CHAPTER ONE
INTRODUCTION

1.1 Background of Study

Hippocrates who lived from 460 – 370 BC described different types of biopsy, referring to cancer as *carcinos* meaning crab or crayfish in Greek (The History of Cancer, 2014), the name which is generated from the appearance of the cut surface of a solid malignant tumour (Moss, 1989). The oldest description of biopsies and their treatment is traceable to ancient Egypt and dates back to 1600 BC (Sudhakar, 2009).

Gynaecological biopsies are not rare in Rivers State, Nigeria, where they cause considerable reproductive morbidity. Biopsies of the female genital tract call for concern worldwide and especially in developing countries (Parkin *et al.,* 1992), globally contributing significantly to morbidity and mortality (Pisani *et al.,* 2002). Data on gynaecological biopsies in some developing countries show a preponderance of cancer of the cervix (Egwuatu and Ejeckam, 1980; Ozumba *et al.,* 2011). Cervical carcinoma in developing countries, accounts for 80% of the estimated 231,000 deaths that occur from it annually (Pindiga *et al.,* 1999*;* Seleye-fubara *et al.,* 2003; Mohammed *et al.,* 2006; Agboola *et al.,* 2007). The incidence and prevalence of other female genital biopsies vary from one geographical region to another (Mazur *et al.,* 2005).

Generally, cancer incidence in Nigeria appears low compared to developed countries, which may not truly reflect the burden. Similar to reports from other parts of the world, it is slightly higher in female. Squamous cell carcinoma is the most common (90-91%) histological type while adenocarcinoma represents 2.4% to 5.1%. HPV is a necessary cause of cervical cancer being present in 99.9% of cases. In a study of 233 cases of cervix cancer from Lagos, HPV 16 and 18 were present in 65.2%, this supports data that effective vaccination against these 2 types will reduce the cervical burden in Nigeria (Abdulkareem, 2009). The Federal Ministry of Health has already given license to bring in vaccines. Institution of organized screening programmes to detect the pre-cancerous stage has reduced the mortality and morbidity of this cancer in developed countries. This can also be done in Nigeria with strong commitments, which will reduce deaths in Nigerian women from obstetric complications. Data from Ibadan showed

common female cancers in 1960-69 as cervix and breast. In 1998, breast became the commonest followed by cervix and ovary. Current data shows that female cancers account for about half of the total, the common female cancers reported from the North are cervix, breast, ovary while from Enugu and Lagos breast is commonest followed by cervix both accounting for over 40% (Abdulkareem, 2009).

Persistent Human papillomavirus (HPV) infection is also a notable risk factor for both vulvar and vaginal cancers. In the United States, it has been reported that 40% of vulvar (Wu *et al.*,2008) and vaginal cancers (Saraiya *et al.*, 2008) could be attributed to Human Papillomavirus (HPV), and HPV type 16 (HPV-16) was detected in 50-64% of high-grade vaginal intraepithelial biopsies (VAIN) (Wu *et al.*,2008).

Worldwide, vulvar and vaginal cancers are rare (Andersen *et al.*, 2003). Independent reports from Nigeria, United Kingdom and the United States show these cancers to be rare (Human Papillomavirus and Related Cancers, 2009; Cancer Facts and Figures, 2009 ; Okolo *et al.*, 2013; UK vulval cancer incidence statistics, 2016). In the United States, vulvar cancer accounts for 0.6% of all cancers in women (Saraiya *et al.*, 2008), and vaginal cancer for 0.3% of all invasive cancers among women. Majority of these cancers occur in developing countries. It was reported that 60% of vulvar cancers and 68% of vaginal cancers occur in developing countries (Okolo *et al*., 2013).

Thomas *et al.* (2004) described the prevalence of HPV infection in Nigerian women as well as the distribution of various HPV subtypes among women with normal and abnormal findings on cytology or visual inspection with acetic acid. HPV 16 and 35 were the most common high-risk HPV types, and HPV 42 was the most common low risk type.

Worldwide and in the US, there has been profound excitement and concern surrounding the HPV vaccine. The excitement derives from the potential of the vaccine to reduce the burden of anogenital cancers in countries that have no screening infrastructure. However, if vaccine uptake is lower in those groups at highest risk of developing cervical cancer, current racial/ethnic or geographic disparities could increase (Okolo *et al*., 2013). For Nigerians, the HPV vaccine may be useful in reducing the burden of disease provided we can afford them and the same HPV subtypes (mostly HPV 16 and 18) targeted by these vaccines are important causes of cancer in

Nigeria. Wu *et al.* (2003) studied vaginal cancers among different races in the United States and showed that black, Asian Pacific Island, and Hispanic women as well as older women were more likely to be diagnosed with late-stage disease, and these groups had lower 5-year relative survival rates than their white, non-Hispanic, and younger counterparts.

With early detection, vulvar cancer is curable. When lymph nodes are not involved, the five-year survival rate is slightly higher than 90 percent. Even in developed nations, the management of vulvar carcinoma is hampered by the fact that diagnosis is delayed in most cases and by the choice of the proper surgical procedure. The greatest difficulty in surgical management is with primary wound closure and healing, and wound breakdown and sepsis occur commonly (Gharoro *et al.,* 2001). Most studies from Nigeria show that most patients with vulvar and vaginal cancers are older than 50 years (Kyari and Nggada, 2004; Mohammed *et al*., 2006; Nwosu and Anya, 2004). In the United States of America, both cancers are also most commonly seen in persons older than 50 years (Wu *et al.,* 2008).

1.2 STATEMENT OF THE PROBLEM

The recent alarm on rising global incidence of biopsies by the World Health Organisation (WHO) should worry areas prone to gynaecological biopsies. Cancer killed 7.6 million persons in 2008 worldwide, and there is indication that the figure could double to 13 million by 2030 (Jemal *et al.,* 2011). According to WHO, cancer accounts for 13 percent of all deaths registered globally and 70 percent of that figure occurs in middle and low-income countries (WHO, 2016). It is on record that about 10,000 cancer deaths occurs annually in Nigeria, while 250,000 new cases are recorded yearly, two- third of the deaths and new cancer cases recorded are as a result of shortage of functional cancer control plans (Olakanmi, 2015).

1.3 JUSTIFICATION OF STUDY

Gynecological cancers are among the leading causes of cancer-related deaths worldwide (Rogo *et al*., 1990). Gynaecological complications in developing countries are enormous primarily due to the high incidence and mortality rate, recording 25% of all new cancers diagnosed among women compared to 16% in the developed world (Sankaranarayanan and Ferlay, 2010). The evaluation of the occurrence of gynaecological biopsies is essential for the formulation of health policies and planning. In Port Harcourt and Rivers State at large reports on the occurrence of

gynaecological biopsies are sketchy, while the predictions of cancerous and noncancerous tumours from theses biopsies have never been reported. Hence the rationale for this research.

1.4 AIM

To evaluate gynaecological biopsies in patients attending Obstetrics and Gynaecology Clinic at Braithwaite Memorial Specialist Hospital (BMSH), Port Harcourt, Rivers State.

1.5 SPECIFIC OBJECTIVES OF STUDY

1. To identify the various gynaecological biopsy in BMSH, Port Harcourt, Rivers State.

2. To determine the frequency of gynaecological biopsies and predict their future occurrence to aid policy formulation in Rivers State, Nigeria.

3. To determine percentage area and intensity of histochemical stains with Haematoxylin and Eosin (H&E) on gynaecological biopsies.

1.6 RESEARCH QUESTIONS

1. Are females of all age groups in Port Harcourt prone to gynaecological biopsies?
2. Will there be increase or decrease in gynaecological biopsies by the year 2050?
3. Which histochemical stain has a higher percentage area and intensity on gynaecological biopsies?

1.7 RESEARCH HYPOTHESIS

1. **H_1**: There is a link between age and gynaecological tumours
   H_0: There is no link between age and gynaecological tumours

2. **H_1**: There will be significant change in number of gynaecological biopsies by the year 2050
   H_0: There will be no significant change in number of gynaecological biopsies by the year 2050

3. **H_1**: There is affinity between histochemical dyes and gynaecological biopsies
   H_0: There is no affinity between histochemical dyes and gynaecological biopsies

CHAPTER TWO

LITERATURE REVIEW

2.1 ANATOMY OF THE GYNAECOLOGICAL REGION

The gynaecological region is basically divided into two parts which are the external (vulva) and internal genitalia (Moore *et al*., 2006).

2.2 EXTERNAL GENITALIA

External genitalia, also called the vulva, consist of the mons pubis, clitoris, labia minora, labia majora, and the vestibule with the external urethral meatus, vaginal orifice, and the vestibular bulbs and glands (Espitia *et al.,* 2014). The remnants of hymen are usually around the vaginal opening.

2.2.1 Mons Pubis

The mons pubis is the triangular shaped area of fatty tissue skin on top of the pubic bone. It extends from the glans clitoris inferiorly to the pubic hairline, which forms the base of this triangular shape. It consists of loose connective tissue (mostly adipocytes) in the fascia. Its average length of the base is 16 ± 2 cm and height of the triangle is 13 ± 2 cm (*Seitz et al., 2010,* Sujata *et al*., 2011).

2.2.2 Labia Majora

These are folds consisting of loose connective tissue, hair follicles, and sebaceous glands located between the mons pubis and the perineum. The outer surfaces of the lips of labia majora in adults are covered with pigmented skin, which contain glands and are covered with pubic hair. The inner parts of the labia majora are pink in colour, hairless and smooth (Mottura, 2009).

2.2.3 Labia Minora

These are two folds of skin devoid of fat, situated between the labia majora. They are rich in sebaceous glands and lie medial to the labia majora on each side immediately adjacent to the vestibule. There is a core of connective tissue and vascular erectile tissue with sensory nerve endings to which they are loosely attached. Each labia minora splits anteriorly around the clitoris, uniting with the labia minora from the contralateral side to form the prepuce over and

frenulum under the clitoris. There is large variation in the dimensions of the labia minora (Lloyd *et al.*, 2005) in their study of 50 premenopausal women between ages 18–50 years found the average length of labia minora to be 6.0 cm ± 1.7 (2–10) and average width to be 2.1 cm ± 0.9 (0.7–5) (Lloyd *et al.*,2005). Maximum distance from the base to the edge >4 cm is considered criteria for corrective surgery by most plastic surgery literature (Rouzier *et al.*, 2000*;* Ellsworth *et al.*, 2010).There is a great diversity and variation with the size of the labia minora that surgeons need to be aware of and consider before planning corrective surgery (Liao *et al.*, 2010).

2.2.4 Clitoris

This is a highly neurovascular erectile structure and consists of the vestibular bulbs and the glans (Sujata *et al*., 2011). The glans is the most richly innervated part of the clitoris. Magnetic resonance imaging and cadaveric studies have helped to better understand the detailed structure of the clitoris (O'Connell and De Lancey, 2005). The clitoris plays a major role in female sexual function and is very closely related to the distal urethra and vagina (O'Connell *et al.*, 1998).

The clitoris is suspended by the superficial and deep suspensory ligaments as described by Rees *et al.* (2000). Based on cadaveric dissections they found the superficial suspensory ligament to be attached to the deep fascia of the mons, glans and body of the clitoris further extending into the labia majora. The deep suspensory ligament originates from the symphysis pubis and attaches to the body, bulbs, and glans of the clitoris. These may provide clitoral stability during sexual intercourse. Accurate knowledge of the clitoris, its relations, and neurovascular supply is crucial in performing clitoral reduction for clitoromegaly to achieve normal morphology without affecting sexual function. It is important to preserve the bulbs with the erectile tissue related closely to the ventral aspect of the clitoris for sexual function, and suspensory ligaments to maintain the anatomic position of the clitoris during surgery (Papageorgiou *et al.*, 2000*;* Lean *et al.*, 2007*;* Vaze *et al.*, 2008).

2.2.5 Vestibule

An area extending from the clitoris lying between the two labia minora is called the vestibule. It contains the vaginal orifice, external urethral meatus, vestibularbulbs, openings of the two greater vestibular glands and those of numerous mucous, lesser vestibular glands. There is a shallow vestibular fossa between the vaginal orifice and the frenulum of the labia minora (Moore and Dalley, 2006).The bulbs of the vestibule are paired elongated masses of erectile tissue,

measuring ~3 cm in length located along the sides of the vaginal ostium under the cover of bulbospongiosus muscles. The greater vestibular glands (Bartholin's glands) are two small structures on either side of the vaginal ostium with openings through ducts ~2 cm in length, in the groove between the hymen and the labia minora (Sujata *et al*., 2011).

2.2.6 Neurovascular Supply of External Genitalia

Arterial supply of the vulva is derived from the external and the internal pudenda arteries on each side. The internal pudenda artery is a branch of the anterior division of the internal iliac artery and the vein drains into the internal iliac vein. The vessels follow the course of the pudenda nerve and supply the superficial perinea muscles and the external genitalia via different branches. The perinea artery supplies the superficial perinea muscles, posterior labial branch, artery to the bulb of the vestibule, dorsal and deep arteries of the clitoris; and the urethral artery supplies the respective structures. The superficial and deep external pudenda arteries are branches of the femoral artery; they distribute into the labia majora and anastomose with branches of the internal pudenda artery. There is a network of anastomosis between branches of these arteries throughout the female external genitalia (Jin *et al.*, 2009).

The pudenda nerve is the main sensory and motor nerve of the perineum. It arises from the ventral rami of S2–S4, runs underneath the piriformis, and exits the pelvis through the greater sciatic foramen. It passes just behind the ischial spine and re-enters the pelvis through the lesser sciatic foramen. The pudenda nerve then runs in the Alcock's canal (pudenda canal) in the obturator fascia and ventral to the sacrotuberous ligament (Shafik *et al.,* 1995*;* Mahakkanukrauh *et al.,* 2005). As it enters the perineum, the pudenda nerve lies on the lateral wall of the ischiorectal fossa and divides into three branches: the inferior rectal, perinea, and dorsal nerve of the clitoris (Schraffordt *et al.,* 2004). The dorsal nerve of the clitoris lies on the perineal membrane along the ischiopubic ramus and on the anterolateral surface of the clitoris, one on each side, and supplies the clitoris (Rees *et al.*, 2000).

2.3 INTERNAL GENITALIA

Internal genitalia comprise mainly of the ovaries, fallopian tube, uterus, cervix and vagina (Moore *et al*., 2006)

2.3.1 Vagina

The vagina is a fibromuscular tubular structure that extends from the cervix to the vulva and measures 7–9 cm in length. The upper two-third lies horizontal while the lower third lies vertically with the woman in an upright position. The walls of the vagina are covered with epithelia. Normally, the vaginal walls are collapsed except at the upper end where the cervix keeps them separate. The vaginal wall consists of three layers. The inner mucosal layer consisting of nonkeratinized stratified squamous epithelium on a layer of loose vascular connective tissue called lamina propria; a middle muscular layer of smooth muscle, collagen, and elastin; and an outer adventitial layer of collagen and elastin with neurovascular bundle and lymphatics. The vaginal walls lack glands and most of the lubrication is provided by transudation from the vessels in the vaginal wall, the cervical glands, and Bartholin glands. The tissue between bladder and urethra, and the anterior vaginal wall has historically been called the pubocervical fascia. Posteriorly the tissue between the posterior vaginal wall and rectum is called the rectovaginal septum. The histology of the anterior and the posterior vaginal wall contains a muscularis layer and not a separate layer of fascia (Corton, 2009).

The distal vagina lies in close proximity to the urethra and clitoris and this relationship has been demonstrated well on magnetic resonance imaging (MRI) (O'Connell *et al.*, 2008). These structures share the same blood supply and innervations. The vaginal canal has various levels of support. Level I support includes the uterosacral cardinal complex and suspends the upper 2–3 cm of the vagina to the sacrum and the pelvis sidewall. Level II support is comprised of the attachment of the lateral wall of the vagina to the arcustendineus fasciae pelvis anteriorly and the levatorani fascia posteriorly. These thick tissue attachments are comprised of smooth muscle, collagen, and elastin along with the neurovascular bundle. The anterior attachment corresponds to the pubocervical fascia and posterior to the rectovaginal septum. The terminal 2–3 cm of the vagina is fused to the structures around it without any suspensory ligaments. Level III support is thus provided by the adjacent structures it attaches to: anteriorly the urethra and the perinea membrane, posteriorly the perineum and the perinea body, and laterally to the levatorani. The arterial supply is through the descending branch of the uterine artery, vaginal artery, and internal pudenda artery, while the veins form the vaginal venous plexuses that ultimately drain into the internal iliac veins via the uterine vein. The upper two-thirds of the vagina have visceral

innervation derived from the uterovaginal plexus and the lower one-third derives somatic innervations from the pudenda nerve (Sujata *et al*., 2011).

2.3.2 Uterus

Hippocrates (460-370 BC) thought that the uterus had several cavities that allow only one gestation within each cavity. Each cavity was lined with "tentacles" He described the uterus as a "cupping vessel with two folds that disappear with pregnancy". Leonardo Da Vinci (1452-1519) who was known for his famous drawings and sketches revealed that the uterus contain only one cavity (David *et al*., 1993), contradicting the earlier beliefs by Hippocrates.

The adult uterus is a hollow, pear shaped organ (Jyothi, 2014). Although its size varies considerably, the uterus is approximately 7.5 cm long, 5 cm wide and 2 cm thick and weighs about 70g to 90g. The non-gravid (non-pregnant) uterus usually lies in the lesser pelvis, with its body lying on the urinary bladder and its cervix between the urinary bladder and the rectum. The adult uterus is usually anteverted (tipped anterosuperiorly relative to the axis of the vagina) and anteflexed (flexed or bent anteriorly relative to the cervix) so that its mass lies over the bladder. The position of the uterus changes with the degree of fullness of the bladder and rectum. It is divided into the cervix and the corpus. The portion of the corpus cephalad to a line connecting the insertion of the fallopian tubes is the fundus. The two lateral regions of the fundus associated with the intramural portion of the fallopian tubes are referred to as the cornua. The portion of the corpus that connects with the cervix is called the isthmus (Bravo *et al.,* 2000) or lower uterine segment. The uterine cavity has a triangular shape and length of approximately 6cm. The body lies between the layers of the broad ligament and is freely movable. It has two surfaces: vesical (related to the bladder) and intestinal. The cervix of the uterus is the cylindrical, relatively narrow inferior third of the uterus, approximately 2.5 cm long in an adult non-pregnant woman. For descriptive purposes, two parts are described: a supravaginal part between the isthmus and the vagina, and a vaginal part, which protrudes into the vagina. The rounded vaginal part surrounds the external os of the uterus and is surrounded in turn by a narrow space, the vaginal fornix. The supra-vaginal part is separated from the bladder anteriorly by loose connective tissue and from the rectum posteriorly by the rectouterine pouch (Höckel *et al.,* 2013). The uterine cavity continues inferiorly as the fusiform cervical canal. The canal extends from a narrowing inside the isthmus of the uterine body, the anatomical internal os, through the supravaginal and

vaginal parts of the cervix, communicating with the lumen of the vagina through the external os. The uterine cavity and the lumen of the vagina together constitute the birth canal through which the fetus passes at the end of gestation (Stuart and Reid, 2000; Beckmann *et al*., 2002).

2.3.3 Normal Histology of the Endometrium

The endometrium of the corpus is composed of two layers; the basalis and the overlying functionalis. In the second half of the menstrual cycle, the functionalis may be differentiated into the superficial compacta and the underlying spongiosa, which extends to the basalis. Every layer consists of 2 major structures; the epithelial component, either as glands or as superficial epithelium (Sequeira *et al.*, 2012), and the mesenchymal component of stromal cells. Both cellular components are pluripotential and can undergo various metaplastic changes.

The mucosal lining of the uterus is composed of the glands and the stroma. It is the glands that give rise to the common and significant pathological conditions in the uterus and it is the glands that are looked at to determine the activity of the endometrium and its response to the hormonal environment. The basal layer (stratum basale) is adjacent to the myometrium, and is composed of small, irregular glands in dark stroma, in which the stromal cells are small and compact. The remainder of the endometrium is the functional zone (stratum functionale), which is further subdivided into the superficial compact layer (stratum compactum) and the deeper spongy layer (stratum spongiosum). The spongy layer consists of glands showing the maximum of the secretory activity, with their distended lumina. The stroma in this zone is relatively non-responsive and does not develop a good decidual response apart from those areas immediately adjacent to the spiral arterioles. The compact layer is the most superficial layer and is made up of abundant stroma with little in the way of glandular elements; the glandular component is represented by the small, straight uppermost portions of the glands, which show very little secretory activity. The stroma of the compact layer shows a well developed response to hormonal stimulation with a prominent decidual reaction and numerous endometrial granulocytes (Deligdisch, 1993).

2.3.4 Glandular Cells

The endometrial glandular cells are of three types: The secretory cell, the ciliated cell and the clear cell. The secretory cell is by far the most abundant and its morphology varies with the time

of the menstrual cycle. The ciliated cells are more frequent near the cornua and towards the endocervix as well as being quite common in the surface epithelium. The ciliated cells appear to be under the influence of estrogens and become more prominent in conditions of estrogen excess. They are usually obvious in tissue that shows cystic hyperplasia.

The clear cells are much less common and are thought to be precursors of the ciliated cells. They are most frequently seen in the proliferative phase and in cystic hyperplasia (Anderson, 1991).

2.3.5 Stroma

During the proliferative phase the stromal cells are small, with elongated nuclei and a narrow rim of cytoplasm. As the end of the proliferative phase is reached, the nuclei become a little less dense and slightly larger. The stroma becomes stratified in the second half of the secretory phase and the cells of the compact zone undergo decidual changes. These decidual cells play an important part in controlling the invasiveness of the trophoblast and localizing the advance of the trophoblast to the endometrium (Pijnenborg *et al.*, 1981).

2.3.6 Endometrial Granulocytes

The endometrial granulocytes become increasingly prominent in the endometrial stroma in the second half of the cycle. These are small, rounded cells characterized by hyperchromatic nuclei which are usually kidney-shaped or segmented. The cytoplasm contains phloxinophilic granules, so that the cells may be mistaken for infiltrating PMNs. These cells are bone marrow derived and are a form of large granular lymphocytes and bear early but not mature T-cell markers (Anderson, 1991).

The blood supply of the uterus comes predominantly from the uterine branch of the internal iliac artery on each side. The uterine lymph vessels drain to a rich network of lymph nodes, the main group being parametrial and paracervical; internal (hypogastric), external and common iliac; periaortic; and inguinal.

2.3.7 Fallopian Tubes and Ovaries

These are structures located on each side of the uterus. The fallopian tubes are tubular structures lined with ciliated columnar epithelium extending from the upper lateral end of the uterus to the ovary on each side. Each fallopian tube can be divided into four anatomical parts: interstitial, isthmic, ampullary, and infundibulum with the fimbria. The vascular supply is via the

mesosalpinx through branches of the ovarian artery as it runs in the broad ligament. The ovaries are oval-shaped structures lying in the lateral pelvic wall in the ovarian fossa. Each ovary consists of an inner medulla an outer cortex with follicles and stroma. The ovaries are suspended from the broad ligament via the mesovarian, which completely covers them making them interperitoneal. The ovary is suspended from the uterus by the fibrous band called the uteroovarian ligament and from the pelvic sidewall by the infundibulopelvic ligament. The infundibulopelvic ligament contains loose connective tissue in addition to ovarian artery and vein, and the accompanying lymphatics and nerves, which supply the ovary (Sujata *et al*., 2011).

2.4 DESCRIPTION OF THE DIFFERENT GYNAECOLOGICAL BIOPSIES

Gynaecological biopsies include biopsies of the ovary, cervix, body of the uterus, vagina and vulva (Madhutandra *et al*., 2012).Gynaecological biopsies are important public health issues in the developing world. The major concerns in this regard are lack of cancer awareness in the villages and cities, as well as lack of screening facilities and man power (Leydon *et al.,* 2000; De Nooijer *et al.,* 2002; Madhutandra *et al*., 2012). Even in the industrialized nations of the West, the need for more precise targeting of high risk groups in other to improve the efficiency of programs and conserving funds have become a major issue (Ngokere and Ofordile, 1996). Delayed presentation of cases may results in poor outcome, which could be averted by early detection and prompt treatment.

2.4.1 OVARIAN BIOPSIES

The most common types of ovarian biopsy include functional or benign cysts and tumors. Intrinsic inflammations of the ovary (oophoritis) are not common. Rarely, a primary inflammatory disorder involving ovarian follicles (autoimmune oophoritis) occurs and is associated with infertility (Bodal *et al*., 2014)**.**

2.4.1.1 Cystic Follicles

They are the one of the most common in the ovary. Follicular cysts originate from follicles which do not ovulate but continually grow (Ryan and Raeside, 1991) until they exceed a diameter of about 11 mm (1.1 cm). A diameter range of 15–60 mm (1.5- 6cm) was described (Martinat-Botte *et al*., 1996). They are filled with a clear serous fluid, and are lined by a gray, glistening membrane (Kumar *et al.,* 2014). Follicular cysts can be single, multiple, unilateral or

bilateral. They vary in size (Ryan and Raeside, 1991) and in the degree of luteinization (Ebbert and Bostedt, 1993). Granulosa lining cells may be identified histologically if the intraluminal pressure has not been too great. The outer theca cells may be conspicuous with increased cytoplasm and a pale appearance (luteinized), when this alteration is pronounced (hyperthecosis), it may ultimately result in increased estrogen production and endometrial abnormalities (Kumar *et al.,* 2014).

2.4.1.2 Polycystic Ovarian Disease (PCOD)

This affects 3% to 8% of reproductive-age women worldwide. The abnormality is numerous cystic follicles or follicle cysts, often associated with oligomenorrhea (Young and Scully, 1991; Homburg, 1996; Michelmore *et al.*, 1999). The instigating event in PCOD is not clear. Increased secretion of luteinizing hormone may stimulate the theca-lutein cells of the follicles, with excessive production of androgen (androstenedione), which is converted to estrone (Ovalle and Azziz, 2002).

2.4.1.3 Stromal Hyperthecosis

This is also called cortical stromal hyperplasia or Ovarian stromal hyperthecosis is a disorder of ovarian stroma which is characterized by uniform enlargement of the ovary (Young and Scully, 1991), as well as the presence of luteinized thecal cells within the ovarian stroma separate from the follicles and is usually accompanied by stromal hyperplasia (Clement, 2002). The clinical importance of stromal hyperthecosis may vary. In premenopausal women, it is often accompanied by hyperandrogenism, and symptoms may resemble those of polycystic ovary syndrome (PCOS) (Penault*et al.,* 2003).Clinically florid cases of stromal hyperthecosis usually occur in women of reproductive age. In postmenopausal women, stromal hyperthecosis is often mild and of noclinical importance (Clement, 2002), although estrogenic effects and virilization have occasionally been reported.

2.4.1.4 Ovarian Tumors

Among cancers of the female genital tract, the incidence of ovarian cancer ranks below only carcinoma of the cervix and the endometrium. Ovarian cancer accounts for 6% of all cancers in the female and is the fifth most common form of cancer in women in the United States (excluding skin cancer). About 70%deaths are of patients presenting with advanced-stage, high-grade serous ovarian cancer (HGS-OvCa) (Seidman, 2004).

There are numerous types of ovarian tumours, both benign and malignant. About 80% are benign, and these occur mostly in young women between the ages of 20 and 45 years. The malignant tumours are more common in older women between the ages of 40 and 65 years (Kumar *et al.*, 2014).

Risk factors for ovarian cancer are not clear than for other genital tumors. Family history and inheritable mutations play a role in tumour development (Azizi *et al.*, 2001; Narod and Boyd, 2002). There is a higher frequency of carcinoma in unmarried women and in married women with low parity. Gonadal dysgenesis in children is associated with a higher risk of ovarian cancer. Women 40 to 59 years of age who have taken oral contraceptives or undergone tubal ligation have a reduced risk of developing ovarian cancer (Ness *et al*., 2001; Narod *et al*., 2001). Mutations in both *BRCA1* and *BRCA2* increase susceptibility to ovarian cancer (Azizi *et al*., 2001; Narod and Boyd, 2002). *BRCA1* mutations occur in about 5% of patients younger than 70 years of age with ovarian cancer. The estimated risk of ovarian cancer in women bearing *BRCA1* or *BRCA2* mutations is 20% to 60% by the age of 70 years (Narod and Boyd, 2002). Most of these cancers are serous cystadenocarcinomas. Approximately 30% of ovarian adenocarcinomas express high levels of *HER2/neu* (ERB-B2) oncogene, which correlates with a poor prognosis. Mutations in the tumor-suppressor gene *p53* are found in 50% of ovarian carcinomas (Narod and Boyd, 2002).

The World Health Organization (WHO) Histological Classification, which separates ovarian neoplasm according to the most probable tissue of origin. It is now believed that tumors of the ovary arise ultimately from one of three ovarian components: Surface epithelium, the germ cells and the stroma of the ovary (Kumar *et al.*, 2014).

2.4.2 FALLOPIAN TUBES BIOPSIES

The most common disorders in these structures are inflammations, followed in frequency by ectopic (tubal) pregnancy and endometriosis.

2.4.2.1 Tumors and Cysts

The most of the fallopian tube cysts are minute measuring 0.1- to 2-cm, translucent cysts are filled with clear serous fluid, called paratubal cysts. The larger cysts are mostly found in the fimbriated end of the fallopian tube and are referred to as hydatids of Morgagni. These cysts are

presumed to arise in remnants of the müllerian duct and are of little significance. Tumors of the fallopian tube are not common. Benign tumors include adenomatoid tumors (mesotheliomas), which occur subserosally on the tube or sometimes in the mesosalpinx. Primary adenocarcinoma of the fallopian tubes is rare and is defined as an adenocarcinoma with a dominant tubal mass and luminal and mucosal involvement. These tumors are detected by pelvic exam, abnormal discharge or bleeding, and occasionally, cervical cytology. Approximately one half are stage I at diagnosis, but nearly 40% of these patients will not survive 5 years. Higher stage tumors have a poor prognosis (Obermair *et al*., 2001). Recently, occult carcinoma of the fallopian tube has been associated with *BRCA* mutations, requiring attention to this site as a potential source of tumors in patients with *BRCA* germ-line mutations (Aziz *et al.,* 2001).

2.4.3 UTERIAN BIOPSIES

Several recent researches suggest that incidence of intraepithelial cervical biopsies rises during adolescence (Wright *et al.,* 2005), which is directly related to the frequency of sexual activity and to an increase in the incidence of human papilloma virus infection among that population (Brown *et al.,* 2005).

2.4.3.1 Endocervical Polyps

Endocervical polyps are relatively harmless and occur in 2% to 5% of adult women. They are not neoplasias but rather only focal hyperplasias of the mucosa that develop in circumscribed regions in response to hormonal stimuli. They may be single or multiple, small or large, and short or long enough to protrude through the cervix. The most important clinical symptoms that polyps produce are bleeding, and occasionally labour-like pains, secondary changes may develop in polyps, leading to haemorrhage and inflammation, and ultimately to extensive necrosis or diffuse endometritis. Endometrial polyps may be divided into those that appear to be responsive to ovarian hormones (functional) and those that are not responsive (nonfunctional). Non-functional polyps are common of the two (Anderson, 1991). Endometrial polyps are classified as sessile or pedunculated based on shape and hyperplastic, functional, fibrousor mixed based on histology. A hyperplastic polyp refers to actively proliferating glands in hypercellular endometrial type stroma. A functional polyp exhibits a normal mid secretory phase glandular pattern or decidualized stroma of the late secretory phase. A fibrous polyp exhibits a dense collagenous stroma surrounding glands lined by single layer of flat to cuboidal epithelium and has few

glands, which may be either cystic or atrophic. A mixed polyp represents combination of the above (Kim *et al.*, 2004).

Atypical polypoid Adenomyoma (APA) is a rare entity that is believed to follow a benign course. The epithelial component of the APA may show cytological atypicality, including carcinoma-in-situ. (Robert, 1991; Khush, 1995), exceptionally, endometrial polyps contain scattered atypical (bizarre) stromal cells. Mitotic activity within the atypical stromal cells is not noted. On IHC, 100% of atypical stromal cells stain with vimentin, estrogen receptor, progesterone receptor and androgen receptor.(Tai and Tavassoli, 2002; Rosai and Ackerman, 2005), Gross Endometrial polyps are recognized grossly as polypoid structures with smooth, glistening, grey white surfaces. They protrude into the endometrial cavity and often exhibit secondary changes. The glands usually show some degree of cystic change. They may be lined by an active pseudostratified epithelium containing mitotic figures or in the postmenopausal patient, by a flat, inactive epithelium (Rosai and Ackerman, 2005). The diagnostic parameters for the polyp also include thick-walled blood vessels, densely fibrous collagenous stroma, hypercellular stroma of endometrial type, glandular irregularities and "out of phase" features. Kim *et al.* in 2004 concluded that parallel arrangement of endometrial glands' long axis to the surface epithelium, if present is an important additional histological feature useful in the diagnosis of endometrial polyp especially in curettage specimens.

2.4.3.2 Endometrial Hyperplasia

Endometrial hyperplasia is recently termed endometrial intraepithelial neoplasia (EIN). Its commonest presenting symptom is abnormal bleeding. Numerous studies have confirmed the malignant potential of endometrial hyperplasia and the concept of a continuum of glandular atypia culminating in some cases, in carcinoma (Robbins and Cotran, 2005). Simplified WHO classification of endometrial hyperplasia is as follows:

a) Simple non-atypical hyperplasias (also called cystic\ mild hyperplasia, which is of lower grade).
b) Complex atypical hyperplasias (also called Endometrial Intraepithelial Neoplasia-EIN, which is of higher grade).

Simple hyperplasias are characterized by architectural changes in glands of various sizes, producing irregularity in gland shape, with cystic alterations. Epithelial growth pattern and

cytology are similar to those of proliferative endometrium, although mitoses are not as prominent. These simple cystic hyperplasias frequently evolve into cystic atrophy in which both the epithelium and stroma become atrophic (Robbins and Cotran, 2005).

Complex atypical hyperplasias (CAH) exhibits an increase in the number and size of endometrial glands with gland crowding, enlargement and irregular shape. There is increased cell stratification and nuclear enlargement and may demonstrate complexity of the lining epithelium with scalloped or tufted surface. Glands remain distinct and non-confluent characteristic of an intraepithelial neoplasm. Mitotic figures are common. Atypical endometrial hyperplasias are closely related to endometrioid carcinoma and should be considered precancerous biopsies. The critical turning point is the stage of atypical hyperplasia or carcinoma-in-situ. After this, the subsequent growth is estrogen independent. Cystic hyperplasia is the first manifestation of unopposed estrogen stimulation (Matai and Mittal, 1997; Huseyin *et al*., 2001).

2.4.3.3 Endometrial Carcinoma (EC)

Carcinoma of the endometrium is the most common gynaecologic malignancy in the developed countries (Munshi *et al*., 2005).The median age at onset is 63 years. 85% of the patients are >50 years. 75% of the patients are postmenopausal and 50% of the cases occur in high risk individuals. About 20-25% will be diagnosed before menopause. Postmenopausal bleeding and abnormal premenopausal bleeding are the primary symptoms of EC (Pellerin and Finan, 2005).

2.4.3.4 Endometrial Adenocarcinoma

Carcinoma of the corpus uteri is commonly found in the fundus, arising from the mucosa of a tubal recess. The tumors may project as spongy, polypoid or papillary masses into the uterine cavity. They may however be flat or ulcerated or grow primarily into the uterine wall. Growth takes place relatively slowly and metastases often appear late.

Endometrial adenocarcinomas may be subdivided into several morphologic subtypes, each of which may vary in the degree of differentiation (Christopher and Fletcher, 2003). Most endometrioid carcinomas are characterized histologically by well defined glands lined by cytologically malignant stratified columnarepithelial cells. They are classified into well differentiated, moderately differentiated and poorly differentiated. It may contain collection of foamy cells (Fletcher, 2003).Adenocarcinoma is the most common histologic type of EC, which develops in the background of prolonged estrogen stimulation and atypical endometrial

hyperplasia (Pellerin and Finan, 2005).Between 5 and 10% of cases have a papillary (villo-glandular) architecture. Villoglandular carcinomas are frequently described as tumors composed of long, slender papillae with fine delicate fibrovascular cores (Robert *et al*., 1994). The microglandular variant of endometrioid type of EC (Mc Cluggage and Perenyei, 2000).It is a rarely described variant which morphologically closely mimics cervical microglandular hyperplasia. It shows closely packed microglandular structures lined by cells with small regular nuclei and abundant clear to eosinophilic cytoplasm. A striking feature is the presence of abundant neutrophils within epithelial cells, glandular lumina and the intervening stroma. Mitotic figures are not seen.

2.4.3.5 Mucinous Adenocarcinoma

It is a tumor subtype characterized by abundant mucin secretion. It is distinguished from mucinous metaplasia by virtue of its architectural and cytologic atypia. The distinction between endometrial mucinous adenocarcinoma and primary endocervical adenocarcinoma depends on differential biopsy and fractional curettage.

2.4.3.6 Papillary Serous Carcinoma (PSC)

It is an aggressive endometrial neoplasm that resembles ovarian serous carcinoma morphologically (Sherman *et al.*, 1992). Most of the tumors are large, bulky, partly necrotic masses that fill the endometrial cavity.

Most present as exophytic growths and few as flat endophytic biopsies. The tumor is histologically characterized by densely fibrotic, thick, edematous fibrovascular papillae and large branching glands lined by papillary tufts composed predominantly of cuboidal shaped cells.PSC frequently contain areas of clear cells The invasive component consists almost entirely of glands.. Prominent areas of necrosis are common. The tumor is associated with intraepithelial carcinoma. The tumors express both estrogen and progesterone receptors. These tumors strongly express p16 and p53.

Tumor consists of highly cellular solid sheets of small uniform cells with round to elongated nuclei; contain finely granular chromatin and inconspicuous nucleoli. The cytoplasm is scanty and ill-defined. Mitotic activity is brisk, and numerous apoptotic bodies are present. Focally, geographic pattern of tumor necrosis may be present. It is strongly positive for the neuroendocrine markers such as , Chromogranin and Synaptophysin (Shaco-Levy *et al*., 2004).

2.4.3.7 Squamous Cell Carcinoma (SCC)

It was first described by Fluhmann in 1928. Primary SCC of endometrium is extremely rare. The uterus is markedly enlarged and the mucosal lining can be irregular with multiple granular excrescences. SCC is seen involving the entire endometrial cavity with no normal mendometrial glandular epithelium. The tumor can penetrate the myometrium. It is believed that the potential cells lying beneath the columnar epithelium may be transformed to squamous metaplasia under the influence of senile involutions, pelvic irradiation, vitamin A deficiency, or a chronic irritating process such as pyometra, uterine prolapse or eversion, IUD and external infection which are potential predisposing factors of SCC (Manuel *et al.,* 2003). Squamous cell carcinoma may occur at any age from the second decade of life to senility. The peak incidence is occurring at an increasingly younger age: 40 to 45 years for invasive cancer and about 30 years for high-grade precancers.

2.4.3.8 Giant Cell Carcinoma

It is a rare pleomorphic form of high grade endometrial adenocarcinoma, featuring poorly cohesive sheets and nests of bizarre multinucleated giant cells (Jones *et al*., 1991).

2.4.3.9 Endometrial Stromal Tumors (ESTs)

Uterine Endometrial Stromal Tumors are among the rarest neoplasms in the female genital tract. Malignant Mesenchymal Tumors comprise less than 5% of primary uterine cancers, with Endometrial Stromal Sarcomas (ESSs) accounting for <10% thereof.EST are composed of cells resembling those of proliferative phase endometrial stroma. These tumors are subdivided into benign and malignant categories based on the type of tumor margin (Kim *et al*., 2004). Uterine EST with pushing margins are benign and designated Endometrial Stromal Nodule. In contrast, ESS infiltrates the myometrium and are divided into low and high (undifferentiated) grade tumors mainly based on mitotic count.

The recent WHO classification of tumors of Breast and Female Genital Organs divides uterine stromal neoplasms into three groups.

a) Benign Endometrial Stromal Nodule (ESN)
b) Low Grade Endometrial Stromal Sarcoma (ESS)

c) Undifferentiated endometrial sarcoma (UES)

Uterine stromal neoplasms, particularly low grade ESS, often express estrogen and progesterone receptors (ER, PR). 41% of ESS and UES also express androgen receptors. They also frequently express EGFR (HER-1).ESSs are negative for oxytocin receptors (OTR) and h-caldesmon, and show desmin positivity mainly in regions of smooth muscle metaplasia (Christoph et al., 2003).

2.4.3.10 Endometrial Stromal Nodule (ESN)

Solitary sharply circumscribed masses of soft consistency and a characteristic yellow to orange colour. They do not invade veins, lymphatics, or the myometrium. They may be situated in the endometrium or in the myometrium, in the latter position they may be confused by the naked eye with leiomyomas. (Anderson, 1991).

ESN are typically densely cellular. About 20% are hypocellular and often fibrous. The tumor cells are generally very similar to those of the endometrial stroma and they are of uniform size, shape and staining, without appreciable cytological atypia. Mitotic activity is either absent or minimal. Although, the endometrial stromal nodule is usually vascular, blood vessel invasion is not seen (Dionigi *et al.*, 2002).

2.4.3.11 Endometrial Stromal Sarcoma (Low Grade)

(Also previously called endolymphatic stromal myosis, endolymphatic stromatosis or stromal endometriosis).Although the tumor may present as a polypoid mass and protrude into the uterine cavity, an infiltrating growth pattern is more characteristic, resulting in an area of thickening of the uterine wall (Anderson, 1991).When the tumor permeates the lymph vessels, grossly it can be detected by the presence of yellowish, ropy, or ball-like masses filling dilated channels. The local invasion may extend into the broad ligament, tubes and ovaries. Pelvic and abdominal recurrences are common.

Occasionally pulmonary metastasis is found years after hysterectomy (De Sá *et al*., 1990).

Their low power appearance is very distinctive, in the sense of showing extensive myometrial permeation by sharply defined tumor islands with pointed edges. The cells of the tumor resemble those of the normal endometrial stroma and nuclear atypia is usually slight. The tumor may show the presence of following features: Extensive hyaline/hyaline bands, tumor cell necrosis, haemorrhage, inflammation, calcification, cells with decidual features, foam cells, epithelioid

areas, glandular areas, smooth muscle features and sex cord-like areas. (Huseyin, 2001)The most striking feature of low grade ESS is the nature of the infiltrating margin of the tumor. The stromal cells infiltrate extensively into the myometrium, and particularly into the lymphatic spaces.

2.4.3.12 Endometrial Stromal Sarcoma (Undifferentiated / High Grade)

The uterus harbouring a high grade ESS is usually enlarged and the tumor appears as a polypoid mass extending into the uterine cavity from the endometrium. The mass is characteristically round with a smooth surface. Necrosis of the tumor is often a prominent naked eye feature.

The resemblance to endometrial stromal cells is less obvious than is seen in low grade ESS. The cells are oval or spindle shaped and may show considerable pleomorphism. Coarse chromatin clumping is seen and there are frequently large nucleoli. Mitotic figures are numerous, always exceeding 10/10HPFs. Vascular and lymphatic channel involvement is much less frequently seen than in low grade variant. Areas of necrosis are frequently seen. Islands of collagen may occasionally be found. ESTs may show morphologic variations or unusual features. These include epithelial differentiation with either a sex cord-like pattern or the presence of endometrioid glands, smooth muscle differentiation, fibrous or myxoid change, cells with granular eosinophilic or clear cytoplasm, cells with a rhabdoid phenotype, skeletal muscle differentiation, cells with bizarre nuclei and lastly fatty metaplasia (Baker *et al.,* 2005).

2.4.3.13 Mixed Mullerian Tumors (Mmts) Malignant Mixed Mullerian Tumors (Mmmts) / Carcinosarcomas

Female genital tract carcinosarcomas otherwise known as Malignant Mixed Mullerian tumours are highly aggressive biphasic neoplasms composed of carcinomatous and sarcomatous components. Most immunohistochemical studies have shown simultaneous expression of epithelial and mesenchymal markers (Keratin and Vimentin respectively) (Kounelis, 1998).MMMTs are practically always seen in postmenopausal patients who present with uterine bleeding and enlargement. They present as large, soft polypoid growths involving the endometrium and myometrium, sometimes protruding from the cervix. Foci of necrosis and haemorrhage are common.

The characteristic feature of MMMTs is the admixture of carcinomatous and sarcoma-like elements, resulting in a characteristic biphasic appearance. The carcinomatous component is usually of glandular type, whether endometrioid, clear cell or papillary serous. As a rule, it has a poorly differentiated appearance and is of high grade nature. The sarcomatous component may be homologous or heterologous. The homologous MMMT contain a mesenchymal element that is composed of cell types that are normally found in the uterus, such as LMS, ESS, fibrosarcoma and undifferentiated sarcoma. The heterologous elements are rhabdomyosarcoma, osteosarcoma, chondrosarcoma and liposarcoma (Pellerin and Finan, 2005).

2.4.3.14 Mullerian Adenosarcoma and Mullerian Adenofibroma

Mullerian adenosarcoma is characterized by a benign, but occasionally atypical, glandular component and a sarcomatous, usually low grade, stromal component. Mullerian adenosarcomas are usually tumors of low malignant potential. The closely related Mullerian adenofibroma (Papillary adenofibroma, cystadenofibroma) is characterized by benign epithelial and benign stromal components (Clement and Scully, 1990).

2.4.3.15 Mullerian Adenosarcoma

The uterine cavity is distended and filled by a coarsely lobulated, soft, polypoid mass, often with areas of necrosis and hemorrhage. The margin with the myometrium is characteristic and is clearly circumscribed and pushing, and myometrial invasion is not seen.

Cardinal feature in the diagnosis of Mullerian adenosarcoma is the benign appearance of the glandular component and the malignant nature of the stromal element. The glands are widely separated by the abundant stromal component and are lined by cuboidal or low columnar epithelium. The stroma is composed of spindled cells and round cells. The presence of periglandular stromal cellularity forming a cuff of so called cambium layer around the glands and intraglandular stromal polypoid projections within adenosarcomas is one of the characteristic features of Mullerian adenosarcoma. The cellular zone around the glands is where the maximum nuclear atypia and mitotic activity (≥4/10HPFs) is found (Christopher, 2003; Clement and Scully, 1990).

2.4.3.16 Mullerian Adenofibroma

The tumor occupies and distends the uterine cavity, arising as a broad based polypoid mass, often lobulated or papillary. It is soft, firm or rubbery in consistency and cut surface may be spongy or overtly cystic. Broad, papillary stromal fronds are covered byendometrial type of epithelium but may be of endocervical pattern, ciliated or even squamous. Cells of the endometrial stromal type and fibroblast, make up the stromal element. Mitotic figures are usually absent.

2.4.3.17 Mullerian Carcinofibroma or Carcinomesenchymoma

This tumour is composed of malignant glandular elements and benign stromal elements. The epithelial component is usually of the endometrioid type, but clear cell type has been described. The behaviour of these tumors appears to be no different from that of a carcinoma.

2.4.4 Tumors of the Myometrium

2.4.4.1 Leiomyomas

Uterine leiomyomas (commonly called *fibroids*) are perhaps the most common tumor affecting the health of millions of women and leading indication for hysterectomy in the world. These benign tumors may be present in about 75% of females of reproductive age, and each uterus harbors an average of 6.5 tumors. Each uterine leiomyoma is a unique clonal neoplasm. Most leiomyomas have normal karyotypes, but approximately 40% have a simple chromosomal abnormality. Six cytogenetic subgroups have been recognized: a balanced translocation between chromosomes 12 and 14, partial deletions of the long arm of chromosome 7, trisomy 12, and rearrangements of 6p, 3q and 10q. The number and variety of cytogenetic abnormalities suggest that more than one genetic mechanism can lead to leiomyoma growth (Ligon and Morton, 2000).

Leiomyomas are discrete, circumscribed, firm and gray-white tumors varying in size from small, barely visible nodules to massive benign neoplasms of smooth muscle that which frequently occur in the viscera of the gastrointestinal tract and uterus. They have also been reported to occur in the ovary (Moore *et al.*, 2006), vulva, and cervix (Cooper and Valentine, 2002).Although most uterine leiomyomas are asymptomatic, signs that can be seen in affected patients include abnormal uterine bleeding, anemia, bowel dysfunction, increased urinary frequency and urgency(Lefebvre *et al.,* 2003.), and decreased efficiency of subsequent assisted-reproduction cycles (Young *et al.,* 1996). The effect of uterine leiomyomas on overall fertility in women is

under debate. Although most patients remain asymptomatic, it is important to differentiate leiomyomas from their malignant counterparts, leiomyosarcomas. The differentiation between the 2 types of smooth muscle tumors can generally be made with reasonable certainty according to gross and light microscopic features. More specifically, mitotic index and determination of nucleolar organizer regions have both been shown to be useful in differentiating leiomyomas from leiomyosarcomas (Cooper and Valentine, 2002; Tyler *et al.,* 2010).

Whatever their size, the characteristic whorled pattern of smooth muscle bundles on cut section usually makes these biopsies readily identifiable on gross inspection. Large tumors may develop areas of yellow-brown to red softening (red degeneration).

The leiomyoma is composed of whorled bundles of smooth muscle cells that resemble the uninvolved myometrium. Usually, the individual muscle cells are uniform in size and shape and have the characteristic oval nucleus and long, slender bipolar cytoplasmic processes. Mitotic figures are scarce. Benign variants of leiomyoma include atypical or bizarre (symplastic) tumors with nuclear atypia and giant cells and cellular leiomyomas. Importantly, both have a low mitotic index. Leiomyomas of the uterus, even when they are extensive, may be asymptomatic. The most important symptoms are produced by submucosal leiomyomas (abnormal bleeding), compression of the bladder (urinary frequency), sudden pain if disruption of blood supply occurs, and impaired fertility. Myomas in pregnant women increase the frequency of spontaneous abortion, fetal malpresentation, uterine inertia, and postpartum hemorrhage. Malignant transformation (leiomyosarcoma) within a leiomyoma is extremely rare.

2.4.4.2 Leiomyosarcomas

Leiomyosarcomas may arise from the uterine myometrium de novo or may be transformed from a preexisting benign leiomyoma. In contrast to leiomyomas, leiomyosarcomas have karyotypes that are complex and more random relative to those described above for leiomyomas. These include deletions identified on a number of chromosomes that are not seen in the benign tumors (Quade *et al.*, 1999).

Leiomyosarcomas grow within the uterus in two somewhat distinctive patterns: bulky, fleshy masses that invade the uterine wall, or polypoid masses that project into the uterine lumen. They

contain a wide range of atypia, from those that are extremely well differentiated to anaplastic biopsies that have the cytologic abnormalities of wildly growing sarcomas. The distinction of leiomyosarcomas from leiomyomas is based on the combination of degree of nuclear atypia, mitotic index, and zonal necrosis. With few exceptions, the presence of ten or more mitoses per ten high-power (X400) fields indicates malignancy, with or without cellular atypism. If the tumor contains nuclear atypia or large (epithelioid) cells, five mitoses per ten high-power fields are sufficient to justify a diagnosis of malignancy.

2.4.4.3 Intraepithelial Neoplasia of the Cervix

Hippocrates and Galen described invasive cancers of the cervix, but the existence of asymptomatic neoplasms within the cervical epithelium was not recognized until early in this century, and the preinvasive nature of these biopsies has been clarified only in the last decades. Only recently, with the development of techniques that allow molecular biologists to explore genomic changes in dysplastic cells, has the fundamental biology of cervical intraepithelial neoplasia (CIN) begun to emerge (Massad and Cejtin, 2014).

Cervical intraepithelial neoplasms are atypical proliferations of immature squamous epithelium that do not penetrate the basement membrane of the epithelium. Cervical CIS was described in the early 1900s; the clinical importance of these biopsies was not appreciated until useful means for detecting these asymptomatic, invisible biopsies were developed. Beforehand, cervical cancer detection relied on inspection and palpation, with biopsy of obvious invasive cancers. Schiller developed a technique for iodine staining as a gross means for detecting areas of abnormal epithelium, but this test could not distinguish metaplastic from neoplastic areas of the cervix and could not distinguish small areas of invasion present in a field of diffuse nonstaining epithelium. In this era, the nature of intraepithelial biopsies was controversial, often described at the margin of invasive biopsies but at times noted as a precursor to invasion. Nevertheless, the description in the 1920s and 1930s of what came to be known as CIN provided the foundation for the development of cytologic study. Although cytologic examination of exfoliated cervical epithelial cells was first described by Babes in 1928 in the French literature,only with the appearance in 1941 of the findings of Papanicolaou and Traut did this technique enter clinical practice as a means for the early diagnosis of cervical cancer (Massad and Cejtin, 2014).

To understand the pathogenesis of cervical cancer, it is important to know the factors involved in its development, which have been identified from a series of clinical, epidemiologic, pathologic, and molecular studies. Epidemiologic data have long implicated a sexually transmitted agent, which is now established to be the human papillomavirus. HPV is currently considered to be the most important agent in cervical oncogenesis. As noted earlier, this virus is the known cause of the sexually transmitted vulvar condyloma acuminatum and has been isolated from vulvar and vaginal squamous cell carcinomas; it is also suspected of being an oncogenic agent in a variety of other squamous tumors or proliferative biopsies of skin and mucous membranes. A wealth of molecular epidemiologic data has established the following risk factors for cervical neoplasia, all of which indicate a complex interaction between host and virus(Koutsky,1997; Crum, 2002). Early age at first intercourse, Multiple sexual partners, Increased parity, A male partner with multiple previous sexual partners, The presence of a cancer-associated HPV, The persistent detection of a high-risk HPV, particularly in high concentration (viral load), Certain HLA and viral subtypes, Exposure to oral contraceptives and nicotine, Genital infections (chlamydia). There is mounting molecular evidence linking HPV to cancer in general and cervical cancer in particular.

1. HPV DNA is detected by hybridization techniques in over 95% of cervical cancers.
2. Specific HPV types are associated with cervical cancer (high risk) versus condylomata (low risk); low (include types 6, 11, 42, 44, 53, 54, 62, and 66) and high-risk types (include types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68). (Zur, 1996)
3. Experimental data indicate that viral (*E6* and *E7*) genes of high risk HPVs can disrupt the cell cycle via binding to RB with up-regulation of Cyclin E (E7) and p16INK4; interrupt cell death pathways by binding to p53 (E6); induce centrosome duplication and genomic instability (E6, E7); and prevent replicative senescence by up-regulation of telomerase (E6)(Munger and Howley, 2002.). HPV E6 induces rapid degradation of p53 via ubiquitin-dependent proteolysis, reducing p53 levels by two- to three-fold. E7 complexes with the hypophosphorylated (active) form of RB, promoting its proteolysis via the proteosome pathway. Because hypophosphorylated RB normally inhibits S-phase entry via binding to the E2F transcription factor, the two viral oncogenes cooperate to promote DNA synthesis while interrupting p53-mediated growth arrest and apoptosis of

genetically altered cells. Thus, the viral oncogenes are critical in extending the life span of genital epithelial cells—a necessary component of tumor development.

4. The physical state of the virus differs in different biopsies, being integrated into the host DNA in cancers, and present as free (episomal) viral DNA in condylomata and most precancerous biopsies.
5. Certain chromosome abnormalities, including deletions at 3p and amplifications of 3q, have been associated with cancers containing specific (HPV-16) papillomaviruses.
6. Most compelling, recent data indicate that vaccines directed against papillomaviruses can prevent infection and the development of precancerous disorders.

However, the evidence does not implicate HPV as the only factor. A high percentage of young women are infected with one or more HPV types during their reproductive years, and only a few develop cancer.

HPV biopsies are perhaps the earliest form of cervical intraepithelial neoplasia and are often indistinguishable from mild dysplasia. Mild dysplasia is characterized by pathologic changes confined to the lower-third of the epithelium. The biopsy of moderate dysplasia involves the lower two-thirds of the epithelium. The pathologic changes associated with severe dysplasia and carcinoma *in situ* (CIS) occupy the full thickness of the epithelium. Carcinoma *in situ* and severe dysplasia is biologically and histologically indistinguishable (Connor and Hartenbach, 2008)

This biopsy may exist in the non-invasive stage for as long as 20 years and shed abnormal cells that can be detected on cytologic examination. These precancerous changes should be viewed with the following in mind: (1) they represent a continuum of morphologic change with indistinct boundaries; (2) they do not invariably progress to cancer and may spontaneously regress, with the risk of persistence or progression to cancer increasing with the severity of the precancerous change; (3) they are associated with papillomaviruses, and high-risk HPV types are found in increasing frequency in the higher-grade precursors. Cervical precancers have been classified in a variety of ways. The oldest is the *dysplasia/carcinoma in situ* system with mild dysplasia on one end and severe dysplasia/carcinoma in situ on the other. Another is the *cervical intraepithelial neoplasia* (CIN) classification, with mild dysplasias termed CIN grade I and carcinoma in situ biopsies termed CIN III. Still another reduces these entities to two, terming

them low-grade and high-grade intraepithelial biopsies. Because these systems describe noninvasive biopsies of indeterminate biology that are usually easily treated, none of these classifications is indispensable to clinical management or immune to revision (Kumar *et al.*, 2014).

2.4.4.4 Invasive Cervical Carcinoma

Manifests in three somewhat distinctive patterns: fungating (or exophytic), ulcerating, and infiltrative cancers. With the advent of widespread screening, many squamous cell carcinomas are detected at a subclinical stage, often during evaluation of an abnormal Papanicolaou smear. When obvious to the naked eye, the most common variant is the fungating tumor, which produces an obviously neoplastic mass that projects above the surrounding mucosa . Advanced cervical carcinoma extends by direct spread to involve every contiguous structure, including the peritoneum, urinary bladder, ureters, rectum, and vagina. Local and distant lymph nodes are also involved. Distant metastasis occurs to the liver, lungs, bone marrow, and other structures. Histologically, about 95% of squamous carcinomas are composed of relatively large cells, either keratinizing (well-differentiated) or nonkeratinizing (moderately differentiated) patterns. A small subset of tumors (less than 5%) are poorly differentiated small cell squamous or, more rarely, small cell undifferentiated carcinomas (neuroendocrine or oat cell carcinomas). The latter closely resemble oat cell carcinomas of the lung and have an unusually poor prognosis owing to early spread by lymphatics and systemic spread. These tumors are also frequently associated with a specific high-risk HPV, type 18.

2.5 VULVA AND VAGINA BIOPSIES

2.5.1 Vulva

Vulvar cancer accounts for approximately 5% of all female genital malignancies. It occurs in about 1.5 per 100,000 women-years in developed countries but is 2-3 times more frequent in underdeveloped countries. With the exception of the rare sarcomas, this cancer appears most frequently in women aged 65-75 years, and, in some series, almost half of the patients are aged 70 years or older. Vulvar cancer can appear in younger patients, and, in some large cancer referral institutions, approximately 15% of all vulvar cancers occur in women younger than 40 years. These young patients tend to have early microcarcinomas, which may be associated with diffuse intraepithelial neoplasia of the vulva (William *et al.*, 2013).

High-risk human papillomavirus (HRHPV) is an established cause of a significant proportion of vulvar intraepithelial neoplasia (VIN) (Koutsky, 1997; van der *et al.*, 2006; Skapa *et al*., 2007). The incidence of VIN has been increasing, along with a decrease in age at diagnosis (Bodelon *et al*., 2009). High-grade VIN, VIN 3 in particular, is considered the immediate precursor of HRHPV-related squamous cell carcinoma of the vulva. Similar to cervical high-grade squamous intraepithelial biopsies (HSIL), the majority of VIN 3 biopsies contain HPV 16 (Barzon et al., 2010). While it has been recognized that, in the cervix, HRHPV infection is responsible for a spectrum of squamous intraepithelial biopsy grades (low-grade squamous intraepithelial biopsy/cervical intraepithelial neoplasia 1 [LSIL/CIN 1], high-grade squamous intraepithelial biopsy/cervical intraepithelial neoplasia 2 [HSIL/CIN 2], and high-grade squamous intraepithelial biopsy/cervical intraepithelial neoplasia 3 [HSIL/CIN 3]), the majority of vulvar HRHPV- related biopsies are high-grade (VIN 2 and VIN 3) and the existence of VIN 1 has been questioned.

Low-risk human papillomavirus (LRHPV) infection is extremely common in the vulva and is responsible for the development of vulvar condyloma acuminatum (Garland et al., 2009). These biopsies most commonly contain HPV6 and HPV11 and have virtually no risk of neoplastic progression (Pirog et al., 2000).

Diseases of the vulva in the aggregate constitute only a small fraction of gynaecologic practice. Many inflammatory dermatologic diseases that affect hair-bearing skin elsewhere on the body may also occur on the vulva, so vulvitis may be encountered in psoriasis, eczema, and allergic dermatitis. Most skin cysts (epidermal inclusion cysts) and tumors can also occur in the vulva.

2.5.2 Bartholin Cyst

Bartholin's glands (BG) are the most important gland of the vulva. Inflammatory process and duct cysts are by far the most frequent biopsies in this location and carcinomas are the most prevalent solid tumors. Between the rare benign tumors, nodular hyperplasia (NH) of BG appears to be the most common biopsy (Santos *et al.*, 2006).Acute infection of the Bartholin gland produces an acute inflammation of the gland (adenitis) and may result in a Bartholin abscess. Bartholin cysts are relatively common, occur at all ages, and result from obstruction of the Bartholin duct, usually by a preceding infection. These cysts may become large, up to 3 to 5

cm in diameter. The cyst is lined by either the transitional epithelium of the normal duct or squamous metaplasia. The cysts produce pain and local discomfort; the cysts are either excised or opened permanently (marsupialization).

2.5.3 Papillary Hidradenoma of the Vulva

Papillary hidradenoma of the vulva is a rare, benign neoplasm arising from apocrine sweat glands of the skin. Frequently, this biopsy has been mistaken for carcinoma (Kaufmann et al., 1987). Hidradenoma presents as a sharply circumscribed nodule, most commonly on the labia majora or interlabial folds, and may be confused clinically with carcinoma because of its tendency to ulcerate. Hidradenomas consist of tubular ducts lined by a single or double layer of nonciliated columnar cells, with a layer of flattened "myoepithelial cells" underlying the epithelium. These myoepithelial elements are characteristic of sweat glands and sweat gland tumors.

2.5.4 Condyloma Acuminatum

Condyloma acuminatum is firm and randomly localized. The color of the condyloma acuminatum biopsies can vary and individual papillary projections often coalesce in a common base. In most cases of condyloma acuminate, whitening can be observed by the acetic acid test (Moyal-Barracco et al., 1990). This benign raised or wartlike (verrucous) conditions of the vulva occur in three forms: (1) Condyloma acuminatum, a papillomavirus-induced squamous biopsy also called venereal wart, is, by far, the most common; (2) mucosal polyps, which are benign stromal proliferations covered with squamous epithelium; and (3) syphilitic condyloma latum,

Fifty per cent of women with vulvar condyloma acuminatum also have cervical intraepithelial neoplasia. Typical exophytic condyloma acuminatum have a fibrovascular stalk, and the epithelial surface is acanthotic and often hyperkeratotic. The fibrovascular stalk is lacking in the flat condyloma acuminatum. Both exhibit similar epithelial changes.

They are benign virus-induced epithelial tumours. The association with HPV type 6 and 11 has been established in 75-95% of cases (Buscema *et al.*, 1988; Ried *et al.*,1994).These types of viruses belong to “low-risk HPV” since they are rarely associated with carcinoma. In some cases, condyloma were found to be induced by other “high- orintermediate-risk” HPV. It should be stressed that themorphologic appearance does not necessarily correlate with the HPV type. The

clinical implication of 6 and 11 HPV infection of the vulva is that it is associated with an increased susceptibility to the acquisition of the HPV oncogenic virus (Li Vigni *et al*., 1992). HPV 16 is associated in up to 10-12% of these biopsies (Campion, 1988). The morphology is typical and the clinical features are usually sufficient for diagnosis. Condylomata accuminata are most often visible with the naked eye and usually form multiple papillary of verrucous biopsies on vulva. They are frequently multiple. Condylomas are pointed, soft, pink or white, elongated, moist excrescences. Prominently vascularised, they have finger like projections on the surface. Each of these projections is in fact a small condyloma with a central capillary loop which can only be seen colposcopically. Their appearance differs according to the site affected. On the hair-bearing skin they are flesh coloured and somewhat camouflaged. They appear as red hypervascular plaques, white keratoticmacules or pigmented papule. On hairless skin they tend tobe soft papular and strikingly white. On mucous membranes they are often fleshy, vascular and filiform. Often, they appear along the rim of the labia minora and may be spread to the interlabial sulcus or around the introitus. Typical proliferations which resemble coral may be seen. If more papillae are fused, biopsies may get cauliflower shape.

Condylomata acuminate which are sexually transmitted, may be solitary, they are more frequently multiple and often coalesce; they involve perineal, vulvar, and perianal regions as well as the vagina and, less commonly, the cervix. The biopsies are identical to those found on the penis and around the anus in males. They consist of a branching, treelike proliferation of stratified squamous epithelium supported by a fibrous stroma. Acanthosis, parakeratosis, hyperkeratosis, and, most specifically, nuclear atypia in the surface cells with perinuclear vacuolization (called *koilocytosis*) are present. The virus life cycle is completed in the mature superficial cells of the epithelium. This dependence of viral growth on squamous maturation is typical of HPV and produces a distinct cytologic change in the mature cells*koilocytotic atypia* (nuclear atypia and perinuclear vacuolization) that is considered a viral "cytopathic" effect. Except in immunosuppressed individuals, condylomata acuminata frequently regress spontaneously, and are not considered to be precancerous biopsies. They are, however, a marker for sexually transmitted disease (.Zur, 1996.).

2.5.5 Extra mammary Paget Disease

This curious and rare biopsy of the vulva, and sometimes the perianal region, is similar in its skin manifestations to Paget disease of the breast. As a vulvar neoplasm, it manifests as a pruritic, red, crusted, sharply demarcated, map like area, occurring usually on the labia majora. It may be accompanied by a palpable submucosal thickening or tumor.

The diagnostic microscopic feature of this biopsy is the presence of large tumor cells lying singly or in small clusters within the epidermis and its appendages. These cells are distinguished by a clear separation ("halo") from the surrounding epithelial cells and a finely granular cytoplasm containing mucopolysaccharide that stains with periodic acid-Schiff, Alcian blue or mucicarmine. Ultrastructurally, Paget cells display apocrine, eccrine, and keratinocyte differentiation and presumably arise from primitive epithelial progenitor cells.

In contrast to Paget disease of the nipple, in which 100% of patients show an underlying ductal breast carcinoma, vulvar biopsies are most frequently confined to the epidermis of the skin and adjacent hair follicles and sweat glands. The prognosis of Paget disease is poor in the uncommon cases with associated carcinoma, but intraepidermal Paget disease may persist for many years, even decades, without the development of invasion. However, because Paget cells may extend beyond the confines of the grossly visible biopsy, often into skin appendages, they are prone to recurrence.

2.5.6 Vagina

The vagina is a portion of the female genital tract that is remarkably free from primary disease. In the adult, inflammations often affect the vulva and perivulvar structures and spread to the cervix without significant involvement of the vagina. The major serious primary biopsy of this structure is the uncommon primary carcinoma. The remaining entities can therefore be cited briefly.

Gartner duct cysts are relatively common biopsies found along the lateral walls of the vagina and derived from wolffian duct rests. They are 1- to 2-cm fluid-filled cysts that occur submucosally. Other cysts include mucous cysts, which occur in the proximal vagina, are derived from

müllerian epithelium, and often contain squamous metaplasia. Another müllerian-derived biopsy (endometriosis, described later) may occur in the vagina and simulate a neoplasm.

2.5.7 Premalignant and Malignant Neoplasms Of The Vagina

Most benign tumors of the vagina occur in reproductive-age women and are skeletal muscle tumors (rhabdomyomas) or stromal tumors (stromal polyps). The latter may exhibit cellular atypia but are benign, localized, and self-limited. Others include benign leiomyomas, hemangiomas, and rare mixed tumors (Nucci and Fletcher, 2000).Clinically important malignant tumors in terms of frequency and biologic behavior are carcinoma and embryonal rhabdomyosarcoma (sarcoma botryoides).

2.5.8 Vaginal Intraepithelial Neoplasia and Squamous Cell Carcinoma

Primary carcinoma of the vagina is an extremely uncommon cancer (about 0.6 per 100,000 women yearly) accounting for about 1% of malignant neoplasms in the female genital tract, and of these, 95% are squamous cell carcinomas. Most are associated with HPV. The greatest risk factor is a previous carcinoma of the cervix or vulva; 1% to 2% of patients with an invasive cervical carcinoma eventually develop a vaginal squamous carcinoma.

Most often, the tumor affects the upper posterior vagina, particularly along the posterior wall at the junction with the ectocervix. It begins as a focus of epithelial thickening, often in association with dysplastic changes, progressing to a plaquelike mass that extends centrifugally and invades, by direct continuity, the cervix and perivaginal structures. The biopsies in the lower two-thirds metastasize to the inguinal nodes, whereas upper biopsies tend to involve the regional iliac nodes.

These tumors first come to the patient's attention by the appearance of irregular spotting or the development of a frank vaginal discharge (leukorrhea). At other times, they remain totally silent and become clinically manifest only with the onset of urinary or rectal fistulas.

2.5.9 Adenocarcinoma

Adenocarcinomas are rare but have received attention because of the increased frequency of clear cell adenocarcinomas in young women whose mothers had been treated with diethylstilbestrol (DES) during pregnancy (for a threatened abortion) (Mittendof and Herbst,

1994). Fortunately, less than 0.14% of such DES-exposed young women develop adenocarcinoma.

The tumors are most often located on the anterior wall of the vagina, usually in the upper third, and vary in size from 0.2 to 10 cm in greatest diameter. They are usually discovered between the ages of 15 and 20 years and are often composed of vacuolated, glycogen-containing cells, hence the term clear cell carcinoma. These cancers can also arise in the cervix. A probable precursor of the tumor is vaginal adenosis, a condition in which glandular columnar epithelium of müllerian type either appears beneath the squamous epithelium or replaces it. Adenosis presents clinically as red, granular foci contrasting with the normal pale pink, opaque vaginal mucosa. On microscopic examination, the glandular epithelium may be either mucus secreting, resembling endocervical mucosa, or socalled tuboendometrial, often containing cilia. Adenosis has been reported in 35% to 90% of the offspring of estrogen-treated mothers, but as mentioned earlier, malignant transformation is extremely rare.

Because of its insidious, invasive growth, vaginal cancer (squamous and adenocarcinomatous) is difficult to cure. Thus, early detection by careful follow-up is mandatory in DES-exposed women. Surgery and irradiation have successfully eradicated DES-related tumors in up to 80% of patients. Extension of cervical carcinoma to the vagina is much more common than are primary malignant neoplasms of the vagina. Accordingly, before a diagnosis of primary vaginal carcinoma can be made, a preexisting cervical biopsy must be ruled out.

2.5.10 Embryonal Rhabdomyosarcoma of the Vagina

Also called sarcoma botryoides, this is an interesting but uncommon vaginal tumor most frequently found in infants and in children younger than 5 years of age. The tumor consists predominantly of malignant embryonal rhabdomyoblasts and is thus a type of rhabdomyosarcoma (Copeland, 1985)

These tumors tend to grow as polypoid, rounded, bulky masses that sometimes fill and project out of the vagina; they have the appearance and consistency of grapelike clusters (hence the designation botryoides, meaning grapelike. The tumor cells are small and have oval nuclei, with small protrusions of cytoplasm from one end, so they resemble a tennis racket. Rarely, striations

can be seen within the cytoplasm. Beneath the vaginal epithelium, the tumor cells are crowded in a so-called cambium layer; but in the deep regions, they lie within a loose fibromyxomatous stroma that is edematous and may contain many inflammatory cells. For this reason, the biopsies can be mistaken for benign inflammatory polyps, leading to unfortunate delays in diagnosis and treatment. These tumors tend to invade locally and cause death by penetration into the peritoneal cavity or by obstruction of the urinary tract.

Conservative surgery, coupled with chemotherapy, appears to offer the best results in cases diagnosed sufficiently early (Andrassy *et al.,* 1995).

2.6 BURDEN OF GYNAECOLOGICAL BIOPSIES IN NIGERIA AND OTHER PARTS OF THE WORLD

Gynaecological biopsies are public health problem worldwide affecting all categories of females, it is a common cause of death in developed and among the leading causes of death in developing countries. WHO reported that about 24.6 million people live with cancer worldwide (WHO, 2005). Parkin *et al*.(2005) reported that in indigenous Africans, 650,000 people of estimated 965million are diagnosed of cancer annually and lifetime risk of dying from cancer in African women is 2 times higher than in developed countries (Abdulkareem *et al.,* 2009). The burden of gynaecological biopsies in Nigeria is unknown, mainly because of lack of statistics or under reporting. In a study of cancer registry literature updated from all over the world, only 1% of the literature emanated from Africa compare to 34% and 42% from Europe and Asia respectively (Howlader, *et al*., 2011). This is partly due to inaccurate population statistics which makes age specific incidence rates impossible or if available inaccurate. Large proportion of the population still never seek orthodox medical care and so are not recorded, other reasons are inadequate diagnostic facilities, limited access to care, inadequate technical manpower and infrastructure as well as quality of cancer data systems all contribute to inaccurate data on cancer burden. There are 11 cancer registries in Nigeria; located in various tertiary hospitals in various parts of the country, most of the Registries are poorly funded and except probably the Ibadan Cancer Registry, they all produce hospital-based data. The centres are as follows; Cancer Registry, Lagos University Teaching Hospital, Lagos. Cancer Registry, Jos University Teaching Hospital, Jos. Cancer Registry, Ahmadu Bello University Teaching Hospital, Zaria. Ife/Ijesha Cancer

Registry, Obafemi Awolowo Teaching Hospital Complex, Ile-Ife. Cancer Registry, University of Nigeria Teaching Hospital, Enugu. The Cancer Registry, University of Ilorin Teaching Hospital, Ilorin. Cancer Registry, University of Maiduguri Teaching Hospital, Maiduguri. Cancer Registry, University of Benin Teaching Hospital, Benin City. Cancer Registry, Aminu Kano University Teaching Hospital, Kano. Cancer Registry, Nnamdi Azikwe University Teaching Hospital, Nnewi. Cancer Registry, University of Calabar Teaching Hospital, Calabar. Cancer Registry, Usman Danfodio University Teaching Hospital, Sokoto.

The earliest study from Nigeria was from the Ibadan Cancer Registry-1960-69(ICR),higher rates of cancer in females with age standardized rates (ASR) of 105.1 and 78 per 100,000 females and males respectively was reported. In 1998, 74.5 per 100,000 females and 63.9 for males was recorded from the same centre. In Zaria, 1976-78 data reported 1575 cases with 52% of cases in males and 48% in males; a latter study however showed more cancers in females than males (Afolanya, 1992). Newer data (2001-2005) from Ibadan showed increasing incidence and the ASR for all cancers as 81.6 per 100,000 for males and 115.1 per 100,000 for females with 65.9% and 34.1% in females and males respectively. From Kano, of 1001 cancers recorded for period 1995-2004, male cancers accounted for 50.3% and 49.7% in females. A total of 1162 and 1657 cancer cases respectively for males and females for the period between 1995 and 2002 from the Cancer Registry in Jos University Teaching Hospital been reported. Report from University of Benin Teaching Hospital showed 2258 cases over a 20year period with female cancers predominating(64%) while that from Calabar showed a total of 588 cancers between 2004-2006 with 50.9% and 49.1% respectively for males and females. The WHO estimated incidence of cancer from all sites in 2002 for Nigeria was 90.7 and 100.9 per 10,000 for males and females respectively while mortality rates were 72.2 and 76 respectively-Globocan. This is comparable to 89.1 and 104.1/100,000 incidence for males and females and 72.2 and 79.6 crude mortality rates recorded for Ghana but much less than figures recorded for United Kingdom and USA (Abdulkareem, 2009).

2.7 PREVALENCE OF GYNAECOLOGICAL TUMOURS

The comprehensive global cancer statistics from the International Agency for Research on Cancer indicate that gynaecological cancers accounted for 19% of the 5.1 million estimated new cancer cases, 2.9 million cancer deaths and 13 million 5-year prevalent cancer cases among

women in the world in 2002 (Ferlay *et al.*, 2004). Cervical cancer accounted for 493 000 new cases and 273 000 deaths; uterine body cancer for 199 000 new cases and 50 000 deaths; ovarian cancer for 204 000 new cases and 125 000 deaths; cancers of the vagina, vulva and choriocarcinoma together constituted 45 900 cases. More than 80% of the cervical cancer cases occurred in developing countries and two thirds of corpus uteri cases occurred in the developed world.

According to report, developing countries accounted for 820 265 cases (77.7%) of global estimates for new cases of the commonest gynaecological cancers including cervical, corpus and ovarian cancer in 2009. This constituted 12.1% of the 6.8 million cases of cancer in developing countries. This review intends to explore the pattern, magnitude and significance of the current burden of gynaecological cancers in developing countries (Parkin *et al*,.2005).

Cervical cancer: Cervical cancer is the commonest gynaecological malignancy in developing countries where organized screening programmes do not exist. According to the IARC, there were 453 531 cases of cervical cancer in developing countries in 2008 representing 89% of global estimates (International Agency for Research, 2015). Also 273 000 deaths occur worldwide every year due to cervical cancer out of which 83% occur in developing countries (Ferlay *et al*., 2004). Case fatality rates of cervical cancer are quite high in these countries with case fatalities up to 60% reported. Conversely in developed countries where nationally organized screening programmes exist, cervical cancer is not as common and case fatality rates are as low as 32%. About 80%-95% of cervical cancers are squamous cell carcinoma (Sankaranarayanan and Ferlay, 2006).

Across different regions of the world, developing countries individually report heavy burdens of high incidences and mortality from cervical cancer. The highest incidence rates are found in Sub Saharan Africa, Latin America and the Caribbean, South Central and South East Asia ((Sankaranarayanan and Ferlay, 2006).

South and South East Asia are thought to experience over 200 000 new cases of cervical cancer yearly (more than one-third of the global burden) (Ferlay *et al.,* 2004). Age-adjusted cervical cancer mortality rates exceed 15 per 100 000 in most developing countries, with rates as high as

35/100 000 in East Africa (Sankaranarayanan and Ferlay, 2006). A nationwide survey in India published recently evaluated the cause of 122 429 deaths in 1.1 million randomly selected homes across the country between 2001 and 2003: cervical cancer made the highest contribution to cancer deaths among women at 17.5% (Dikshit *et al.,* 2012). In Latin America and the Caribbean, Haiti, Nicaragua and Bolivia had the highest mortality due to cervical cancer with rates of 40, 28 and 22 percent respectively (Ferlay *et al.,* 2004) . The very high mortality rates of cervical cancer in developing countries are due to the fact that most patients present at advanced clinical stages of the disease, and to the fact that a significant proportion of patients do not receive or complete prescribed courses of treatment due to deficiencies in treatment availability, accessibility, and affordability Africa (Sankaranarayanan and Ferlay, 2006).

A report in Nigeria gave the incidence of cervical cancer as 25/100 000 per year which translates to a disease burden for an estimated 32 million women in 2005 to about 8000 cases per year (Adewole *et al.,* 2005). A hospital based study in Lagos Nigeria showed that, overall, cancer was the leading cause of death among gynaecological inpatients and that cervical cancer contributed over 44% to all gynaecological mortality (Anorlu *et al.,* 2010).

Ovarian cancers: Over 80% of cases of ovarian cancer are epithelial in origin (Bast *et al.,* 2009; Gubbels *et al.*, 2001). Ovarian cancer is the second commonest gynaecological cancer in developing countries including Nigeria (Babarinsa *et al.,* 1998). It accounts for 18.8% of all gynaecological cancers in developing countries and 28.7% in developed countries (Sankaranarayanan and Ferlay, 2006). Recent estimates indicated that of 240 476 cases of ovarian cancer in 2009, 155 835 (64.8%) occurred in developing countries compared to 84 641 in developed countries. Accounts that ovarian cancer is commoner in developed countries than in developing countries may not, therefore, be supported by the most current estimates. Ovarian cancer has a case-fatality rate of 59.2% in developing countries which is similar to the 54.8% in developed countries. The high case fatality rate of ovarian cancer is primarily due to the fact that the disease only becomes manifest in advanced stages of the disease (Bast *et al.,* 2009; Gubbels *et al.,* 2001).

Vaginal cancer: Vaginal cancer is rare and constitutes less than 2% of gynaecological cancers worldwide. Of 13 200 cases globally in 2002, 9000 (68%) occurred in developing countries. Incidence rates do not exceed 0.8/100 000 in any region of the world. Case fatality rate in developing countries is 44.7% compared to 15.4% in the developed world. More than 75% of cases occur in women older than 60 years (Sankaranarayanan and Ferlay, 2006).

Vulva cancer: This constitutes 3% of gynaecological cancers worldwide. In 2002, there were 26 800 cases out of which 11 100 (41.4%) occurred in developing countries. Incidence rate is less than 1/100 000 in developing countries. More than 50% are seen in women over 70 years and more than two-thirds occur in the labia majora (Sankaranarayanan and Ferlay, 2006).

Choriocarcinoma: This represents 0.6% of all gynaecological cancers. Approximately 5800 cases occurred worldwide in 2002 out of which 5400 (96.4%) occurred in developing countries. Incidence rates are highest in South East Asia where rates of (0.43-1.7)/100 000 are quoted compared to 0.04/100 000 in Africa and Europe (Sankaranarayanan and Ferlay, 2006).

Leiomyomas (fibroids) are the commonest benign tumors in women. Leiomyomas are the most common tumors in women of reproductive age. They are symptomatic in 50% of cases, with the peak incidence of symptoms occurring among women in their 30s and 40s (Wise *et al*., 2005). It has been postulated that they occur in over 70% of women by the onset of menopause (Flake *et al.,* 2003; Baird *et al.,* 2003) The exact etiology of the tumors is unknown; however, several interesting associations have been noted. There is a great predilection of fibroids for women of African descent. Theories attribute this to genetic predisposition, diet, or environmental factors. However, few studies have addressed these relationships (Heinemann *et al*., 2003; Payson *et al*., 2006). Leiomyomas occur in 20– 25% of women over the age of 30years, although most are symptomless (Buttran and Reiter, 1981)

2.8 Staining Methods in the Evaluation of Gynaecological Biopsies

Staining is used to highlight important features of the tissue as well as to enhance the tissue contrast. Staining is a commonly used medical process in the medical diagnosis of tumors in which a dye color is applied on the tissues sample to locate the diseased or tumorous cells or other pathological cells (Musumeci, 2014).

Hematoxylin and eosin (H&E) stains have been used for at least a century and are still essential for recognizing various tissue types and the morphologic changes that form the basis of contemporary cancer diagnosis. The stain has been unchanged for many years because it works well with a variety of fixatives and displays a broad range of cytoplasmic, nuclear, and extracellular matrix features. Biopsies are stained with haematoxylin and eosin (H&E) to enhance the visual contrast for histopathological evaluations. Haematoxylin stains the nuclei purple while eosin stains the intracellular and extracellular protein pink. Morphological features, such as cell shape, nuclear size and nuclear-to-cytoplasm (N/C) ratio are commonly used as diagnostic criteria by histopathologists to identify abnormal cells. A limitation of hematoxylin staining is that it is incompatible with immunofluorescence. It is useful, however, to stain one serial paraffin section from a tissue in which immunofluorescence will be performed. Hematoxylin, generally without eosin, is useful as a counterstain for many immunohistochemical or hybridization procedures that use colorimetric substrates (such as alkaline phosphatase or peroxidase). This protocol describes H&E staining of tissue and cell sections. (Boone *et al.,* 1997; Evan *et al.,* 2001).

The Masson trichrome (MT) stain is one of the most utilized special stains in the histology and histopathology Laboratory. Most of the common uses for requesting a trichrome stain are liver biopsies, renal biopsies, dermatopathology, gynaecological biopsies, cardiac biopsies and muscle and nerve biopsies, and widely utilized techniques are the Masson, Gomori One Step, Martius Scarlet Blue and Mallory (Jones, 2010). The purpose of the trichrome stain is primarily to demonstrate collagen and muscle in normal tissue or to differentiate collagen and muscle in tumours. It is also used to identify an increase in collagenous tissue or indicate fibrotic change in cirrhosis of the liver or in a renal disease. The trichrome stain is also used to distinguish tumors that have arisen from muscle cells and fibroblasts.

The difference between H&E and MT staining were more related to the steps and dyes used in the staining preparation. Standard H&E staining involves two types of dyes which are haematoxylin and eosin . This staining method involves application of haemalum, which is a complex formed from aluminium ions and oxidised haematoxylin. The dye stains nucleus of cells and a few other objects, such as keratohyalin granules dark blue or purple in colour. The nuclear staining is followed by counterstaining with an aqueous or alcoholic solution of eosin Y,

which colours eosinophilic and other structures in various shades of red, pink and orange (Junqueira and Carneiro, 2007). However, the modified MT staining involves three colours of staining dyes, as the name implies, "trichrome". The principle of trichrome staining is that the less porous tissues are coloured by the smallest dye molecule and followed by the larger molecule (Sheehan and Hrapcahk, 1980). Theoretically, most of the stains are based on the attraction of the opposite charges in the tissues to the dyes applied. In MT staining the sections are first stained with an acidic dye such as acid Fucshin. In this step, all acidophilic tissue elements such as cytoplasm, muscle and collagen will bind to the acid dyes. The section is then treated with phosophomolybidic acid to decolourise the collagen but not to the cytoplasm. The decolorised collagen is then stained with fiber stain such as methyl blue, anilline blue or fast green dye (Masson, 1929). The blue colour of collagen can be enhanced by preliminary treatment of the section in hot Bouin's solution which is absent in the H&E staining protocol. The blue colour intensity of the collagen can be measured by a computerised imaging analyser with the aid of software. Several studies used this computerised method to measure collagen content in order to quantify dermal wound recovering for application to pharmacological products such as toxicity and efficacy tests in wound healing (Bae *et al.,* 2005).

Immunohistochemistry (IHC) combines microscopic morphology with accurate molecular identification and allows in situ visualisation of any specific protein antigen. The introduction of IHC in diagnostic pathology has revolutionised routine practice, and IHC studies have significantly contributed to a better understanding and subtyping of many malignancies, initially lymphoid neoplasms. Furthermore, IHC has become an integral part of the definition of the majority of solid tumours and is progressively gaining a foothold in guiding anticancer therapy. Among other examples, HER2/neu and oestrogen receptor (ER) expression is routinely used to identify patients with breast cancer eligible to trastuzumab and tamoxifen, respectively. With the boost and consequential widespread use of advanced technologies, molecular studies that claim to have discovered novel candidate makers with diagnostic, predictive, prognostic or therapeutic value are published daily. Besides making tissue diagnosis, they are also in charge of (1) guaranteeing the adequacy of samples used for diagnostic tests, which will be translated into therapeutic decisions, (2) performing IHC biomarker analysis and (3) assisting the development of novel tissue biomarkers. Over the last decade, molecular studies have unveiled the molecular

genetic pathway of gynaecological malignancies and enriched the portfolio of IHC markers useful in the differential diagnosis of gynaecological diseases. Accordingly, IHC represents a solid adjunct for the classification of gynaecological malignancies that improves interobserver reproducibility1 and has the potential of revealing unexpected features. However, interpretation in the light of knowledge-based specificity of each single marker along with histopathology expertise and stringency is still the sine qua non. A satisfactory IHC must localise cells and tissue targets, clearly and specifically, keeping the non-specific background to a minimum level. Here, we will describe the panels of IHC markers used in the most common scenarios of differential diagnosis seen in routine gynaecological pathology, along with their rationale. Though beyond the scope of this paper, clinical information and macroscopical and microscopical features will be outlined at times since they still represent a keystone for the correct diagnosis and characterisation of many pathological entities.

The most difficult differential diagnosis in the ovarian cancer field concerns mucinous tumours since both morphological and immunophenotypical features are shared between primary and metastatic tumours. Indeed, macroscopic features and clinical correlation remain fundamental for a correct diagnosis (Kurman *et al.,* 2014). Immunohistochemically, there is a significant overlap in the immunophenotypes between primary mucinous ovarian carcinoma and metastatic gastrointestinal carcinoma. Typically, CK20, CDX2 and SATB2 are expressed by colorectal adenocarcinoma and show an intense and diffuse pattern. Notably, they are negative, or only focal and weak, and in any case less intense and diffuse than CK7, in primary ovarian carcinomas, with the only exception being the rare intestinal-type mucinous ovarian tumours originating from ovarian teratomas (Moh *et al.,* 2016). In primary ovarian mucinous tumours, besides cytokeratin 7 (CK7) and CA125, PAX8 is expressed in 65% of cases, but not in colorectal adenocarcinomas (Strickland *et al*., 2016). Notably, CA125 is not ovarian specific; even breast, lung, pancreas, cervix and uterine carcinomas and mesothelioma may be positive. Therefore, though CK20+/CK7− is prototypical for metastatic adenocarcinomas from the lower intestinal tract and this immunoprofile can be definitive for correct diagnosis, often it is necessary to resort to lineage-specific markers PAX8 and SATB2, both highly specific but defectively sensitive (Strickland *et al*., 2016). In this situation, ER and PR are of limited value

since they are negative in both intestinal-type primary and metastatic carcinomas, whereas CDX2 is a site-unspecific marker of intestine differentiation (Vang *et al.,* 2006).

Likewise, endocervical adenocarcinoma in situ (AIS) must be distinguished from potential innocuous mimics such as reactive and reparative glandular changes, tubal metaplasia, microglandular hyperplasia and endometriosis. Immunohistochemically, AIS shows increased Ki-67 and diffuse p16 and mCEA, but negative vimentin and ER. Conversely, p16 in benign biopsies tends to be negative or focal, and Ki-67 proliferation index is low (Loureiro and Oliva, 2014).

Immunohistochemistry for Ki67 (MKI67), a nuclear antigen which is present in all but the G0 phase of the cell cycle and therefore expressed in proliferating cells, can be used to determine tumor proliferation index (Gerdes *et al.,* 1984). Ki67 is a prognostic and predictive marker in breast cancer patients used in both clinical practice and clinical trials. However, Ki67 staining is subject to intra-tumoral heterogeneity and Ki67 scoring is prone to inter- and intra-observer variability, especially with 'eyeballing' (Dowsett et al., 2011). The cellular proliferation status could reflect the proliferative potential of a tumor, as well as the sensitivity to chemotherapy; therefore, it is a potential prognostic tool. Ki67 is a nuclear located protein that is closely linked to cell proliferation. It is present during all active phases of the cell cycle but absent from resting cells (Scholzen and Gerdes, 2000). Recently, Ki67 was identified as an important prognostic factor for many tumor entities with respect to chemosensitivity and disease recurrence/death. Some investigations have considered higher Ki67 expression a risk factor for survival since highly proliferative tumors are associated with a worse outcome. However, other studies have indicated that high-grade serous cancer (HGSC) patients with higher Ki67 expression tended to experience longer progression-free survival (PFS) because highly proliferative tumors seemed to respond better to first line chemotherapy (Feng *et al*., 2016).

In a study, Ki-67 was assessed using immunohistochemistry from paraffin-embedded tissue in 20 patients with uterine leiomyosarcomas (LMS), 22 cases of smooth muscle tumors of uncertain malignant potential (STUMP) and 25 cases of leiomyomas. They recorded a significantly elevated Ki-67 antigen expression in LMS, which correlates well with the rapid growth of these malignant tumors, as such Ki-67 may be a useful immunohistochemical parameter to distinguish

between cases of malignant smooth muscle tumors and those of uncertain or borderline histology (Klaus *et al*., 2004).

Yabushita *et al*. (1992) examined the growth potential of uterine endometrial cancer, the population of cells in proliferating cycle (% PC) with Ki-67, using flow cytometry. The %PC of 27.18 ± 12.00% in 22 endometrial cancers was significantly higher than the 14.5 ± 5.94% found in 28 normal endometrial tissues. In premenopausal endometrial tissue, the %PC in the proliferatory phase was significantly higher than the %PC found in the secretory phase. In endometrial cancers, an increase of %PC was found in cases with deep myometrial invasion, and the %PC was elevated in groups containing histologically poorly differentiated types when compared to groups of well-differentiated and moderately differentiated types. Sorted cells reactive with Ki-67 antibody were large and had a high nuclear/cytoplasmic ratio. On the bases of these results, it was concluded that a Ki-67 Ag/DNA dual-color assay would be useful to examine the growth fraction in endometrial carcinoma and that an increased growth fraction was related to deep myometrial invasion or poorly differentiated types.

CHAPTER THREE
MATERIALS AND METHODS

3.1 Area of Study

Braithwaite Memorial Specialist Hospital (BMSH) is located in Port Harcourt, Rivers State. The hospital is a Specialist Health Institution with the mandate to deliver health services to the urban city of Port Harcourt and its surrounding rural areas of Rivers State.

Rivers State is one of the six states that make up the South-South geopolitical zone of Nigeria. Rivers State lies at latitude 4°45' north and longitude 6°50' east and covers an area of 10,432.3 square kilometres. It has a population of 5,198,716 as at 2010, 3.7% of Nigeria's total and a population density of 468 people per square kilometre (Menegbo and Doosu**,** 2015). Port Harcourt is the capital of Rivers State and lies at latitude 4°47'21" north and longitude 6°59'55" east, with a population of 1,382,592.

The natives of Rivers State are mainly farmers and fishermen, with over 23 languages. The State is known as the treasure base of Nigeria due to its abundant oil and gas resources. Oil explorations in Rivers State began in 1956 and since then, there has been a paradigm shift in the occupation and life style of the natives resulting from reckless environmental pollution and industrialization.

3.2 Sample size

The sample size for this study was statistically determined using "Taro Yamane" formula for a finite population (Yamane, 1967)

The formula is given as:

$$n = \frac{N}{1 + N(e)^2}$$

Where n = the sample size,

N = the finite population,

e = Level of significance (or Limit of the tolerable error)

I = Unity (a constant)

N = 697

e = 0.05

$$n = \frac{697}{1+697(0.0025)} = \frac{697}{1.75} = 398$$

Since there is a known (finite) population (697), 398can be sampled out of it. This is adequate to represent the entire population based on this formula.

3.3 Data and Tissue Collection

A total of six hundred and ninety seven (697) gynaecological data set and representative paraffin wax tissue blocks of patients who had partial or total hysterectomy or diagnosed of gynaecological biopsy from 2010 to 2014 were collected from the archives of Histopathology Laboratory of Braithwaite Memorial Specialist Hospital (BMSH), Port Harcourt, Rivers State.

3.4 Ethical Approval

Ethical approval was sought and obtained from the Hospital Management Board of Rivers State, through the Ethics Committee of BMSH.

3.5 Tissue Sections

The tissue blocks of already established biopsies collected from BMSH were sectioned at 5µm thickness using the rotary microtome and prepared for staining according to the method of Drury and Wallington, 1973.

3.6 Staining Methods Employed

The seven (7) staining techniques used to demonstrate the various gynaecological biopsies include; Haematoxylin & Eosin for general tissue structure, Masson's Trichrome for demonstration of collagen and muscle fibres, Periodic Acid Schiff (PAS) for demonstration of neutral mucosubstances and basement membranes, phosphotungstic acid haematoxylin (PTAH) for striated muscle fibres, and Verhoeff Van Gieson Elastin for demonstration of elastic tissue. Others are Cytokeratin (CKs) and cellular marker for proliferation (Ki67) for demonstration of cytokeratin and proliferation of malignant cells respectively.

3.6.1 Erhlich's Haematoxylin & Eosin (H&E) (Erhlich, 1877)

Principle

Haematoxylin is oxidized to Haematein by using natural oxidation or chemical oxidation. It requires a mordant, which is usually a metal, to enable Haematein dye to be well demonstrated

on the acidic nucleus to give a blue colour. Eosin which stains pink is acidic and has the ability to demonstrated the cytoplasm of different types of tissues (Avwioro, 2010).

Procedure

The already cut sections were dewaxed in two changes of xylene, hydrated in descending grades of alcohol (Abs, 90% and 70%). The sections were rinsed in water for 1 minute. They were stained in Erhlich's Haematoxylin for 30 minutes, they were rinsed in water for 1 minute and differentiated in 1% acid alcohol for 30 seconds blue in Scot tap water for 10 minutes and counter stained in 1% aq. Eosin for 5 minutes. The sections were rinsed in water for 2 minutes, dehydrated in ascending grades of alcohol (70%, 90% and Abs) for 2 minutes each, cleared in two changes of Xylene and mounted in dibutyl phthalate xylene (DPX).

3.6.2 Phosphotungstic Acid Haematoxylin (PTAH) (Mallory, 1897)

Principle

The phosphotungstic acid binds all of the available hematein to form a blue lake pigment. This lake stains the muscle cross striations, fibrin, nuclei, and other tissue elements blue. The rest of the phosphotungstic acid stains the red-brown components, such as collagen (Puchtler *et al.*, 1980)

Solutions

Solution A (Acid dichromate solution): 10% HCl in absolute alcohol 12ml and 3% aqueous potassium dichromate 36ml

Solution B (Acid permanganate solution): 0.5 aqueous potassium permanganate 50ml and 3% sulphuric acid 2.5ml

Solution C (Staining solution): Haematoxylin 0.5g, Phosphotungstic acid 5g, Distilled water 500ml

Preparation of solution

The haematoxylin was dissolved in 100ml of distilled water and the phosphotungstic acid in the remaining 400ml; the two solutions were mixed and 50ml of potassium permanganate solution was added.

Staining procedure

The dried sections were dewaxed in two changes of xylene 5 minutes each, hydrated in descending grades of alcohol (Abs, 90% and 70%) for 2 minutes each, they were placed in acid dichromate solution for 30 minutes. They were rinsed in tap water for 2 minutes and treated with acid permanganate solution for 1 minute, rinsed in tap water for 2 minutes. The sections were bleached in 1% oxalic acid for 5 minutes and well rinsed in tap water for 2 minutes. They were stained in PTAH solution over night, dehydrated in ascending grades of alcohol (70%, 90% and Abs) for 2 minutes each, cleared in two changes of xylene 1 and 2 for 2 minutes and were mounted in DPX

3.6.3 Periodic Acid Schiff (PAS) (McManu, 1946)

Principle

The principle of the PAS reaction is the conversion or loss of the quinoid structure and the masking of chromophores. This forms a colourless compound called leuco-fuchsin, which can be changed to the classic red reaction by washing in running water to remove the sulphurous groups and restore the quinoid groups. Excess Schiff reagent is removed by potassium metabisulfite rinses, thus preventing a false positive by oxidation of the reagent in the tissue (Torres-Bugarín *et al.*, 2014).

Solutions

Periodic acid solution: Periodic acid 1g, distilled water for 100ml Schiff's reagent

Staining procedure

The dried sections were dewaxed in two changes of xylene for 5 minutes each. Hydrated in descending grades of alcohol and then distilled water for 2 minutes each. Oxidized with periodic acid for 5 minutes and rinsed in several changes distilled water. The sections were covered with Schiff reagent for 15 minutes, rinsed in running tap water for 5 minutes. Stained in haematoxylin for 15 minutes and blue for 10 minutes, dehydrated in ascending grades of alcohol (70%, 90% and Absolute) for 2 minutes each, cleared in two changes of xylene 1 and 2 for 2 minutes each and mounted in DPX.

3.6.4 Masson's Trichrome (Masson, 1929)

Principle

As the name implies, three dyes are employed selectively staining muscle, collagen fibers, fibrin, and erythrocytes. The general rule in trichrome staining is that the less porous tissues are colored by the smallest dye molecule; whenever a dye of large molecular size is able to penetrate, it will always do so at the expense of the smaller molecule. Others suggest that the tissue is stained first with the acid dye, Biebrich Scarlet, which binds with the acidophilic tissue components. Then when treated with the phospho acids, the less permeable components retain the red, while the red is pulled out of the collagen. At the same time causing a link with the collagen to bind with (Suvarna *et al*., 2013)

Solution A: Acid fuchsin 0.5g**,** glacial acetic acid 0.5ml and distilled water, 100ml
Solution B: Phosphomolybdic acid 1g and distilled water 100ml
Solution C: Methyl blue 2g, glacial acetic acid 2.5ml and distilled water100ml

Staining Procedure

Sections were dewaxed in two changes of xylene for5 minutes each, hydrated in descending grades of alcohol (Abs, 90% and 70%) for 2 minutes each, rinsed in water for 1 minute after which the sections were stained in haematoxylin for 30 minutes, rinsed in water for 1 minute, differentiated in 1% acid alcohol for 30 seconds. Rinsed in water for 10 minutes and stained in acid fuchsin (solution A) for 5 minutes, the sections were again rinsed in distilled water for 2 minutes and then treated with Phosphomolybdic acid (solution B) for 5 minutes. It was drained and stained in Methyl blue (solution C) for 5 minutes, rinsed in distilled water. They were further treated in 1% acetic acid for 2 minutes. Dehydrated in ascending grades of alcohol (70%, 90% and Abs) for 2 minutes each and were cleared in two changes of xylene for 2 minutes and mounted in DPX.

3.6.5 Verhoeff Van Gieson (Verhoeff, 1908)

Principle

The tissue is stained with a regressive haematoxylin, consisting of ferric chloride and iodine. The differentiating is accomplished by using excess mordant (ferric chloride) to break the tissue-mordant dye complex. The dye will be attracted to the larger amount of mordant in the

differentiating solution and will be removed from the tissue. The elastic tissue has the strongest affinity of the iron-haematoxylin complex and will retain the dye longer than the other tissue elements (Suvarna, 2013).

Solution A: Haematoxylin 5g and absolute alcohol 100ml

Solution B: Ferric chloride 10g and distilled water 100ml

Solution C: (Lugol's iodine solution): Iodine 1g**,** Potassium iodide 2g and distilled water 100ml

Verhoeff's solution: Solution A 20ml**,** Solution B 8ml and Solution C 8ml

The Veroeff's solution was added in the above order.

Staining procedure

Sections were dewaxed in two changes of xylene for 5 minutes each and hydrated in descending grades of alcohol (Abs, 90% and 70%) for 2 minutes each. The sections were rinsed in water for 1 minute and stained in Verhoff's solution for30 minutes, rinsed in water for 1 minute and differentiated in 2% aqueous ferric chloride until elastic tissue fibre colour turns black on gray background. The sections were again rinsed in water 10 minutes and further in rinsed in 95% alcohol. Counter stained with Van Gieson for 5 minutes and blotted to remove excess stain for another 5 minutes. Dehydrated in ascending grades of alcohol rapidly, cleared in two changes of xylene for 2 minutes and mounted in DPX.

3.6.6 Cytokeratin and Ki-67 Immunohistochemistry (Gerdes *et al.*, 1983)

Principle

Antigen detection in tissues and cells is a multi-step immunohistochemical process. The initial step binds the primary antibody to its specific epitope. A secondary antibody may be applied to bind the primary antibody, followed by an enzyme labeled polymer; or an enzyme labeled polymer may be applied directly to bind the primary antibody. The detection of the bound primary antibody is evidenced by an enzyme-mediated colorimetric reaction

Ki67 is a nuclear antigen associated with cell proliferation and is present throughout the active cell cycle (Gap 1, Synthesis, Gap 2 and M phases) but absent in resting cells (Gap 0). Antigen detection in tissues and cells is a multi-step immunohistochemical process. The initial step binds the primary antibody to its specific epitope. After labeling the antigen with a primary antibody, a secondary antibody is added to bind to the primary antibody. An enzyme label is then added to

bind to the secondary antibody; this detection of the bound antibody is evidenced by a colorimetric reaction.

Solutions and Reagents

A. Phosphate Buffered Saline (PBS):1 L
B. Antigen Retrieval Solution: 10mM Sodium Citrate Buffer:
C. 3% Hydrogen Peroxide: 100ml
D. Blocking Solution: 100ml
E. Primary Antibody: anti-human Ki67
F. Secondary Antibody: anti-rabbit IgG
G. Avidin–Biotin Complex (ABC) Reagent: Horseradish Peroxidase (HRP)-streptavidin
H. 0.02% 3,3′-Diaminobenzidine (DAB) 100ml

Procedure

Sections were dewaxed in two changes of xylene for 5 minutes each and hydrated in descending grades of alcohol (Absolute, 95% and 70%) for 2 minutes each. The slide were washed in steamer-citrate buffer antigen retrieval and rinse in PBS for for 5minutes each. Sections were incubated in 3% H2O2 in PBS for 10- minutes to block endogenous peroxidase activity, aftere which it was rinse for 2 minutes. Sections were incubated with 2% normal goat serum in PBS for 20 minutes to block non-specific binding of secondary immunoglobulin and were rinsed for 2 minutes. Primary antibody (rabbit anti-human Ki67 or cytokeratin diluted 1:3000 in PBS) was used to incubate sections with for 1 hour at room temperature and rinsed in 3 changes of PBS for 5 minutes each. The sections were further incubated with secondary antibody (biotinylated goat anti-rabbit IgG diluted 1:400 in PBS) for 30 minutes at room temperature and were rinsed in 3 changes of PBS for 5minutes each. Sections were incubated with HRP-streptavidin reagent diluted 1:400 in PBS for 30 minutes at room temperature and rinsed in 3 changes of PBS for 5minutes each. sections were Incubate with DAB solution for 5 minutes and rinse in distilled water twice for 5 minute. Counter stained with hematoxylin, rinsed in distilled water twice for 5 minutes. The sections were dehydrate through 95% ethanol for 5 minute, 100% ethanol twice for 5 minutes.Sections were cleared in xylene and mounted in DPX.

3.7 Microscopy and Data Acquisition from Photomicrographs

The stained tissue slides were viewed using OMAX 40X-2000X built-in 3.0MP digital camera compound LED Binocular Microscope. The stain intensity and percentage area stained were analyzed using ImageJ 1.48 version (National Institute of Health, USA).

3.8 Statistical Analysis

3.8.1 Analytical Packages used

Data management were performed using Database Plus Software (Data Based Intelligence, Inc., Vestal, New York, United State of America). General Statistical data analyses were conducted using Statistical Analysis System (SAS) 9.4 version (SAS Institute, Cary, North Carolina, United State of America). All measurement system analyses were performed using John Mark Project (JMP) statistical discovery™ software, version 12.0 (SAS Institute, Cary, North Carolina, United State of America). For all tests performed, the probability value of 0.05 was used as threshold for determining statistical significance level.

3.8.2 Types of analyses conducted

Chi-square (X^2) was used to test for association and relationship between data. Predictive modelling was used to predict the future out of biopsies, while measurement variation was carried out to test for the variability of percentage area and intensity of stains. Matched pairs analysis was used to compare staining methods, while Pearson *r* correlation was used to measure the degree of the relationship.

CHAPTER FOUR
RESULTS

4.1 Distribution of Patients Characteristics in 5years (2010-2014)

Figures 4.1 (histogram with a bell curve) and 4.2 (density graph) pointed out and demonstrated the distribution of biopsies and their percentages in five years as well as the patient's ages. Out of the 697 biopsies recorded in 5 years (2010-2014), 157 (22.5%) biopsies occurred in 2010, 150 (21.5%) occurred in 2011 and 158 (22.7%) occurred in 2012. The year 2013 recorded the highest number of biopsies with 186 (26.7%), while in 2014 only 46 (6.6%) biopsies were reported. The χ^2 analysis indicates significant difference ($p<0.0001$) in the various years of distribution, with χ^2 and df values as 83.7 and 4.

The occurrence of biopsy in patients recorded a mean age 39.1±12.8. Out of the total number 665 ages of patients recorded, 12 (1.8%) biopsies occurred in age group 0-19, which is the least when compared to other age groups. Age group 20-29 recorded 124 (18.6%), age group 30-39 was 263 (39.5%) which was reported to be highest in the age category. Age group 40-49 was 148 (22.3%), Age group 50-59 recorded 46 (6.9%), while age groups 60-69 and 70+ were 51(7.7%) and 21 (3.2%) respectively. The χ^2 analysis showed significant difference ($p<0.0001$) for the age category with χ^2 and df values as 511.3 and 6.

The density graph (mapping) shows patients with benign biopsy having the least age mean of 37.27 and patients with inflammatory biopsies having the highest age mean of 52.43. Patients with premalignant and malignant biopsies recorded age mean of 44.87 and 47.65 respectively. The density mapping also showed that in the year 2010, age group 40-49 had the most populated premalignant area while between age group 20-40 had the most populated malignant area. The most populated area for inflammatory and benign biopsies was between age brackets of 30-50 years. In 2011, age bracket 50-70 had the most dense portion for premalignant biopsy, ages between 30-50 years were populated for malignant biopsy and ages 60-70 and 30-40 for inflammatory and benign respectively. In 2012, there was no indication of density clustering for premalignant biopsies but the most dense for malignant was ages between 30-40, and for inflammatory and benign the most populated portions are areas 60-70 and 30-50 ages respectively. In 2013, age group 40 and 60 had similar density for premalignant biopsies,

malignant and inflammatory biopsies were not that populated but there density lies at 70 for malignant and age group 40 for inflammatory. Benign was dense at the level of age 30 -50. In 2014, the density was scanty as there was no cluster at any age bracket except for a few in age group 30-40 for benign, as illustrated in figure 4.2.

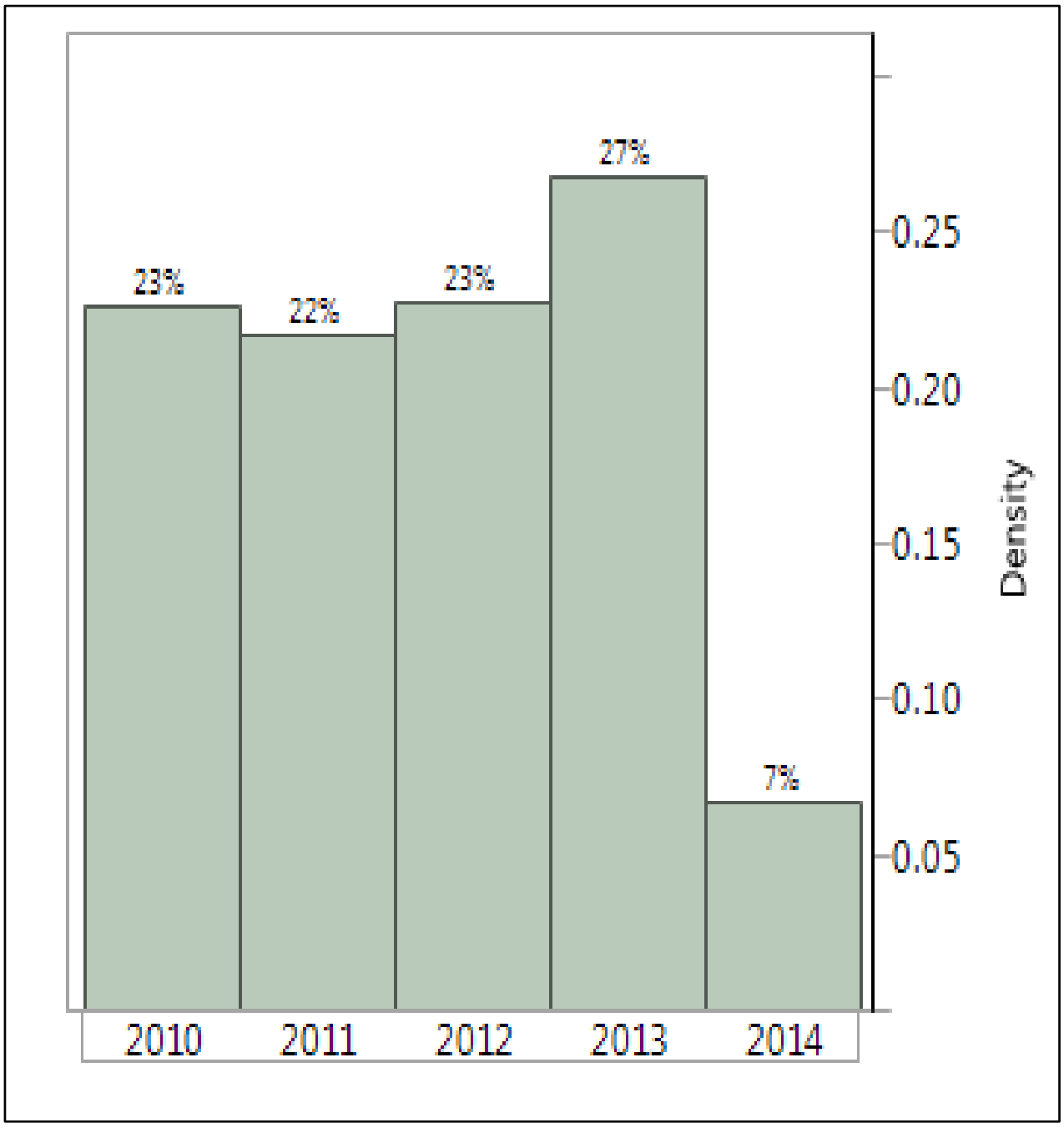


Figure 4.1: Distribution of Number of Biopsies by Year of Diagnosis

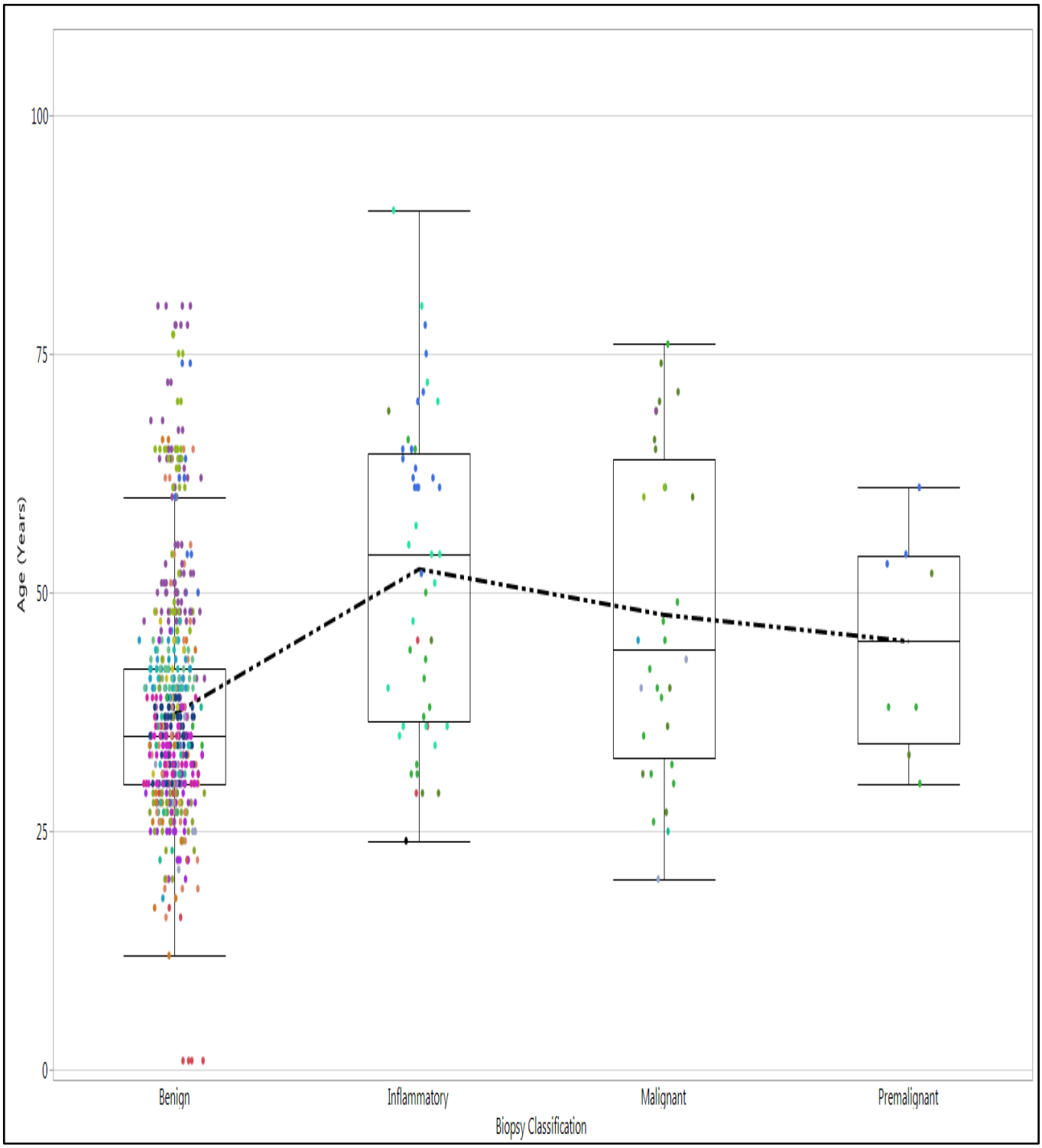


Figure 4.2: Graph of Density Distribution of Biopsies Classification by Patients Age and Year of Diagnosis

Table 4.1: Comparison of Patient Characteristics in 5 year (2010-2014)

Characteristic	Number of Biopsy	Percentage (%)	Test Statistics χ^2 Value (df)	P-value
Developmental Stage				
Infant	2	0.3		
Teenager	5	0.8	1288.4 (2)	0.0001****
Adult	658	98.9		
Reproductive Status				
Menopausal	150	22.6		
Premenarchal	3	0.5	619.1 (2)	0.0001****
Postmenarchal	512	77.0		

*Note: Significance level:****p<0.0001*

4.2 Comparison of Gynaecological Biopsies, Histopathological Characteristics, and Region of Occurrence in 5years (2010-2014)

Table 4.2 reveals the frequency of biopsy and its classification, origin and region in the five years (Nonparametric scatter plot matrix). Out of the total 697 biopsies recorded in this study adenoma and condyloma acuminatum were 5 (0.7%) each. The highest recorded biopsy was leiomyoma 390 (56.0%), followed by ovarian cyst 70 (10.0%), adenocarcinoma was 9 (1.3%), adenomyosis 21 (3.0%), cervical polyp 6 (9%), chronic cervicitis 44 (6.3%), chronic endometritis 7 (1.0%), CIN 9 (1.3%), endometrial hyperplasia 28 (4.0%), endometrial polyp 14 (2.0%), product of conception 56 (8.0%), squamous cell carcinoma 13 (1.9%) and others (Basal cell epithelioma1, Brenner tumour 2, Cervical cyst 1, Chronic Endocervitis 1,Chronic vulvitis 1, Endometrial Carcinoma 3, Epidermal cyst 1, Fibroma 1, Haemangioma 2, Ovaritis 1, Vulva cyst 2,Vulva War 1, Vulvaritis 2, Yolk sac tumour (Hepatoid variant)1, 20 (2.9%)). The χ^2 analysis showed significant difference ($p<0.0001$) when the various biopsies were compared to each other, the χ^2 and df values were 2840.1 and 14 respectively.

When the biopsies were classified based on their nature (benign, inflammatory, premalignant and malignant), the highest occurring was benign biopsies 600 (86.1%), followed by inflammatory with 56 (8.0%), the least was premalignant 9 (1.3%) and malignant biopsies were 32(4.6%). The χ^2 analysis also showed significant difference ($p<0.0001$) when they were compared.

The classification of biopsies according to their tissue origin recorded biopsies of muscle origin as the highest 456 (65.5%), biopsies of epithelia origin were 165 (23.7%), sex cord and / stroma71 (10.2%), biopsy that originated from blood vessels and connective tissues were only 2 (0.3%) each. The χ^2 and df values were1029.6 and 4. It was statistically significant ($p<0.0001$).

The occurrence of biopsies in the various parts of the gynaecological region were analyzed and the endometrium recorded the highest number of biopsies 526 (75.5%), followed by the ovary 80 (11.5%), the cervix was the third 75 (10.8), vulva 13 (1.9%), fallopian tube 2 (0.3%), and vagina 1(0.1%). They were also statistically significant ($p<0.0001$) with χ^2 and df values as 1789.7 and 5 respectively.

Table 4.2: Comparison of Gynaecological Biopsies within the Study Period

Characteristic	Number of Biopsy	Percentage (%)	Test Statistics χ^2 Value (df)	P-value
Biopsy				
Adenocarcinoma	9	1.3		
Adenoma	5	0.7		
Adenomyosis	21	3.0		
Cervical Polyp	6	0.9		
Chronic Cervicitis	44	6.3		
Chronic Endomeritis	7	1.0		
CIN	9	1.3		
Condyloma Acuminatum	5	0.7		
Endometrial Hyperplasia	28	4.0		
Endometrial Polyp	14	2.0		
Leiomyoma	390	56.0		
Ovarian Cyst	70	10.0		
Product of Conception	56	8.0		
Squamous Cell Carcinoma	13	1.9		
Others	20	2.9	2840.1 (14)	0.0001****

*Note: Significance level:****p<0.0001*

Table 4.3: Histopathological Characteristics, and Region of Occurrence in 5 years (2010-2014)

Characteristic	Number of Biopsy	Percentage (%)	Test Statistics χ^2 Value (df)	P-value
Biopsy Classification				
Benign	600	86.1		
Inflammatory	56	8.0		
Premalignant	9	1.3		
Malignant	32	4.6	1393.3 (3)	0.0001****
Origin of Tissue				
Blood Vessels	2	0.3		
Connective Tissue	2	0.3		
Epithelial Tissue	165	23.7		
Muscle	456	65.5		
Sex Cord/Stroma	71	10.2	1029.6 (4)	0.0001****
Region				
Cervix	75	10.8		
Endometrium	526	75.5		
Fallopian Tube	2	0.3		
Ovary	80	11.5		
Vagina	1	0.1		
Vulva	13	1.9	1789.7 (5)	0.0001****

*Note: Significance level:****p<0.0001*

4.3 Comparison between Patient's Age and Reproductive Status by Year of Diagnosis

Table 4.4 – 4.8 shows age category, in 2010 age group 0-19 years was 4 (2.6%), while age group 20-29 was 21 (13.7%), age group 30-39 recorded 71 (46.4%), age group 40-49 34 (22.2%), age group 50-59 4 (2.6%), age group 60-69, 15 (9.8%) and age group 70 years and above was 4 (4.6%). In 2011, age group 0-19 was 4 (2.9%), age group 20-29 38 (27.0%), age group 30-39, 42 (30.4%), age group 40-49, 28 (20.3%), age group 50-59, 6 (4.3%), age group 60-69, 15 (10.9%) and age group 70 and above 5(4.6%). In 2012, age groups 0-19 2 (1.4%), age group 29 (19.7%), age group 30-39, 55 (37.4%), age group 40-49, 33 (22.4%), age group 50-59, 14 (9.5%), age group 60-69, 9 (6.1%) and age group 70 and above 5 (3.4%). In 2013, age group 0-19 recorded only 1 (0.8%), age group 20-29 33 (18.2%), age group 30-39, 74 (40.9%), age group 40-49, 36 (19.9%), age group 50-59, 20 (11.0%), age group 60-69, 10 (5.5%) and age group 70 and above 7 (3.9%). In 2014, age group 0-19 recorded 1 (2.2%), age group 20-29 was 3 (6.5%), age group 30-39, 21 (45.7%), age group 40-49, 17 (37.0%), age groups 50-59 and 60-69 recorded 2 (4.3%) biopsies each, age group 70 and above did not record any biopsy in the year 2014. The age categories were statistically significant ($p<0.0001$) when compared, with χ^2 and df values as 44.10 and 24 respectively.

The reproductive status of patients as illustrated in table 4.4 shows that in 2010 menopausal was 29 (19.0%) while premenarchal was only 2 (1.3%), and postmenarchal was 122 (79.7%). In 2011, menopausal was 35 (25.4%), while premenarchal was 1 (0.7%) and postmenarchal 102 (73.9%). In 2012, menopausal was 38 (25.9%), while premenarchal did not record any biopsy, postmenarchal was 109 (74.1%). In 2013, menopausal was 39 (21.5%), premenarchal did not also record any biopsy, postmenarchal was 142 (78.5%). In 2014, menopausal was 9 (19.6%), premenarchal was still zero (0%) while postmenarchal was 37 (80.4%). They were not statistically significant ($p>0.05$) when compared with each other, with χ^2 , df and p values as 7.33, 8 and 0.0502 respectively.

Table 4.4: Comparison of Patient's Age and Reproductive Status in 2010

Characteristic	n (%)	Test Statistics	
		χ^2 Value (df)	P-value
Age Category			
0-19 yrs	4 (2.6)		
20-29 yrs	21 (13.7)		
30-39 yrs	71 (46.4)		
40-49 yrs	34 (22.2)		
50-59 yrs	4 (2.6)		
60-69 yrs	15 (9.8)		
70+ yrs	4 (4.6)	163.2 (6)	<0.0001****
Reproductive Status			
Menopausal	29 (19.0)		
Premenarchal	2 (1.3)		
Postmenarchal	122 (79.7)	155.4 (2)	<0.0001****

Significance Level: ****= p<0.0001

Table 4.5: Comparison of Patient's Age and Reproductive Status in 2011

Characteristic	n (%)	Test Statistics	
		χ^2 Value (df)	P-value
Age Category			
0-19 yrs	4 (2.9)		
20-29 yrs	38 (27.5)		
30-39 yrs	42 (30.4)		
40-49 yrs	28 (20.4)		
50-59 yrs	6 (4.3)		
60-69 yrs	15 (10.9)		
70+ yrs	5 (3.6)	79.8 (6)	<0.0001****
Reproductive Status			
Menopausal	35 (25.4)		
Premenarchal	1 (0.7)		
Postmenarchal	102 (73.9	114.8 (2)	<0.0001****

Significance Level: ****= p<0.0001

Table 4.6: Comparison of Patient's Age and Reproductive Status in 2012

		Test Statistics	
Characteristic	**n (%)**	χ^2 Value (df)	P-value
Age Category			
0-19 yrs	2 (1.4)		
20-29 yrs	29 (19.8)		
30-39 yrs	55 (37.4)		
40-49 yrs	33 (22.4)		
50-59 yrs	14 (9.5)		
60-69 yrs	9 (6.1)		
70+ yrs	5 (3.4)	103.5 (6)	<0.0001****
Reproductive Status			
Menopausal	38 (25.9)		
Premenarchal	0(0)		
Postmenarchal	109(74.1)	34.3 (1)	<0.0001****

Significance Level: ****= p<0.0001

Table 4.7: Comparison of Patient's Age and Reproductive Status in 2013

		Test Statistics	
Characteristic	**n (%)**	χ^2 Value (df)	P-value
Age Category			
0-19 yrs	1 (0.6)		
20-29 yrs	33 (18.2)		
30-39 yrs	74 (40.9)		
40-49 yrs	36 (19.9)		
50-59 yrs	20 (11.0)		
60-69 yrs	10 (5.5)		
70+ yrs	7 (3.9)	144.3 (6)	<0.0001****
Reproductive Status			
Menopausal	39 (21.5)		
Premenarchal	0 (0)		
Postmenarchal	142 (78.5)	58.6 (1)	<0.0001****

Significance Level: ****= p<0.0001

Table 4.8: Comparison of Patient's Age and Reproductive Status in 2015

		Test Statistics	
Characteristic	**(%)**	χ^2 Value (df)	P-value
Age Category			
0-19 yrs	1 (2.2)		
20-29 yrs	3 (6.5)		
30-39 yrs	21 (45.7)		
40-49 yrs	17 (37.0)		
50-59 yrs	2 (4.3)		
60-69 yrs	2 (4.3)		
70+ yrs	0(0)	51.6 (5)	<0.0001****
Reproductive Status			
Menopausal	9 (19.6)		
Premenarchal	0 (0)		
Postmenarchal	37 (80.4)		
		17.0 (1)	<0.0001****

Significance Level: ****= p<0.0001

4.4 Comparison of Types of Gynaecological Biopsy and Histopathological Characteristics among Year of Diagnosis

The prevalence of the various types of biopsies in year of occurrence were analyzed as illustrated in table 4.9-4.14 and can be extracted from figures 4.4 and 4.5. In 2010, adenocarcinoma was 3 (1.9%), adenoma 2(1.3%), adenomyosis 7 (4.5%), cervical polyp 3(1.9%), chronic cervicitis 10 (6.4%), chronic endometritis 4 (2.5%), CIN 1 (0.6%), condyloma acuminatum had zero, endometrial hyperplasia 15 (9.6%), endometrial polyp 4 (2.5%), leiomyoma recorded the highest with 74 (47.1%), ovarian cyst 5 (3.2%), product of conception 14 (8.9%), squamous cell carcinoma 5(3.2%), and others (Basal cell epithelioma1, Brenner tumour, Cervical cyst, Chronic Endocervitis, Chronic vulvitis, Endometrial Carcinoma, Epidermal cyst, Fibroma, Haemangioma, Ovaritis, Vulva cyst, Vulva Wart, Vulvaritis and Yolk sac tumour (Hepatoid variant))10 (6.4%).In 2011, adenocarcinoma was 1 (0.7%), adenoma 2(1.3%), adenomyosis 3 (2.0%), cervical polyp 2(1.3%), chronic cervicitis 11 (7.3%), chronic endometritis 3 (2.0%), CIN 6 (4.0%), condyloma acuminatum 3(2.0%), endometrial hyperplasia 9 (6.0%), endometrial polyp 4 (2.7%), leiomyoma 66 (44.0%), ovarian cyst 16 (10.7%), product of conception 16 (10.7%), squamous cell carcinoma 4(2.7%), and others (Basal cell epithelioma1, Brenner tumour, Cervical cyst, Chronic Endocervitis, Chronic vulvitis, Endometrial Carcinoma, Epidermal cyst, Fibroma, Haemangioma, Ovaritis, Vulva cyst, Vulva Wart, Vulvaritis and Yolk sac tumour (Hepatoid variant))4 (2.7%).In 2012, adenocarcinoma 3 (1.9%) was reported, adenoma 1(0.6%), adenomyosis 3(1.9%), cervical polyp 1(0.6%), chronic cervicitis 12 (7.6%), chronic endometritis 0 (0.0%), CIN 0 (0.0%), condyloma acuminatum 1(0.6%), endometrial hyperplasia 3 (1.9%), endometrial polyp 3 (1.9%), leiomyoma 99 (62.7%), ovarian cyst 17 (10.8%), product of conception 11 (7.0%), squamous cell carcinoma 1(0.6%), and others (Basal cell epithelioma1, Brenner tumour, Cervical cyst, Chronic Endocervitis, Chronic vulvitis, Endometrial Carcinoma, Epidermal cyst, Fibroma, Haemangioma, Ovaritis, Vulva cyst, Vulva Wart, Vulvaritis and Yolk sac tumour (Hepatoid variant))3 (1.9%).In 2013,adenocarcinoma 1 (0.5%) was reported, adenoma 0(0.0%), adenomyosis 7(3.8%), cervical polyp 0(0.0%), chronic cervicitis 8 (4.3%), chronic endometritis 0 (0.0%), CIN 2 (1.1%), condyloma acuminatum 1(0.5%), endometrial hyperplasia 1 (0.5%), endometrial polyp 3 (1.6%), leiomyoma 119 (64.0%), ovarian cyst 24 (12.9%), product of conception 14 (7.5%), squamous cell carcinoma 3 (1.6%), and others (Basal

cell epithelioma1, Brenner tumour, Cervical cyst, Chronic Endocervitis, Chronic vulvitis, Endometrial Carcinoma, Epidermal cyst, Fibroma, Haemangioma, Ovaritis, Vulva cyst, Vulva Wart, Vulvaritis and Yolk sac tumour (Hepatoid variant))3 (1.5%).In 2014, adenocarcinoma was 1 (2.2%), adenomyosis 1(2.2%), chronic cervicitis 3 (6.5%), leiomyoma 32 (69.6%), ovarian cyst 8 (17.4%) and product of conception 1 (2.2%). Adenoma, cervical polyp, chronic endometritis, CIN, condyloma acuminatum, endometrial hyperplasia, endometrial polyp, squamous cell carcinoma and others (Basal cell epithelioma1, Brenner tumour, Cervical cyst, Chronic Endocervitis, Chronic vulvitis, Endometrial Carcinoma, Epidermal cyst, Fibroma, Haemangioma, Ovaritis, Vulva cyst, Vulva Wart, Vulvaritis and Yolk sac tumour (Hepatoid variant)) had no recorded cases. The frequency of biopsy in the various years were statistically significant ($p<0.0001$) when compared, with χ^2 and df values as 104.73 and 56 respectively.

The classification of biopsies according to their nature revealed that in 2010, benign 128 (81.5%), inflammatory 16 (10.2%), premalignant 1(0.6%) and malignant 12 (7.6%). While in 2011 benign 121 (80.7%), inflammatory 16 (10.7%), premalignant 6 (4.0%) and malignant 7(4.7%). In 2012, benign 138 (88.0%), inflammatory 13 (8.2%), premalignant 0(0.0%) and malignant 6(3.8%). In 2013, benign 170 (91.4%), inflammatory 8(4.3%), premalignant 2(1.1%) and malignant 6(3.2%) and in 2014, benign 42 (91.3%), inflammatory 3(6.5%), premalignant 0(0.0%) and malignant 1(2.2%).The classification in the various years were statistically significant ($p<0.05$) when compared, with χ^2 and df values as 23.77 and 12 respectively.

The origin of tissues of the various biopsies in 2010 revealed that biopsies from blood vessels origin were 2 (1.3%), connective tissue 1(0.6%), epithelia tissue 46 (29.3%), muscle tissue 102 (65.0%), sex cord/ stroma 6 (3.8%). In 2011, blood vessels and connective tissue were 0 (0%), epithelia tissue 51 (34.2), muscle tissue 82 (55.0%) and sex cord/ stroma 16 (10.7%). In 2012, blood vessels was 0 (0%), connective tissue was 1 (0.6%), epithelia tissue 32 (20.3%), muscle tissue 108 (68.4%) and sex cord/ stroma 17 (23.9%). In 2013, blood vessels and connective tissue were 0 (0%), epithelia tissue 31 (16.7%), muscle tissue 131 (70.4%) and sex cord/ stroma 24 (12.9%). In 2014, blood vessels and connective tissue were also 0 (0%), epithelia tissue 5 (10.9%), muscle tissue 33 (71.7%) and sex cord/ stroma 8 (17.4%). The various years were statistically significant ($p<0.001$) when compared, with χ^2 and df values as 39.87 and 16 respectively.

The region of occurrence of these biopsies indicates that in 2010, 17 (10.8%) biopsies occurred in the cervix, endometrium was 121 (77.1%), fallopian tube 1 (0.6%), ovary 12 (7.6%), vagina 0 (0%), vulva 6 (3.8%).In 2011, cervix was 25 (16.7%), endometrium 101 (67.3%), fallopian tube 0 (0%), ovary 20 (13.3%), vagina 1 (0.7%), vulva 3 (2.0%).In 2012, cervix was 14 (8.9%), endometrium 120 (75.9%), fallopian tube 1 (0.6%), ovary 20 (12.7%), vagina 0 (0%), vulva 3 (1.9%).In 2013, cervix was 15 (8.1%), endometrium 150 (80.6%), fallopian tube 0 (0%), ovary 20 (10.8%), vagina 0 (0%), vulva 1 (0.5%).In 2014, cervix was 4 (8.7%), endometrium 34 (73.9%), fallopian tube 0 (0%), ovary 8 (17.4%), vagina and vulva were both 0. The various years were statistically not significant ($p>0.05$) when compared, with χ^2 , df and p values as 24.95, 20 and 0.204 respectively.

Table 4.9: Yearly Distribution of Biopsies

	Year					Test Statistics	
	2010	**2011**	**2012**	**2013**	**2014**	χ^2 Value	P-value
Characteristic	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	(df)	
Biopsy							
Adenocarcinoma	3 (1.9)	1 (0.7)	3 (1.9)	1 (0.5)	1 (2.2)		
Adenoma	2 (1.4)	2 (1.3)	1 (0.6)	0 (0.0)	0 (0.0)		
Adenomyosis	7 (4.5)	3 (2.0)	3 (1.9)	7 (3.8)	1 (2.2)		
Cervical Polyp	3 (1.9)	2 (1.3)	1 (0.6)	0 (0.0)	0 (0.0)		
Chronic Cervicitis	10 (6.4)	11 (7.3)	12 (7.6)	8 (4.3)	3 (6.5)		
Chronic Endomeritis	4 (2.8)	3 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)		
CIN	1 (0.7)	6 (4.0)	0 (0.0)	2 (1.1)	0 (0.0)		
Condyloma A.	0 (0.0)	3 (2.0)	1 (0.6)	1 (0.5)	0 (0.0)		
Endometrial Hyper.	15 (9.6)	9 (6.0)	3 (1.9)	1 (0.5)	0 (0.0)		
Endometrial Polyp	4 (2.5)	4 (2.7)	3 (1.9)	3 (1.6)	0 (0.0)		
Leiomyoma	74(47.1)	66 (44.0)	99 (62.7)	119(64.0)	32(69.6)		
Ovarian Cyst	5 (3.2)	16 (10.7)	17 (10.8)	24 (12.9)	8 (17.4)		
Product of Conception	14 (8.9)	16 (10.7)	11 (7.0)	14 (7.5)	1 (2.2)		
Squamous Cell C.	5 (3.4)	4 (2.7)	1 (0.6)	3 (1.6)	0 (0.0)		
Others	10 (6.4	4 (2.7)	3 (1.9)	3 (1.6)	0 (0.0)	104.73 (56)	0.0001****

*Significance level: ****p<0.0001*

Table 4.10: Comparison of Histopathological Characteristics of Biopsies in 2010

Characteristic	n (%)	Test Statistics	
		χ^2 Value (df)	P-value
Lesion Classification			
Benign	128(81.5)		
Inflammatory	16(10.2)		
Premalignant	1 (0.6)	270.6 (3)	<0.0001****
Malignant	12 (7.6)		
Origin of Tissue			
Blood Vessels	2 (1.3)		
Connective Tissue	1 (0.6)		
Epithelial Tissue	46 (29.3)		
Muscle	102 (65.0)	243.0 (4)	<0.0001****
Sex Cord/Stroma	6 (3.8)		
Region			
Cervix	17 (10.8)		
Endometrium	121 (77.1)		
Fallopian Tube	1 (0.6)		
Ovary	12 (7.6)		
Vagina	0 (0.0)	324.2 (4)	<0.0001****
Vulva	6 (3.8)		

Significance Level: ****= p<0.0001

Table 4.11: Comparison of Histopathological Characteristics of Biopsies in 2011

		Test Statistics	
Characteristic	**n (%)**	**χ^2 Value (df)**	**P-value**
Lesion Classification			
Benign	121(80.7)		
Inflammatory	16 (10.7)		
Premalignant	6 (4.0)		
Malignant	7 (4.7)	249.5 (3)	<0.0001****
Origin of Tissue			
Blood Vessels	0 (0)		
Connective Tissue	0 (0)		
Epithelial Tissue	51 (34.2)		
Muscle	82 (55.0)	43.9 (2)	<0.0001****
Sex Cord/Stroma	16 (10.7)		
Region			
Cervix	25 (16.7)		
Endometrium	101(67.3)		
Fallopian Tube	0 (0.0)		
Ovary	20 (13.3)		
Vagina	1 (0.7)		
Vulva	3 (2.0)	224.5 (4)	<0.0001****

Significance Level: ****= p<0.0001

Table 4.12: Comparison of Histopathological Characteristics of Biopsies in 2012

		Test Statistics	
Characteristic	**n (%)**	**χ^2 Value (df)**	**P-value**
Lesion Classification			
Benign	139(88.0)		
Inflammatory	13 (8.2)		
Premalignant	0 (0)		
Malignant	6 (3.8)	212.7 (2)	<0.0001****
Origin of Tissue			
Blood Vessels	0(0)		
Connective Tissue	1 (0.6)		
Epithelial Tissue	32 (20.3)		
Muscle	108(68.4)		
Sex Cord/Stroma	17 (23.9)	170.6 (3)	<0.0001****
Region			
Cervix	14 (8.9)		
Endometrium	120(75.9)		
Fallopian Tube	1 (0.6)		
Ovary	20 (12.7)		
Vagina	0(0)		
Vulva	3 (1.9)	316.9 (4)	<0.0001****

Significance Level: ****= p<0.0001

Table 4.13: Comparison of Histopathological Characteristics of Biopsies in 2013

		Test Statistics	
Characteristic	**n (%)**	**χ^2 Value (df)**	**P-value**
Lesion Classification			
Benign	170 (91.4)		
Inflammatory	8 (4.3)		
Premalignant	2 (1.1)		
Malignant	6 (3.2)	437.7 (3)	<0.0001****
Origin of Tissue			
Blood Vessels	0 (0)		
Connective Tissue	0(0)		
Epithelial Tissue	31 (16.7)		
Muscle	131 (70.4)		
Sex Cord/Stroma	24 (12.9)	115.6 (2)	<0.0001****
Region			
Cervix	15 (8.1)		
Endometrium	150 (80.6)		
Fallopian Tube	0(0)		
Ovary	20 (10.8)		
Vagina	0(0)		
Vulva	1 (0.5)	311.3 (3)	<0.0001****

Significance Level: ****= p<0.0001

Table 4.14: Comparison of Histopathological Characteristics of Biopsies in 2014

		Test Statistics	
Characteristic	**n (%)**	**χ^2 Value (df)**	**P-value**
Lesion Classification			
Benign	42 (91.3)		
Inflammatory	3 (6.5)		
Premalignant	0(0)	69.7 (2)	<0.0001****
Malignant	1 (2.2)		
Origin of Tissue			
Blood Vessels	0(0)		
Connective Tissue	0(0)		
Epithelial Tissue	5 (10.9)		
Muscle	33 (71.7)		
Sex Cord/Stroma	8 (17.4)	30.8 (2)	<0.0001****
Region			
Cervix	4 (8.7)		
Endometrium	34 (73.9)		
Fallopian Tube	0(0)		
Ovary	8 (17.4)		
Vagina	0(0)	34.6 (2)	<0.0001****
Vulva	0(0)		

Significance Level: ****= p<0.0001.

4.5 Comparison of Gynaecological Biopsies and Patients Age at Diagnosis

The result of table 4.5, which can be extracted from figures 4.3-4.5reveals that age group0-19 recorded 0 (0%) for menopausal, 3 premenarchal and 9 (75%) postmenarchal. In age group 20-29, no patient under menopausal and premenarchal had gynaecological biopsy but 124 (100%) patients under postmenarchal had biopsies. Similar to age group 20-29, age group 30-39 did not record any biopsy under menopausal and premenarchal groups, but postmenarchal recorded 263(100%) biopsies. In age group 40-49 menopausal recorded 34 (23.0%) and postmenarchal was 144 (77.0%), while premenarchal recorded 0 (0%). Age group 50-59 recorded only 46 (100%) biopsies in menopausal, while premenarchal and postmenarchal had no biopsy. Age group 60-69 also recorded 50 (98.0%) for menopausal, 1 (2.0%) for premenarchal and none for postmenarchal. Similarly, 20 (95.2%), 1 (4.8%) and 0(0%) was reported for menopausal, premenarchal and postmenarchal respectively in age group 70 and above. Statistically the occurrence of biopsies in the above age groups under their various reproductive status was significant ($p<0.0001$) when compared, with χ^2 and df values as 667.13 and 12 respectively.

The classification of benign, inflammatory, premalignant and malignant biopsies according to the ages of the patients at the time of diagnosis revealed that in age group 0-19 all 12(100%) biopsy recorded were benign. Inflammatory, premalignant and malignant were not reported. In age group 20-29, benign was also high 116 (93.5%).Inflammatory and malignant 4 (3.2%) each and premalignant nil. In age group 30-39, benign was 241 (91.6%). Inflammatory 11 (4.2%), premalignant 4 (1.5%) and malignant 7 (2.7%). Age group 40-49, benign recorded 132 (89.2%), inflammatory 7(4.7), premalignant 0 (0%) and malignant 9 (6.1%). Age group 50-59, benign recorded 35 (76.1%), inflammatory 8 (17.4%), premalignant 3 (6.5%) and malignant 0 (0%). In age group 60-69, benign recorded 27 (52.9%), inflammatory 15 (29.4%), premalignant 1 (2.0%) and malignant 8 (15.7%).Age group 70 and above had the least benign case 9(42.9%), inflammatory 8 (38.1%), premalignant 0 (0%) and malignant 4 (19.0%). Statistically the different classes of biopsies in age groups when compared to each other were significant ($p<0.0001$), with χ^2 and df values as 126.18 and 18 respectively.

The origin of biopsies according to the type tissue or source was analysed and blood vessel in age group 0-19 was 1 (8.3%), connective tissue 0 (0%), epithelia tissue 3 (25.0%), muscle 1 (8.3%), sex cord/stroma 7 (58.3%)In age group 20-29 blood vessel was 1 (0.8%), connective

tissue 0 (0%), epithelia tissue 28 (22.8%), muscle 71(57.7%), sex cord/stroma 23 (18.7%). In age group 30-39 blood vessel was 0 (0%), connective tissue 2 (0.8%), epithelia tissue 51(19.4%), muscle 188 (71.5%), sex cord/stroma 22 (8.4%). In age group 40-49 blood vessel and connective tissue were 0 (0%), epithelia tissue 19 (12.8%), muscle 120 (81.1%), sex cord/stroma 9 (6.1%). In age group 50-59 blood vessel and connective tissue were 0 (0%), epithelia tissue 15 (32.6%), muscle 26 (56.5%), sex cord/stroma 5 (10.9%). In age group 60-69 blood vessel and connective tissue were 0 (0%), epithelia tissue 24 (47.1%), muscle 24 (47.1%), sex cord/stroma 3 (5.9%). In age group 70 and above blood vessel and connective tissue were also 0 (0%), epithelia tissue 13 (61.9%), muscle 8 (38.1%) and sex cord/stroma 0 (0%). Statistically the different origin of biopsies in age groups when compared to each other were significant ($p<0.0001$), with χ^2 and df values as 129.10 and 24 respectively.

The prevalence of the most affected gynaecological region according to age groups were analysed and in age group 0-19, out of 12 biopsies the cervix had 0 (0%), endometrium 1 (8.3%), fallopian tube 0 (0%), ovary 7(58.3%), vagina 0 (0%) and vulva 4 (33.3%). Out of 124 biopsies in age group 20-29, the cervix had 3 (2.4%), endometrium 89(71.8%), fallopian tube 2 (1.6%), ovary 26(21.0%), vagina 0 (0%) and vulva 4 (3.2%). Out of 263 biopsies in age group 30-39 cervix had 18 (6.8%), endometrium 219(83.3%), fallopian tube 0 (0%), ovary 24(9.1%), vagina and vulva recorded 1 (0.4%) each. Out of 148 biopsies in age group 40-49, the cervix had 9 (6.1%), endometrium 128 (86.5%), fallopian tube 0(0%), ovary 10 (6.8%), vagina 0 (0%) and vulva 1 (0.7%). Out of 46 biopsies in age group 50-59, the cervix had 12 (26.1%), endometrium 28 (60.9%), fallopian tube 0(0%), ovary 5 (10.9%), vagina 0 (0%) and vulva 1 (2.2%).Out of 51 biopsies in age group 60-69, the cervix had 17 (33.3%), endometrium 28 (54.9%), fallopian tube 0(0%), ovary 5 (9.8%), vagina 0 (0%) and vulva 1 (2.0%). Out of 21 biopsies in age group 70 and above, the cervix had 12 (54.1%), endometrium 7 (33.3%), fallopian tube and vagina 0(0%), ovary and vulva 1 (4.8%) each. Statistically the different gynaecological regions where the biopsies occurred according to age groups were compared to each other and were found statistically significant ($p<0.0001$), with χ^2 and df values as 228.12 and 30 respectively.

Table 4.15: Comparison of Gynaecological Biopsies, Histopathological Characteristics among Patients Age at Diagnosis

	Total	Age Group (Years)							Test Statistics	
		0-19	20-29	30-39	40-49	50-59	60-69	70+	χ^2Value	P-value
Characteristics	N (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	(df)	
Reproductive Status										
Menopausal	150(22.6)	0 (0.0)	0 (0.0)	0 (0.0)	34 (23.0)	46(100)	50(98.0)	20(95.2)		
Premenarchal	3(0.5)	3(25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	667.13	
Postmenarchal	512(77.0)	9(75.0)	124(100)	263(100)	144(77.0)	0 (0.0)	1 (2.0)	1 (4.8)	(12)	0.0001 ****
Origin of Tissue										
Blood Vessels										
Connective T.	2 (0.3)	1 (8.3)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Epithelial T.	2 (0.3)	0 (0.0)	0 (0.0)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Muscle	153(23.0)	3 (25.0)	28 (22.8)	51 (19.4)	19 (12.8)	15(32.6)	24(47.1)	13(61.9)		
SexCord/Stroma	438(66.0)	1 (8.3)	71 (57.7)	188(71.5)	120(81.1)	26(56.5)	24(47.1)	8 (38.1)	129.10	0.0001
	69 (10.4	7 (58.3)	23 (18.7)	22 (8.4)	9 (6.1)	5 (10.9	3 (5.9)	0 (0.0)	(24)	****
Region										
Cervix	71 (10.7)	0 (0.0)	3 (2.4)	18 (6.8)	9 (6.1)	12 (26.1)	17 (33.3)	12 (54.1)		
Endometrium	500 (75.2)	1 (8.3)	89 (71.8)	219 (83.3)	128 (86.5)	28 (60.9)	28 (54.9)	7 (33.3)		
Fallopian Tube	2 (0.3)	0 (0.0)	2 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Ovary	78 (11.7)	7 (58.3)	26 (21.0)	24 (9.1)	10 (6.8)	5 (10.9)	5 (9.8)	1 (4.8)		
Vagina	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Vulva	13 (2.0)	4 (33.3)	4 (3.2)	1 (0.4)	1 (0.7)	1 (2.2)	1 (2.0)	1 (4.8)	228.12 (30)	0.0001 ****

*Note: Significance level: ***=p<0.001; p<0.000*

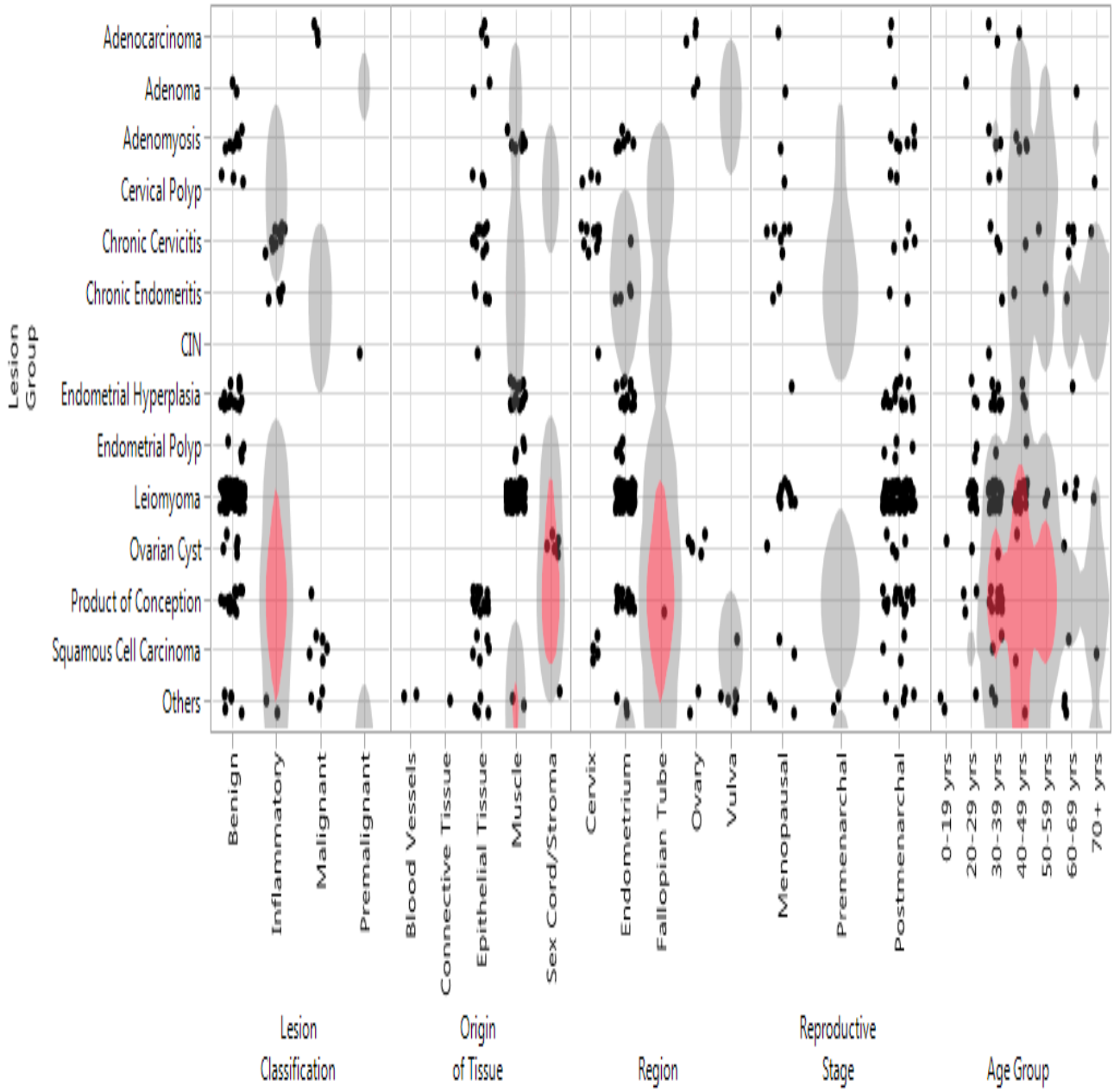


Figure 4.3: **Scatter plot Matrix of Biopsies by Origin of Tissue, Region of Diagnosis, Reproductive Stage and Age Category of patients by Year of Diagnosis (2010)**

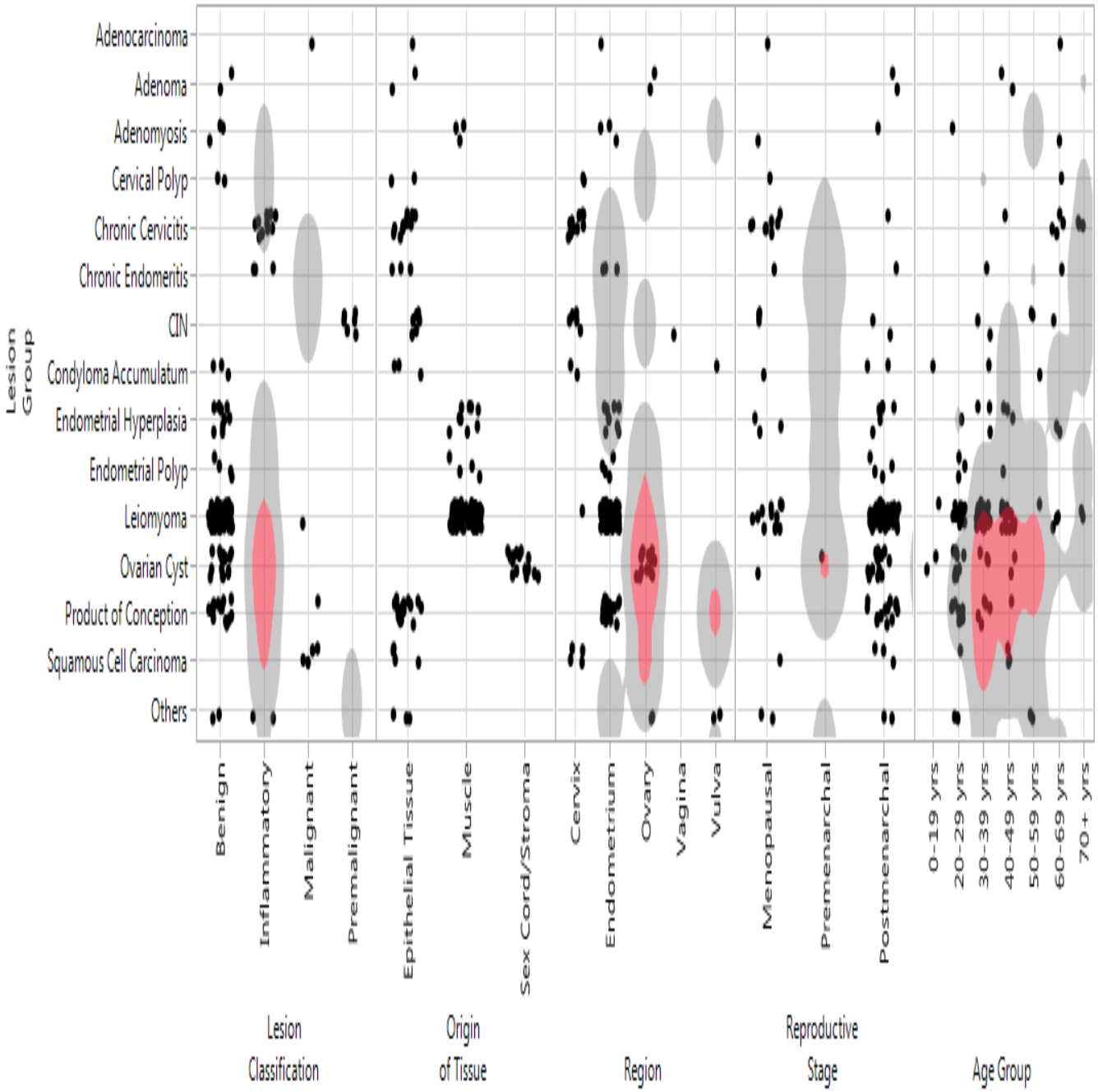


Figure 4.4: **Scatter plot Matrix of Biopsies by Origin of Tissue, Region of Diagnosis, Reproductive Stage and Age Category of patients by Year of Diagnosis (2011)**

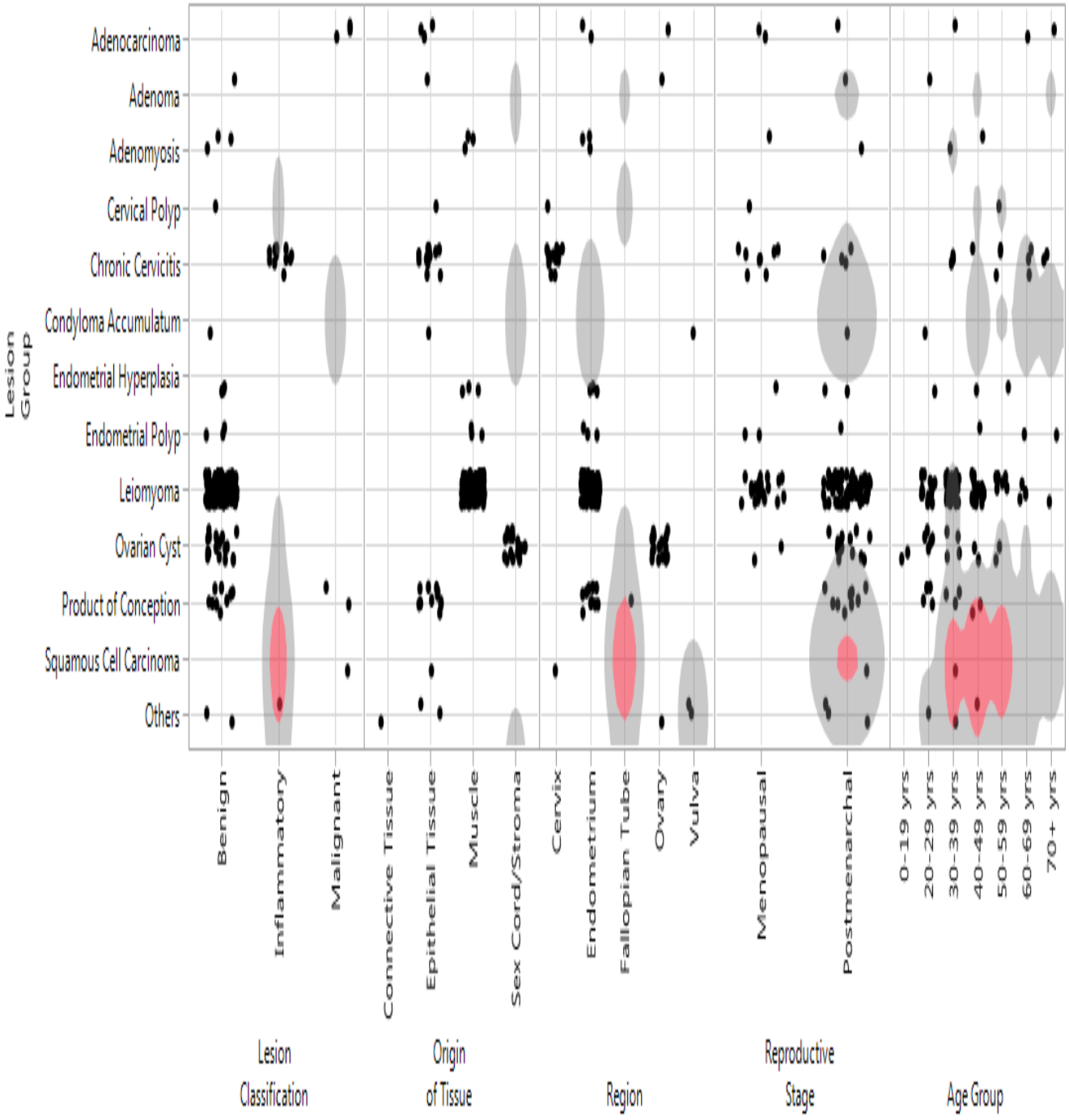


Figure 4.5: **Scatterplot Matrix of Biopsies by Origin of Tissue, Region of Diagnosis, Reproductive Stage and Age Category of patients by Year of Diagnosis (2012)**

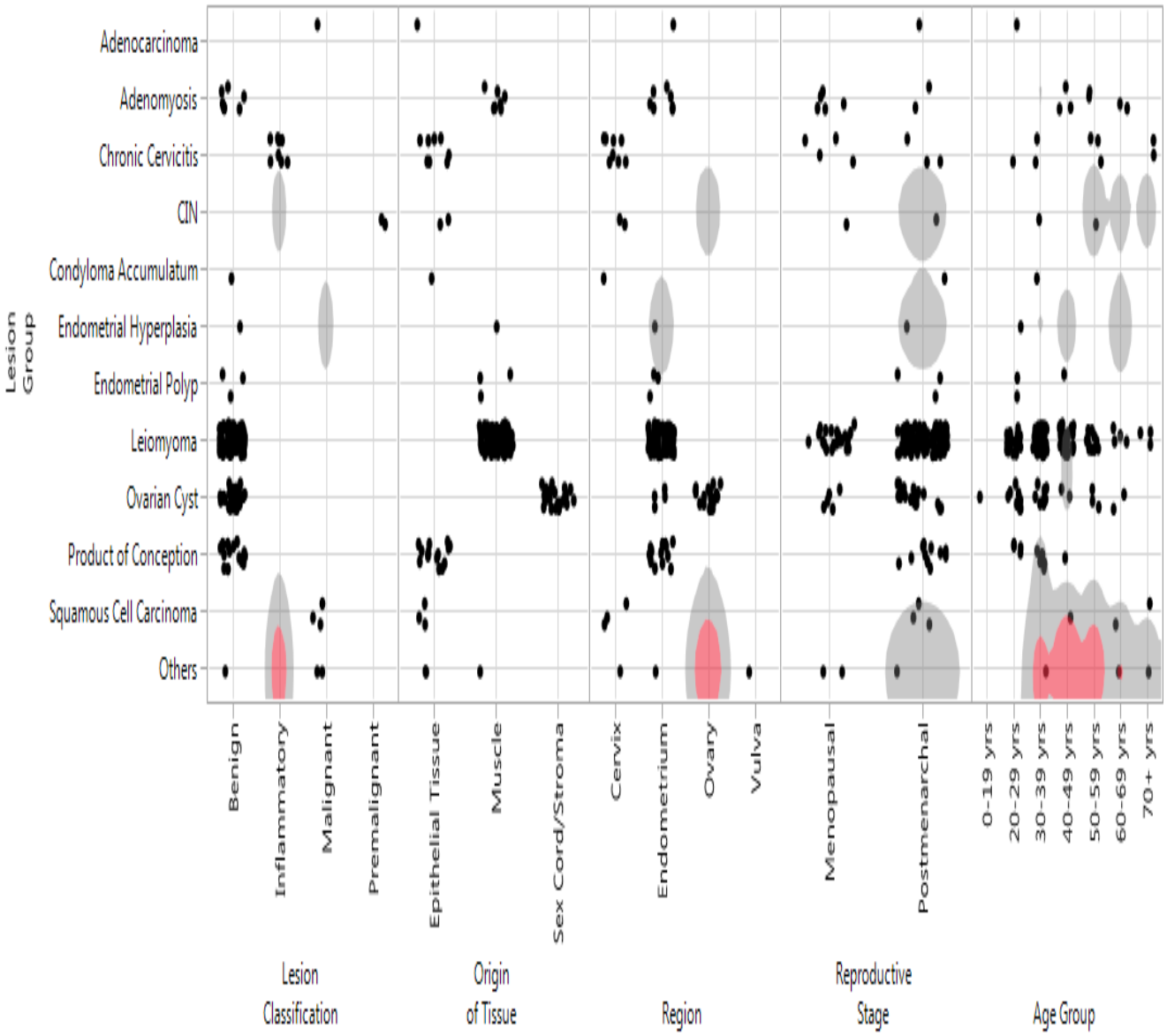


Figure 4.6: **Scatterplot Matrix of Biopsies by Origin of Tissue, Region of Diagnosis, Reproductive Stage and Age Category of patients by Year of Diagnosis (2013**

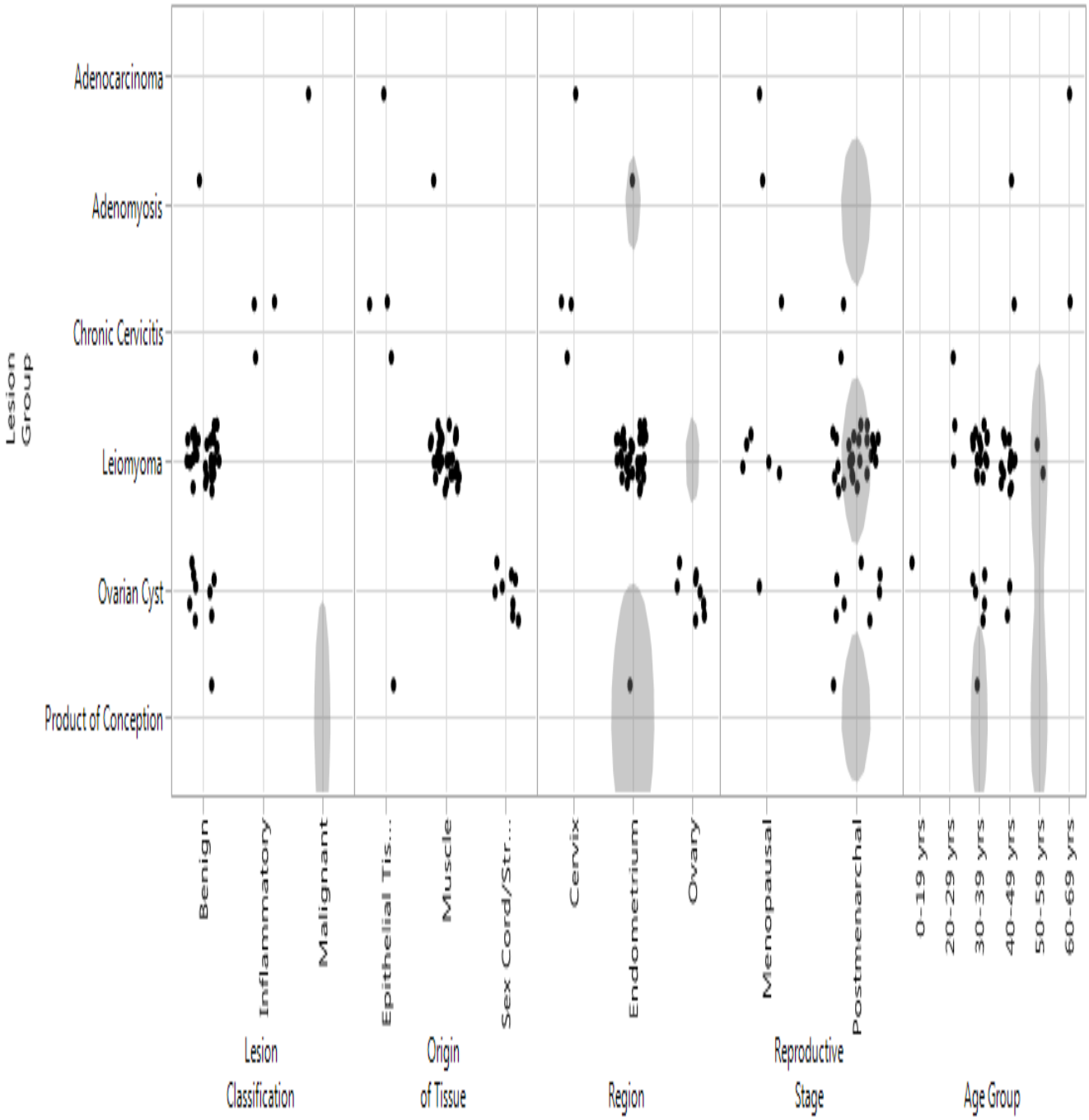


Figure 4.7: **Scatterplot Matrix of Biopsies by Origin of Tissue, Region of Diagnosis, Reproductive Stage and Age Category of patients by Year of Diagnosis (2014)**

4.6 Prediction Modelling Outcomes

Prediction of biopsies up to the year 2050 was forecasted, based on standardized mean and rate of 5 years of this study. The prediction of gynaecological biopsies from BMSH based on standardized mean and rate, revealed that the mean of leiomyoma (235.401) in the period of study will increase to 470.803 by the year 2020. It will go up to 706.204 by 2025, will further increase to 941.605 by 2030, in the year 2035. Leiomyoma biopsy will be 1177.007, by 2040 it will still increase to 1412.408, in 2045 and 2050 the record of leiomyoma in BMSH will rise to 1647.809 and 1883.210 respectively. Similarly, ovarian cyst, which is second to leiomyoma in this research, will increase from 57.640 to 115.279 in 2020. It will further increase to 172.919 in 2025, by 2030 it will rise to 230.558 and 288.198 in 2035. In 2040, 2045 and 2050 ovarian cyst in BMSH will rise to 354.838, 403.477 and 461.117 respectively. Product of conception will increase from 34.729 at the rate of 0.075 to 277.834 by the year 2050. Chronic cervicitis, which is more in age group 70 years and above will increase from 27.610 at the rate of 0.060 to 220.879 by the year 2050, endometrial hyperplasia, will also increase from 20.345 at the rate of 0.044 to 162.761 by 2050. Adenomyosis has been predicted to rise from 13.981 at the rate of 0.030 to 111.845 by the 2050. Similarly, Adenocarcinoma from 9.195 at the rate of 0.020 to 73.562 by the year 2050. Adenoma will rise from 1.943 at 0.004 rates to 15.540 by 2050, while Cervical Polyp at the rate of 0.009 will rise from 4.337 to 34.694 by 2050. Chronic endomeritis will increase from 6.509 to 52.073 by the year 2050 at the rate of 0.014 and CIN from 9.880 to 79.040 by 2050 at the rate of 0.021.Condyloma A. will increase from 6.193 at the rate of 0.013 to 49.541 by the year 2050. Endometrial polyp has been predicted to rise from 12.797 to 102.374 by the year 2050 at the rate of 0.028 while squamous cell carcinoma will rise at the rate of 0.019 from 8.968 to 71.743 by 2050 (Table 4.6-4.9).

Table 4.16: Prediction Equation Expression

```
2679.7657627463
+ -1.327239488117 * Year
+ Match[ Lesion ][
    "Adenocarcinoma"          ⇒ -7.5599126548852
    "Adenoma"                 ⇒ -9.0204854763356
    "Adenomyosis"             ⇒ -5.1599126548852
    "Cervical Polyp"          ⇒ -8.6871521430022
    "Chronic Cervicitis"      ⇒ -0.5599126548852
    "Chronic Endomeritis"     ⇒ -7.8507718870607
    "CIN"                     ⇒ -7.2447389802966
    "Condyloma Accumulatum"   ⇒ -7.6932459882186
    "Endometrial Hyperplasia" ⇒ -3.0235323989437
    "Endometrial Polyp"       ⇒ -6.5235323989437
    "Leiomyoma"               ⇒ 68.6400873451148
    "Others"                  ⇒ -5.0235323989437
    "Ovarian Cyst"            ⇒ 4.64008734511476
    "Product of Conception"   ⇒ 1.84008734511477
    "Squamous Cell Carcinoma" ⇒ -6.7735323989437
    else                      ⇒ .
]
```

David *et al.*, 2012

Table 4.17: Summary of Prediction Model: Standardized and Predicted Estimates for Diagnosed Biopsies

	Standardized *			Predicted Estimates (Numbers) by Year**						
Biopsy	**Mean**	**SD**	**Rates**	**2020**	**2025**	**2030**	**2035**	**2040**	**2045**	**2050**
Adenocarcinoma	9.195	0.138	0.020	18.390	27.586	36.781	45.976	55.171	64.366	73.562
Adenoma	1.943	0.385	0.004	3.885	5.828	7.770	9.713	11.655	13.598	15.540
Adenomyosis	13.981	0.300	0.030	27.961	41.942	55.922	69.903	83.884	97.864	111.845
Cervical Polyp	4.337	0.546	0.009	8.674	13.010	17.347	21.684	26.021	30.358	34.694
Chronic Cervicitis	27.610	0.103	0.060	55.220	82.830	110.440	138.050	165.659	193.269	220.879
Chronic Endomeritis	6.509	0.318	0.014	13.018	19.527	26.036	32.546	39.055	45.564	52.073
CIN	9.880	0.280	0.021	19.760	29.640	39.520	49.400	59.280	69.160	79.040
Condyloma A.	6.193	0.436	0.013	12.385	18.578	24.770	30.963	37.156	43.348	49.541
Endometrial Hyperplasia	20.345	0.585	0.044	40.690	61.035	81.380	101.726	122.071	142.416	162.761
Endometrial Polyp	12.797	0.644	0.028	25.594	38.390	51.187	63.984	76.781	89.578	102.374
Leiomyoma	235.401	0.438	0.508	470.803	706.204	941.605	1177.007	1412.408	1647.809	1883.210
Others	14.112	0.151	0.030	28.224	42.336	56.448	70.560	84.672	98.784	112.896
Ovarian Cyst	57.640	0.638	0.124	115.279	172.919	230.558	288.198	345.838	403.477	461.117
Product of Conception	34.729	0.518	0.075	69.458	104.188	138.917	173.646	208.375	243.104	277.834
Squamous Cell Carcinoma	8.968	0.522	0.019	17.936	26.904	35.872	44.840	53.807	62.775	71.743
Total	**463.639**	**6.003**	**1.000**	**927.277**	**1390.916**	**1854.554**	**2318.193**	**2781.832**	**3245.470**	**3709.109**

Model Information: *R-Square =0.8370; Adjusted R-Square=0.7814; Root Mean Square Error = 10.5294; Mean of Response = 11.6166.SD=Standard Deviation of Mean; *Standardized Rates are based on prediction equation (Table 4.8) using observed data from 2010-2014 at maximum desirability score of 0.099296.**Note that the estimates are based on standardized meanrates, and thus, represent the hospital sample population (which is limited by the number of available medical charts abstracted by the researcher) and not the general population.*

4.7 Photomicrographs of Gynaecological Various Biopsies Demonstrated with Different Staining Techniques

The different techniques used as seen in plates 4.1-4.7 (Haematoxylin and Eosin, Masson's Trichrome, Periodic Acid Schiff, Phosphotungstic Acid Haematoxylin, Voehoff's Van Gieson) demonstrated the various tissues in different shades. Cytokeratin and Ki67 were used to validate the presence of cell proliferation as well as cytokeratin

The photomicrograph of choriocarcinoma (Plate 4.1) shows malignant trophoblast, connective tissue core of chorionic villi, intravillous space, syncytiotrophoblast and cytotrophoblast, layer of syncytiotrophoblastic cells with mitotic and necrotic cells. Plate 4.2 displays condyloma acuminatum with acantosis and koilocytosis, Epidermal and dermal inflammatory cells are also visible as well as the inflammation of the dermal papilla and statum basale. In plate 4.3, Photomicrograph of Brenner tumour showing follicle with portions of mixed cells of transitional, squamous and cuboidal epithelium with malignant cells are scattered in the stroma. Mucinous epithelia and connective tissue invasion are also visible. Photomicrograph of Endometrial hyperplasia with proliferation of cystically dilated and non-dilated endometrial glands with proliferating pseudostratified epithelial cells. Photomicrograph of Squamous Cell Carcinoma show portions of squamous cell invasion and keratinous pearl while photomicrograph of Leiomyoma and Adenoma displays interlacing bundles of smooth muscle and proliferation of glands respectively as illustrated in plates 4.1-4.7.

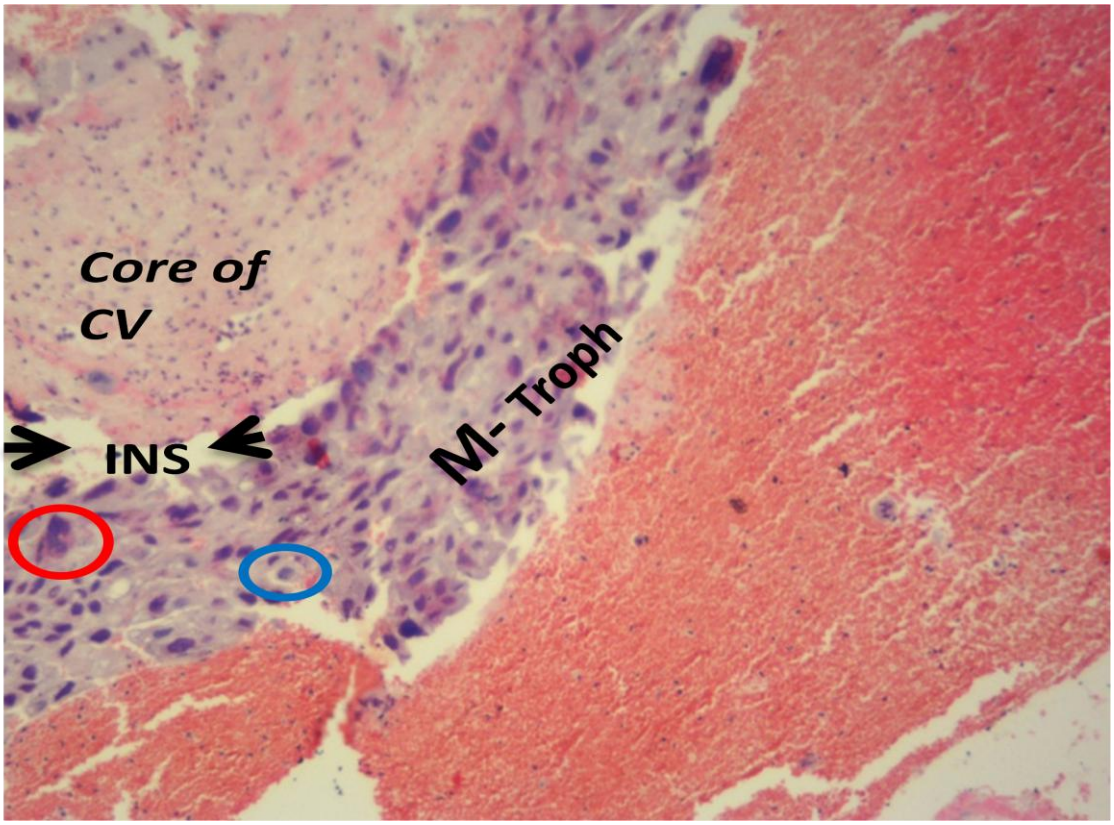


Plate 4.1A: **Photomicrograph of Choriocarcinoma with** Malignant trophoblast (**M-Troph**), Connective tissue core of chorionic villi (**Core of CV**), Intravillous space (**INS**), Syncytiotrophoblast and Cytotrophpblast (**Black circle**) (**Haematoxylin and Eosin, X100).**

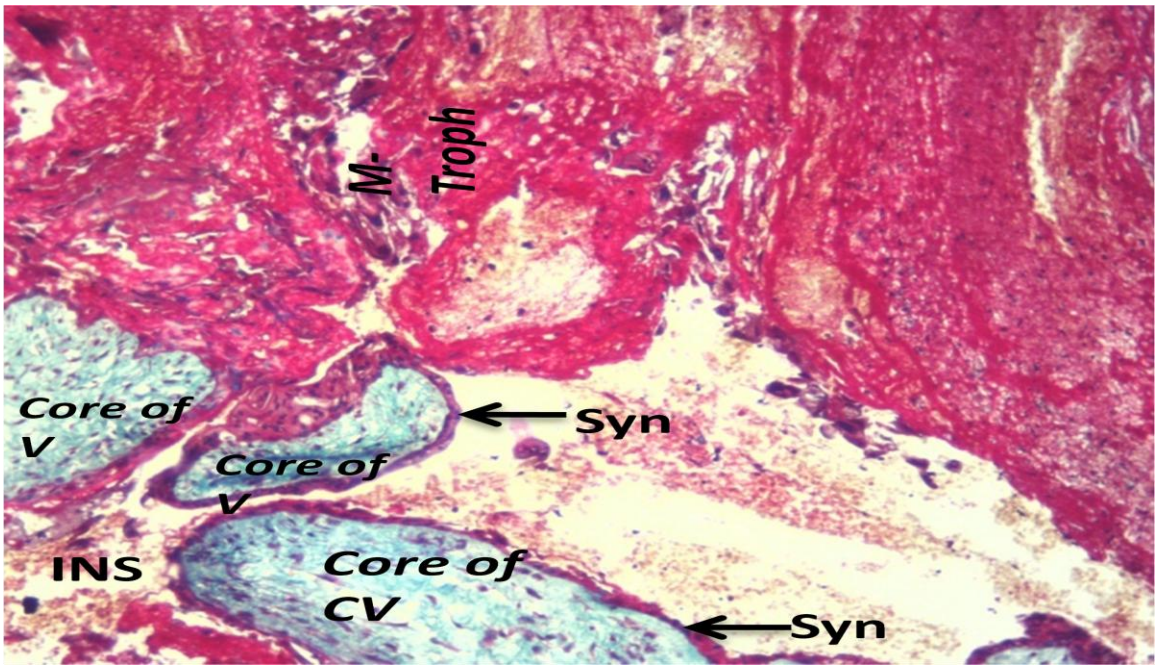


Plate 4.1B: **Photomicrograph of Choriocarcinoma**). Malignant trophoblast (**M-Troph**), Connective tissue core of chorionic villi (**Core of CV**), Intravillous space (**INS**), Layer of Syncytiotrophoblastic cells (**Syn**) (**Masson Trichrome, X100**).

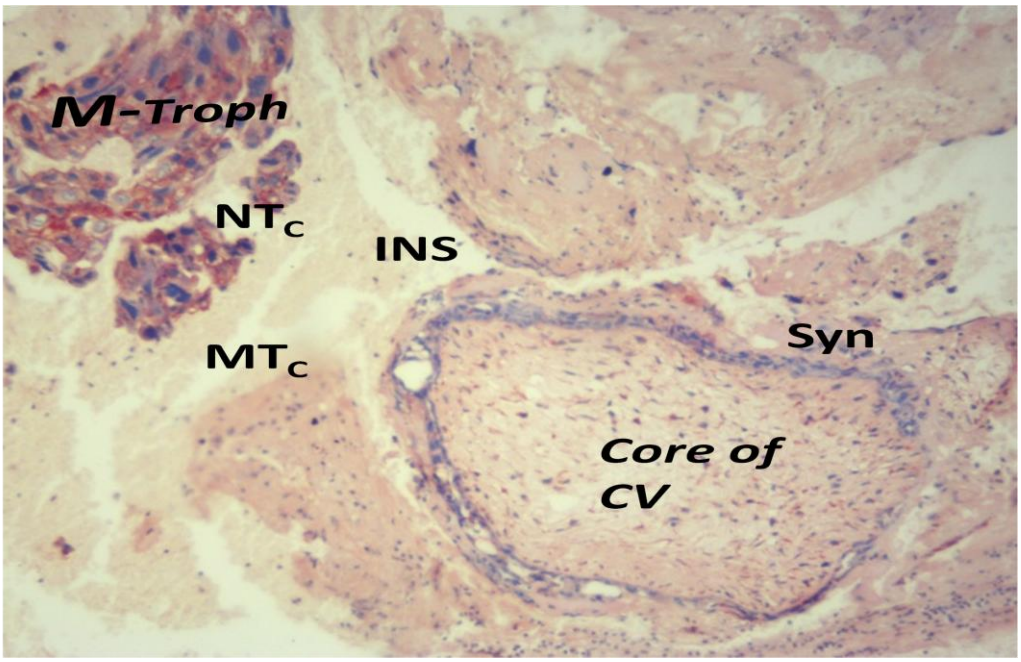


Plate 4.1C: **Photomicrograph of Choriocarcinoma.** Connective tissue core of chorionic villi (**Core of CV**), Intravillous space (**INS**), Layer of Syncytiotrophoblastic cells (**Syn**). Mitotic cell (**MT_C**), and nicrotic cells (**NT_C**), Malignant trophoblast (**M-Troph**) (**Periodic Acid Schiff, X100**)

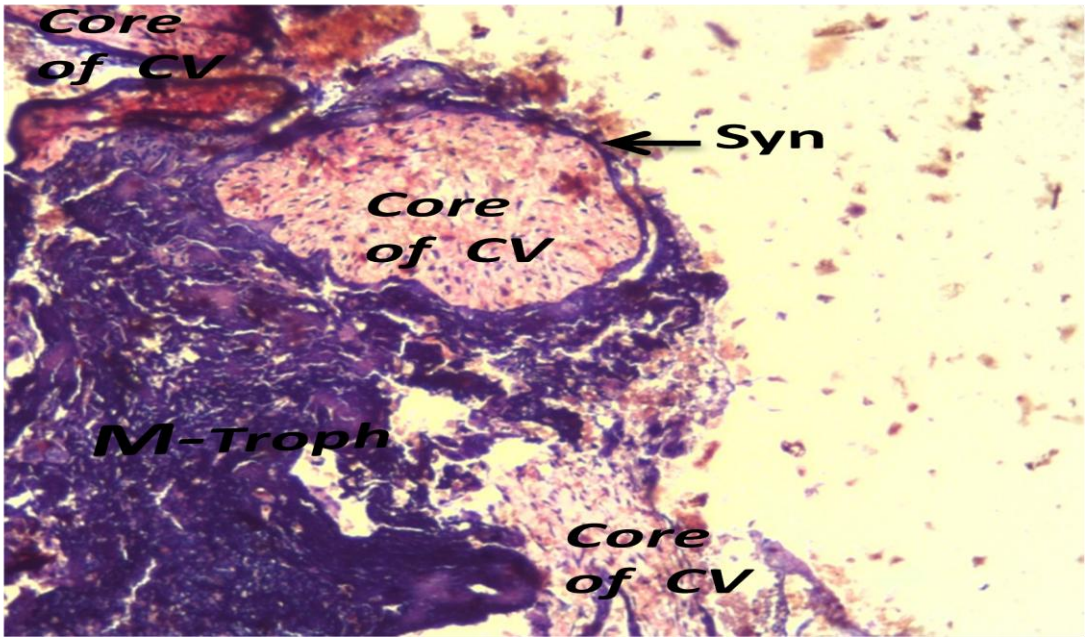


Plate 4.1D: **Photomicrograph of Choriocarcinoma.** Connective tissue core of chorionic villi (**Core of CV**), Intravillous space (**INS**), Layer of Syncytiotrophoblastic cells (**Syn**) and Malignant trophoblast (**M-Troph**) **(Phosphotungstic Acid Heamatoxylin, X100**).

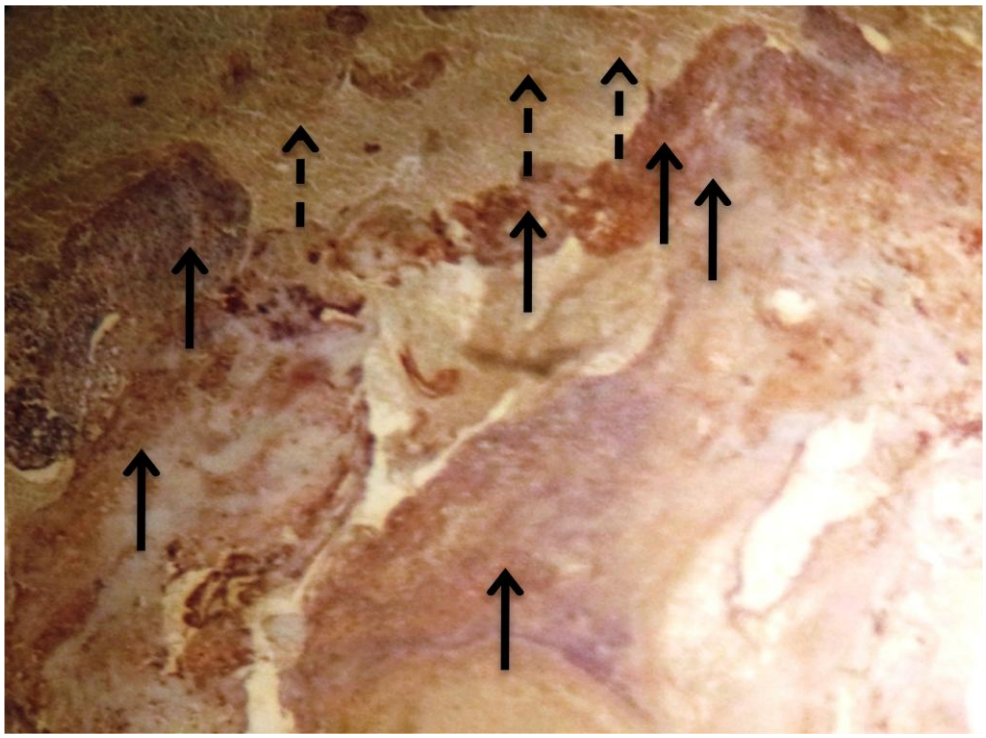


Plate 4.1E: Photomicrograph of Choriocarcinoma: Trophoblast positive cells (Arrow), negative cells (Dash arrow) (**Cytokeratin, X100**)

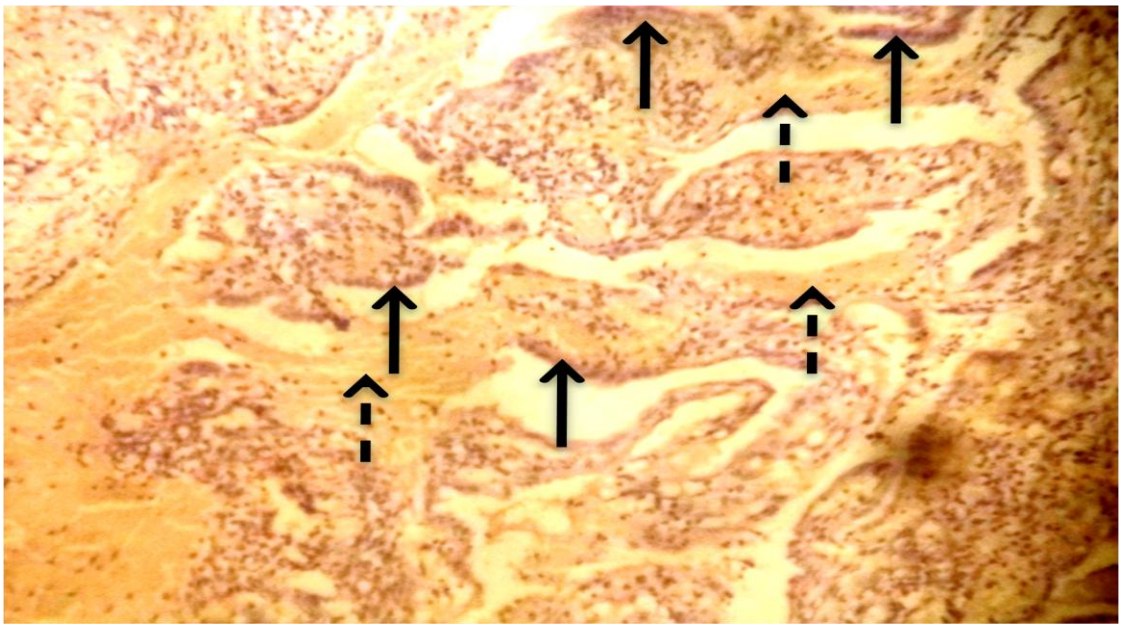


Plate 4.1F: **Photomicrograph of Choriocarcinoma**. Cellularly marked proliferating cells positive for Ki67 (Arrow), negative cells (Dash arrow) (**Ki67, X100**)

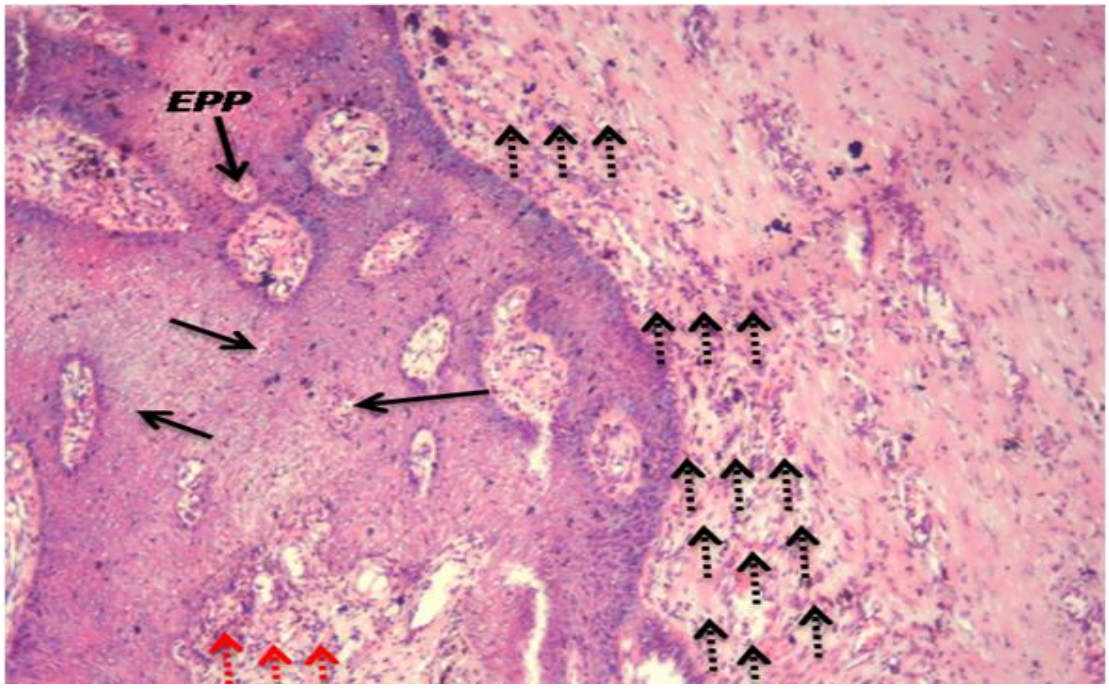


Plate 4.2A: **Photomicrograph of Condyloma Acuminatum.** Koilocytosis (**arrows**), Epidermal papilla (**EPP**), inflammatory cells (**Red dash arrows**). Dermal inflammatory cells (**Black dash arrows**), Epidermal Inflammation of the Dermal papilla (**SB**) (**Haematoxylin and Eosin, X100**)

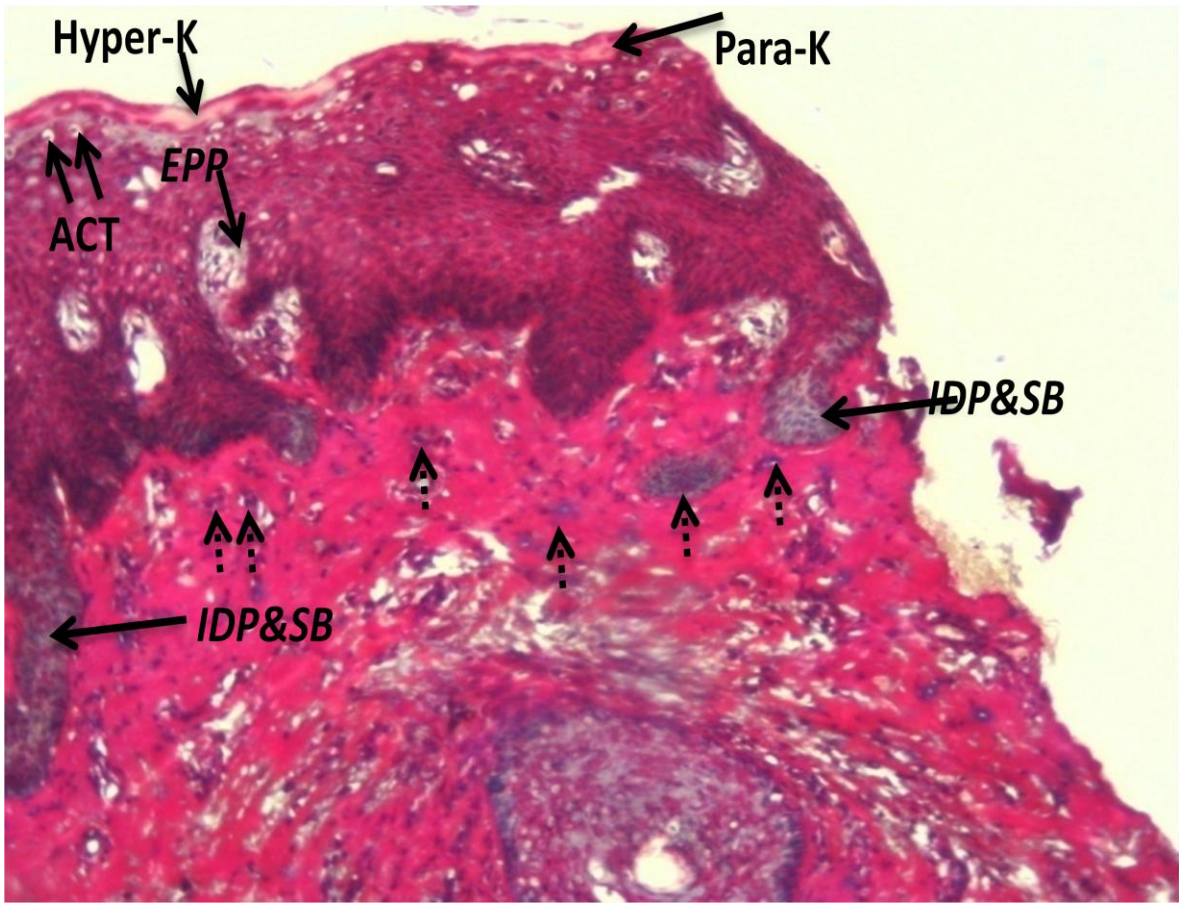


Plate 4.2B: Photomicrograph of Condyloma Acuminatum. Acantosis (**ACT**), Koilocytosis (**arrows**). Dermal inflammatory cells (**dash arrows**), Inflammation of the Dermal papilla and statum basale (**IDP & SB**). Hyper keratinisation (**Hyper-K**), Parakeratin (**Para-K)** and Epidermal papilla (**EPP**) (**Masson Trichrome X100**),

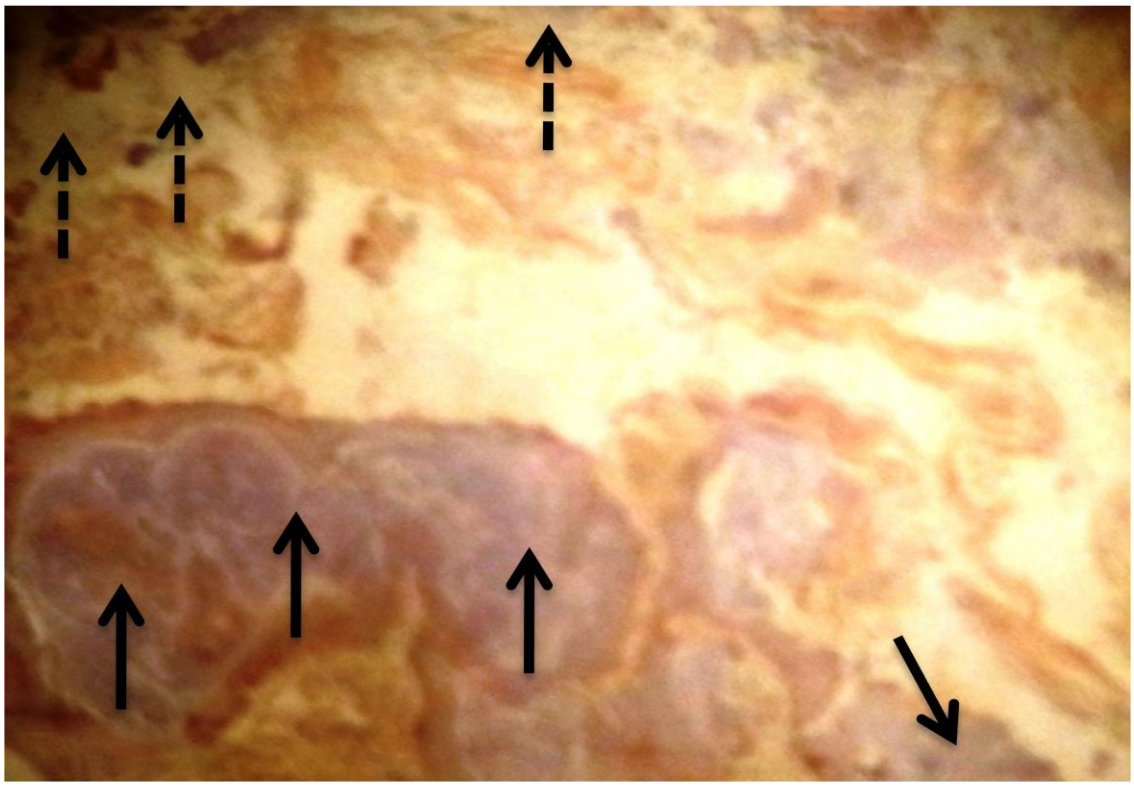


Plate 4.2C: Photomicrograph of Condyloma Acuminatum. Para and hyperkeratinizaion positive (Arrow), Negative areas (Dash arrows) (Cytokeratin X100).

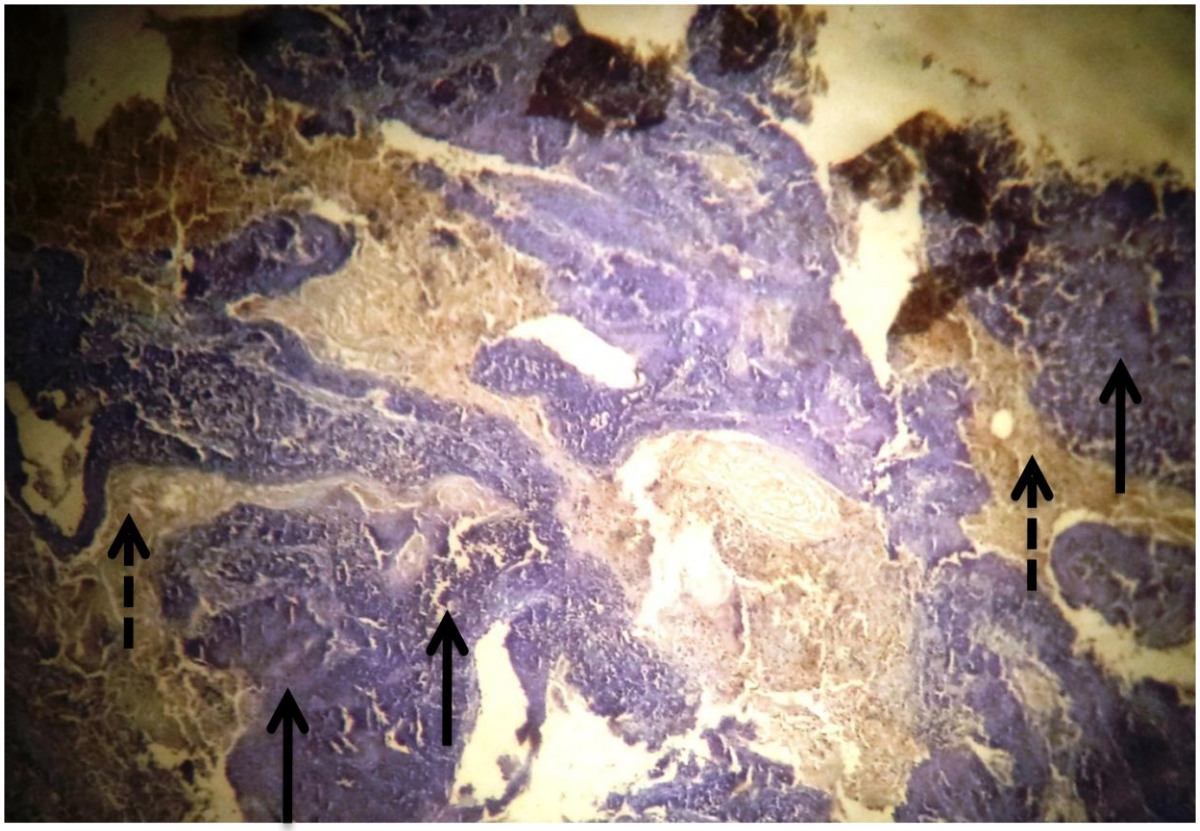


Plate 4.2D: Photomicrograph of Condyloma Acuminatum. X100. Heavily marked proliferating cells positive (Arrow), Negative areas (Dash arrows) (**Ki67 X100**).

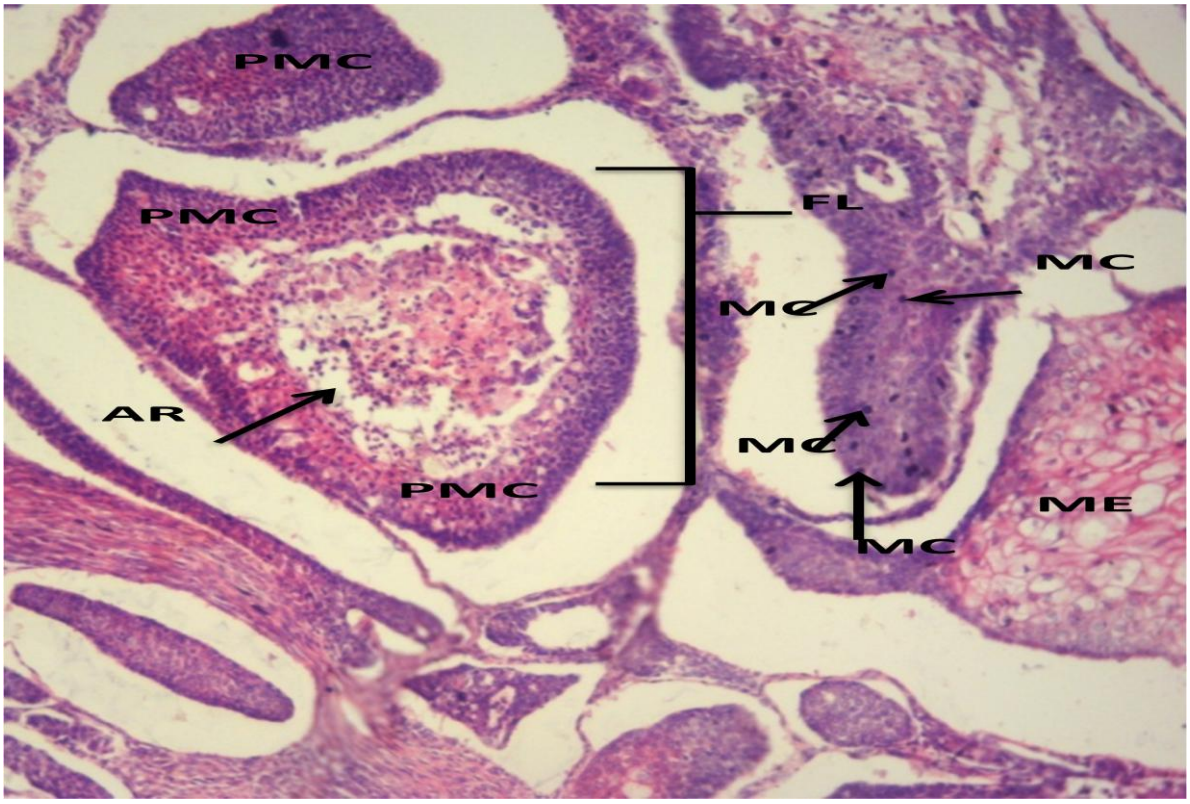


Plate 4.3A: **Photomicrograph of Brenner Tumour.** Follicle (**FL**) showing Portions of mixed cells of transitional, squamous and cuboida epithelium (**PMC**), Atrium of the follicle (**AR**), Malignant cells scattered in the stroma (**MC**), Mucinous epithelia (**ME**) (**Haematoxylin and Eosin, x100).**

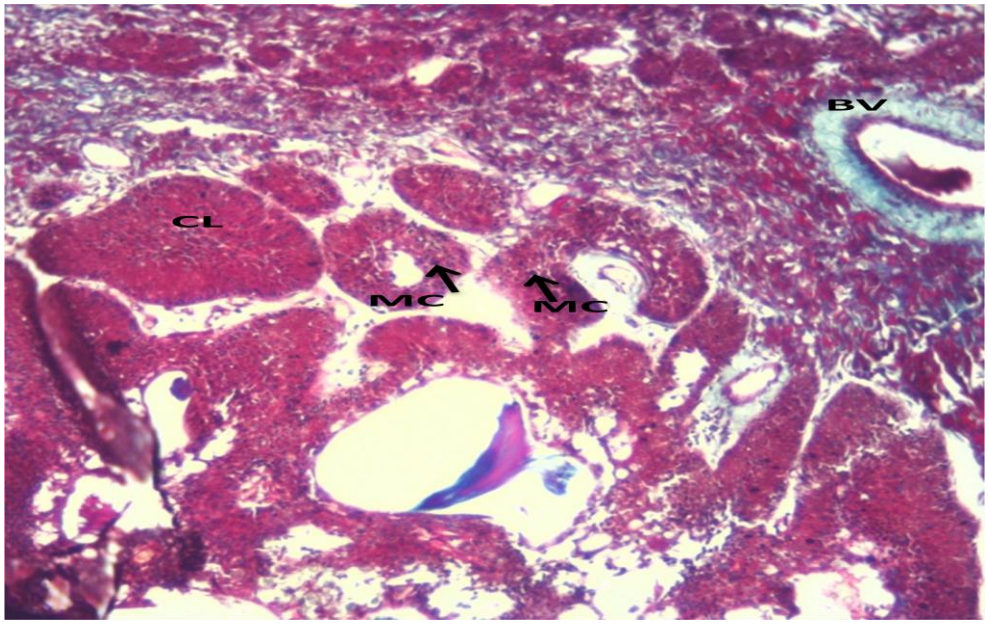


Plate 4.3B: **Photomicrograph of Brenner Tumour.** Malignant cells scattered in the stroma (**MC**), Mucinous epithelia (**ME**). Blood vessel (**BV**) and Corpus luteum (**CL**). (**Masson Trichrome, X100)**

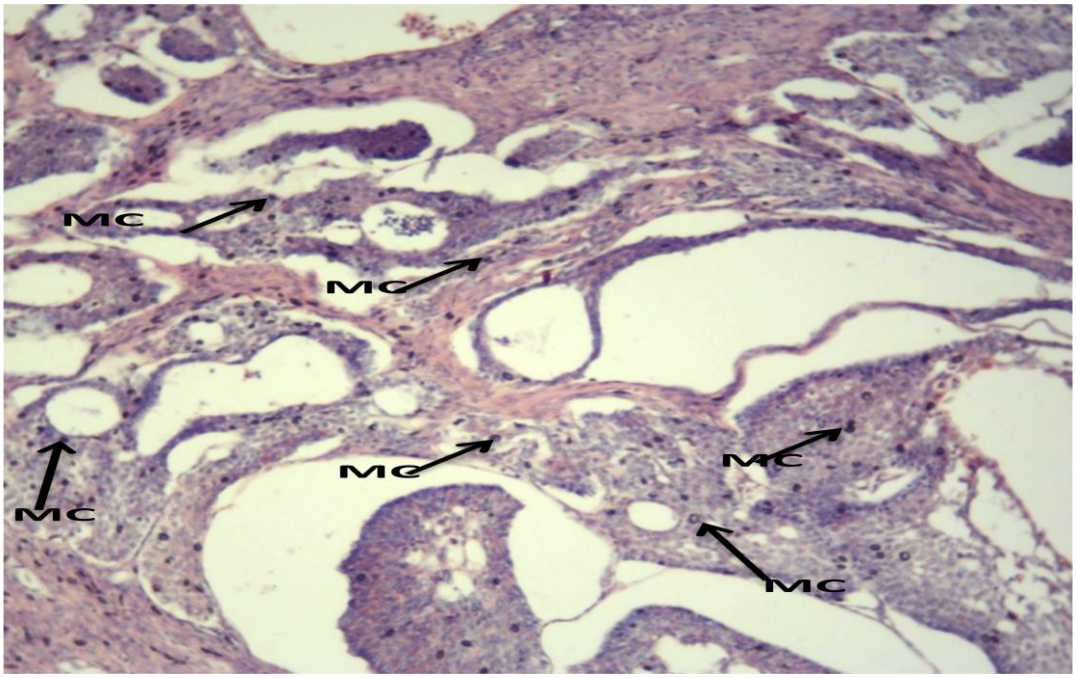


Plate 4.3C: Photomicrograph of Brenner Tumour. Malignant cells scattered in the stroma (**MC**), Mucinous epithelia (**ME**) (**Periodic Acid Schiff, X100**).

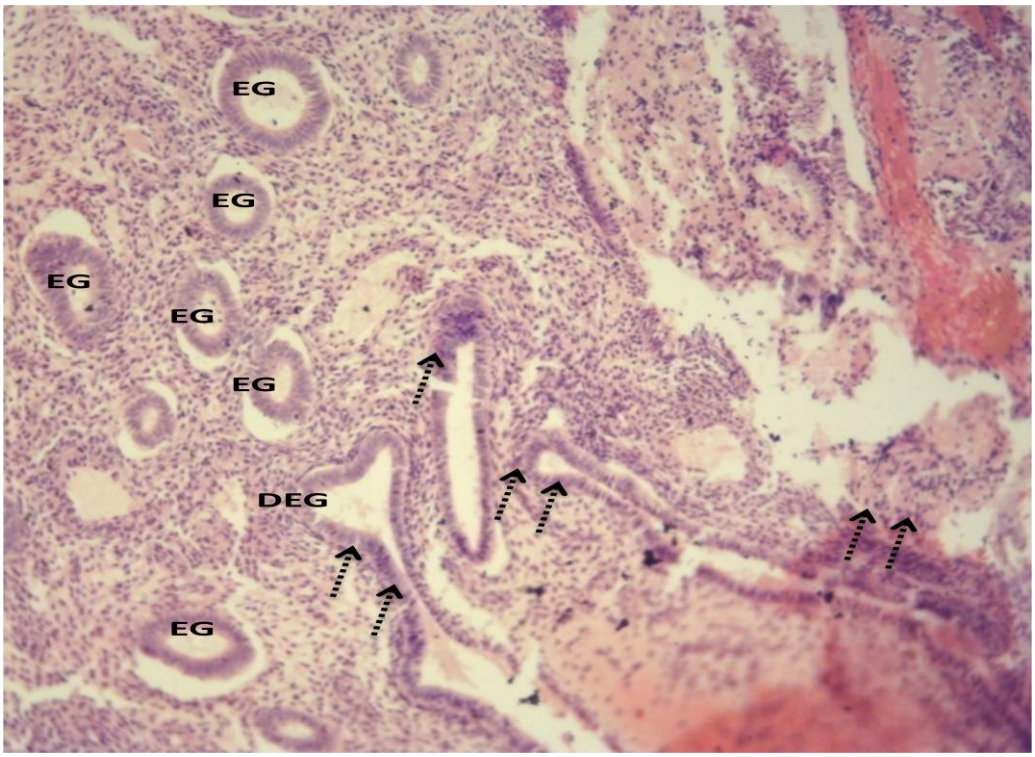


Plate 4.4A: **Photomicrograph of Endometrial Hyperplasia.** Proliferation of cystically dilated and non-dilated endometrial glands (**DEG** and **EG**).
There are also proliferating pseudostratified epithelial cells (**Dash arrow**) (**Haematoxylin and Eosin, X100**).

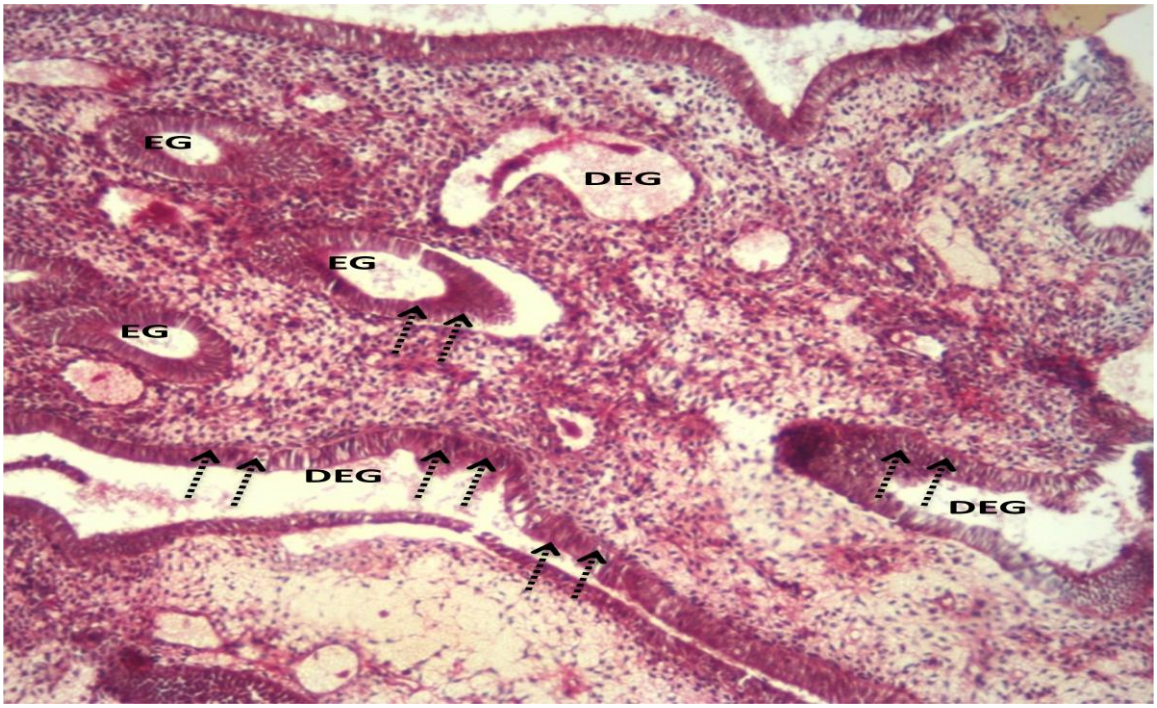


Plate 4.4B: Photomicrograph of Endometrial Hyperplasia. Proliferation of cystically dilated and non-dilated endometrial glands (**DEG** and **EG**). There are also proliferating pseudostratified epithelial cells (**Dash arrow**) (**Masson Trichrome, X100**).

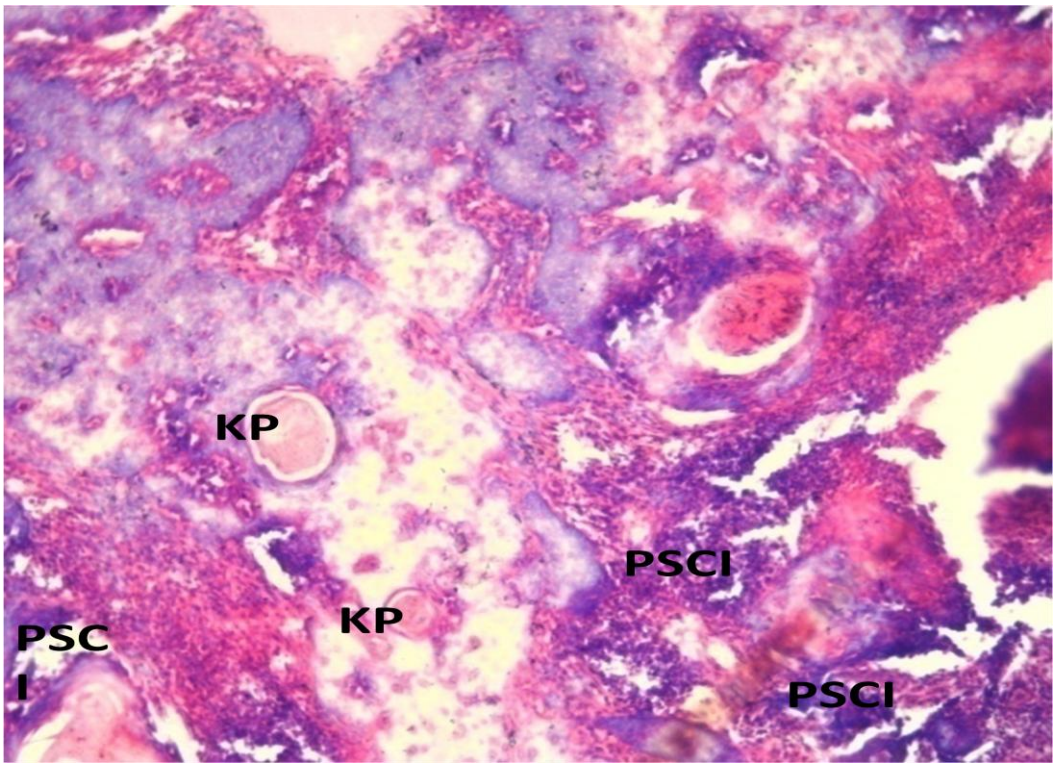


Plate 4.5A: **Photomicrograph of Squamous Cell Carcinoma.**) Portions of squamous cell invasion (**PSCI**) and keratinous pearl (**KP**) (**Haematoxylin and Eosin, X100**)

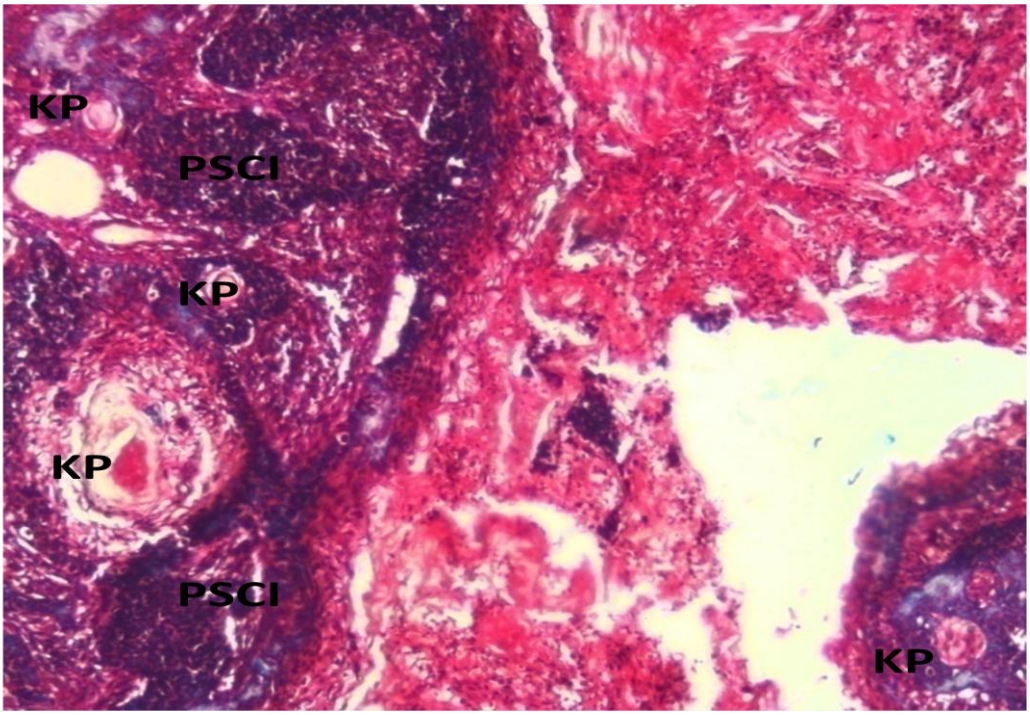


Plate 4.5B: **Photomicrograph of Squamous Cell Carcinoma**. Portions of squamous cell invasion (**PSCI**) and keratinous pearl (**KP**) (**Masson Trichrome, X100**)

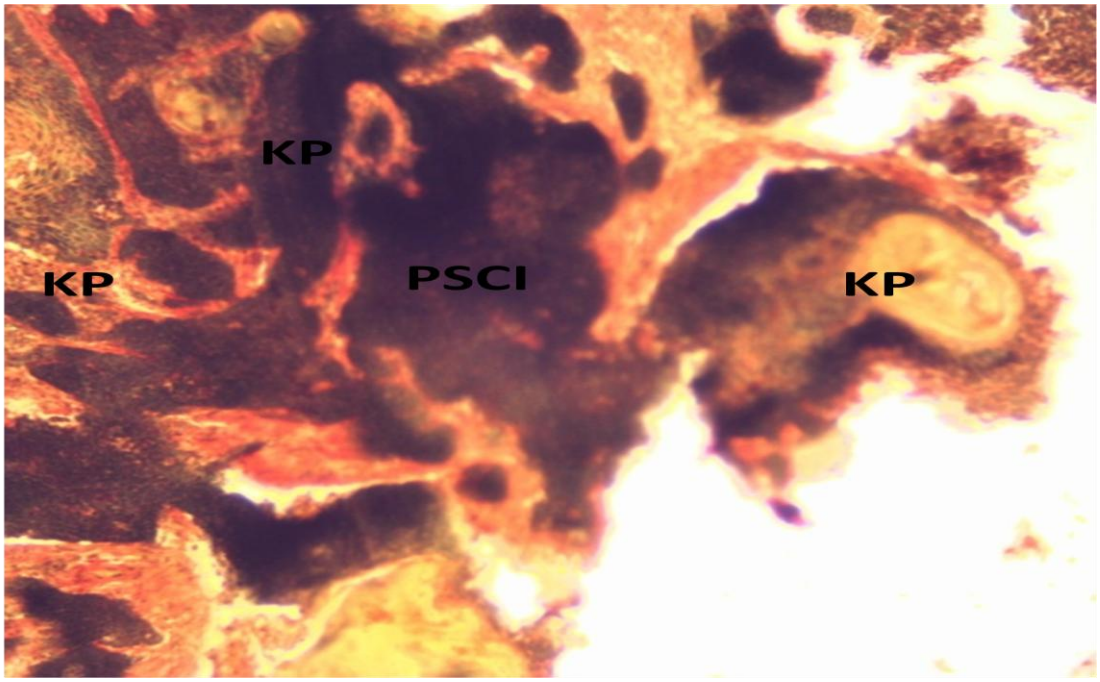


Plate 4.5C: Photomicrograph of Squamous Cell Carcinoma. Portions of squamous cell invasion (**PSCI**) and keratinous pearl (**KP**) (**Verhoeff Van Gieson, X100).**

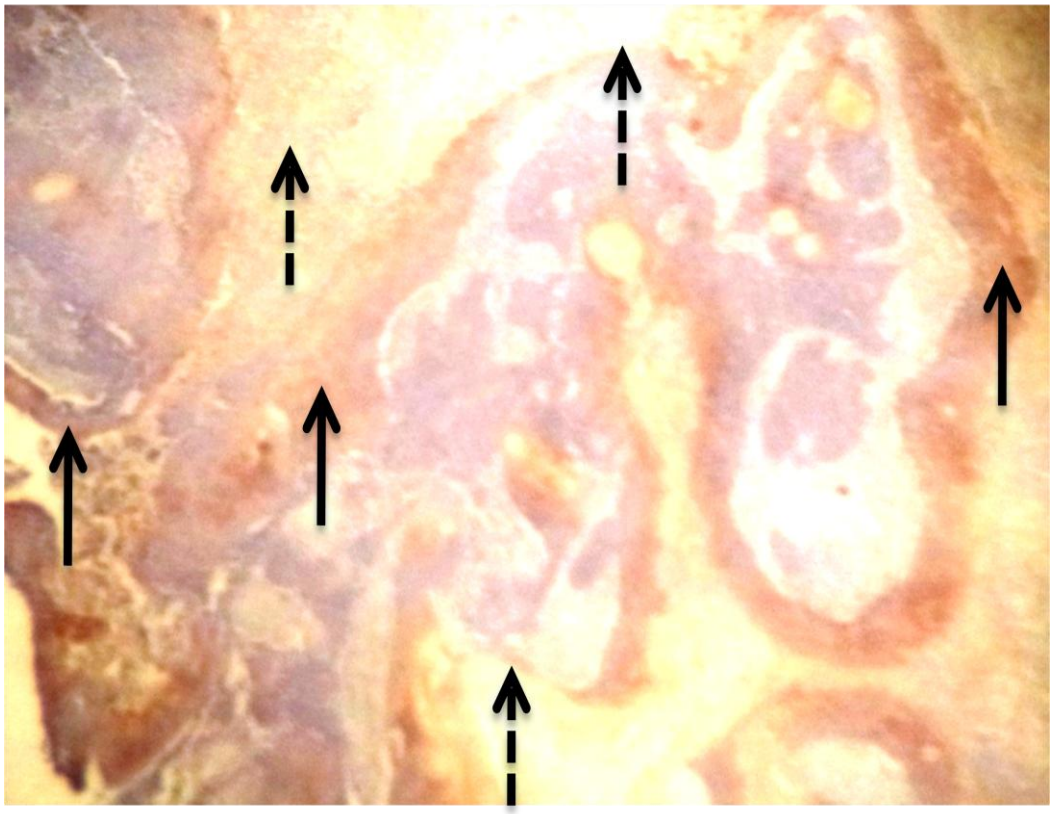


Plate 4.5D: **Photomicrograph of Squamous Cell Carcinoma.** keratinous pearl positive cells (Arrow), Negative cells (Dash arrows) (**Cytokeratin X100**).

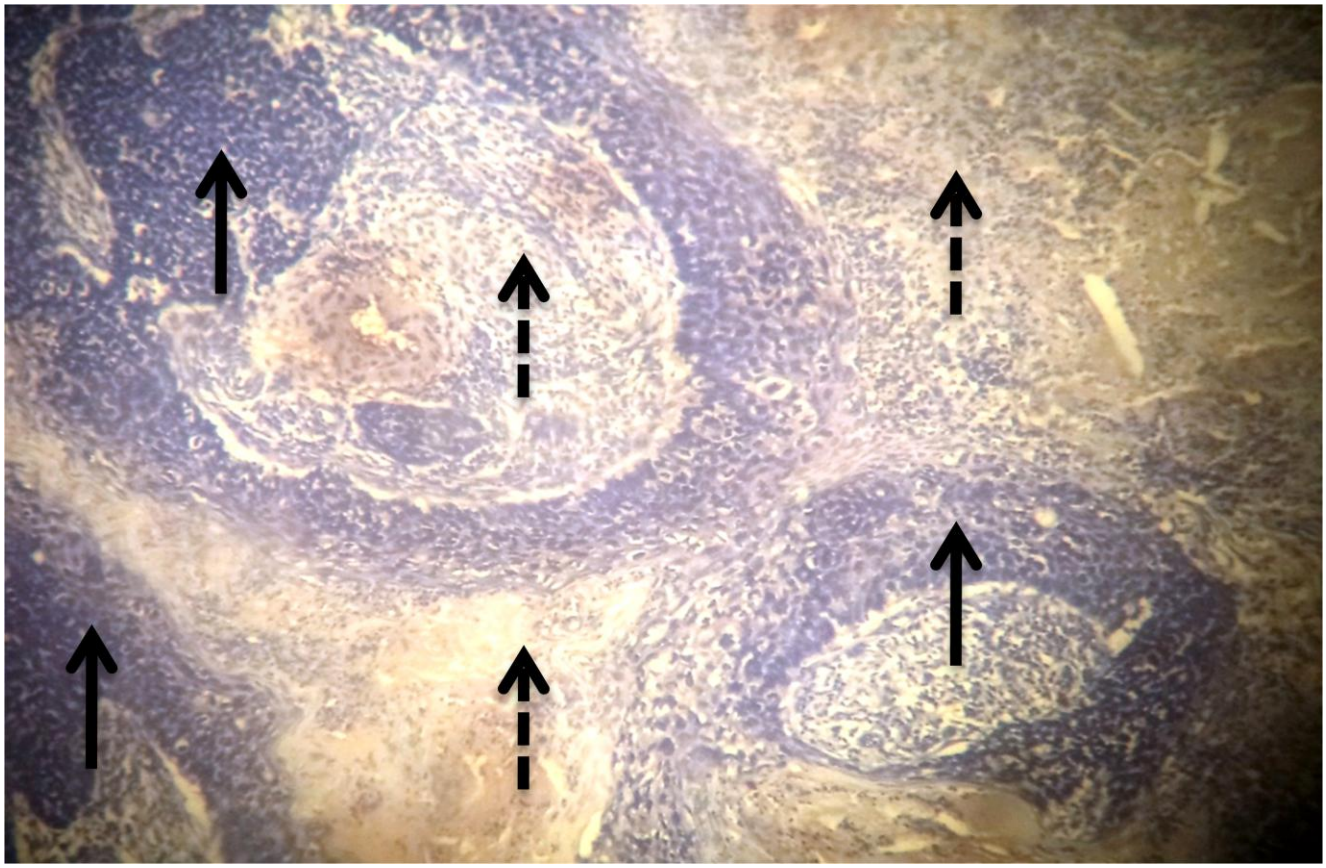


Plate 4.5E: **Photomicrograph of Squamous Cell Carcinoma X100.** (VVG) Heavily marked proliferating squamous cell invasion (**PSCI**), positive cells (Arrow), Negative areas (Dash arrows) (**Ki67 X100**).

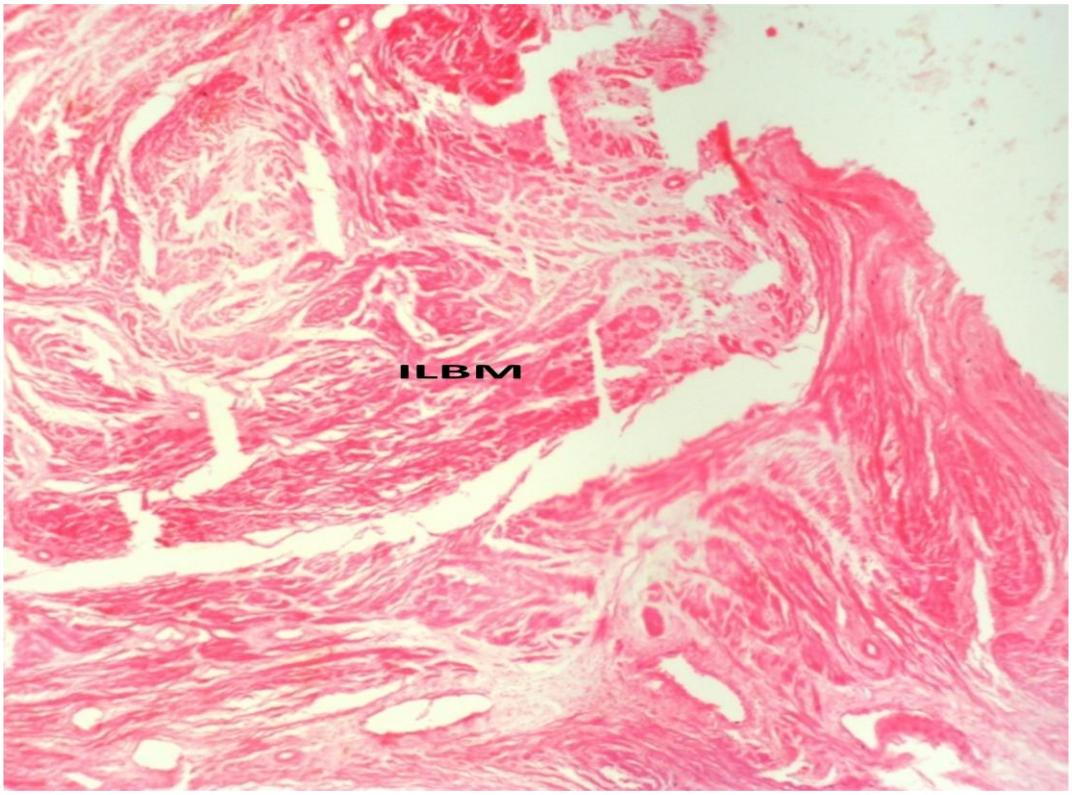


Plate 4.6A: **Photomicrograph of Leiomyoma.** Interlacing bundles (ILBM) **(Haematoxylin and Eosin X100**)

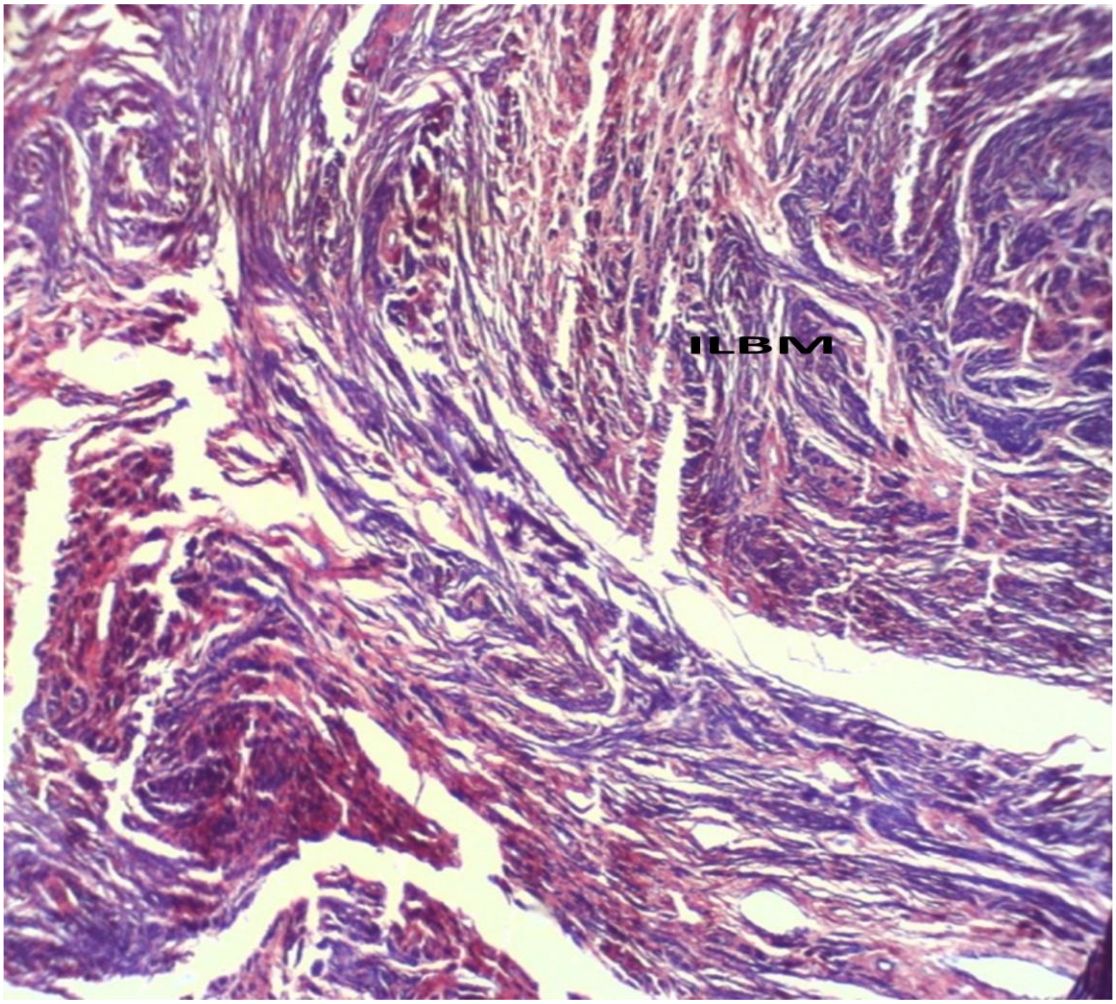


Plate 4.6B: **Photomicrograph of Leiomyoma.** Interlacing bundle of smooth muscle (**ILBM**) **(Phosphotungstic Acid Haematoxylin, X 100**).

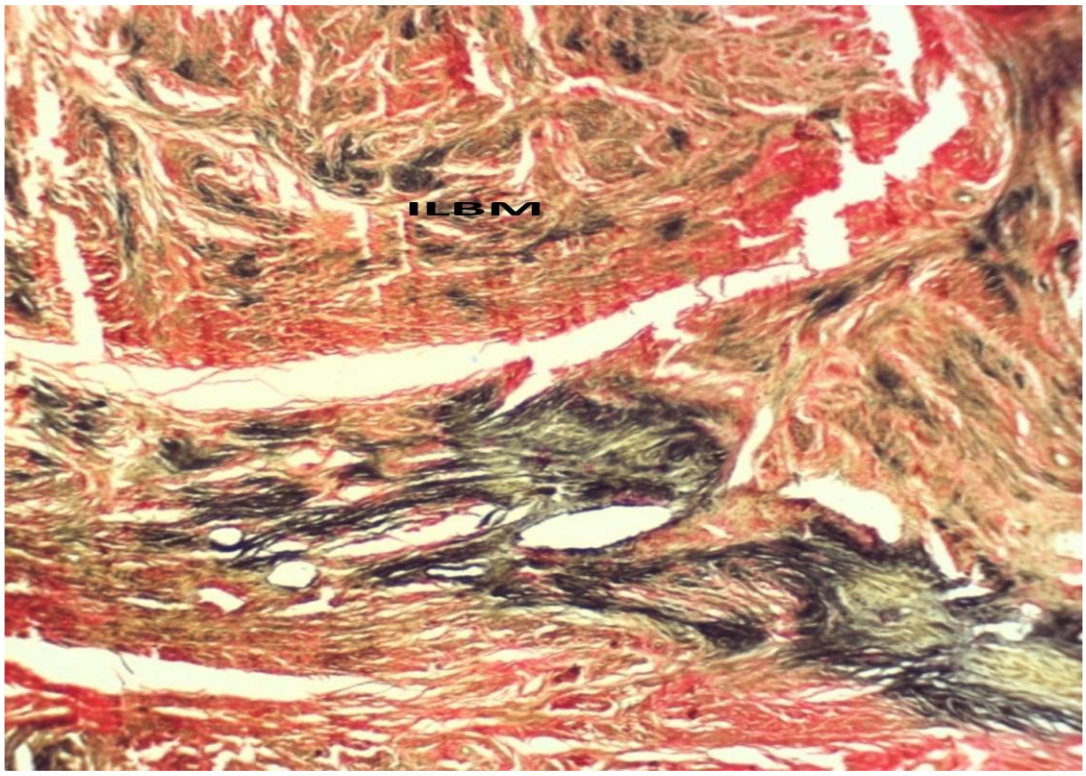


Plate 4.6C: **Photomicrograph of Leiomyoma X100. (VVG)** Interlacing bundles of smooth muscle (**ILBM**) (**Verhoeff Van Gieson, X100.)**

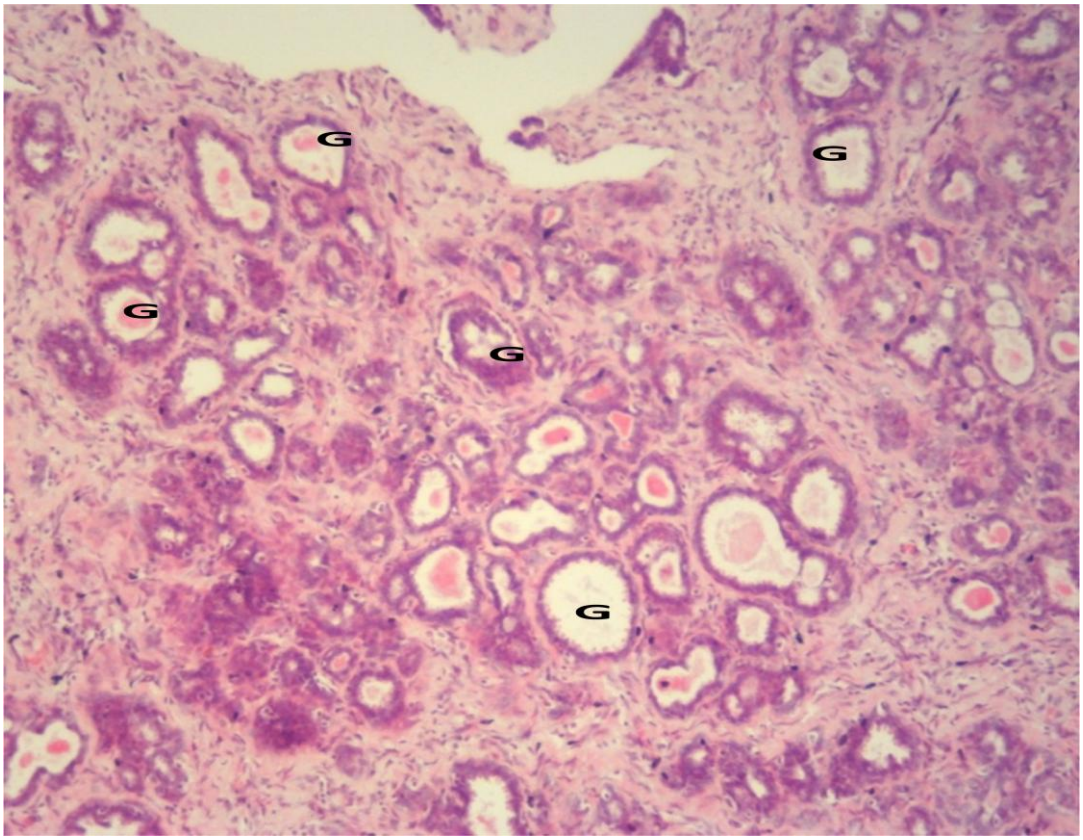


Plate 4.7A: Photomicrograph of Adenoma. Proliferation of glands **G) (Haematoxylin and Eosin, X100).**

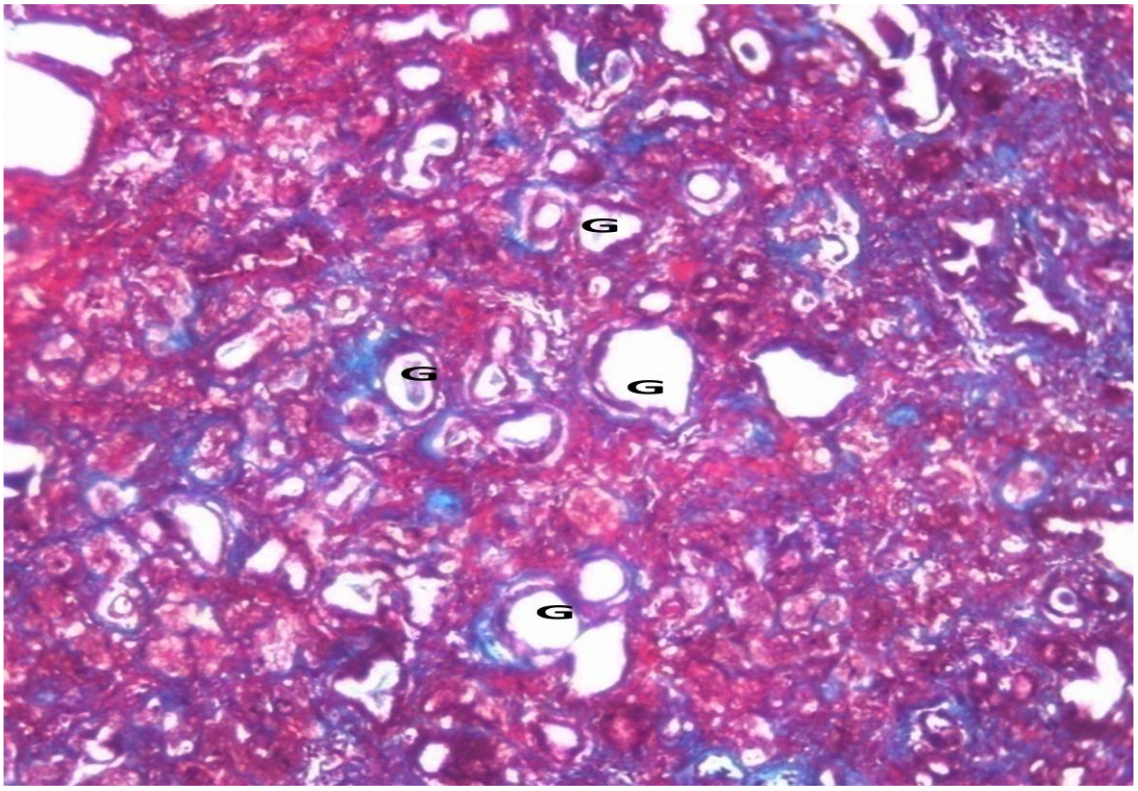


Plate 4.7B: Photomicrograph of Adenoma Proliferation of glands (**G**). **(Masson Trichrome, X100)**

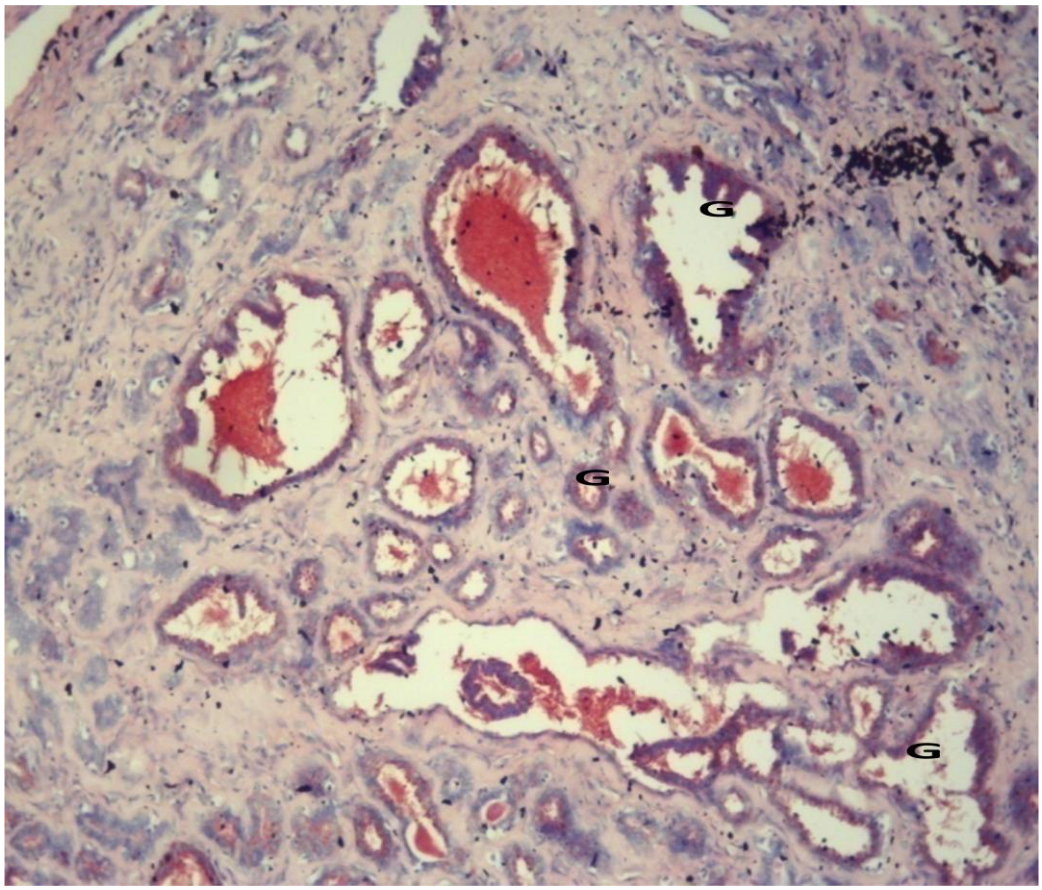


Plate 4.7C: Photomicrograph of Adenoma Proliferation of glands **(G)(Periodic Acid Schiff, X100).**

4.8 Variability Analysis of Percentage (%) Area by different Staining Techniques

The % area of the tissue covered by stain is dependent on the type of stain and tissue. The mean % area for adenocarcinoma covered by different stains was 39.867%, adenoma 52.927%, adenomyosis 50.116%, Brenner tumour 56.353%, choricarcinoma 43.815%, condyloma A. 45.641%, Demoid cyst 37.826%, Endometria hyperplasia 46.144%, endometria polyp 53.977%, fibroma, 38.979%, leiomyoma 57.984%, mucinous cyst 46.389% and squamous cell carcinoma 52.429%.

The % area covered by H&E was 42.645%, MT 64.384%, PAS 40.722%, PTAH 54.183% and VVG 53.653%. In adenoma the % area covered by H&E was 44.114%, MT 79.111%, PAS 33.890%, PTAH 53.730%and VVG 74.328%. In adenomyosis H&E stained 44.352%, MT 80.862%, PAS 44.754%, PTAH 56.359% and VVG 36.626%. In Brenner tumour the % area stained by H&E was 54.354% of the area, MT was67.659%, PAS 56.808%, PTAH 56.629% and VVG 65.894%. In choricarcinoma, H&E stained 49.678% of the area; MT was 58.231%, PAS 30.009%, PTAH 37.589% and VVG 51.073%. In condyloma A, H&E stained 46.147% of the tissue, MT 53.043%, PAS 37.433%, PTAH 69.851%and VVG 50.346%. In demoid cyst biopsy, H&E stained 33.745%, MT 53.670%, PAS 23.395%, PTAH 36.603%and VVG 49.576. In endometria hyperplasia, H&E stained 42.374%, MT 54.051%, PAS 39.768%, PTAH 51.162% and VVG 55.622%. In endometria polyp H&E covered 49.494% of the tissue, MT 55.407%, PAS 39.195%, PTAH 53.353% and VVG 71.302%. In fibroma, H&E stained 36.913%, MT 52.301%, PAS 19.298%, PTAH 77.153% and VVG 39.332%. In leiomyoma, H&E stained 51.340%, MT 71.025%, PAS 56.120%, PTAH 59.727 and VVG 55.763%. The % area stained by H&E in mucinous cyst 23.438%, MT 77.992%, PAS 49.357%, PTAH 57.193% and VVG 49.435%. In squamous cell carcinoma, H&E stained 57.082% of the area, MT 74.269%, PAS 80.665%, PTAH 47.021% and VVG 57.684%. These are presented in table 4.10 and figures 4.8-4.11. Table 4.11 shows the statistical comparison of biopsy and the staining method, which was significant.

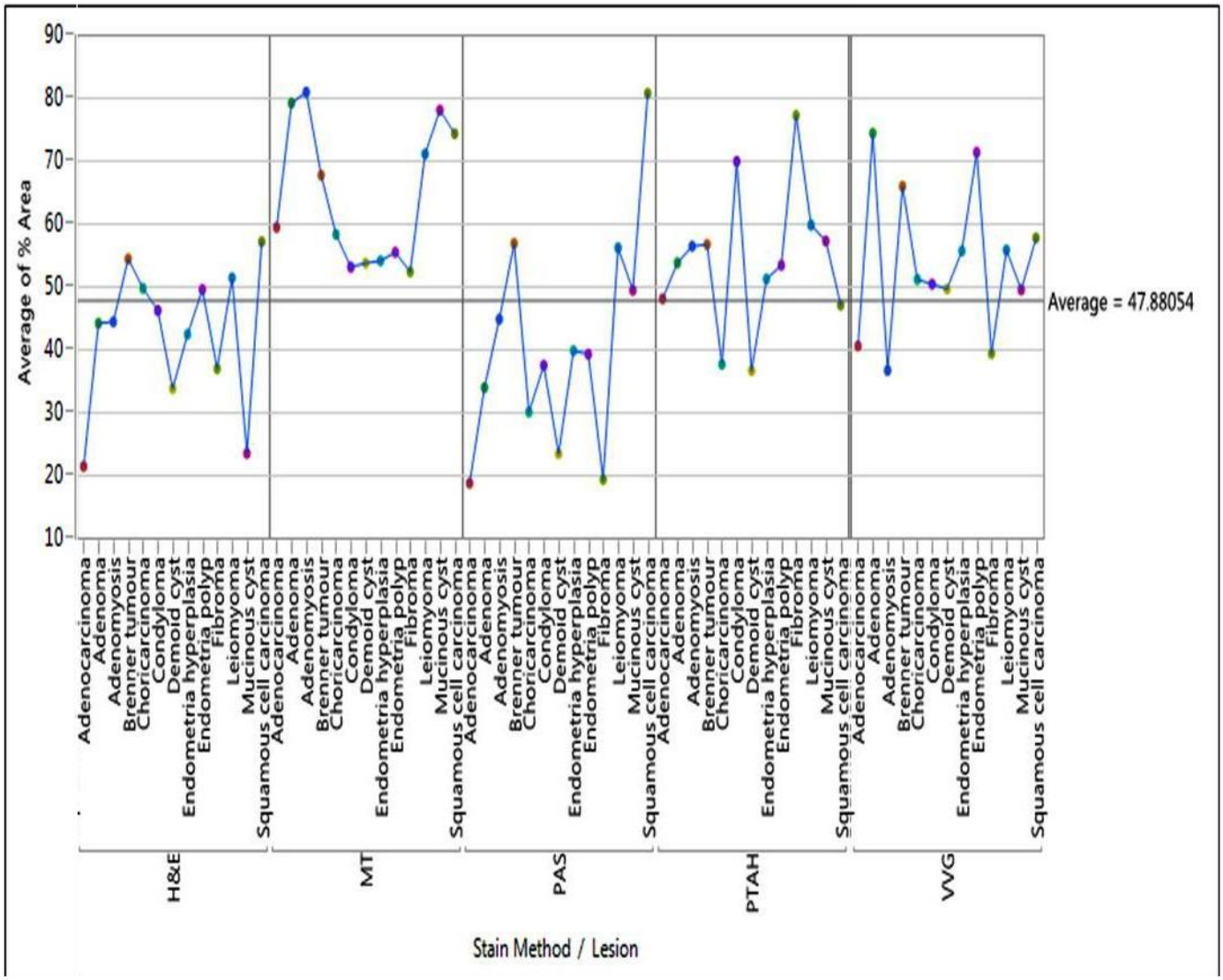
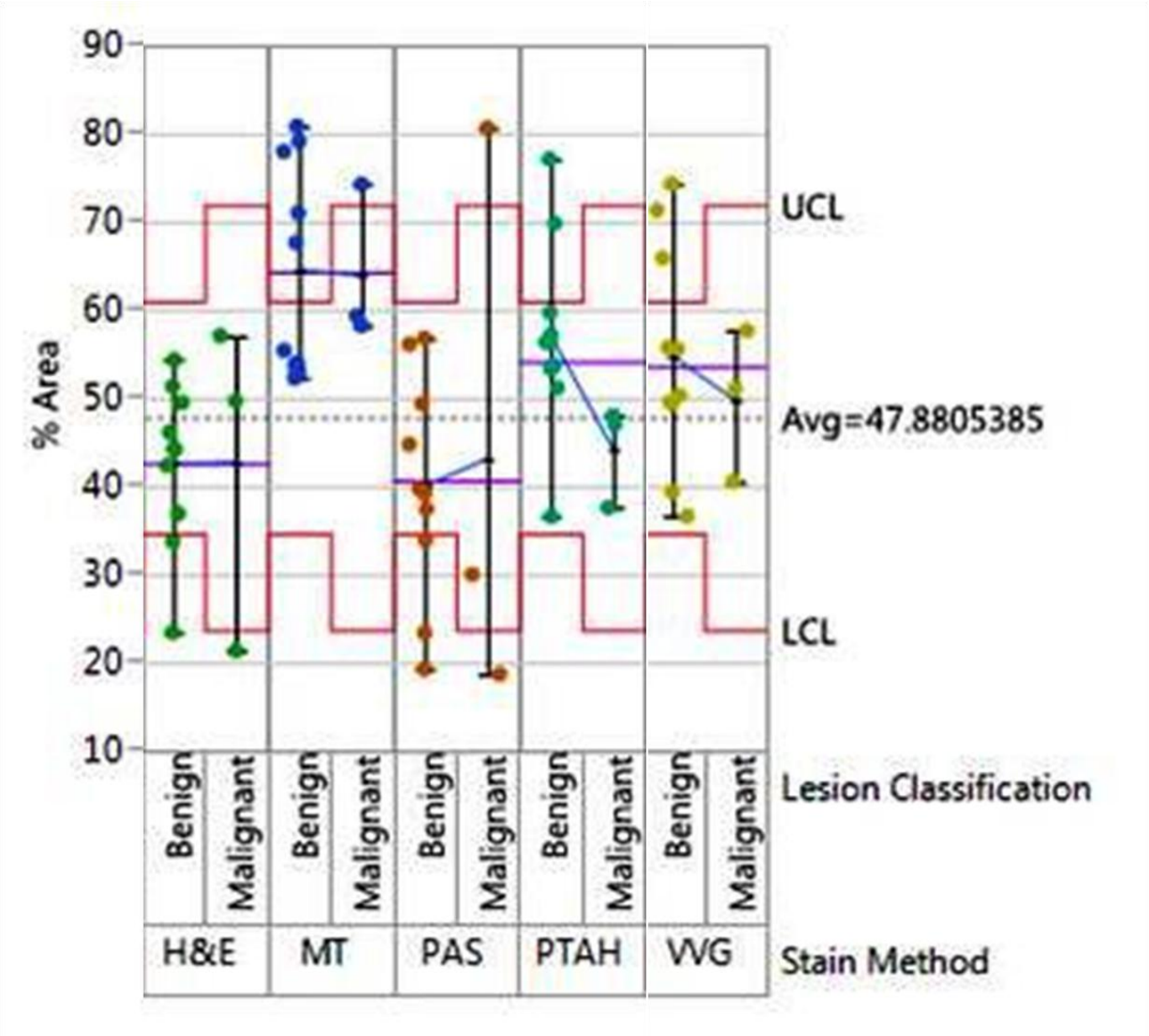


Figure 4.8: Chart for % Area Measurement by Biopsy within Staining Methods

4.9 Variability Analysis for % Area Measurement of Benign and Malignant

As presented in table 4.12 and showed in figure 4.9, the mean % area of the benign and malignant biopsies stained by H&E were 42.6271% and 42.706% respectively. While MT stained a % area of 64.5121 in benign biopsies, malignant was 63.95633. PAS stained a % area of 40.0018 for benign and 43.12433 for malignant. PTAH covered % area of 57.176 in benign and 44.208 in malignant. VVG stained a % area of 54.8224 in benign and 49.759 in malignant biopsies.



H&E= Haematoxylin and Eosin; MT= Masson Trichrome; PAS= Periodic Acid Schiff; PTAH= Phosphotungstic Acid Haematoxylin; VVG= Verhoff's Van Gieson

Figure 4.9: Variability Chart for Percentage Area Measurement

Table 4.18: Variability Summary for % Area Measurement of Benign and Malignant

Stain Method By Biopsy Classification	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%	Minimum	Maximum	Range	Median
[H&E][Benign]	42.6271	9.177226	2.902094	36.06211	49.19209	23.438	54.354	30.916	44.233
[H&E][Malignant]	42.706	18.85491	10.88589	-4.13219	89.54419	21.358	57.082	35.724	49.678
[MT][Benign]	64.5121	12.04167	3.807909	55.89801	73.12619	52.301	80.862	28.561	61.533
[MT][Malignant]	63.95633	8.949139	5.166788	41.72544	86.18723	58.231	74.269	16.038	59.369
[PAS][Benign]	40.0018	12.4786	3.94608	31.07515	48.92845	19.298	56.808	37.51	39.4815
[PAS][Malignant]	43.12433	32.99932	19.05217	-38.8505	125.0992	18.699	80.665	61.966	30.009
[PTAH][Benign]	57.176	10.81726	3.420717	49.4378	64.9142	36.603	77.153	40.55	56.494
[PTAH][Malignant]	44.208	5.753684	3.321891	29.91506	58.50094	37.589	48.014	10.425	47.021
[VVG][Benign]	54.8224	12.57775	3.977434	45.82482	63.81998	36.626	74.328	37.702	52.984
[VVG][Malignant]	49.759	8.657117	4.998189	28.25353	71.26447	40.52	57.684	17.164	51.073

4.10 Matched Pairs Analysis of Stains on Percentage Area

The matched pairs analysis of % area measurements by staining methods. Using H&E as the standard (mean = 42.6%), we compared the six staining methods. Results from this analysis indicate that the mean % areas of tissues covered were significantly improved by 50% with MT (64.4%, p =0.0002), 27% with PTAH (54.2%, p = 0.021) and 26% with VVG (53.7%, p =0.004) when compared to H&E. However, PAS performed poorly by producing mean % areas that were below or failed to match that of H&E (p > 0.005) Figures 4.10-4.15.

Comparison of Stain Methods based on % area Measurements

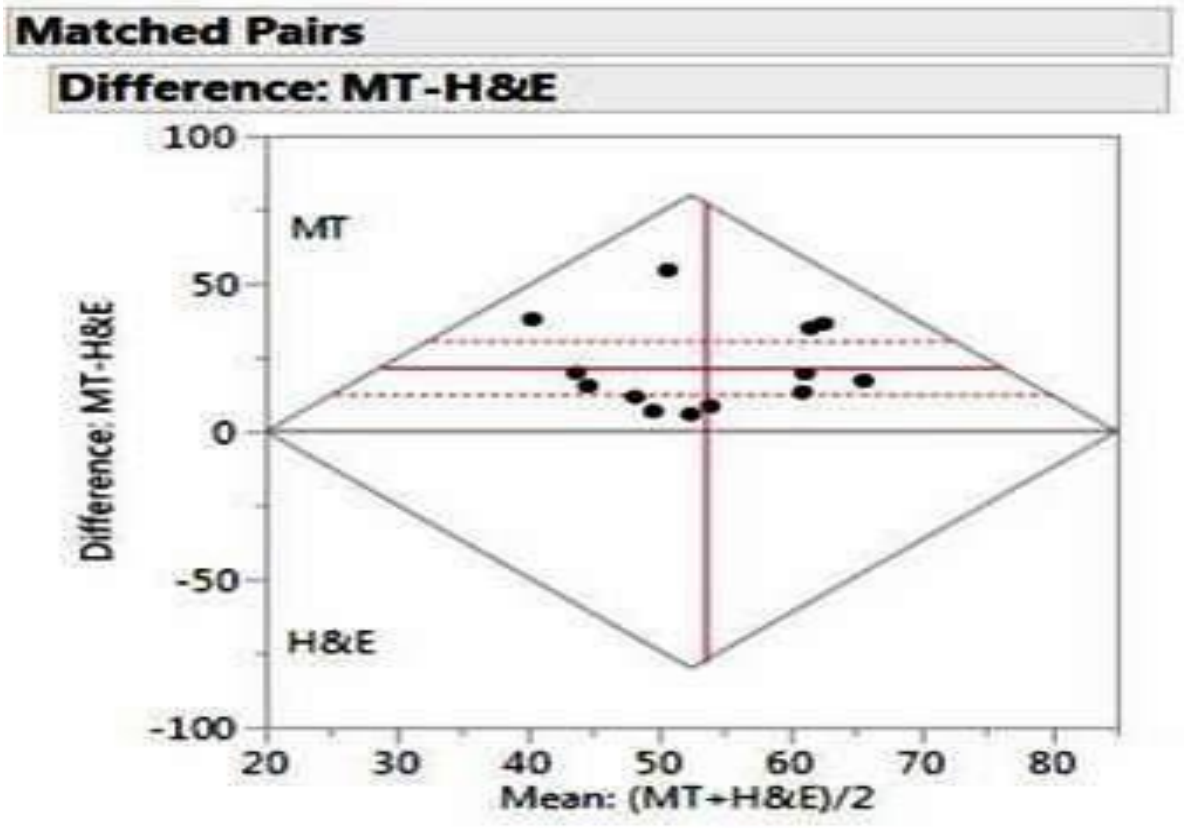


Figure 4.10: Comparison of MT and H&E on % Area Measurement.
MT 64.3838, **H&E**42.6453, **Mean Difference** 21.7385, **Mean of Means** 53.51455, **Std Error** 4.09905,**Upper 95%** 30.6696, **Lower 95%** 12.8075, **t-Ratio** 5.303308, **Prob**> 0.0002*

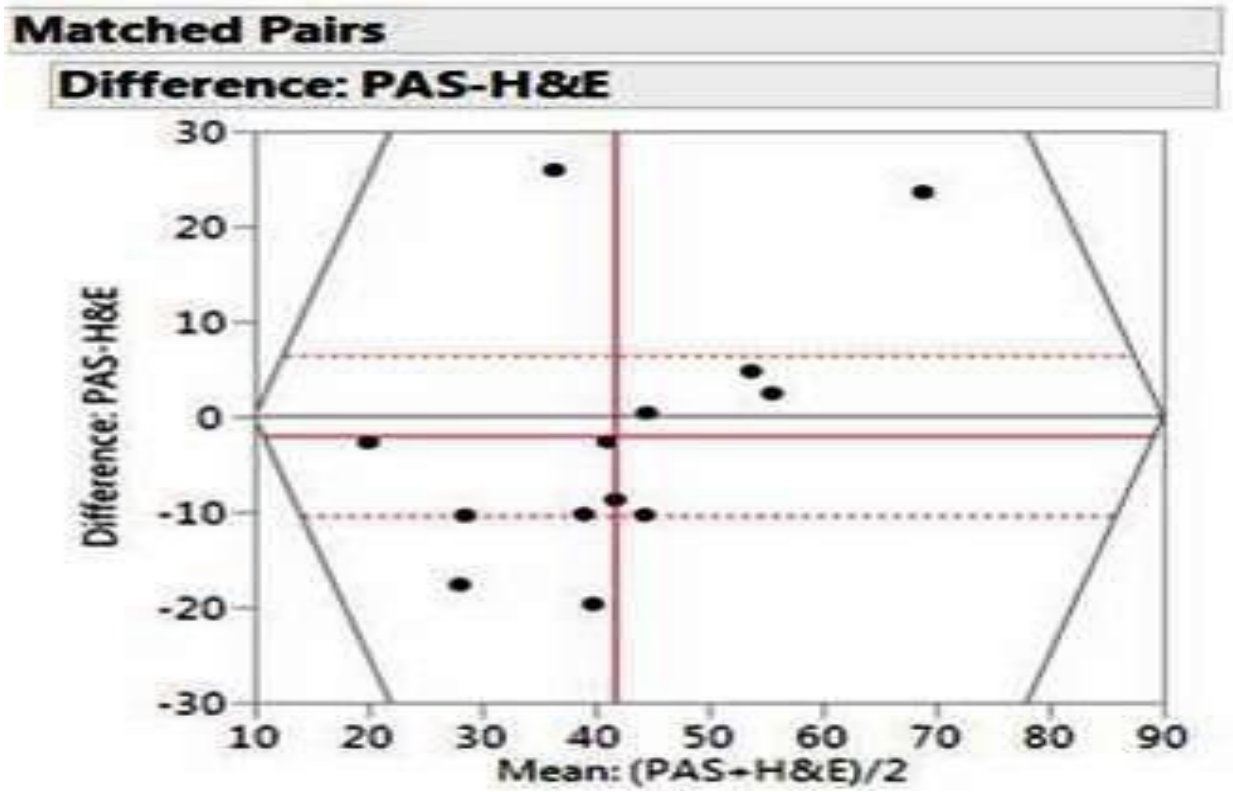


Figure 4.11: Comparison of PAS and H&E on % Area Measurement.
PAS 40.7224, **H&E**42.6453, **Mean Difference** -1.9229, **Mean of Means** 41.68385, **Std Error** 3.85107,**Upper 95%** 6.46783, **Lower 95%** -10.314, **t-Ratio** -0.49932, **Prob**>0.6266

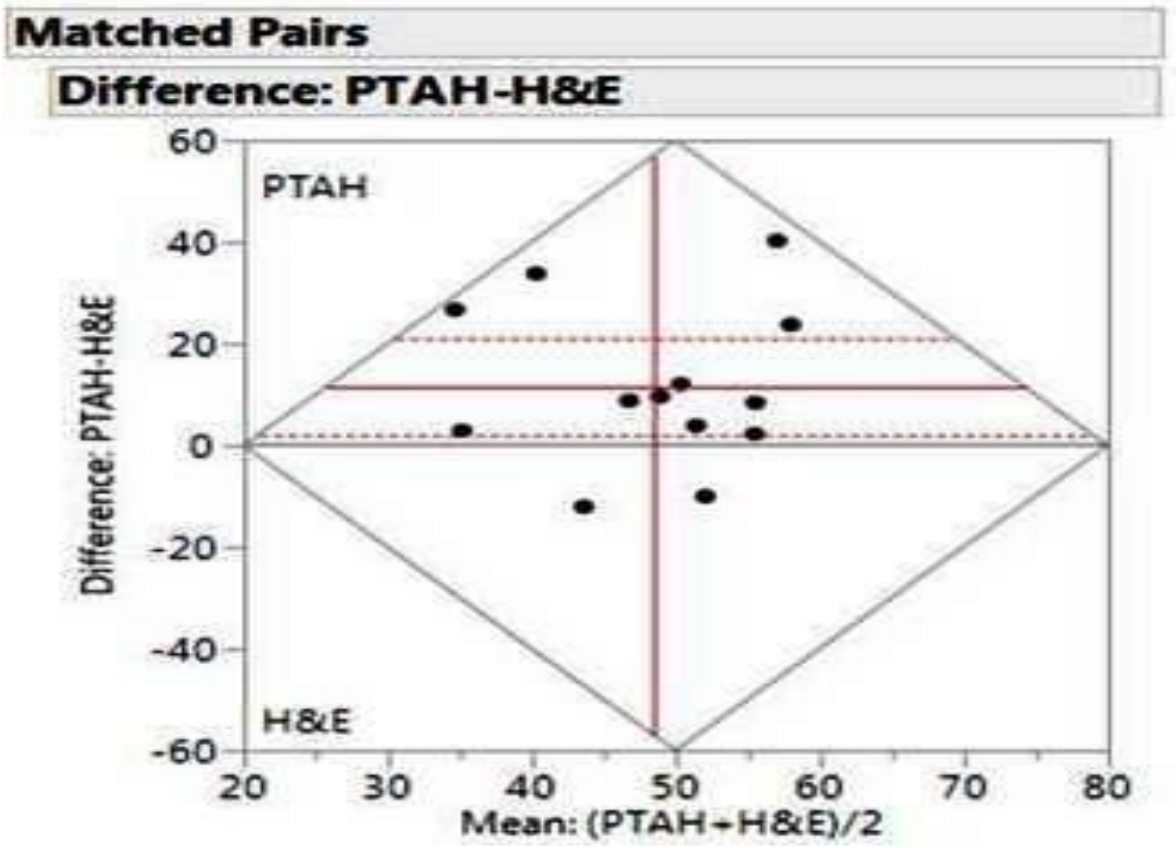


Figure 4.12: Comparison of PTAH and H&E on % Area Measurement.
PTAH 54.1834, **H&E**42.6453, **Mean Difference** 11.5381, **Mean of Means** 48.41435, **Std Error** 4.35613,**Upper 95%** 21.0293, **Lower 95%** 2.04689, **t-Ratio** 2.628699, **Prob**>0.0212*

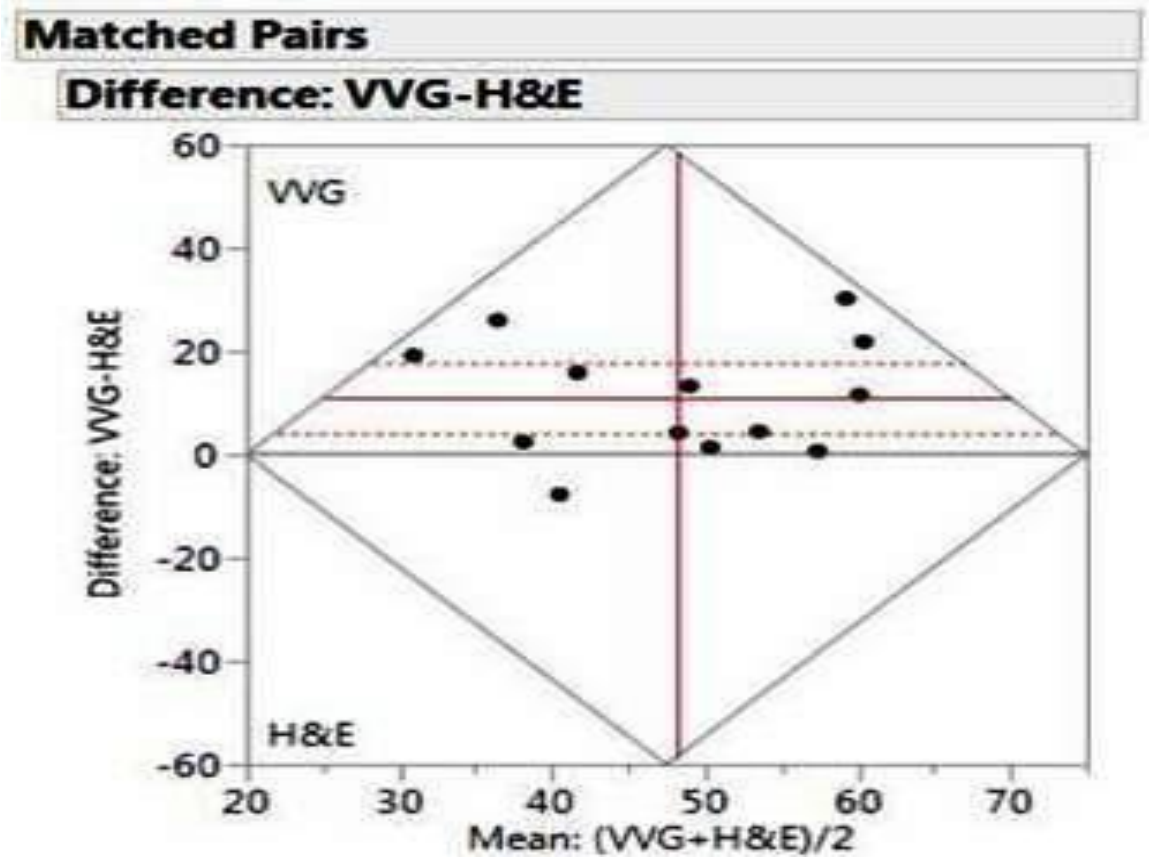


Figure 4.13: Comparison of VVG and H&E on % Area Measurement.
VVG 53.6539, **H&E**42.6453, **Mean Difference** 11.0086, **Mean of Means** 48.1496, **Std Error** 3.12187,**Upper 95%** 17.8106, **Lower 95%** 4.20665, **t-Ratio** 3.526294, **Prob**>t 0.0021*

4.11 Variability Analysis of Intensity by different Staining Techniques

The intensity measurement of stain similar to % area is dependent on the type of stain and tissue. The mean intensity measurement for the different types of gynaecological tissues impacted by the different stains was 122.232. While mean intensity measurement for stains used on adenocarcinoma was 128.042, adenoma 122.173, adenomyosis 139.927, Brenner tumour 110.195, choricarcinoma 123.204, condyloma A. 120.767, demoid cyst 131.570, endometria hyperplasia 120.093, endometria polyp 126.251, fibroma 132.957, leiomyoma 118.318, mucinous cyst 124.189 and squamous cell carcinoma 91.3286.

The intensity of H&E stain in adenocarcinoma was 111.172, MT 106.119, PAS 127.586, PTAH 118.249 and VVG 131.193. In adenoma the intensity was 120.828for H&E, MT 80.290, PAS 107.343, PTAH 97.295and VVG 150.602. In adenomyosis H&E intensity was 161.410, MT 107.908, PAS 181.255, PTAH 102.001 and VVG 134.354. In Brenner tumour the intensity of H&E was 101.007, MT was 78.468, PAS 132.407, PTAH 61.856 and VVG 97.253. In choricarcinoma, the intensity was 108.529 for H&E, MT was 72.472, PAS 145.026, PTAH 90.955 and VVG 128.349. In Condyloma, H&E intensity was 118.809, MT 61.951, PAS 139.943, PTAH 86.234 and VVG 120.478. In demoid cyst biopsy, H&E intensity was 140.502, MT 74.824, PAS 160.405, PTAH 98.384 and VVG 163.407. In endometrial hyperplasia, H&E intensity was 127.362, MT 88.764, PAS 145.724, PTAH 96.836 and VVG 125.222. In endometrial polyp H&E was 118.905, MT 89.446, PAS 140.975, PTAH 71.680 and VVG 135.743. In fibroma, H&E intensity was 162.312, MT 65.361, PAS 175.104, PTAH 88.549 and VVG 149.600. In leiomyoma, H&E intensity 109.216, MT 95.682, PAS 56.120%, PATH 89.307 and VVG 113.424. The intensity of H&E on mucinous cyst was 115.391, MT 74.924, PAS 201.830, PTAH 65.544 and VVG 121.427. In squamous cell carcinoma, H&E intensity was 92.077, MT 55.557, PAS 69.710, PTAH 67.722 and VVG 75.052 as presented in table 4.13. Table 4.16 shows the statistical comparison of biopsy and the stain intensity, which was significant.

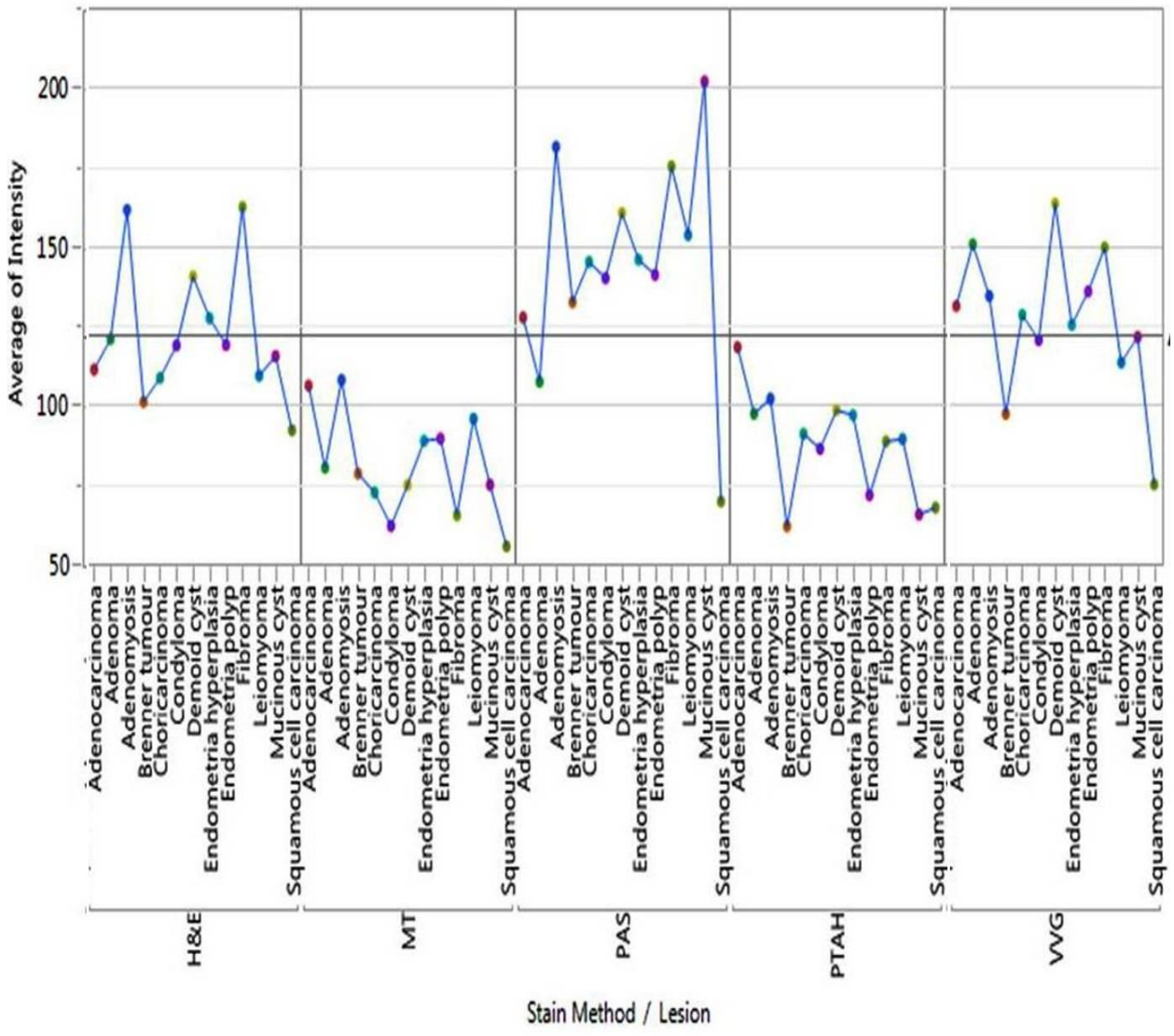


Figure 4.14: Chart for Average Intensity Measurement by Biopsy within Stain Methods

4.12 Variability Analysis for Intensity Measurement of Benign and Malignant

Table 4.17 and figure 4.15 shows the mean intensity measurement of benign and malignant biopsies. The mean intensity of 127.5742 and 103.926 in benign and malignant biopsies respectively. While MT mean intensity was 81.7618 in benign biopsies and 78.04933 malignant. PAS mean intensity was 153.852 in benign and 114.1073 in malignant. PTAH mean intensity was 85.7686 in benign and 92.30867 in malignant. VVG mean intensity was 131.151 in benign and 111.5313 in malignant biopsies.

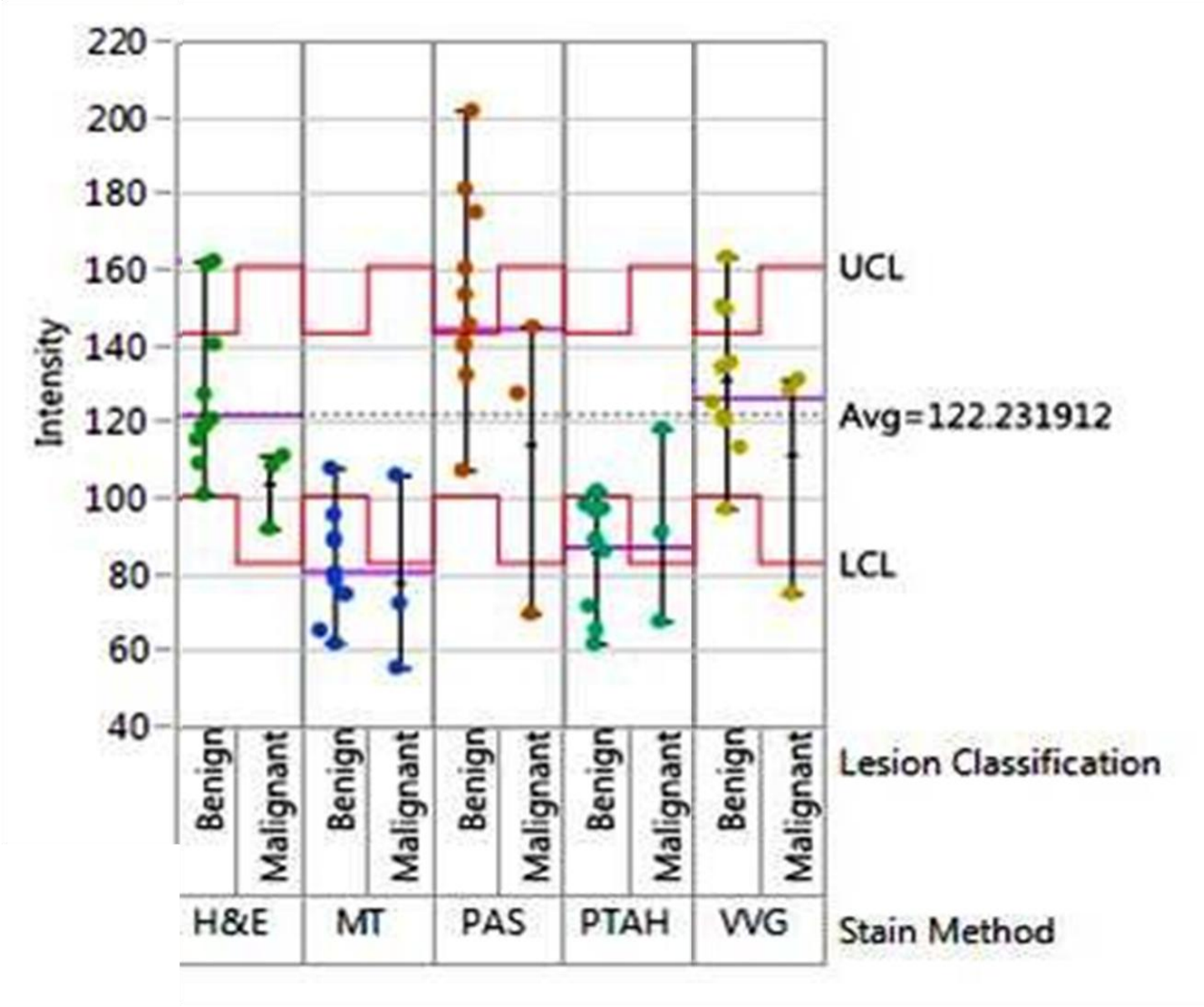


Figure 4.15: **Variability Chart for Intensity Measurement for Benign and Malignant Biopsy**

Table 4.11: Variability Summary for Intensity Measurement for Benign and Malignant Biopsies

Stain Method By Biopsy Classification	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%	Minimum	Maximum	Range	Median
[H&E] [Benign]	127.5742	20.8367	6.589144	112.6685	142.4799	101.007	162.312	61.305	119.8665
[H&E] [Malignant]	103.926	10.34628	5.973426	78.22442	129.6276	92.077	111.172	19.095	108.529
[MT] [Benign]	81.7618	13.96357	4.415668	71.77286	91.75074	61.951	107.908	45.957	79.379
[MT] [Malignant]	78.04933	25.73828	14.86	14.11191	141.9868	55.557	106.119	50.562	72.472
[PAS] [Benign]	153.852	27.07155	8.560776	134.4862	173.2178	107.343	201.83	94.487	149.629
[PAS] [Malignant]	114.1073	39.42564	22.7624	16.16862	212.046	69.71	145.026	75.316	127.586
[PTAH] [Benign]	85.7686	14.44448	4.567746	75.43564	96.10156	61.856	102.001	40.145	88.928
[PTAH] [Malignant]	92.30867	25.29068	14.60158	29.48312	155.1342	67.722	118.249	50.527	90.955
[VVG] [Benign]	131.151	19.71307	6.233819	117.0491	145.2529	97.253	163.407	66.154	129.788
[VVG] [Malignant]	111.5313	31.62402	18.25813	32.97292	190.0897	75.052	131.193	56.141	128.349

4.13 Matched Pairs Analysis of Stains Intensity

The matched pairs analysis of the intensity measurements by staining methods. Tissues stained using MT and PTAH techniques produced the most intense mean measurements that were 34% (80.9 pts) and 29% (87.3 pts) better than those produced from tissues stained with H&E, which served as the standard. On the other hand, intensity measurement for tissues stained with PAS performed poorly being 33% (162.9 pts) and 18% (144.7 pts) less intense than those stained with H&E (Figures 4.16-4.19).

4. 14 Pair-wise correlation of staining methods

Tables 4.12 and 4.13, show the pair-wise correlation of % area and intensity measurement by staining methods. With reference to % area, except for significant correlations noted between PAS and H&E ($r = 0.599$, $p = 0.030$) and PAS and MT ($r = 0.572$, $p=0.041$), all other staining methods were not statistically significant ($p > 0.05$). Similarly, our study noted significant correlations in intensity measurements by staining methods as follows; PAS and H&E ($r = 0.615$, $p=0.025$), VVG and H&E ($r = 0.707$, $p = 0.007$) and, VVG and PTAH ($r = 0.577$, $p =0.038$).

Comparison of Stain Methods based on Intensity Measurements

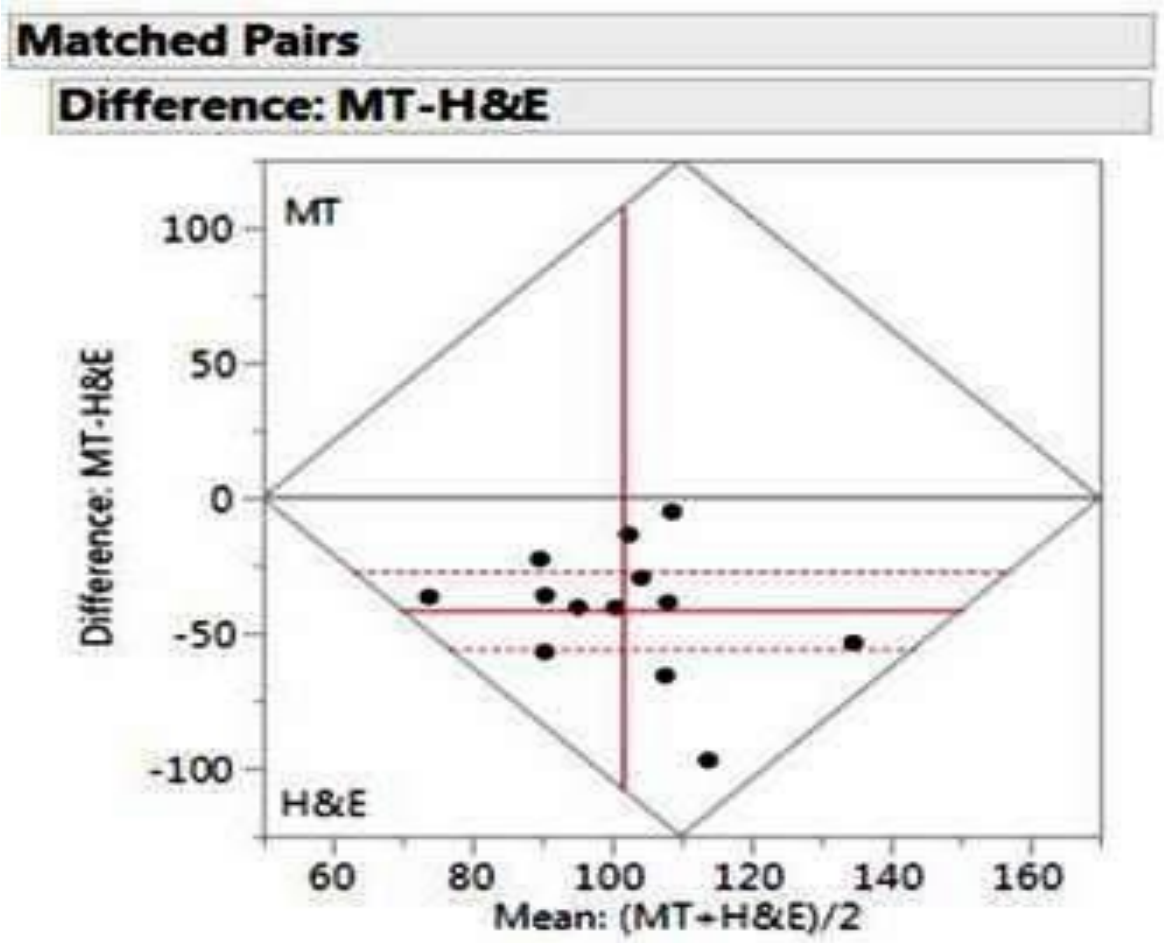


Figure 4.16: Comparison of MT and H&E on Intensity Measurement.
MT 80.9051, **H&E** 122.117, **Mean Difference** -41.212, **Mean of Means** 101.511, **Std Error** 6.56235, **Upper 95%** -26.914, **Lower 95%** -55.51, **t-Ratio** -6.28004, **Prob**> 0.0001*

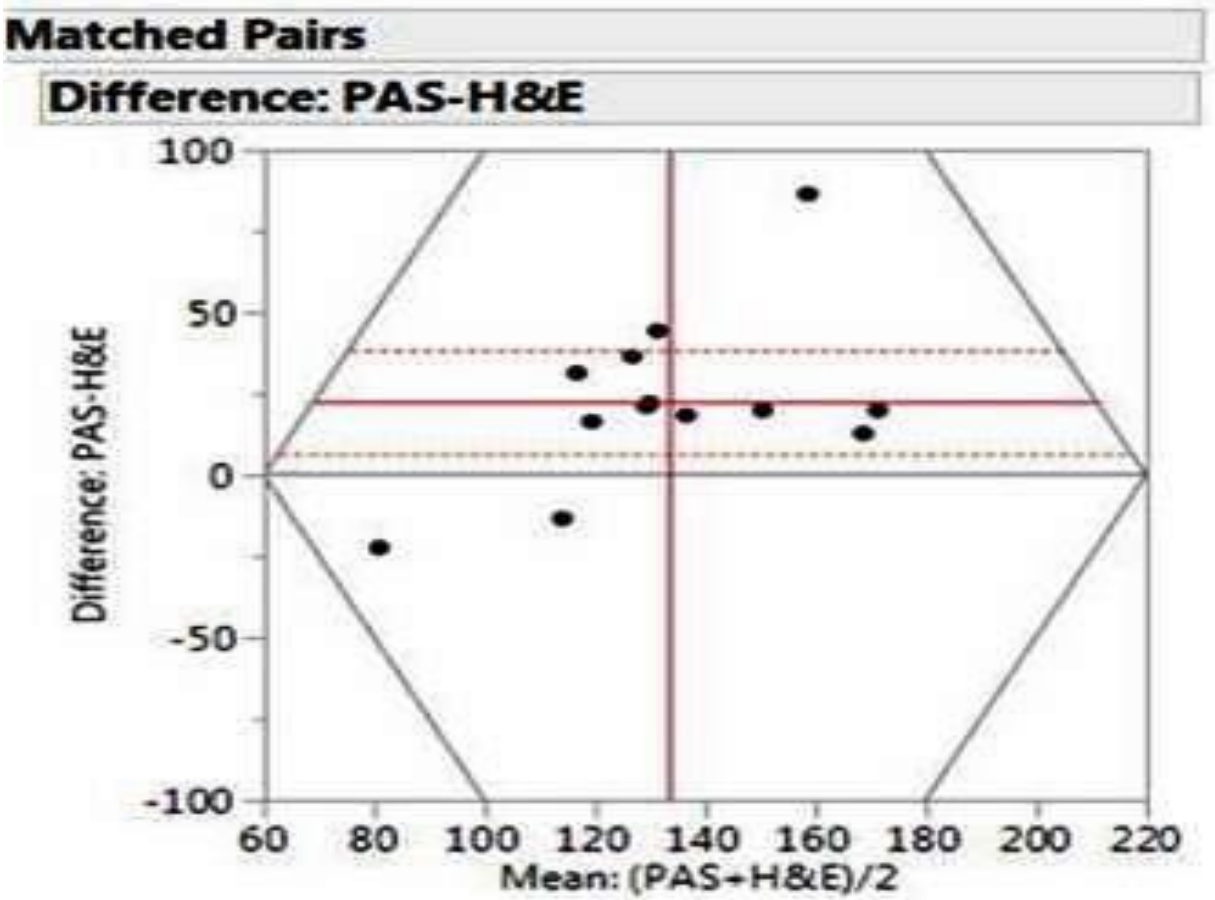


Figure 4.17: Comparison of PAS and H&E on Intensity Measurement.
PAS 144.68, **H&E** 122.117, **Mean Difference** 22.5632, **Mean of Means** 133.3985, **Std Error** 7.29924, **Upper 95%** 38.4669, **Lower 95%** 6.65955, **t-Ratio** 3.091174, **Prob**>t 0.0047*

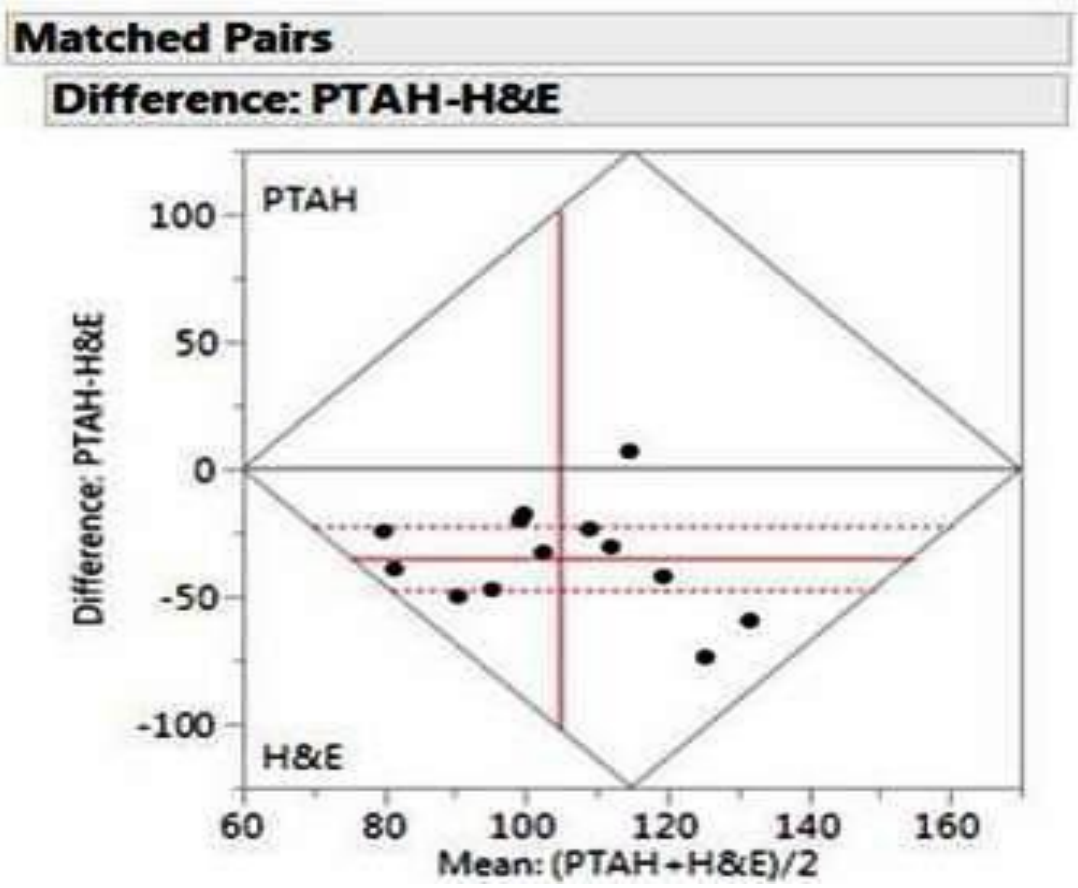


Figure 4.18: Comparison of PTAH and H&E on Intensity Measurement.
PTAH 87.2778, **H&E** 122.117, **Mean Difference** -34.839, **Mean of Means** 104.6974, **Std Error** 5.72242, **Upper 95%** -22.371, **Lower 95%** -47.307, **t-Ratio** -6.08817, **Prob**> 0.0001*

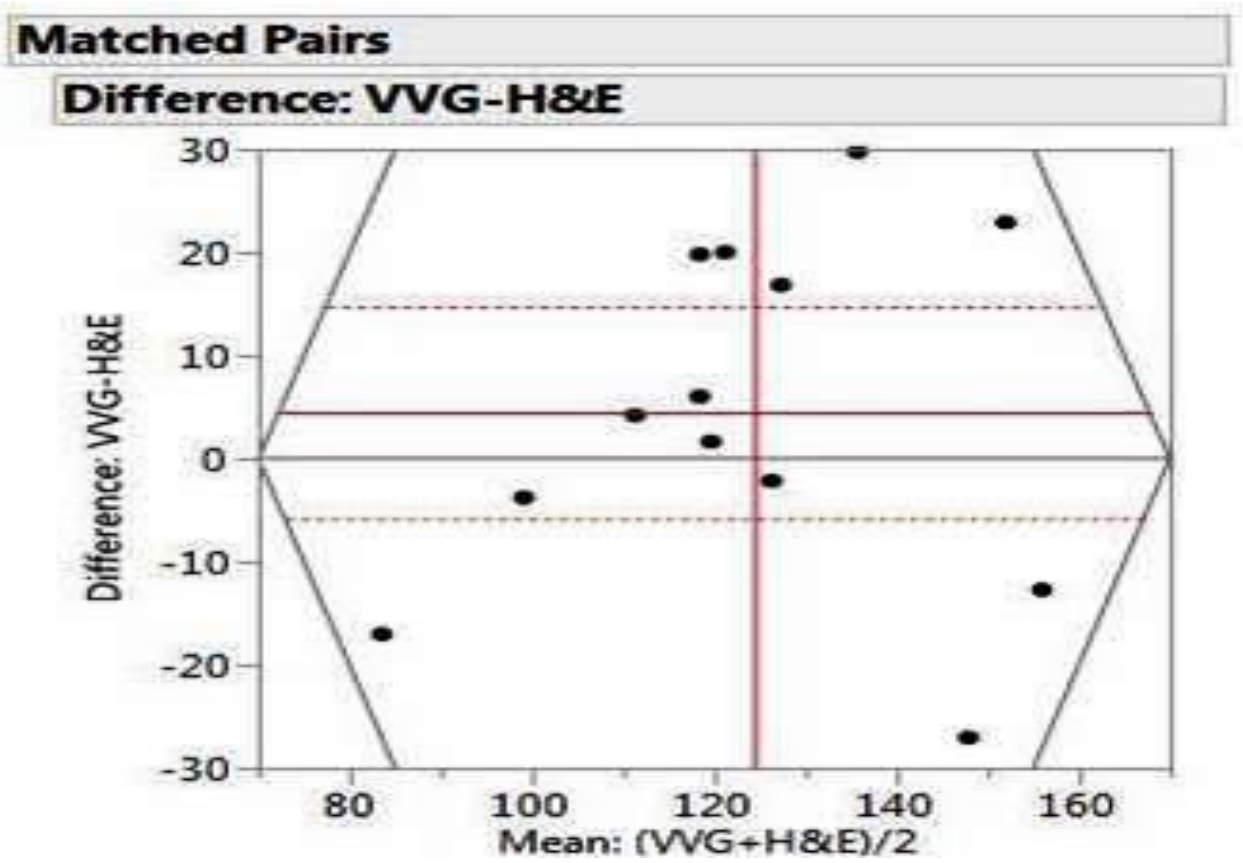


Figure 4.19: Comparison of VVG and H&E on Intensity Measurement.
VVG 126.623, **H&E** 122.117, **Mean Difference** 4.50646, **Mean of Means** 124.37, **Std Error** 4.7254, **Upper 95%** 14.8022, **Lower 95%** -5.7893, **t-Ratio** 0.953668, **Prob**< 0.8205

Table 4.12: Pair wise Correlation of % Area Measurements by Stain Methods

Variable	by Variable	Correlation	Lower 95%	Upper 95%	Significant Probability	Graphical Representation
MT	H&E	0.1069	-0.4719	0.6213	0.7281	
PAS	H&E	0.5993	0.0722	0.8648	0.0304*	
PAS	MT	0.5722	0.0310	0.8540	0.0410*	
PTAH	H&E	0.0054	-0.5472	0.5548	0.9859	
PTAH	MT	-0.0343	-0.5744	0.5266	0.9114	
PTAH	PAS	-0.0192	-0.5642	0.5375	0.9503	
VVG	H&E	0.5106	-0.0562	0.8285	0.0746	
VVG	MT	0.1407	-0.4448	0.6419	0.6467	
VVG	PAS	0.3383	-0.2614	0.7496	0.2582	
VVG	PTAH	-0.1608	-0.6538	0.4282	0.5998	

Table 4.13: Pair wise Correlation of Intensity Measurements by Stain Methods

Variable	by Variable	Correlation	Lower 95%	Upper 95%	Significant Probability	Graphical Representation
MT	H&E	0.2200	-0.3766	0.6876	0.4702	
PAS	H&E	0.6147	0.0964	0.8708	0.0254*	
PAS	MT	0.2783	-0.3221	0.7190	0.3572	
PTAH	H&E	0.4240	-0.1657	0.7903	0.1488	
PTAH	MT	0.5446	-0.0091	0.8427	0.0543	
PTAH	PAS	0.0723	-0.4986	0.5994	0.8145	
VVG	H&E	0.7072	0.2559	0.9054	0.0069*	
VVG	MT	0.2495	-0.3496	0.7037	0.4111	
VVG	PAS	0.4759	-0.1018	0.8136	0.1002	
VVG	PTAH	0.5772	0.0384	0.8560	0.0389*	

CHAPTER FIVE

5.0 DISCUSSION

The results of this research revealed that out of 697 gynaecological biopsies reported in the period of study, the highest (26.7%) occurred in 2013, it was closely followed by 22.7% in 2012, third most occurring year was 2010 (22.5%) which is approximately the same as 2012. The year 2011 recorded 21.5% and the least occurred in 2014 with only 6.6% and there was significant difference ($p<0.0001$) in the various years of distribution. Apart from 2014 that recorded a sharp drop in the number of biopsies, which was due to industrial action, the outcome was comparatively stable as they were all in the same range despite slight increase. This is at variance with an earlier work on cervical cancer in Port Harcourt where a fluctuating outcome from 2007 to 2009 was reported (Onyije *et al.,* 2010).

A massive 98.9% of the gynaecological biopsies occurred in adults with only 1.1% occurring in both infants and teenagers. This is in agreement with the research of You *et al.* (2005) who reported that gynaecological biopsies in children and adolescents are rare compared to adults.

The mean occurring age of gynaecological biopsies recorded in this research was 39.1 years and the peak age group was 30-39 years accounting for 39.5%. Age group 30-39 years recorded the highest in all the years studied. In 2010 it was 46.4% while 2011 30.4% was reported, in 2012, 2013 and 2014 the age group maintained the lead with 37.4%, 40.9% and 45.7% respectively. There has not been any holistic report on the peak age for the entire gynaecological biopsies rather in parts. Nwachokor and Forae (2013) reported a peak age range of non-neoplastic cervical biopsies in Warri as 40-49 years accounting for 33.7%. Okeke *et al*. (2013) in Enugu reported a peak age of 51-60 years for female genital malignancies. They observed that the late presentation might be due to low awareness, perception to seek for medical advice, lack of health care providers and policy makers, absence or poor quality of screening programs, limited access to health care services, and lack of functional referral systems (WHO, 2006).

Sulayman *et al*. (2013); Abubakar *et al. (*2011); Okusanya *et al.* (2006) and Moronkolu and Uzegbu (2006) have reported that the mean age of menarche is 12.53 and 13.67 years in the North, 13.6 in the West, 13.9 and 13.4 in the South. Other investigators noted that mean age for menopause is 46.2 in North, 48.4 in West and 49.4 in South (Achie *et al*., 2011; Ozumba *et al*., 2004). In the light of the above, the biopsies were regrouped into reproductive status classified as menopausal, premenarchal and postmenarchal. Postmenarchal recorded the highest with 512 biopsies representing 77% in 5 years. In 2010 79.7% of biopsies were from

postmenarchal women while in 2011 postmenarchal was still highest with 73.9%. In 2012, 2013 and 2014, were 74.1%, 78.5% and 80.4% respectively.

Forae and Aligbe (2013) reported that endometrial biopsies are ranked among the most common gynaecological disorders that affect women globally, cutting across all ages and contribute significantly to increased maternal morbidity and mortality. In this present study, the endometrium was seen as the site most prone to biopsies with 526 out of 697 biopsies representing 75.5%. The second most prone part was the ovary with 11.5% and closely followed by the cervix 10.8%. The vulva was the fourth with only 1.9% of the biopsies, fallopian tube and vagina were 0.3% and 0.1% respectively. The high prevalence of the biopsies on the endomentrium has been attributed to several causes including exogenous estrogen without progesterone (Lethaby *et al*., 2004), defective immune response (Sinaii *et al.*, 2002), retrograde menstruation, apoptosis suppression and alteration of endometrial cell fate, familial aggregation amongst others (Samer *et al.,* 2014). Zanotti (2010) reported that endometrial cancer is the most common of the gynecologic malignancies. She further added that approximately 2 to 3% of women in the United States will develop cancer of the endometrium at some point during their lives. It is the fourth most common malignancy among women. It predominantly affects older women, with 75% of cases occurring in the postmenopausal years. The result of this research also agrees with the result of Nnamdi *et al*. (2014), who recorded 11.4% and 0.3% for the ovary and vagina respectively.

On year-to-year basis, the endometrium was also the most affected site with 77.1% in 2010, 67.3% in 2011, 75.9% in 2012, 80.6% in 2013 and 73.9% in 2014.This is not in line with the findings in Sokoto by Nnamdi *et al*. (2014), where 69% of the biopsies were seen in the cervix. Our result for the vagina is also similar to the research on the pathology of vagina cancers by Seleye-Fubara *et al*. (2007) where 0.63% was reported. In Enugu Okeke *et al.* (2013) reported 0% biopsy on the vagina. Most of the biopsies (66.0%) in this research originated from muscle tissue and 23% originated from epithelial tissue. Sex cord stroma biopsies were 10.4% while the least were biopsies from connective tissue (0.3%) and blood vessel (0.3%) origin. This result did not agree with the result of Sanni *et al.* (2013) who reported biopsies of epithelia origin (61.2%) as the highest in malignancies and their least were tissue of sex cord/ stroma origin (16.1%).

There was disparity in the region of occurrence based on age, as the youngest and oldest groups were not endometrial predominant. Ovarian cyst (58.3%) was prevalent among age 0-19 years, while in the oldest group (70 and above years) the biopsies of the cervix were more prevalent with 54.1%. The other age groups; age 20-29, 30-39, 40-49, 50-59 and 60-69 years all recorded high prevalence in endometrium 71.8%, 83.3%, 86.5%, 60.9% and 54.9% respectively. Typically, ovarian cysts are frequently seen in young females due to failure of ovulation. However, fewer cases could also be seen in older women, studies have shown that 90% of these cysts are resolved spontaneously (Forae and Aligbe, 2014).

Biopsies are classified into benign, premalignant, malignant and inflammatory (Rao, 2012; Philippi *et al*., 2003). Out 697 biopsies, benign biopsies were 600 representing 86.1%, followed by inflammatory with 56 biopsies representing 8.0%. The third was malignant with 32 representing 4.6%, and the least was premalignant with only 9 biopsies representing 1.3%. This data obviously shows that benign biopsies are more prevalent than their malignant counterpart. Having the bulk of the biopsies in 2010 (81.5%), 80.7% in 2011 and 88.0% in 2012. In the same vein, 2013 was 91.4% while 2014 was 91.3%.The age categories also validates the preponderance of benign biopsies as all the age groups recorded high number of benign biopsies.This finding agrees with previous report by Ozumba *et al*. (2011) in Enugu, Nigeria, where benign biopsies were 82.6% as against 17.4% for malignant biopsies. Nwachokor and Forae (2013) in Warri also reported that benign biopsies (56.3%) were more common than malignant biopsies (43.7%).

Leiomyoma, which is uterine fibroid, is the most common biopsy in this research with 390 cases representing 56.0%. The second most common was ovarian cyst with 70 biopsies representing 10.0%. The preponderance of leiomyoma was on the steady increase from 2011. In 2010 it was 47.1% and in 2011 44.0%, 2012, 2013 and 2014 recorded 62.7%, 64.0% and 69.6% respectively. This is similar to the result of Mohammed *et al.* (2005) where leiomyoma (52.6%) was the highest among 19 biopsies in Zaria, Nigeria. In Gombe Nigeria, 54% of operative findings were fibroid (Bukar *et al*., 2010). In eastern part of Nigeria, it was lower with 25.9% (Ozumba *et al.*, 2011) when compared with the results from the north and the present research, though the highest among other biopsies. The result of this research is also in line with the research of Nnoli *et al*. (2013), where it was reported that 1 in every 5 women of child bearing age of over 30 years had fibroids and that 20-30% of women of this age harbour uterine fibroids thus accounting for 3.2 –7.6% of new gynaecological cases and

68.1% of hysterectomies (Akinyemi *et al.,* 2004). On the other hand, ovarian cyst, which is the second highest (10.0%), did not agree with the result of Ikechebelu (2005) in Nnewi where 0.67% was reported as the prevalence of ovarian cyst in gynaecological diseases.
Retained Products of conception which is the 3rd most prevalent biopsy in this study are complication of labour and delivery. The retained tissue can cause prolonged postpartum hemorrhage and endometritis. The usual treatment is curettage, which results in further complications in 7% of patients, including uterine perforation, cervical laceration, and subsequent synechia formation. Retained products of conception are suspected when routine examination of the placenta at delivery reveals an incomplete placenta or when a patient has signs of endometritis or prolonged vaginal bleeding in the postpartum period (Durfee *et al*., 2005). In most centres, it is a routine practice to submit tissues obtained by uterine evacuation for histopathologic examination to confirm the presence of intrauterine fetal tissue. The main rationale is to detect an ectopic pregnancy, which requires immediate further management, or a molar pregnancy, which necessitates special follow up. Other reasons include detecting surgical complications, such as incomplete or failed pregnancy evacuation; determining the cause of recurrent pregnancy loss; or detecting unexpected fetal pathology (Sharifa, 2014).
Retained products of conception in this present research recorded 56 cases representing 8.0% with peak age range of 20-39 years (figure 4.5), which is lower than the findings of other authors. This may not reflect the number of criminal abortions in Port Harcourt as some may be due to miscarriages from married women. Forae and Aligbe (2013) reported that product of conception was the most commonly encountered among reproductive women in Benin city with 27.7%, Ozumba *et al.* (2011) reported 20.7% in Enugu with mean age range of 24.9-36.9 years.

Cervical inflammation may be acute or chronic. Each of these may be as a result of non-infective or infective causes. Non-infective cervicitis is most often caused by chemical while infective consist commonly of sexually transmitted diseases (Omoniyi-Esan *et al.,* 2006). Chronic Cervicitis was the fourth most prevalent biopsy in this research with 6.3% is lower compared to 17.1% reported by Jesmin *et al*. (2014). Nwachokor and Forae (2013), also reported a higher prevalence of 52.2% for chronic cervicitis.

Four percent of the biopsies recorded in this work were endometrial hyperplasia, while 2% were endometrial polyp. This is low compared to the research of Abid *et al.* (2014) who reported 14% for endometrial polyp and 5% for endometrial hyperplasia. Azim *et al*. (2011)

also reported increased frequency of endometrial polyp with advancing age 5%, 8% and 11% in reproductive, perimenopausal and postmenopausal age groups respectively.

The development of adenocarcinoma arising from adenomyosis is a relatively rare occurrence (Natsuki *et al*., 2013). In this present research, the frequency of adenocarcinoma, adenoma and adenomyosis were 1.3, 0.7 and 3.0% respectively. The finding for adenocarcinoma agrees with the report of Yakasai *et al*. (2013) who also recorded low frequency of 3.5%. Prevalence of CIN in this study was lower (1.3%) than the result of Adisa *et al*. (2013) who reported 12.8% in Zaria, but the result of the prevalence of condyloma A. (0.7%) agree with the findings of Vittori *et al.* (2008) who reported a prevalence range between 0.03% and 0.6% this is further corroborated by Pasciullo *et al*. (2011) and Lee *et al*.(2010).

Cervical cancer has been reported severally by researchers as the commonest malignancy of the female genital tract in developing countries. However, this has been mostly through pap smear screening. The histopathological tissue block screening of squamous cell carcinoma in this present research show low prevalence of 1.9%. This is similar to the 5% (20 cases) of squamous cell carcinoma reported in a clinico-pathological assessment of hysterectomies (Samaila *et al*., 2009).

5.1 PREDICTION OF GYNAECOLOGICAL LESIONS

Over the next fifty years, gynaecological biopsies are projected to change due to population growth, which is one of the largest contributors to the increasing total number of gynaecological cases (ACS, 2007; Boyle and Levin, 2008). The world population as at 2015 was 7.3 billion and Nigeria was 183.5 million, this number is expected to increase to 9.7 billion and 440 millions in the world and Nigeria respectively by 2050 (CBP, 2016; WPP, 2016; United Nations, 2015).

Leiomyoma which has been predicted to rise from 235 to 1883 by 2050, generally research has shown that high incidence of leiomyoma occurs within age 35 (Day *et al*., 2003; Laughlin *et al*., 2010), and early menarche has also been identified as a factor (Schwartz, 2001; Purdie and Green, 2001; Colditz, 1993). According to Baird and Dunson (2003); Parazzini (2006) and Wise *et al*. (2004) parity and pregnancy are contributory factors to the rise in cases of leiomyoma. Other factors include caffeine intake (Laughlin *et al.,* 2010), estrogen and progesterone. Research has shown that estrogen influences the growth of leiomyoma and decreased estrogen regresses it's growth (Medikare et al., 2011). Flake *et al* (2003) reported

high concentrations of estrogen receptor in leiomyomata than other biopsies (Medikare *et al*., 2011). Estrogen dominance is a complex situation caused by excess exposure to environmental xenoestrogens (made up of hydrocarbons) which may arise from oil and gas exploration (Holly, 2016). Ngokere *et al*. (2014) has earlier reported increased estradiol and decreased progesterone in rabbits administered with escravos crude oil.
The use of synthetic estrogens such as the birth control pill and hormone replacement therapy; anovulation which is common among women older than 35; unresolved emotional issues; poor diet; and negative lifestyle factors such as smoking and alcohol are also contributing factors use among others.

There has been little or no documentation on prediction estimation of biopsies in Nigerian tertiary hospitals. In the United States of America, it was reported that leiomyoma related hospitalized cases will rise from 37,134 in 2010 to 49,154 in 2050 with an increase of 22% in black women and 8% in white women (Wechter *et al*., 2011). This is lower compare to the 700% increase (235 to 1883 by 2050) in the present work.

Similarly, ovarian cysts which were predicted to increase from 57 to 461 by 2050 is higher than the projection for Ireland, where it was reported that ovarian cyst will increase from 407 cases in 2015 to 662 by 2040 (Cancer projections for Ireland, 2016). Product of Conception will increase from 34.729 at the rate of 0.075 to 277.834 by the year 2050.
The study of histopathology requires the use of dyes to aid differentiation of cells and tissue components. Choriocarcinoma which is a malignant trophoblastic tumor, usually of the placenta. Its characteristic feature is the identification syncytiotrophoblasts and cytotrophoblasts (Clement and Young, 2014). Choriocarcinoma stained with H&E and PAS displayed malignant trophoblast (M-Troph) and mitotic cell better than other techniques used in this work. While the core of chorionic villi (CV) was better revealed in Masson's trichrome and phosphotungstic acid haematoxylin, the Syncytiotrophoblast (Syn) was also better stained in Masson's trichrome and PAS than others. Southgate's Mucicarmine, Alcian Blue and Voehoff's Van Gieson did not reveal distinct components of choriocarcinoma (Figure 4.11). Condyloma A. was adequately demonstrated in H&E and PAS but the features (acantosis and koilocytosis, epidermal inflammatory cells and dermal inflammatory cells, inflammation of the dermal papilla and stratum basale) were better demonstrated in Masson's trichrome and VVG. The features of condyloma were poorly demonstrated in alcian blue, PTAH and Southgate's Mucicarmine. In Brenner tumour, the features (follicle with portions

of mixed cells of transitional, squamous and cuboida epithelium. Atrium of the follicle with malignant cells scattered in the stroma. Mucinous epithelia and connective tissue invasion) were well demonstrated in all the staining techniques except in PTAH. While in endometrial hyperplasia, Masson's trichrome displayed the features (proliferation of cystically dilated and non-dilated endometrial glands with proliferating pseudostratified epithelial cells) more distinctly. Alcian blue did not display the glands of endometrial hyperplasia. Photomicrograph of squamous cell carcinoma in all staining technique in the current study demonstrated the features (squamous cell invasion and keratinous pearls) adequately. Leiomyoma features were better displayed in PTAH and VVG than in other staining techniques, as the inter lacing buddles of smooth muscles were well demonstrated. This is similar to the report of Dettmeyer (2011) who reported that PTAH demonstrates smooth and striated muscle. Robert *et al.* (2013) also reported that VVG can be used to distinguish between elastic, collagen and muscle fibres. The proliferation of glands in adenoma was properly demonstrated in all the techniques except in PTAH and Alcian blue (Figures 4.11-17).

The human eye is sensitive to a number of factors including luminosity and variation in contrast and brightness. Hence, critical visual analysis is open to subjective interpretation. The essence of morphometry is to eliminate subjectivity and increase the reproducibility of measurements (Andrea *et al.,* 2008). The quantification of percentage area covered by different stains on different tissues as well as the intensity measurement have not been given due attention which has resulted to lack of improvement in routine staining procedures. Recent advances in computer image analysis techniques allow more accurate quantification of histopathological biopsies (Jensen, 2013; Rangan and Tesch, 2007). ImageJ is a public domain, Java-based image processing program developed at the National Institute of Health (Schneider *et al.,* 2012; Collins, 2007) in 1997 but Prior to the release of ImageJ, a similar freeware image analysis program known as *NIH Image* had been developed (NIH, 2016). ImageJ is used in quantitative analysis of histological staining among others (Ellen, 2013).

The % area of the tissue covered by stain is dependent on the type of stain and tissue. In this present research, the mean % area for the different types of tissues covered by the different stains was 47.881%. The tissue with the highest % area cover was Leiomyoma with 57.984%, followed closely by Brenner tumour with 56.353%, the least was Demoid cyst 37.826%.This in is an indication that muscle cells of leiomyoma has the capacity to absorbed stain and has a

large surface area, as a result of its dense, whorled and anastomosing fascicles with elongated cytoplasm and nuclei that have finely dispersed chromatin (Vanni, 2016). Ijomone and Obi(2013) reported a mean % area of 52.88% in the hippocampus which is lower than the % area of leiomayoma (57.984%) and Brenner tumour (56.353%) but higher than Demoid cyst (37.826 %.).

Similarly, the intensity measurement of stain is also dependant on the stain and type of tissue, using the standard scale of 0 to 255 from less brighter (that is more intensity) to more brighter (that is less intensity).The mean intensity measurement for stains used on adenocarcinoma was 128.042, adenoma 122.173, adenomyosis 139.927, Brenner tumour 110.195, choricarcinoma 123.204, Condyloma A. 120.767, Demoid cyst 131.570, Endometria hyperplasia 120.093, Endometria polyp 126.251, fibroma 132.957, Leiomyoma 118.318, Mucinous cyst 124.189 and Squamous cell carcinoma 91.3286. The intensity of stains on Squamous cell carcinoma (91.3286.) was more compared to other biopsies in this research. This can be attributed to the numerous deeply stained malignant cells of squamous cell carcinoma by the various staining technique. This is in agreement with the publication of The New Science of the British Association for the Advancement of Science which stated that premalignant cells take up stains two to three times more than normal cells (New Scientist, 2016).

The mechanisms of staining of tissue are histochemical in nature, which is the application of chemical substances on to a tissue in order to give a visible out come. To achieve this, tissue take up the stain either through chemical or through physical (adsorption, absorption, solubility, osmotic pressure and capillary attraction) (Avwioro, 2010) which could also affect the intensity and area covered.

The imageJ used measured the stained areas and intensity of the various biopsies. The three biopsies that had the largest % area covered by H&E were squamous cell carcinoma (57.082%), Brenner tumour (54.354%) and leiomyoma (51.340%).The most intensely stained biopsy was also squamous cell carcinoma (92.077) followed by Brenner tumour (101.007) and thirdly Choricarcinoma (108.529). Leiomyoma had the highest % area covered by MT stain with 69.415%, it was followed by Endometria hyperplasia with 53.224%. The three biopsies that covered the largest area in MT were adenomyosis (80.862%), Adenoma (79.111%) and Mucinous cyst (77.992%). Squamous cell carcinoma (55.557) was intensified in MT followed by condyloma A. (61.951) and fibroma (65.361). In PAS the greatest

percentage covered was in squamous cell carcinoma (80.665%), followed by Brenner tumour (56.808%) and Leiomyoma (80.665%). However, the three most intensified biopsies by PAS were Adenoma (107.343), Adenocarcinoma (127.586) and (132.407).While in PTAH, it was Fibroma (77.153%), Condyloma (69.851%) and Leiomyoma (80.665%) had more areas covered. Brenner tumour (61.856) was more intensely stained, the second was Mucinous cyst (65.544) and thirdly squamous cell carcinoma (67.722). VVG covered more of Adenoma (74.328%) followed by Endometria polyp (71.302%) and Brenner tumour (65.894%). The intensity of VVG was more on Squamous cell carcinoma (75.052), followed by Brenner tumour (97.253) and Leiomyoma (75.052). Based on the percentage area covered and the intensity of the various stains on gynaecological biopsies MT is the best stain for gynaecological biopsies. On the individual biopsies, MT was also the best stain for Adenocarcinoma, Adenoma, Choricarcinoma, Demoid cyst, Fibroma and Squamous cell carcinoma. The % area covered by stains and intensity aids the visualization of cells and tissue demonstrated. Poor coverage and intensity may obscure accurate and reliable diagnosis.

The tissues were regrouped into benign and malignant biopsies and percentage area covered by stain was measured. H&E recorded the same mean % area (42.6271 and 42.706) for both benign and malignant biopsies. In line with the use of H&E for general tissue architecture, this study reveals that H&E covers benign and malignant tissue equally. On the intensity, the mean intensity for malignant biopsies (103.926) was higher than that the mean intensity for benign biopsies (127.5742), which is due to the metachromatic nature of malignant cells. In the same vein MT also covered a very close % area (64.5121 and 63.95633) for benign and malignant tissue similar to H&E. In addition, the intensity measurement of malignant biopsies (78.04933) was more than the benign gynaecological biopsies (81.7618). Based on the findings in this work, MT has a higher coverage % area and intensity than H&E though the matched pair analysis indicates significant difference in both % area and intensity measurement, it was also observed that there was no strong correlation ($r = 0.10691$) between the % area of H&E and MT. It was the same on the intensity ($r = 0.22$) though better than % area. This result is similar to the result of Ouyang *et al.* (2010) who reported that MT is superior to H&E in all cases, they further summarized by stating that MT is a valuable tool when faced with difficulty in analysing autopsy tissues.

PAS covered % area of 40.0018% for benign and 43.12433% for malignant, while the intensity was 153.852 in benign and 114.1073 in malignant. On the other hand, PTAH

covered % area of 57.176% in benign and 44.208% in malignant. PTAH intensity was 85.7686 in benign and 92.30867 in malignant. VVG stained a % area of 54.8224 in benign and 49.759 in malignant biopsies. The intensity was 131.151in benign and 111.5313 in malignant biopsies. Comparing the staining techniques used in this series MT was the best for gynaecological biopsies, which further validates the statement of Ouyang *et al.* (2010) as earlier emphasised.

The matched pair analysis of the various stains on gynaecological biopsies indicated that the strongest correlation (r = 0.59934) exist between H&E and PAS in % area covered and in intensity measurement the strongest correlation (r = 0.707) was between H&E and VVG. This has not been reported previously.

5.2 CONCLUSION

Leiomyoma and ovarian cyst are the most prevalent gynaecological biopsies in BMSH and have been predicted to increase in the population to the range of 797%-815% in thirty-five years time. There has been little or no information on the prediction estimate of gynaecological biopsies in Nigerian tertiary hospitals. Therefore, our study is the first attempt at filling this knowledge gap, and we are hopeful that the data obtained will provide the needed basic information to engender interest among researchers and government agencies in addressing this important public health problem. However, application of effective intervention and control measures such as alteration of life style, vaccination against human papillomavirus (HPV), cytological screening, early clinical detection and treatment and improved therapy could help reduce incidence and mortality rates associated with these diseases. In addition, health care practitioners specializing in cancer care for women need to be alert to every opportunity to improve cancer screening and prevention among the growing, and aging female populations in Nigeria.

The quantitative and comparative analysis of MT in both % area and intensity measurements with other techniques in this study clearly demonstrates that MT is better than other staining methods. Therefore, MT is recommended for routine use alongside with H&E in diagnosis of gynaecological biopsies.

5.3 RECOMMENDATION

In line with the outcome of this work, the following are recommended;

1. The girl child should be encouraged to attend girls' school at the secondary level and special topics on reproductive health should be incorporated and taught in all their classes.
2. All women associations in churches, mosques and market places etc should take reproductive health education as one of their objectives emphasising on prevention, predisposing factors and regular check up.
3. Government should step up on strong advocacy for good reproductive health by ensuring that unending jingles in government owned radio and television stations are constantly heard.
4. A policy on reproductive health should be formulated and endorsed such that every woman attending clinic will have a few minutes check on her reproductive health.
5. Every gynaecological biopsy for analyses in the laboratory should be demonstrated with a second stain especially Masson's trichrome rather than just haematoxylin and eosin alone.
6. The need for quantitative examination and use of technology in the analysis of tissues in histopathology should be adopted as other disciplines have all gone automated.

5.4 CONTRIBUTIONS TO KNOWLEDGE

1. Leiomyoma and Ovarian Cyst are the most occurred gynaecological tumours in BMSH
2. Benign Lesions occur more in ypunger women, while inflammatory lesions occur more in older women.
3. Prediction of gynaecological lesions upto the year 2050 to aid policy formulation
4. Masson trichrome has the highest percentage area and the best intensity on gynaecological biopsies

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APPENDIX I

Table 1.1: Raw Dataset from BMSH Port Harcourt, Rivers State

S/N	Year	Age	Developmental Stage	Age group	Reproductive Status	Biopsy	Tissue Origin	Biopsy Class	Tissue Type
1.	2010	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
2.	2010	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
3.	2010	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
4.	2010	64	Adult	60+	Menopausal	Chronic Cervicities	Epithelial	Inflamatory	Cervix
5.	2010	64	Adult	60+	Menopausal	Brenner tumour	Epithelial	Benign	Ovary
6.	2010	64	Adult	60+	Menopausal	Endometrial hyperplasia	Muscle	Benign	Endometrium
7.	2010	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
8.	2010	37	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
9.	2010	44	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
10.	2010	44	Adult	40-49	Postmenarchal	Ovarian Cyst	Sex cord/Stroma	Benign	Ovary
11.	2010	44	Adult	40-49	Postmenarchal	Chronic cervicities	Epithelial	Inflamatory	Cervix
12.	2010	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
13.	2010	37	Adult	30-39	Postmenarchal	Chronic cervicities	Epithelial	Inflamatory	Cervix
14.	2010	37	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
15.	2010	74	Adult	60+	Menopausal	Cervical polyp	Epithelial	Benign	Cervix
16.	2010	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
17.	2010	38	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
18.	2010	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
19.	2010	32	Adult	30-39	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
20.	2010	25	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Malignant	Endometrium
21.	2010	26	Adult	20-29	Postmenarchal	Haemangioma	Blood vessels	Benign	Vulva
22.	2010	38	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
23.	2010	28	Adult	20-29	Postmenarchal	Ovarian cyst (serous)	Sex cord/Stroma	Benign	Ovary
24.	2010	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
25.	2010	52	Adult	50-59	Menopausal	Chronic Cervicities	Epithelial	Inflamatory	Cervix
26.	2010	30	Adult	30-39	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium

27.	2010	30	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
28.	2010	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
29.	2010	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
30.	2010	31	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
31.	2010	36	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
32.	2010	41	Adult	40-49	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
33.	2010	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
34.	2010	32	Adult	30-39	Postmenarchal	Yolk sac tumour (Hepatoid variant)	Sex cord/Stroma	Malignant	Ovary
35.	2010	1	Infant	0-19	Premenarchal	Vulva Wart	Epithelial	Benign	Vulva
36.	2010	25	Adult	20-29	Postmenarchal	Adenoma (serous)	Epithelial	Benign	Ovary
37.	2010	39	Adult	30-39	Postmenarchal	Cervical polyp	Epithelial	Benign	Cervix
38.	2010	42	Adult	40-49	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
39.	2010	39	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
40.	2010	31	Adult	30-39	Postmenarchal	Chronic endometritis	Epithelial	Inflamatory	Endometrium
41.	2010	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
42.	2010	76	Adult	60+	Menopsual	Squamous cell carcinoma	Epithelial	Malignant	Cervix
43.	2010	30	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
44.	2010	31	Adult	30-39	Postmenarchal	Product of conception(Partial hydatidiform mole)	Epithelial	Benign	Endometrium
45.	2010	36	Adult	30-39	Postmenarchal	Cervical polyp	Epithelial	Benign	Cervix
46.	2010	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
47.	2010	31	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
48.	2010	34	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
49.	2010	31	Adult	30-39	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Endometrium
50.	2010	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
51.	2010	34	Adult	30-39	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
52.	2010	43	Adult	40-49	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
53.	2010	30	Adult	30-39	Postmenarchal	Squamous cell carcinoma (Small cell)	Epithelial	Malignant	Cervix
54.	2010	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

55.	2010	44	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
56.	2010	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
57.	2010	62	Adult	60+	Menopausal	Adenoma (serous)	Epithelial	Benign	Ovary
58.	2010	35	Adult	30-39	Postmenarchal	Adenocarcinoma (serous)	Epithelial	Malignant	Ovary
59.	2010	46	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
60.	2010	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
61.	2010	50	Adult	50-59	Menopausal	Chronic Endometritis	Epithelial	Inflamatory	Endometrium
62.	2010	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
63.	2010	60	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
64.	2010	31	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
65.	2010	20	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
66.	2010	-				Leiomyoma	Muscle	Benign	Endometrium
67.	2010	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
68.	2010	36	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
69.	2010	66	Adult	60+	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
70.	2010	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
71.	2010	66	Adult	60+	Menopausal	Chronic Endomeritis	Epithelial	Inflamatory	Endometrium
72.	2010	1	Infant	0-19	Premenarchal	Haemangioma	Blood vessels	Benign	Vulva
73.	2010	61	Adult	60+	Menopausal	Chronic Cervicitis	Epithelial	Inflamatory	Cervix
74.	2010	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
75.	2010	46	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
76.	2010	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
77.	2010	54	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
78.	2010	32	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
79.	2010	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
80.	2010	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
81.	2010	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
82.	2010	43	Adult	40-49	Postmenarchal	Chronic Endocervitis	Epithelial	Inflamatory	Endometrium

83.	2010	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
84.	2010	36	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
85.	2010	27	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
86.	2010	34	Adult	30-39	Postmenarchal	Product of conception(Partial hydatidiform mole)	Epithelial	Benign	Endometrium
87.	2010	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
88.	2010	40	Adult	40-49	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
89.	2010	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
90.	2010	41	Adult	40-49	Postmenarchal	Chronic Endocercitis	Epithelial	Inflamatory	Endometrium
91.	2010	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
92.	2010	60	Adult	60+	Menopausal	Endometrial Carcinoma	Muscle	Malignant	Endometrium
93.	2010	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
94.	2010	61	Adult	60+	Menopausal	Endometrial Carcinoma	Muscle	Malignant	Endometrium
95.	2010	61	Adult	60+	Menopsual	Squamous cell Carcinoma	Epithelial	Malignant	Vulva
96.	2010	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
97.	2010	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
98.	2010	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
99.	2010	38	Adult	30-39	Postmenarchal	Chronic cervictis	Epithelial	Inflamatory	Cervix
100.	2010	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
101.	2010	61	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
102.	2010	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
103.	2010	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
104.	2010	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
105.	2010	36	Adult	30-39	Postmenarchal	Chronic vulvitis	Connective	Inflamatory	Vulva
106.	2010	22	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
107.	2010	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
108.	2010	22	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Fallopian tube
109.	2010	46	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
110.	2010	28	Adult	20-29	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium

111.	2010	39	Adult	30-39	Postmenarchal	Squamous cell carcinoma (small varient)	Epithelial	Malignant	Cervix
112.	2010	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
113.	2010	-				Leiomyoma	Muscle	Benign	Endometrium
114.	2010	27	Adult	20-29	Postmenarchal	Product of conception(Partial hydatidiform mole)	Epithelial	Benign	Endometrium
115.	2010	61	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
116.	2010	61	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
117.	2010	26	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
118.	2010	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
119.	2010	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
120.	2010	35	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
121.	2010	46	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
122.	2010	31	Adult	30-39	Postmenarchal	Adenocarcinoma (Mucinous cyst)	Epithelial	Malignant	Ovary
123.	2010	-				Leiomyoma	Muscle	Benign	Endometrium
124.	2010	22	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
125.	2010	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
126.	2010	27	Adult	20-29	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
127.	2010	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
128.	2010	-				Leiomyoma	Muscle	Benign	Endometrium
129.	2010	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
130.	2010	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
131.	2010	38	Adult	30-39	Postmenarchal	CIN	Epithelial	Premalignant	Cervix
132.	2010	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
133.	2010	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
134.	2010	47	Adult	40-49	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
135.	2010	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
136.	2010	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
137.	2010	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
138.	2010	46	Adult	40-49	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium

139.	2010	40	Adult	40-49	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
140.	2010	16	Teenager	0-19	Postmenarchal	Vulva cyst	Epithelial	Benign	Vulva
141.	2010	70	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
142.	2010	70	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
143.	2010	42	Adult	40-49	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
144.	2010	39	Adult	30-39	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
145.	2010	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
146.	2010	25	Adult	20-29	Postmenarchal	Endometrial Polyp	Muscle	Benign	Endometrium
147.	2010	27	Adult	20-29	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
148.	2010	28	Adult	20-29	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
149.	2010	63	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
150.	2010	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
151.	2010	18	Adult	0-19	Postmenarchal	Ovarian Cyst	Sex cord/Stroma	Benign	Ovary
152.	2010	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
153.	2010	49	Adult	40-49	Menopausal	Adenocarcinoma (Serous)	Epithelial	Malignant	Ovary
154.	2010	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
155.	2010	35	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
156.	2010	30	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
157.	2010	45	Adult	40-49	Postmenarchal	Squamous cell Carcinoma (Small cell)	Epithelial	Malignant	Cervix
158.	2011	40	Adult	40-49	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
159.	2011	43	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
160.	2011	27	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
161.	2011	37	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
162.	2011	30	Adult	30-39	Postmenarchal	CIN	Epithelial	Premalignant	Cervix
163.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
164.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
165.	2011	45	Adult	40-49	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
166.	2011	43	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

167.	2011	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
168.	2011	43	Adult	40-49	Postmenarchal	Product of conception (Choriocacinoma)	Epithelial	Malignant	Endometrium
169.	2011	30	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
170.	2011	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
171.	2011	-				Leiomyoma	Muscle	Benign	Endometrium
172.	2011	-				Product of conception	Epithelial	Benign	Endometrium
173.	2011	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
174.	2011	28	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
175.	2011	-				Chronic Endometritis	Epithelial	Inflamatory	Endometrium
176.	2011	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
177.	2011	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
178.	2011	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
179.	2011	27	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
180.	2011	30	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
181.	2011	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
182.	2011	-				Leiomyoma	Muscle	Benign	Endometrium
183.	2011	-				Product of conception	Epithelial	Benign	Endometrium
184.	2011	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
185.	2011	28	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
186.	2011	27	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
187.	2011	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
188.	2011	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
189.	2011	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
190.	2011	23	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
191.	2011	49	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
192.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
193.	2011	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
194.	2011	35	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium

195.	2011	40	Adult	40-49	Postmenarchal	Adenoma	Epithelial	Benign	Ovary
196.	2011	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
197.	2011	54	Adult	50-59	Menopausal	CIN	Epithelial	Premalignant	Cervix
198.	2011	24	Adult	20-29	Postmenarchal	Ovaritis		Inflamatory	Ovary
199.	2011	-				Leiomyoma	Muscle	Benign	Endometrium
200.	2011	41	Adult	40-49	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
201.	2011	17	Teenager	0-19	Postmenarchal	Condyloma accumulatum	Epithelial	Benign	Vulva
202.	2011	44	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
203.	2011	-				Chronic cervicitis	Epithelial	Inflamatory	Cervix
204.	2011	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
205.	2011	43	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
206.	2011	60	Adult	60+	Menopausal	Cervical polyp	Epithelial	Benign	Cervix
207.	2011	32	Adult	30-39	Postmenarchal	Chronic Endometritis	Epithelial	Inflamatory	Endometrium
208.	2011	54	Adult	50-59	Menopausal	Condyloma accumulatum	Epithelial	Benign	Cervix
209.	2011	71	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
210.	2011	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
211.	2011	26	Adult	20-29	Postmenarchal	Squamous cell carcinoma	Epithelial	Malignant	Cervix
212.	2011	34	Adult	30-39	Postmenarchal	Condyloma accumulatum	Epithelial	Benign	Cervix
213.	2011	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
214.	2011	54	Adult	50-59	Menopausal	Brenner tumour	Epithelial	Benign	Ovary
215.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
216.	2011	61	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
217.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
218.	2011	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
219.	2011	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
220.	2011	26	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
221.	2011	40	Adult	40-49	Postmenarchal	Squamous cell carcinoma	Epithelial	Malignant	Cervix
222.	2011	17	Teenager	0-19	Postmenarchal	Ovarian cyst(Teratoma)	Sex cord/Stroma	Benign	Ovary

223.	2011	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
224.	2011	42	Adult	40-49	Postmenarchal	Squamous cell carcinoma	Epithelial	Malignant	Cervix
225.	2011	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
226.	2011	65	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
227.	2011	77	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Cervix
228.	2011	34	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
229.	2011	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
230.	2011	12	Teenager	0-19	Premenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
231.	2011	45	Adult	40-49	Postmenarchal	Leiomyosarcoma	Muscle	Malignant	Endometrium
232.	2011	47	Adult	40-49	Menopsual	Squamous cell carcinoma	Epithelial	Malignant	Cervix
233.	2011	53	Adult	50-59	Menopausal	CIN	Epithelial	Premalignant	Cervix
234.	2011	65	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
235.	2011	65	Adult	60+	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
236.	2011	50	Adult	50-59	Menopausal	Epidermal cyst	Epithelial	Benign	Vulva
237.	2011	45	Adult	40-49	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
238.	2011	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
239.	2011	38	Adult	30-39	Postmenarchal	CIN	Epithelial	Premalignant	Vagina
240.	2011	28	Adult	20-29	Postmenarchal	Endometerial hyperplasia	Muscle	Benign	Endometrium
241.	2011	60	Adult	60+	Menopausal	Adenocarcinoma	Epithelial	Malignant	Endometrium
242.	2011	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
243.	2011	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
244.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
245.	2011	47	Adult	40-49	Menopausal	Endometrial hyperplasia	Muscle	Benign	Endometrium
246.	2011	26	Adult	20-29	Postmenarchal	Ovarian cyst(Teratoma)	Sex cord/Stroma	Benign	Ovary
247.	2011	26	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
248.	2011	41	Adult	40-49	Postmenarchal	Adenoma	Epithelial	Benign	Ovary
249.	2011	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
250.	2011	22	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

251.	2011	22	Adult	20-29	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
252.	2011	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
253.	2011	34	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
254.	2011	52	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
255.	2011	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
256.	2011	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
257.	2011	45	Adult	40-49	Postmenarchal	Endometrial Polyp	Muscle	Benign	Endometrium
258.	2011	20	Adult	20-29	Postmenarchal	Endometrial Polyp	Muscle	Benign	Endometrium
259.	2011	27	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
260.	2011	33	Adult	30-39	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
261.	2011	65	Adult	60+	Menopausal	Chronic Endometritis	Epithelial	Inflamatory	Endometrium
262.	2011	65	Adult	60+	Menopausal	Endometrial hyperplasia	Muscle	Benign	Endometrium
263.	2011	28	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
264.	2011	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
265.	2011	-				Adenomyosis	Muscle	Benign	Endometrium
266.	2011	27	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
267.	2011	29	Adult	20-29	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium
268.	2011	78	Adult	60+	Menopausal	Chronic Cervicitis	Epithelial	Inflamatory	Cervix
269.	2011	44	Adult	40-49	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
270.	2011	26	Adult	20-29	Postmenarchal	Ovarian Cyst	Sex cord/Stroma	Benign	Ovary
271.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
272.	2011	61	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
273.	2011	61	Adult	60+	Menopausal	Chronic Cervicitis	Epithelial	Inflamatory	Cervix
274.	2011	22	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
275.	2011	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
276.	2011	27	Adult	20-29	Postmenarchal	Ovarian Cyst	Sex cord/Stroma	Benign	Ovary
277.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
278.	2011	22	Adult	20-29	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium

279.	2011	34	Adult	30-39	Postmenarchal	Product of Conception	Epithelial	Benign	Endometrium
280.	2011	24	Adult	20-29	Postmenarchal	Ovarian cyst(Teratoma)	Sex cord/Stroma	Benign	Ovary
281.	2011	28	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
282.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
283.	2011	34	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
284.	2011	-				Leiomyoma	Muscle	Benign	Endometrium
285.	2011	-				CIN	Epithelial	Premalignant	Cervix
286.	2011	-				Chronic Cervicitis	Epithelial	Inflamatory	Cervix
287.	2011	29	Adult	20-29	Postmenarchal	Ovarian Cyst	Sex cord/Stroma	Benign	Ovary
288.	2011	61	Adult	60+	Menopausal	Chronic Cervicitis	Epithelial	Inflamatory	Cervix
289.	2011	61	Adult	60+	Menopausal	CIN	Epithelial	Premalignant	Cervix
290.	2011	31	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
291.	2011	65	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
292.	2011	65	Adult	60+	Menopausal	Chronic Cervicitis	Epithelial	Inflamatory	Cervix
293.	2011	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
294.	2011	18	Adult	0-19	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
295.	2011	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
296.	2011	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
297.	2011	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
298.	2011	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
299.	2011	29	Adult	20-29	Postmenarchal	Vulvitis	Epithelial	Inflamatory	Vulva
300.	2011	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
301.	2011	64	Adult	60+	Menopausal	Endometrial hyperplasia	Muscle	Benign	Endometrium
302.	2011	35	Adult	30-39	Postmenarchal	Ovarian cyst (Teratoma)	Sex cord/Stroma	Benign	Ovary
303.	2011	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
304.	2011	75	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
305.	2011	75	Adult	60+	Menopausal	Chronic Cervicitis	Epithelial	Inflamatory	Cervix
306.	2011	24	Adult	20-29	Postmenarchal	Ovarian cyst (Teratoma)	Sex cord/Stroma	Benign	Ovary

307.	2011	-				Cervical polyp	Epithelial	Benign	Cervix
308.	2012	25	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
309.	2012	49	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
310.	2012	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
311.	2012	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
312.	2012	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
313.	2012	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
314.	2012	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
315.	2012	31	Adult	30-39	Postmenarchal	Squamous cell carcinoma	Epithelial	Malignant	Cervix
316.	2012	19	Adult	0-19	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
317.	2012	62	Adult	60+	Menopausal	Endomentrial polyp	Muscle	Benign	Endometrium
318.	2012	-				Leiomyoma	Muscle	Benign	Endometrium
319.	2012	72	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
320.	2012	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
321.	2012	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
322.	2012	-				Leiomyoma	Muscle	Benign	Endometrium
323.	2012	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
324.	2012	35	Adult	30-39	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
325.	2012	-				Ovarian cyst	Sex cord/Stroma	Benign	Ovary
326.	2012	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
327.	2012	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
328.	2012	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
329.	2012	47	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
330.	2012	47	Adult	40-49	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
331.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
332.	2012	67	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
333.	2012	-				Leiomyoma	Muscle	Benign	Endometrium
334.	2012	55	Adult	50-59	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix

335.	2012	30	Adult	30-39	Postmenarchal	Fibroma	Connective	Benign	Ovary
336.	2012	47	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
337.	2012	36	Adult	30-39	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
338.	2012	66	Adult	60+	Menopausal	Adenocarcinoma	Epithelial	Malignant	Endometrium
339.	2012	47	Adult	40-49	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
340.	2012	57	Adult	50-59	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
341.	2012	-				Adenomyosis	Muscle	Benign	Endometrium
342.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
343.	2012	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
344.	2012	63	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
345.	2012	63	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
346.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
347.	2012	51	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
348.	2012	20	Adult	20-29	Postmenarchal	Product of conception (Choriocacinoma)	Epithelial	Malignant	Endometrium
349.	2012	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
350.	2012	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
351.	2012	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
352.	2012	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
353.	2012	34	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
354.	2012	-				Product of conception	Epithelial	Benign	Endometrium
355.	2012	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
356.	2012	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
357.	2012	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
358.	2012	30	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
359.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
360.	2012	43	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
361.	2012	24	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
362.	2012	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

363.	2012	38	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
364.	2012	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
365.	2012	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
366.	2012	26	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
367.	2012	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
368.	2012	50	Adult	50-59	Menopausal	Cervical polyp	Epithelial	Benign	Cervix
369.	2012	21	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
370.	2012	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
371.	2012	20	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
372.	2012	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
373.	2012	52	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
374.	2012	28	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Fallopian tube
375.	2012	32	Adult	30-39	Postmenarchal	Ovarian cyst (teratoma)	Sex cord/Stroma	Benign	Ovary
376.	2012	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
377.	2012	51	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
378.	2012	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
379.	2012	53	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
380.	2012	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
381.	2012	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
382.	2012	38	Adult	30-39	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
383.	2012	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
384.	2012	26	Adult	20-29	Postmenarchal	Ovarian cyst (teratoma)	Sex cord/Stroma	Benign	Ovary
385.	2012	45	Adult	40-49	Postmenarchal	Vulvaritis	Epithelial	Inflamatory	Vulva
386.	2012	27	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
387.	2012	-				Leiomyoma	Muscle	Benign	Endometrium
388.	2012	60	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
389.	2012	78	Adult	60+	Menopausal	Endometrial polyp	Muscle	Benign	Endometrium
390.	2012	51	Adult	50-59	Menopausal	Endometrial hyperplasia	Muscle	Benign	Endometrium

391.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
392.	2012	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
393.	2012	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
394.	2012	47	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
395.	2012	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
396.	2012	36	Adult	30-39	Postmenarchal	Adenocarcinoma	Epithelial	Malignant	Endometrium
397.	2012	74	Adult	60+	Menopausal	Adenocarcinoma	Epithelial	Malignant	Ovary
398.	2012	62	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
399.	2012	62	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
400.	2012	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
401.	2012	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
402.	2012	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
403.	2012	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
404.	2012	54	Adult	50-59	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
405.	2012	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
406.	2012	45	Adult	40-49	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
407.	2012	28	Adult	20-29	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
408.	2012	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
409.	2012	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
410.	2012	40	Adult	40-49	Postmenarchal	Product of conception	Epithelial	Malignant	Endometrium
411.	2012	40	Adult	40-49	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
412.	2012	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
413.	2012	52	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
414.	2012	29	Adult	20-29	Postmenarchal	Condyloma acuminatum	Epithelial	Benign	Vulva
415.	2012	29	Adult	20-29	Postmenarchal	Vulva cyst	Epithelial	Benign	Vulva
416.	2012	54	Adult	50-59	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
417.	2012	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
418.	2012	22	Adult	20-29	Postmenarchal	Adenoma	Epithelial	Benign	Ovary

419.	2012	55	Adult	50-59	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
420.	2012	34	Adult	30-39	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
421.	2012	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
422.	2012	23	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
423.	2012	70	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
424.	2012	40	Adult	40-49	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
425.	2012	62	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
426.	2012	78	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
427.	2012	35	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
428.	2012	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
429.	2012	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
430.	2012	38	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
431.	2012	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
432.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
433.	2012	-				Leiomyoma	Muscle	Benign	Endometrium
434.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
435.	2012	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
436.	2012	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
437.	2012	26	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
438.	2012	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
439.	2012	28	Adult	20-29	Postmenarchal	Ovarian cyst (teratoma)	Sex cord/Stroma	Benign	Ovary
440.	2012	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
441.	2012	-				Leiomyoma	Muscle	Benign	Endometrium
442.	2012	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
443.	2012	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
444.	2012	47	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
445.	2012	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
446.	2012	40	Adult	40-49	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium

447.	2012	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
448.	2012	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
449.	2012	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
450.	2012	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
451.	2012	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
452.	2012	27	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
453.	2012	47	Adult	40-49	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
454.	2012	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
455.	2012	-				Ovarian cyst (teraatoma)	Sex cord/Stroma	Benign	Ovary
456.	2012	27	Adult	20-29	Postmenarchal	Ovarian cyst (teraatoma)	Sex cord/Stroma	Benign	Ovary
457.	2012	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
458.	2012	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
459.	2012	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
460.	2012	19	Adult	0-19	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
461.	2012	-				Product of conception	Epithelial	Benign	Endometrium
462.	2012	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
463.	2012	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
464.	2012	33	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
465.	2012	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
466.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
467.	2013	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
468.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
469.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
470.	2013	68	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
471.	2013	26	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
472.	2013	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
473.	2013	36	Adult	30-39	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
474.	2013	64	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium

475.	2013	19	Adult	0-19	Postmenarchal	Ovarian cyst (Theco fibroma)	Sex cord/Stroma	Benign	Ovary
476.	2013	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
477.	2013	-				Product of conception	Epithelial	Benign	Endometrium
478.	2013	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
479.	2013	26	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
480.	2013	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
481.	2013	26	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
482.	2013	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
483.	2013	90	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
484.	2013	70	Adult	60+	Menopausal	Basal cell epithelioma	Epithelial	Malignant	Vulva
485.	2013	64	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
486.	2013	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
487.	2013	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
488.	2013	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
489.	2013	27	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
490.	2013	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
491.	2013	27	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
492.	2013	43	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
493.	2013	43	Adult	40-49	Postmenarchal	Ovarian cyst (serous)	Sex cord/Stroma	Benign	Endometrium
494.	2013	37	Adult	30-39	Postmenarchal	Ovarian cyst (serous)	Sex cord/Stroma	Benign	Endometrium
495.	2013	54	Adult	50-59	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
496.	2013	32	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
497.	2013	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
498.	2013	33	Adult/	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
499.	2013	41	Adult	40-49	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
500.	2013	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
501.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
502.	2013	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium

503.	2013	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
504.	2013	30	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
505.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
506.	2013	51	Adult	50-59	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
507.	2013	51	Adult	50-59	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
508.	2013	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
509.	2013	22	Adult	20-29	Postmenarchal	Ovarian cyst (Theco fibroma)	Sex cord/Stroma	Benign	Ovary
510.	2013	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
511.	2013	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
512.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
513.	2013	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
514.	2013	61	Adult	60+	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
515.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
516.	2013	69	Adult	60+	Menopausal	Endometrial carcinoma	Muscle	Malignant	Endometrium
517.	2013	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
518.	2013	30	Adult	30-39	Postmenarchal	Condyloma acuminaum	Epithelial	Benign	Cervix
519.	2013	41	Adult	40-49	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
520.	2013	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
521.	2013	30	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
522.	2013	43	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
523.	2013	53	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
524.	2013	53	Adult	50-59	Menopsual	Ovarian cyst (serous)	Sex cord/Stroma	Benign	Ovary
525.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
526.	2013	55	Adult	50-59	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
527.	2013	55	Adult	50-59	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
528.	2013	69	Adult	60+	Postmenarchal	Squamous cell carcinoma (small cell)	Epithelial	Malignant	Cervix
529.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

530.	2013	24	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
531.	2013	29	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
532.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
533.	2013	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
534.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
535.	2013	51	Adult	50-59	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
536.	2013	27	Adult	20-29	Postmenarchal	Adenocarcinoma	Epithelial	Malignant	Endometrium
537.	2013	80	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
538.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
539.	2013	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
540.	2013	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
541.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
542.	2013	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
543.	2013	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
544.	2013	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
545.	2013	55	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
546.	2013	50	Adult	50-59	Menopsual	Ovarian Cyst	Sex cord/Stroma	Benign	Endometrium
547.	2013	44	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
548.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
549.	2013	60	Adult	60+	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
550.	2013	52	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
551.	2013	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
552.	2013	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
553.	2013	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
554.	2013	62	Adult	60+	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
555.	2013	28	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
556.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
557.	2013	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

558.	2013	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
559.	2013	23	Adult	20-29	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium
560.	2013	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
561.	2013	26	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
562.	2013	55	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
563.	2013	26	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
564.	2013	52	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
565.	2013	25	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
566.	2013	30	Adult	30-39	Postmenarchal	Ovarian cyst (Teratoma)	Sex cord/Stroma	Benign	Ovary
567.	2013	51	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
568.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
569.	2013	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
570.	2013	25	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
571.	2013	26	Adult	20-29	Postmenarchal	Ovarian cyst (Teratoma)	Sex cord/Stroma	Benign	Ovary
572.	2013	43	Adult	40-49	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium
573.	2013	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
574.	2013	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
575.	2013	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
576.	2013	44	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
577.	2013	-				Leiomyoma	Muscle	Benign	Endometrium
578.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
579.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
580.	2013	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
581.	2013	25	Adult	20-29	Postmenarchal	Endometrial polyp	Muscle	Benign	Endometrium
582.	2013	30	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
583.	2013	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
584.	2013	45	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
585.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

586.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
587.	2013	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
588.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
589.	2013	65	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
590.	2013	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
591.	2013	65	Adult	60+	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
592.	2013	25	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
593.	2013	44	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
594.	2013	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
595.	2013	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
596.	2013	28	Adult	20-29	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
597.	2013	71	Adult	60+	Postmenarchal	Squamous cell carcinoma (small cell)	Epithelial	Malignant	Cervix
598.	2013	33	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
599.	2013	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
600.	2013	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
601.	2013	32	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
602.	2013	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
603.	2013	52	Adult	50-59	Menopausal	CIN	Epithelial	Premalignant	Cervix
604.	2013	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
605.	2013	29	Adult	20-29	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
606.	2013	24	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
607.	2013	41	Adult	40-49	Postmenarchal	Adenomyosis	Muscle	Benign	Endometrium
608.	2013	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
609.	2013	30	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
610.	2013	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
611.	2013	27	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
612.	2013	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
613.	2013	-				Product of conception	Epithelial	Benign	Endometrium

614.	2013	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
615.	2013	29	Adult	20-29	Postmenarchal	Endometrial hyperplasia	Muscle	Benign	Endometrium
616.	2013	34	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
617.	2013	30	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
618.	2013	35	Adult	30-39	Postmenarchal	Cervical cyst	Epithelial	Benign	Cervix
619.	2013	47	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
620.	2013	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
621.	2013	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
622.	2013	20	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
623.	2013	45	Adult	40-49	Postmenarchal	Ovarian cyst (Teratoma)	Sex cord/Stroma	Benign	Endometrium
624.	2013	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
625.	2013	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
626.	2013	26	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
627.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
628.	2013	20	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
629.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
630.	2013	31	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
631.	2013	40	Adult	40-49	Postmenarchal	Squamous cell carcinoma (Small cell)	Epithelial	Malignant	Cervix
632.	2013	80	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
633.	2013	80	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
634.	2013	48	Adult	40-49	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
635.	2013	-				Leiomyoma	Muscle	Benign	Endometrium
636.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
637.	2013	32	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
638.	2013	-				Product of conception	Epithelial	Benign	Endometrium
639.	2013	31	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
640.	2013	36	Adult	30-39	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
641.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

642.	2013	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
643.	2013	37	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
644.	2013	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
645.	2013	27	Adult	20-29	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
646.	2013	27	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
647.	2013	33	Adult	30-39	Postmenarchal	CIN	Epithelial	Premalignant	Cervix
648.	2013	72	Adult	60+	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
649.	2013	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
650.	2013	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
651.	2013	14	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
652.	2014	46	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
653.	2014	48	Adult	40-49	Menopausal	Adenomyosis	Muscle	Benign	Endometrium
654.	2014	48	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
655.	2014	31	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
656.	2014	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
657.	2014	69	Adult	60+	Menopausal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
658.	2014	65	Adult	60+	Menopausal	Adenocarcinoma (well differentiated)	Epithelial	Malignant	Cervix
659.	2014	41	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
660.	2014	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
661.	2014	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
662.	2014	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
663.	2014	38	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
664.	2014	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
665.	2014	47	Adult	40-49	Postmenarchal	Ovarian cyst (teratoma)	Sex cord/Stroma	Benign	Ovary
666.	2014	42	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
667.	2014	44	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
668.	2014	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
669.	2014	30	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

670.	2014	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
671.	2014	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
672.	2014	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
673.	2014	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
674.	2014	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
675.	2014	37	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
676.	2014	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
677.	2014	36	Adult	30-39	Postmenarchal	Ovarian cyst (teratoma)	Sex cord/Stroma	Benign	Ovary
678.	2014	45	Adult	40-49	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
679.	2014	32	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
680.	2014	40	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
681.	2014	48	Adult	40-49	Menopsual	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
682.	2014	39	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
683.	2014	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
684.	2014	38	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
685.	2014	50	Adult	50-59	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
686.	2014	49	Adult	40-49	Menopsual	Leiomyoma	Muscle	Benign	Endometrium
687.	2014	36	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
688.	2014	43	Adult	40-49	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
689.	2014	38	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
690.	2014	34	Adult	30-39	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
691.	2014	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
692.	2014	34	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
693.	2014	37	Adult	30-39	Postmenarchal	Product of conception	Epithelial	Benign	Endometrium
694.	2014	29	Adult	20-29	Postmenarchal	Chronic cervicitis	Epithelial	Inflamatory	Cervix
695.	2014	29	Adult	20-29	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium
696.	2014	16	Teenager	0-19	Postmenarchal	Ovarian cyst	Sex cord/Stroma	Benign	Ovary
697.	2014	35	Adult	30-39	Postmenarchal	Leiomyoma	Muscle	Benign	Endometrium

APPENDIX II

Table1.2: Distribution of Biopsies Grouped under "Others"

Biopsy	Frequency	Percent
Basal cell epithelioma	1	5.0
Brenner tumour	2	10.0
Cervical cyst	1	5.0
Chronic Endocervitis	1	5.0
Chronic vulvitis	1	5.0
Endometrial Carcinoma	3	15.0
Epidermal cyst	1	5.0
Fibroma	1	5.0
Haemangioma	2	10.0
Ovaritis	1	5.0
Vulva cyst	2	10.0
Vulva Wart	1	5.0
Vulvaritis	2	10.0
Yolk sac tumour (Hepatoid variant)	1	5.0
Total	**20**	**100.0**

APPENDIX III: Copy of Ethical Approval