PATTERNS OF TRANSVAGINAL ULTRASOUND FINDINGS AND ITS RELATIONSHIP WITH SUBFERTILITY TYPES IN SUBFERTILE WOMEN AT MOI TEACHING AND REFERRAL HOSPITAL.

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A THESIS SUBMITTED AS PARTIAL FULFILLMENT FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN RADIOLOGY AND IMAGING OF MOI UNIVERSITY.

DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

This work is dedicated to my husband, Mr Rohan Patel, and my daughter Prahi Patel whose love and support has been my strength all through.

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DEFINITION OF TERMS

Female Subfertility	A disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.
Primary Subfertility	Describes couples who have never been able to become pregnant after at least one year of unprotected sexual intercourse
Secondary Subfertility	Describes couples who have been pregnant at least once, but have not been able to become pregnant again

LIST OF ABBREVIATIONS

AIDS	Acquired Immuno-Deficiency Syndrome
CEO	Chief Executive Officer
DM	Diabetes Mellitus
FSH	Follicular Stimulating Hormone
HIV	Human Immunodeficiency Virus
HSG	Hysterosalpingography
HTN	Hypertension
HyCoSy	Hysterosalpingo-Contrast Sonography
IREC	Institutional Research and Ethics Committee
ISS	Immuno-Suppressed State
KMTC	Kenya Medical Training College
LH	Luteinizing Hormone
MRI	Magnetic Resonance Imaging
MTRH	Moi Teaching and Referral hospital
PCO	Polycystic ovaries
PID	Pelvic Inflammatory Disease
STI/Ds	Sexually Transmitted Infections/ Diseases
TVUS	Transvaginal Ultrasonography
US	Ultrasound
WHO	World Health Organization

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ABSTRACT

Background: Subfertility is defined as failure to attain pregnancy after one year of regular, unprotected intercourse. Subfertility affects about 10-15% of couples. The exact magnitude and importance of subfertility as a public health problem in Africa is poorly understood. Prevalence of primary subfertility is reported as <5%, whereas secondary subfertility is common, ranging from 10-30% depending on the socio-cultural settings.

In Africa, most studies cover prevalence, while few studies have looked at the radiological point of view, especially possible structural causes of subfertility as evidenced on transvaginal ultrasonography (TVUS).

Objectives: To determine patterns of transvaginal ultrasonographic findings and their relationship with subfertility subtypes as seen at MTRH.

Methods: A cross-sectional study conducted at Moi Teaching and Referral Hospital (MTRH) in Eldoret for one year. Sample size was calculated using Fischer's formula and 100 female patients with clinical subfertility and referred for ultrasound were recruited after obtaining consent. Endocavitary vaginal probe of Mindray M7 machine was used to scan the patients. Consecutive sampling technique was used to recruit patients with subfertility. Continuous variables were summarized as means and standard deviations. Categorical variables were summarized in frequency, percentages and tables. Fisher's exact test was used to assess the association between subfertility types and transvaginal ultrasound patterns.

Results: The mean age of the recruited women included in the study was 35.3 years.

Of the 100 patients, 80 had primary subfertility while 20 had secondary subfertility.

On the patterns of transvaginal ultrasonographic findings, 40 (40.0%) had normal ultrasound findings, 14 (14.0%) had leiomyoma, 13 (13.0%) polycystic ovaries, 8 (8.0%) Pouch of Douglas (POD) free fluid noted, 6 (6.0%) functional ovarian cysts, 6 (6.0%) adenomyosis, 5 (5.0%) hydro-salpinx, 3 (3.0%) congenital malformations, 3 (3.0%) Endometrioma, 1 had Tubo-ovarian mass and 1 Hydro-salpinx with functional ovarian cyst.

Regarding the association between the ultrasound findings and the subfertility types, no statistically significant association, P-values of >0.005(Fischer's exact test), was found between the TVUS findings and subfertility types.

Conclusion: Women subfertility in this study is associated with multiple structural abnormalities involving the uterus, ovaries, fallopian tubes. TVUS is a useful diagnostic modality for evaluating abnormalities. Leiomyoma and PCOS are the leading causes of subfertility. The proportion of primary subfertility is high (80%) in this study.

Recommendations: Well-designed large cohort or randomized studies are needed to understand the association between subfertility types and ultrasound findings in patients with subfertility.

CHAPTER ONE: INTRODUCTION

1.1 Background information

Subfertility refers to any grade or form of reduced fertility among women who have tried to conceive but ending up being unsuccessful (Jenkins et al., 2004).

The commonly reported causes of subfertility in women include uterine abnormalities, tubal disease, endometriosis, ovulatory disorders, peritoneal adhesions, and the advancing age of the female. However, in approximately 5-10% of the cases, subfertility is unexplained even after thorough evaluation (Adamson, G. D., & Baker, 2003).

Most global subfertility surveys have reported the prevalence of subfertility to be approximately 8-12%. However, parts of Sub-Saharan Africa have shown high rates of subfertility of up to 30% (Cui, 2010). In Kenya, prevalence rates for subfertility are about 11.9% (Ericksen & Brunette, 1996).

In a Kenyan national survey on subfertility conducted in 2005/2006, it was noted that subfertility is a major reproductive health concern and it also highlighted the subfertility related consultations/visits as follows: at the tertiary level hospitals(teaching and referral) to be 30%, provincial hospitals to be 27%, district hospitals to be 15%, health centres to be 4% and dispensaries to be 2%. Subfertility in Kenya is a remarkable family issue in all communities across the country, majority of the people in the subfertility survey interviewed during 2005/6 cited that subfertility as a problem of women since its difficult to count in the men in the assessment of subfertility. The National reproductive health policy issued in the year 2007 recognized subfertility as an important public health problem in Kenya. It prioritizes the actions as follows; to improve the access to quality subfertility services to all the

levels, to promote awareness in the community especially among men and encouraging all the aspects of research (Otwori et al., 2013).

It is approximated that 15% of Kenyan men and almost one fifth of Kenyan women have subfertility related problems, and according to the recent statistics from the University of Nairobi, while most people are unknown of their fertility status (Odek et al., 2014).

Pelvic inflammation resulting in reproductive organs damage has been a critical contributor to the sub-Saharan Africa region's high subfertility cases (Collet et al., 1988). In most instances, this damage causes secondary subfertility, a type of subfertility that occurs after a woman had given birth (Larsen, 2000).

However, in most Sub-Saharan Africa countries, subfertility is wrongly attributed to diverse cultural beliefs. For example, in Madagascar, breaching the taboo was believed to lead to subfertility, or the condition was attributed to spiritual forces (Greil et al., 2018). For example, the Luhya and Luo communities believe subfertility results from failure to follow taboos or traditions (Kimani et al., 1996). Hence in the African set-up, it is not only a biomedical affair but also a cultural one.

Psychological and social impacts have been linked to subfertility, especially in most developing countries (Inhorn, 2003). It is a cause of immense stress to couples, families, and relatives, especially in Sub-Saharan Africa, where marriage is revered, respected, and tied to childbearing. The emotional, psychological, sexual, social, and financial burden of subfertility on the family are enormous (Ezenyeaku, 2015). This is serious for women in most local communities where motherhood is linked to women gender identity. Such sufferings have been described as gender suffering, excluding women from key social roles (Inhorn, 2003).

Fertility affects both men and women and is caused by either of the couples. However, previous research has demonstrated that the consequences of childlessness are far more severe for women than men, even when they are not the definite cause of the subfertility problem in Sub-Saharan Africa (Larsen, 2000).

A review by Chachamovich et al. found that subfertility is linked with low psychological coping, especially for women with most having a feeling of shame (Chachamovich et al., 2010). The women faced with this condition have a reduction in relationship satisfaction (Greil et al., 2018) and reduced life quality (Mcquillan et al., 2015).

There are four major categories of the causes of subfertility: the female cause, the male cause, the combined cause and the unexplained subfertility. It is cumbersome to assign the exact percentage to these categories, however it is usually reported that female causes constitute in about 35% of cases, and that subfertility is mainly due to the female cause, male factor in approximately 30% of cases, in 20% of cases the abnormalities and seen in both the partners and in approximately 15% of cases there is no actual casue which was found after the whole process of investigations done (Otwori et al., 2013).

In a study conducted by Mati et al in Kenya among subfertile couples found that in approximately 61.9% cause of subfertility was attributed by the female factor, 20.1% constituted by the male cause and 18% was due to the combination of both the male and female factors (Mati, J., Senai, S., Oyieke, J., Sekadde, C., Njoroge, J., & Muta, 1989).

The women with primary subfertility (those who have never had a child) are affected the most with the psychological distress compared with those with secondary

subfertility(Raque-Bogdan & Hoffman, 2015). For those trying to conceive, long subfertility periods (Ramezanzadeh et al., 2004) and unsuccessful treatments (Pasch et al., 2012) results in increased distress. Women with fertility issues experience diverse forms of domestic violence, especially emotional violence (Silwal & Thapa, 2020).

The challenges associated with subfertility are worse in Africa, where most cultures put meaning to marriage as being associated with conceiving and bearing children (Horbst, 2010). Value is placed on children as a source of wealth, power and pride and an assurance of continuity of the family name while women have a social role to be mothers (Lampiao et al., 2013). Hence subfertility is frowned at, resulting in rejection and psychological distress, with a heavy burden on women (Chimbatata & Malimba, 2016).

In sub-Saharan African countries, primary subfertility is relatively low as compared to the high proportion of secondary subfertility in most countries in Africa which ranges from the age 20-44 years in women (Larsen, 2000).

Female subfertility workup is incomplete without the application of ultrasonography (Ezenyeaku, 2015). Ultrasound is no longer used simply to distinguish a cystic and solid mass within the abdomen and pelvis. With improved image resolution and software, subtle differences in tissue texture can be demarcated and pelvic organs clearly identified. Ultrasound is now established as the primary imaging investigation in all cases of suspected female infertility.

Ultrasonography is a useful, safe, inexpensive, radiation-free, non-invasive tool, readily available, easy to use and easily repeatable approach to evaluate causes of female subfertility.

Transvaginal sonography has been increasingly used in the investigation and treatment of subfertility. Transvaginal ultrasound, also referred to as endovaginal ultrasound, is a pelvic ultrasound utilized by medical or radiology specialists in examining the female reproductive organs such as the cervix, ovaries, vagina, fallopian tubes, and uterus. It involves internal examination through the vagina, where the ultrasound probe is inserted approximately 2-3 inches into the canal of the vagina. The approach through the vagina minimizes the distance between the pelvic structures and the probes, enabling higher frequencies. Transvaginal Ultrasound results in an improvement in resolution as a result of the high frequencies used and the absence of deformation of the beam caused by the anterior abdominal wall (Steinkampf, 1988).

The introduction of transvaginal ultrasonography (TVUS) has been gradually displaced other invasive investigations from being the first line investigation for females with subfertility. It has become an important tool for clinicians to interpret images quickly (Ebubedike & Enukegwu, 2019).

For improved diagnostic accuracy in the assessment of endometrial response to follicular development and ovaries, TVUS should be performed preferably in the follicular phase of the regular 28-day cycle (Hrehorcak & Nargund, 2011).

Transvaginal sonography has been found to be superior to transabdominal sonography as an imaging technique (Narayan & Goswamy, 1994). Better visualization of pelvic organs afforded by transvaginal sonography, most likely because of the proximity of the transvaginal probe, is of greatest help when obesity, bowel gas, or adhesions limits transabdominal examination (Mendelson et al., 1988).

Transvaginal ultrasound provides unique advantages for the investigation of female causes of subfertility over other modalities. Thus, most women dealing with subfertility will no longer have to face multiple procedures and tests, at different sites

and in multiple visits. As a consequence, TVUS is considered as a one-stop shopping for the evaluation of a subfertile female (Groszmann & Benacerraf, 2016).

This study aims to help identify the commonest abnormalities of the female reproductive system as seen on transvaginal ultrasonography and assist clinicians on the proper management of subfertility.

1.2 Problem Statement

Subfertility is a neglected reproductive health area of concern in Sub-Saharan Africa, despite the deleterious effects on the individuals who have the condition. Similar is the situation in the low resource countries, where there is a struggle with infectious diseases such as malaria and HIV/AIDS, thus given more focus to them and that manner fail to look after subfertility problems. (Inhorn, 2003).

Patterns of transvaginal ultrasound findings in subfertile women have been studied elsewhere but local data is limited.

A study done in Nigeria by Ebubedike et al, showed the commonest pattern was uterine fibroids followed by ovarian cysts (Ebubedike & Enukegwu, 2019). However, in Kenya and at MTRH, little is known regarding transvaginal ultrasound application and the outcomes of the TVUS in evaluating the causes of subfertility. This information from TVUS is vital in informing management and care.

A study done by Ericksen et al, in California who estimated the national prevalence rates of subfertility in 27 African countries found to be approximately 11.9% in Kenya (Ericksen & Brunette, 1996). This is not a small number, as around 36% of Kenya's population fall into the bracket of reproductive age group.

However, the challenge has always been the identification, diagnosis, and treatment of subfertility conditions among those who have it. The recognition, evaluation and treatment of female subfertility are complicated, complex, stressful, and emotionally devastating for most couples. The causes are multifactorial in origin, with both congenital and acquired problems of the uterus, fallopian tubes, and ovaries.

A detailed evaluation of the uterus, fallopian tubes, and ovaries using TVUS that is radiation-free, inexpensive, readily available, non-invasive, relatively less time consuming and easily repeatable in female subfertility has resulted offer the hope of identifying the causes of subfertility in most women hence informing management. TVUS remains the first line indispensable tool for gynecologic workup, monitoring and treating subfertility. (Okeke et al., 2015).

Use of TVUS as the first subfertility investigation to diagnose the various etiologies to replace more invasive modes of investigation (D Chizen, 2010).

There is a need of reinforcement to the already known knowledge on proper utilization of TVUS (timing of the scan, good preparation, counselling and sensitization of the clinicians) in the evaluation of female subfertility.

1.3 Justification

Female subfertility is immense stress to couples, families, and relatives worldwide. Ultrasound plays an essential role in female subfertility workup with hysterosalpingography (HSG) and magnetic resonance imaging (MRI), each playing a complimentary role in the screening, diagnosis and/or management of female subfertility. Transvaginal sonography has become an invaluable tool for the care of subfertility patients due to its number of advantages. Hence the need for the study to

describe the patterns of transvaginal sonography in the identification of subfertility causing abnormalities in the female reproductive system, which is key in informing care and management.

With limited data on the patterns of disorders observed on TVUS among women with subfertility, this study will help highlight the utilization of TVUS in the identification of such disorders to inform management.

Female subfertility is multifactorial thus need to know the associations between the TVUS findings and subfertility types which would be helpful in guiding management.

1.4 Research Questions

1. What are the transvaginal ultrasonographic findings in subfertile women and its relationship to subfertility subtypes referred for TVUS in MTRH?

1. 5 Objectives

1.5.1 Broad objective:

To describe transvaginal ultrasonographic findings in subfertile women and its relationship with subfertility subtypes referred for TVUS at MTRH.

1.5.2 Specific Objectives

1. To describe demographic profiles of women with subfertility who underwent transvaginal ultrasound.
2. To describe proportions of primary and secondary subfertility among subfertile women who underwent transvaginal ultrasonography.
3. To describe patterns of transvaginal ultrasonographic findings among subfertile women and its relationship with the subfertility subtypes.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The agreed clinical definition of subfertility is "any form or grade of reduced fertility in couples unsuccessfully trying to conceive for a period of 1 year or after 12 unsuccessful menstrual cycles with unprotected coitus within the fertile phase of the menstrual cycles or inability to conceive within one year of exposure to high risk of pregnancy, i.e. unprotected regular coitus, in a woman of reproductive age who is not on contraceptives and is non-lactating (Gnoth et al., 2003).

There are two types of subfertility: Primary and Secondary.

Primary subfertility is defined as the inability to become pregnant after one year of unprotected regular intercourse or despite actively trying for a certain number of years. Secondary subfertility is defined as the inability to become pregnant despite actively trying for years and have been pregnant (or had a child) in the past (Comhaire;, 1987).

2.2 Epidemiology of female subfertility

The prevalence of subfertility is varying worldwide, ranging from 3% to 7%. The consequences of subfertility are societal repercussions, personal suffering, psychological effects, clinical depression and sexual dysfunction. In developed countries, 80-90% of couples attempting to conceive are successful after one year and 95% after two years. The incidence of female subfertility is rising and varies from 10 to 20%. Subfertility, either primary or secondary, will occur for almost 15% of all women worldwide. Female subfertility occurs in about 37% of all subfertile couples. Marital discord is also familiar in subfertile couples, mainly when they are under stress for making medical decisions. Depression is also considerable in subfertile women, similar to women with heart disease or cancer. Subfertility in women

experiences higher rates of psychological distress compared with their fertile counterparts.

Sexually transmitted infections (STIs) are important risk factors for both subfertility and HIV/AIDS in Kenya and entire sub-Saharan Africa (Mati et al., 1989). This is evident from studies conducted by the WHO task force in the 1970s and 1980s on subfertility, which revealed that STIs were the significant causes of subfertility in sub-Saharan Africa (Larsen, 2000; Mati et al., 1989). Between 1973 and the early 1990s, Tanzania had a comparatively higher primary subfertility of about 10% than Kenya and Uganda.

Furthermore, (Gumodoka et al., 1997) found out that subfertile women compared to fertile ones, were more likely to be exposed to STIs because of their tendency to have more sexual partners.

Studies on subfertility based on data from the World Fertility Survey (WFS) in the 1970s involving several developing countries, including Kenya, showed that subfertility among married women aged 40-49 who were sexually active and non-contracepting for at least five years varied from 1.3 to 6.7 per cent (Larsen, 2000).

Moreover, (Larsen & Menken, 1989) found that the risk of childlessness increases with age because the older a woman is, the longer she has been exposed to risks of pelvic inflammatory disease (PID).

For the 1990 national institutes of health (NIH), the prevalence of PCOS for White women was estimated at 5.5% (95% CrI: 4.8– 6.3%). The corresponding figures for Black women and women residing in the Middle East are 7.4% (95% CrI: 6.3–8.7%) and 6.1% (95% CrI: 5.3–7.1%), respectively (Ding et al., 2017).

2.3 Causes of female subfertility

In order for a woman to become pregnant: – 1. The egg must be released from one of her ovaries (ovulation) –2. The egg must go through the fallopian tube toward the uterus –3. Sperm must join with the egg in the fallopian tube (fertilization) –4. The fertilized egg must attach to the uterine wall (implantation).

Subfertility can result from problems that interfere with any of these steps.

Risk factors include age, stress, poor diet, smoking, alcohol, STDs, overweight, underweight, caffeine intake and too much exercise.

In a study of 8500 subfertile couples done by the World Health Organization (WHO), the most common identifiable female factors, which accounted for 81 per cent of female subfertility, included:

- Ovulatory disorders
- Uterine causes
- Leiomyoma
- Endometriosis
- Pelvic adhesions
- Tubal blockage
- Ovarian diseases
- Hormonal imbalances

Ovulatory disorders can be due to a result of infrequent ovulation or absence of ovulation. The World Health Organization (WHO) has come up with a classification on anovulation categorized into three main groups which are as follows: WHO class 1 has been defined in women who have found to be having low or low-normal serum follicle stimulating hormone (FSH) levels of concentration and low estradiol serum concentration levels secondary to reduced hypothalamic secretion of gonadotropin-

releasing hormone (GnRH) or unresponsiveness to GnRH by the pituitary gland. WHO class 2 constitutes of the normogonadotropic normoestrogenic anovulation, and the class 3 includes the type of hypergonadotropic hypoestrogenic ovulation. This classification has been useful for defining and treating the disorders of anovulation according to the endocrine dysfunctioning disorders (Otwori, 2013).

Age of a woman is also a recognized determinant in the cause of female subfertility. The decrease in fecundability as the age increases is mostly due to the reduction in both the quality and quantity of the oocytes. In the mid gestation female fetus the number of germ cell component in the ovary reaches its maximum of 6 to 7 million follicles, which is followed by a steady attrition from around 1-2 million follicles at the time of birth to approximately 300,000 follicles at the start of puberty. This pace of loss of the follicles has found to be accelerating after the female reached her mid-thirties (Ali et al., 2020).

For the conception to take place, there are factors like patent fallopian tubes, fuctional uterus and cervix are essential in the process. Diseases of the fallopian tubes and pelvic adhesions is known to cause subfertility by the prevention of the normal transport of the sperm and oocyte through the fallopian tube. The main cause of the subfertility caused by the tubal factor is pelvic inflammatory disease which is caused mainly by the pathogens namely chlamydia or gonorrhea which are sexually transmitted. There are other known conditions which can interfere with the tubal transport include severe endometriosis , adhesions caused by the previous surgical procedure or nontubal infection like appendicitis, inflammatory bowel disease and also pelvic tuberculosis. Abnormalities of the uterus secondary to the fibroid or

congenital anomalies can result into subfertility due to impaired implantation. There are other causes which fall into the structural abnormalities associated with subfertility include endometrial polyps and synechiae resulte from the prior curettage (Adamson, G. D., & Baker, 2003).

Sexually transmitted infections/diseases (STIs/Ds) are considered as a known casue of secondary subfertility as well as a cause of mortality and morbity in the low middle income countries. Therefore, the need of aggressive awareness amongst the public with the increase use of condoms and proper precautions with also the early identification and treatment of the disease to reduce the consequences and complications which can be fatal (Perslev et al., 2019).

Treatment of subfertility should follow a detailed evaluation and diagnosis. The cause of subfertility is important in the determination of the mode of management. In Kenyatta National Hospital, specific interventions of subfertility are provided for example- ovulation induction, surgery- both laparoscopic and open, menses regulation by hormones, reassurance and counseling (Otwori, 2013).

2.4 Imaging Modalities

2.4.1 Ultrasonography (USG)

Ultrasonography is a useful and first-line investigation tool available to radiologists to assess the causes of female subfertility and to institute some of the treatments used to ameliorate subfertility. It is an effective, safe, inexpensive, radiation-free, non-invasive tool, readily available, easy to use and easily repeatable approach to evaluate female subfertility worldwide.

It is known to offer the following contribution in the diagnosis and management of female subfertility. They are as follows: a) To access the anatomy of the organs of

pelvis, b) To monitor the development of the ovarian follicles, c) In evaluation of endometrium, d) To guide in oocyte retrieval and in the in-vitro fertilization procedure of embryo transfer, e) In avoiding the development of ovarian hyperstimulation syndrome, and f) In indentifying the uterine and fallopian tube disorders- both congenital and aquired (Okeke et al., 2015).

Ultrasonography helps determine the morphology of the uterus and ovaries, uterine and ovarian perfusion, and endometrial thickness, volume, and vascularity. It detects pathological lesions, including tubal lesions and abnormalities of follicular maturation and ovulation.

USG can guide oocyte retrieval and embryo transfer in *in vitro* fertilization procedures and drainage of pelvic collections or cystic lesions as part of the intervention procedures available.

Transvaginal ultrasonography in relation to transabdominal ultrasonography has the following advantages:

a. Excellent tissue characterization of the uterus and ovaries;
b. The closeness of the transducer to the pelvic organs, producing high-resolution sonograms even when there is abundant gas-filled bowel, adhesions, or obesity;
c. Rapid performance of examination without the need for a full bladder, permitting more efficient patient scheduling;
d. Good patient acceptance without the discomfort of a full bladder (Mendelson et al., 1988).

The indications for the transvaginal ultrasound are as follows: 1. Pelvic mass which is palpable or a suspected pelvic mass, 2. In confirmation of the presence of intrauterine contraceptive device in the endometrium, 3. In cases of post menopausal bleeding, 4.

Suspicion of uterine or other pelvic congenital anomaly and 5. In cases of subfertility (Hussain, 2017).

Transvaginal ultrasonography has the advantage of using higher frequency probes resulting in excellent resolution. It has been notably advocated for use in women with subfertility.

Furthermore, women prefer transvaginal ultrasound because they do not need a full bladder, which saves time and is more comfortable (Farquhar et al., 1994).

The first structure to be evaluated while doing the transvaginal ultrasound is the uterus which represents the important landmark of pelvic anatomy. It is located in the middle of the pelvis between the urinary bladder which is noted to be lying before and the large bowel lying behind it.

On a sagittal plane, the uterus has a pyriform shape and the isthmus of the uterus is identified where the body of the uterus and cervix meet.

The uterus can be lying in the anteverted position (bent forward in relation to the axis of vagina) or in retroverted position (bent backwards in relation to the vaginal axis).

The volume of the uterus can be calculated by the formula as follows: Volume = length (cm) x anteroposterior diameter (cm) x transverse diameter (cm) x 0.523or can be automatically calculated by the ultrasound machine. In the reproductive age, the normal measurements for the uterus is 7.5-9 cm long, 3-4 cm deep and 4.5-6 cm wide. The volume ranges from 50-70 cm3.

The next part to evaluate is myometrium of the uterus which is characterized by homogencity and of low echogencity on ultrasound. The inner part of the myometrium adjacent to the endometrium is known as the junctional zone which is a thin area of lower echogenicity as compared to the remaining myometrium.

The ultrasonographic appearance of the endometrium in fertile patients changes with the different phases of the menstrual cycle. Menstruation is characterized by shedding of the functional layer of the endometrium, which is caused by hormonal deprivation and alteration in the spiral arteriolar system. Bleeding is the result of vasoconstriction of the spiral arteries and necrosis of their walls.

During the last menstrual phase, endometrial layers are very thin and ultrasonography shows a single-line with slightly irregular echogenic interphase. At the beginning of the follicular phase, the endometrium appears as a single hyperechoic line since it is difficult to identify the borders between the two layers. As the ovulation approaches near, there is increase in the size an number of the endometrial glands and the endometrium shows a triple line appearance on ultrasound.

In a normal uterus, the endometrial cavity has a triangular shape. In the examination of the ovaries, the following should be evaluated: position, shape and size with also the changes during the ovarian cycle.

The position of the ovary is usually found lateral from the uterus in the ovarian fossa.
The shape of the ovary is an ellipsoid shape with the long axis noted to be oriented downward and forward.
The mean measurements of the ovary are 3 x 2 x 2 cm. In the reproductive age and in the early proliferative phase of the menstrual cycle, the volume of the ovary should be between 6 and 10 cm3. The ultrasonographic appearance of the ovary varies with the ovarian cycle in relation to the ovulation, follicular and corpus luteum formation.

The ovaries are visualized as homogeneous, hypoechogenic ovoid organ with mildly echogenic central part. The small cystic structures which are the developing antral

follicles aid in the identification of the ovaries. Between the day 2 and 4 of a 28-day regular cycle, the number of antral follicles is known to be a reliable marker of the reservoir of ovary and a good prognostic factor of the ovarian response to the hormonal treatment done in the assisted reproductive technology (ART).

As the follicular phase approaches, which is by the end of first week, the smaller follicles regress under the influence of a drop in FSH. Out of those, one will become dominant which is also known as the Graffian follicle, increases in the size at a rate of 2-3mm/day and peaks it to the diameter of 17-27 mm just before the ovulation.

Ovulation is marked by the follicular wall dissolution, eruption and liberation of the oocyte and passage of the follicular fluid into the cavity of the peritoneum. After the ovulation, there are rapid changes noted of the dominant collapsed follicle and the mural granulosa cells go into the morphological changes which are referred to as the luteinization. And therefore, the luteinized granulosa cells which surround the theca-interstitial cells with the invading vasculature give rise to the origin of corpus luteum. It is usually visualized as a small structure with thick irregular hyperechogenic walls known as the ‘ring of fire’ around the corpus luteum, though sometimes it can be difficult to identify with ultrasound as it is confused with the stromal tissue. The fallopian tubes can be seen on ultrasound only when they are distended with fluid (hydrosalpinx) or when there is peritoneal fluid surrounding the adnexae (D’Addario et al., 2020).

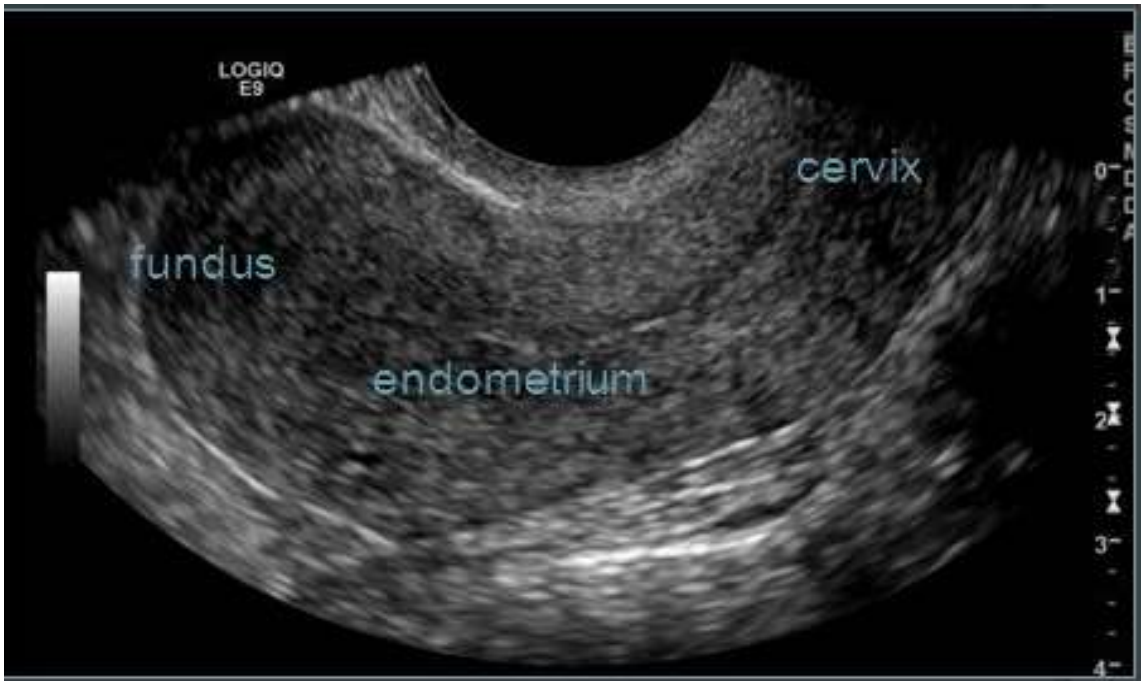

Figure 1:Normal sagittal transvaginal ultrasound of the uterus. Image courtesy of internet.

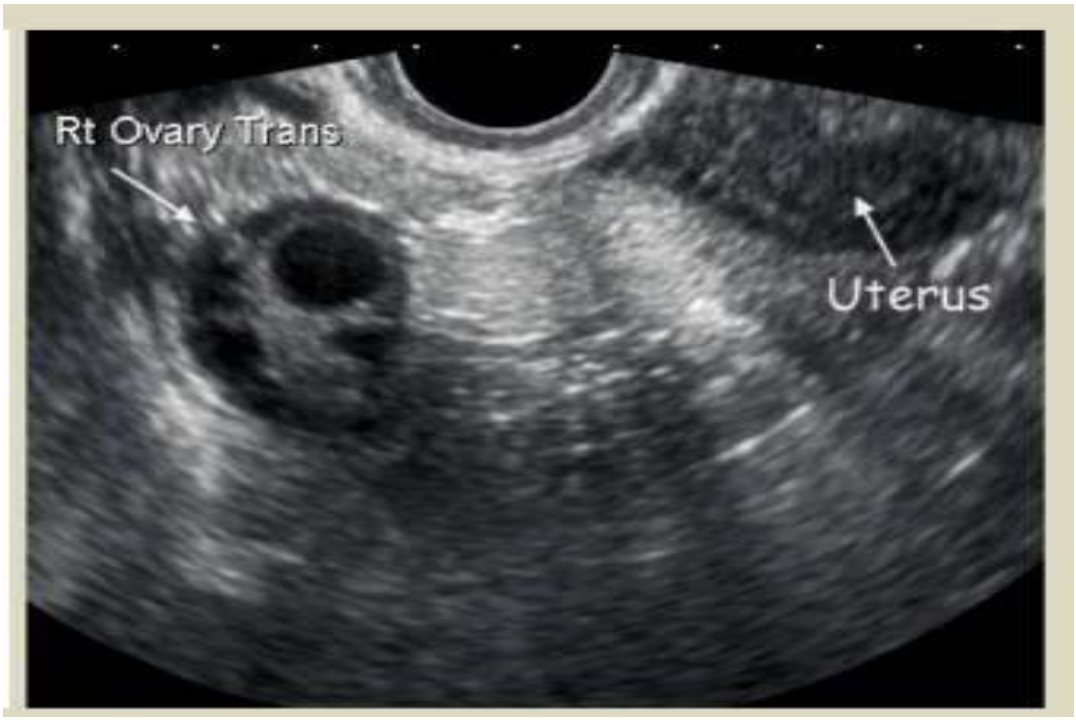

Figure 2:Normal coronal/transverse transvaginal ultrasound showing typical appearance of the ovary- Image courtesy of internet.

Transvaginal Ultrasonography in the diagnosis of female subfertility-

1. **Polycystic ovaries (PCO):**

Polycystic ovarian syndrome is known to be the most common of the endocrine disorders and the presence of the morphology of polycystic ovaries is a cardinal feature of PCOS. It is a common cause of the anovulatory subfertility and thus the high incidence is expected of the polycystic ovarian morphology in women with subfertility undergoing for TVUS as part of the subfertility investigations (Ogueh et al., 2014).

The polycystic ovarian syndrome is characterized by a combination of multiple clinical manifestations (i.e., hirsutism, menstrual disturbances, anovulatory cycles, and subfertility) and hormonal imbalance (an abnormal luteinizing hormone / follicular stimulating hormone (LH/FSH) ratio and excessive androgen secretion) and polycystic ovaries on ultrasound.

Transvaginal Ultrasound examination of polycystic ovaries include:

- Increased follicle number per ovary (FNPO) - usually 20 or greater.
- Individual follicles are generally similar in size and measure 2-9 mm in diameter.
- Peripheral distribution of follicles; this can give a "string of pearls" appearance.
- Background ovarian enlargement (volume greater than 10 mL).
- Central stromal brightness +/- prominence. (Courtesy of Radiopedia).

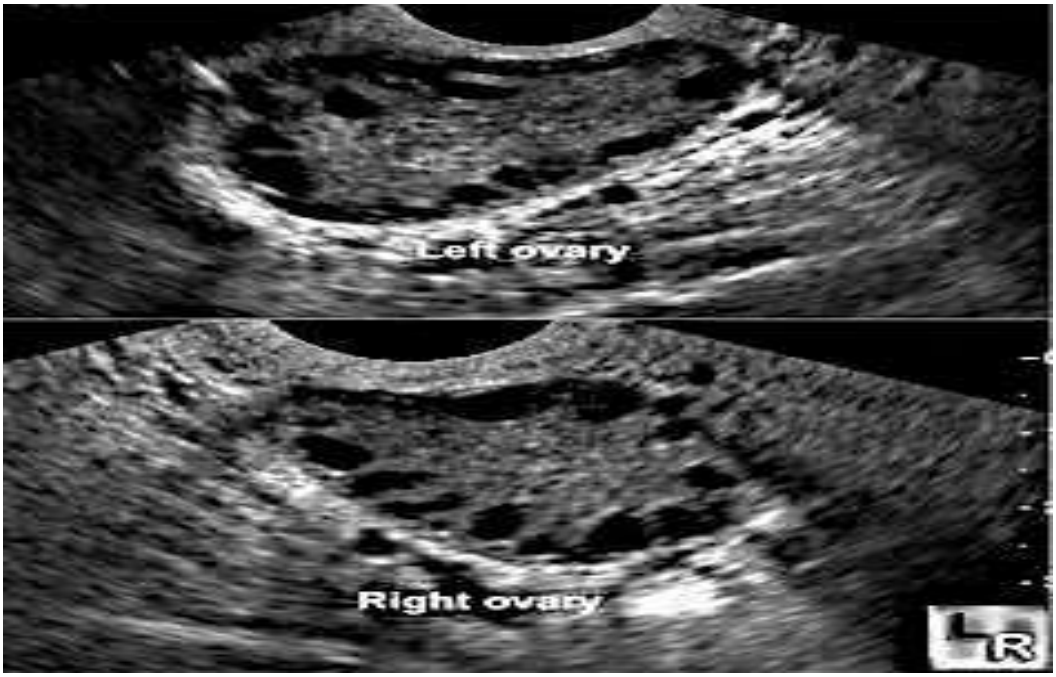

Figure 3:PCO with Cysts Arranged at the Periphery- image courtesy by (Rathour & Singh, 2020).

2. Endometriosis

TVUS is considered as the primary tool for the initial diagnostic evaluation and consequent management of endometriosis which is a complex disease with a wide variety of spectrum of clinical and diagnostic features that can affect the quality of life.

There are four components described of a dedicated TVUS protocol for the evaluation of pelvic endometriosis which include: a) uterus and adnexal evaluation, b)dedicated look out for deep infiltrating endometriosis, c)evaluation of the sliding sign and d) detection of the soft markers on ultrasound (Collins et al., 2019).

It is a chronic disease that affects 10-15% of reproductive-aged women, which is characterized by the demonstration of functional endometrial glands and stroma outside the uterus.

Transvaginal ultrasound is considered the preferred technique not because of its availability but due to its diagnostic accuracy in diagnosing, most cases of ovarian and pelvic endometriosis.

Features of a typical endometrioma are a unilocular cyst with a well-defined wall and ground glass appearance- low-level echoes. In one-third of endometriomas, hyperechogenic wall foci are seen and are thought to be quite distinctive, which is characteristic on TVUS. (Savelli, 2009).

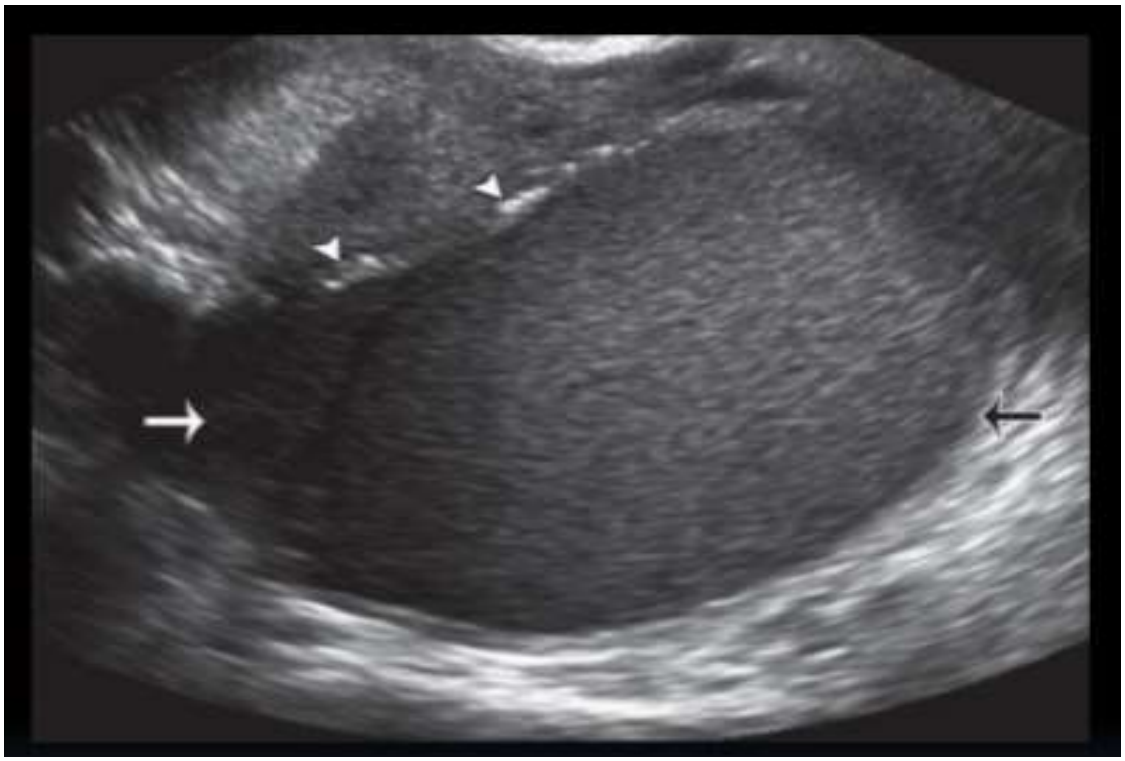

Figure 4:Sagittal transvaginal ultrasound- shows an ovarian mass with fine internal echoes (ground glass appearance) and hyperechoic mural foci- Image courtesy of internet.

4. Leiomyoma

Uterine fibroids or leiomyoma are the common benign tumors of the uterus which can cause severe pain, bleeding and subfertility. Fibroids are known to affect around 35-77% of the reproductive aged females, although the actual prevalence is much higher as many leiomyomas can be asymptomatic.

Leiomyomas are found in approximately 5-10% of the subfertile women and may be the only cause of subfertility in around 1-2.4%. It is known to cause subfertility by the distortion of the endometrial cavity which can lead to an abnormal endometrial development and receptivity (Guo & Segars, 2012).

Submucosal and intramural leiomyomas may cause subfertility by interfering with the transportation of sperms or implantation due to distortions of the uterine contour and cavity. Nowadays, ultrasonography remains the first line in the diagnosis of uterine leiomyomas. Transvaginal ultrasonography is proven to be more sensitive than transabdominal ultrasonography in detecting leiomyomas, even if the size is small. They appear to be well defined, solid, usually hypoechoic masses with wavering amounts of posterior acoustic shadows. The leiomyomas can have differences in echogenicities depending on the amount of calcification they have, either hyperechogenic or isoechogenic. Some leiomyomas can have areas of necrosis which may show as anechogenic areas. In some complicated cases, where the size of the leiomyoma is small and appears isoechogenic to the surrounding myometrium, there can be an only visible sign on ultrasound which is a bulge altering the uterine contour. To distinguish the submucosal fibroids from the polyps, colour Doppler can be useful as the fibroids will show the multiple circular feeding vessels. In contrast, in polyps, there would be a single feeding artery that can be seen (Wozniak & Wozniak, 2017).

There is a little impact of subserosal and pedunculated fibroids on subfertility (Zepiridis et al., 2016).

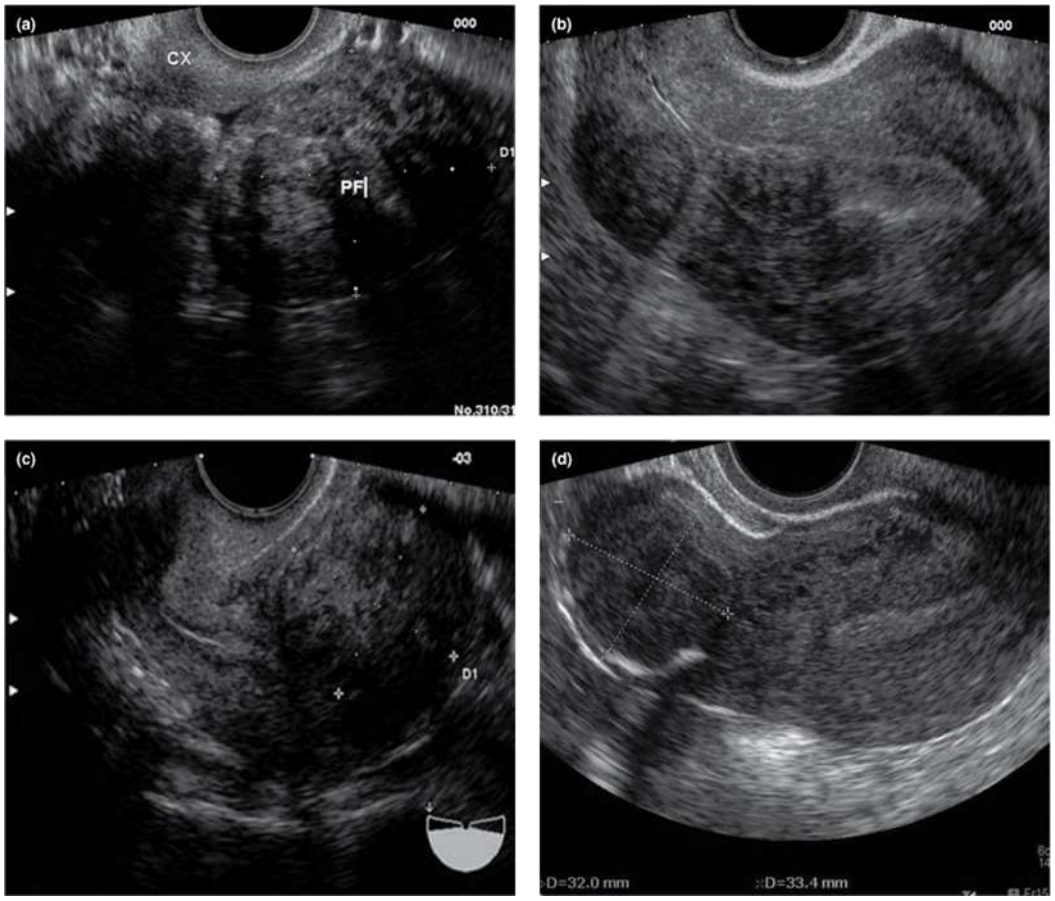

Figure 5:TVUS images of (a) pedunculated fibroid arising from the cervix; (b) submucosal fibroid (with adjacent intramural fibroid in the cervix); (c) intramural fibroid (with indeterminate intrusion on the cavity); and (d) subserosal fibroid. Image courtesy by: Cambridge university press.

5. Adenomyosis

Adenomyosis is a known disorder which is defined by the presence of endometrial glands in the ectopic position and stroma within the myometrium with a component of myometrial hyperplasia. It usually presents with excessive menstrual bleeding, tenderness and pain in the pelvic region. TVUS has been known to be useful in the evaluation and diagnosis of adenomyosis.

Adenomyosis is a disease which is characterized by a diffuse infiltrative process. And it is established that TVUS should be the primary modality of choice in the diagnosis of adenomyosis, though the gold standard is MRI with thickening of the myometrium is recognized as the hallmark of the disease.

Tenderness of the uterus is considered as a hallmark of adenomyosis which can only be assessed by the endovaginal ultrasound and not by MRI. The one doing the ultrasound must always examine the uterus especially looking for areas of focal tenderness. They should also be able to differentiate the actual pain from a sense of deep pressure which is usually a normal reponse (Lara & Szyller, 2016).

It uncommonly causes subfertility, possibly by reducing uterine/endometrial receptivity. TVUS findings include a diffusely enlarged or globular uterus, asymmetric walls (>2.5 cm), ill-defined areas or diffusely altered uterine echogenicity, myometrial or sub endometrial cysts, indistinct endometrial-myometrial interface, sub endometrial echogenic nodules or strands with surrounding hypoechoic myometrium, and undulating outer margin of the endometrium (Rastogi, 2010).

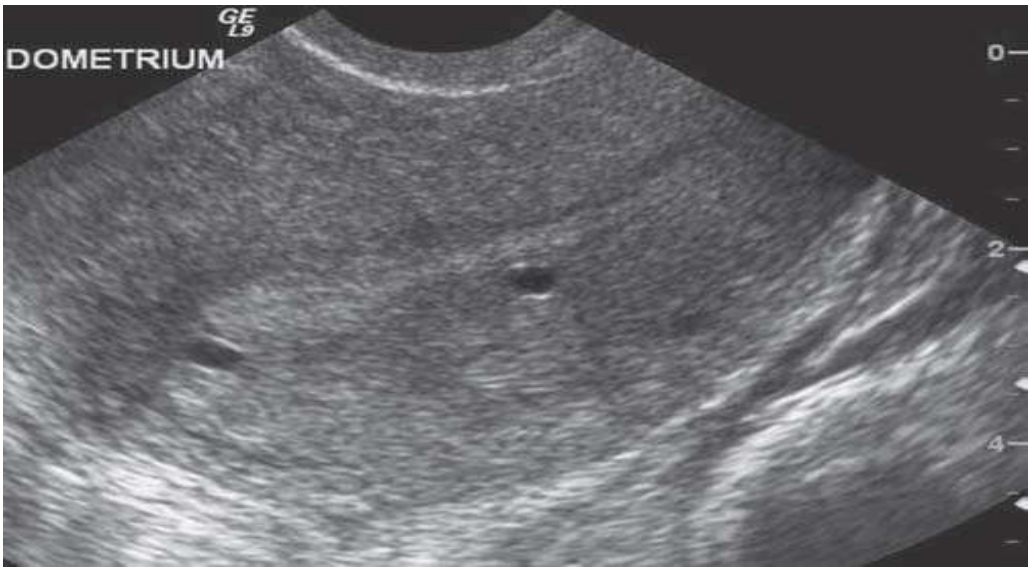

Figure 6:Small myometrial cysts in the junctional zone. The myometrium is also heterogeneous: a case of adenomyosis—image courtesy of- (Lara & Szyller, 2016).

6. Hydrosalpinx

The utility of transvaginal ultrasonography in the diagnosis of hydrosalpinx is done by identifying a tubular structure with an echogenic wall which is well-defined, a folded configuration and echoes protruding into the lumen. It is difficult though to differentiate between the acute and chronic appearances of the disease.

The cogwheel sign is also demonstrated on the ultrasound (Timor-Tritsch et al., 1998).

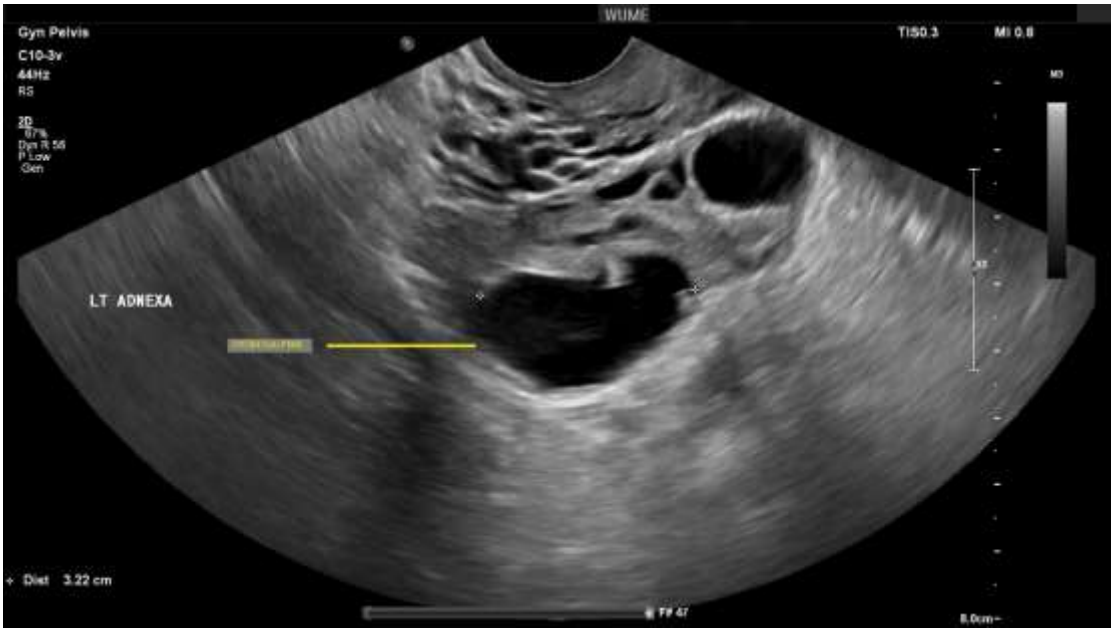

Figure 7: Patient with PID. TVUS showed hydrosalpinx. Image courtesy of internet.

7. Pelvic inflammatory disease

PID is a very common cause of female subfertility and can be manifested as pelvic collections, tubo-ovarian collections, uterine or broad ligament infection.

TVUS and MRI are both considered as equally sensitive in the detection of tubo-ovarian collections. If there is presence of peripheral vascularity on Doppler ultrasound is a characteristic finding suggestive of an infective mass.

There are other signs of PID which include tenderness caused by the probe, thickening of the tubes (mural thickness of more than 5 mm) and masses of tubo-ovarian origin (Rastogi, 2010).

8. Uterine anomalies (Mullerian duct anomalies)

They are considered the cause of subfertility when all the other causes have been ruled out. TVUS specially 3D is considered the most useful modality in the diagnosis of the congenital uterine anomalies, though MRI is the gold standard for those.

American Fertility Society Criteria has developed a classification on the various classes of mullerian duct anomalies:

- ✓ Class I is classified as uterine hypoplasia or agenesis.
- ✓ Class II or unicornuate uterus: characterized by a banana-shaped uterus with a single fallopian tube. A rudimentary horn (communicating or noncommunicating) may be present.
- ✓ Class III or uterus didelphys: which is classified as two complete uteruses, each with its own cervix and a sagittal vaginal septum is seen in most of the cases.
- ✓ Class IV or bicornuate uterus: In this class there are two uterine cavities with one cervix. MRI shows widely placed uterine horns with an intercornual distance of >4 cm and concavity of the fundal contour or an external fundal cleft of >1 cm in depth.
- ✓ Class V or septate uterus: This is defined as the presence of a fibrous septum that appears hypointense on T2W images while the muscular septum appears intermediate in intensity. MRI criteria includes a convex or flat external fundal contour or external fundal cleft of <1 cm in depth.

- ✓ Class VI or arcuate uterus: It is a normal variant and is characterized by an external convex contour of the fundus with fundal endometrial indentation.
- ✓ Class VII or diethylbestrol-induced: Exposure to this synthetic estrogen antenatally can result in a T-shaped, hypoplastic, and constricted uterus (Rastogi, 2010).

2.4.2 3 D- Transvaginal Ultrasonography

The 3-D TVUS allows the conceurrent assessment of the individual sectional planes in order to maximize the information available on the 2D and thus improve on the spatial awareness.

Also, it has a unique feature which allows the demonstration of the coronal plane, perpendicular to the face of the transducer which is used to facilitate in the identification of the mullerian duct anomalies by the visualization of the surface abnormalities.

3D ultrasound offers the following advantages on top of the 2D ultrasonographic features:

- In the precise measurement of the different organ dimensions and volumes.
- Improved information on the anatomy and blood flow parameters.
- Assessment of the different uterine congenital anomalies.
- In the assessment of endometrial receptivity (Momtaz, 2006).

2.4.3 Magnetic resonance imaging (MRI)

It is best for delineating the morphology and orientation of pelvic structures.

MRI also detects pathological lesions, including tubal lesions and pituitary adenoma. It helps in predicting the prognosis in conservatively treated cases of leiomyoma, adenomyosis, and endometriosis (Rastogi, 2010).

MRI is excellent in not just getting at a defnitive diagnosis in sonographically undiagnosed tubo-ovarian masses, but also in delineating the stage, severity, and extent of spread of pelvic inflammatory disease. There are characteristic MRI appearances in tubo-ovarian abscesses which include, complex cystic solid masses in adnexal region, with ovaries not separately seen. These lesions are noted to be heterogeneously hypointense on T1W sequences, hyperintense on T2W sequences, and show heterogeneous contrast enhancement of the tubal walls and septae on gadolinium administration.

The information provided is useful in the assessment of tubal and peritubal pathologies, complex tubo-ovarian abscesses and masses, and for the diagnosis and localization of deep-seated endometriosis and its associated complications. In the delineation of Mullerian anomalies and the mapping of uterine leiomyomas, the capability of MRI remains remarkable.

Though it is non-invasive and radiation-free, it has limited availability, and high cost and hence cannot be repeated easily. Longer examination time, failure to delineate sub-centimetre uterine lesions, and inability to characterize endometriomas at some stages are other limitations. MRI is contraindicated in patients with cardiac pacemakers and cochlear implants. (Grover et al., 2020).

2.4.4 Hysterosalpingography(HSG)

Hysterosalpingography (HSG) is a special contrast examination that is used to assess the cervical canal, uterine cavity and both fallopian tubes; usually, an invasive procedure and is achieved by cannulating the cervical os and retrogradely injecting the contrast medium to outline the female reproductive tract, (cervix, uterus and both tubes). It is usually done under fluoroscopy with image intensification.

Common indications for this procedure include evaluation of tubal patency, identification of congenital anomalies of the genital tract, assessment of uterine cavity, efficiency of tubal sterilization, reversal of tubal surgery, assessment of secondary amenorrhoea, among others. Known contrast allergy is an absolute contraindication. It is, however, contra-indicated in pelvic inflammatory infection (PID) and pregnancy. Noted among its complications are pelvic disease, severe pain, Hemorrhage and vasovagal attacks (Ezenyeaku, 2015).

The patients are usually scheduled for the procedure on 7^{th} to 12^{th} day of the regular 28-day menstrual cycle and before having sexual intercourse to make sure that there is thin endometrium to facilitate proper interpretation. The patients are usually advised to take a nonsteroidal- anti inflammatory medicine half an hour before the procedure to reduce the discomfort caused due to the procedure.

The patient is placed in the lithotomy position at the foot end of the table and using aseptic technique, a vaginal speculum is inserted after applying a local anesthetic agent. A syringe filled with 15 ml of 60% urografin is fixed to the end of the cannula and remove air from the cannula. With a gentle traction on a vulsellum forceps placed on the anterior cervical lip, the cannula is then inserted and fixed to the cervix and the patient is moved up the table. Patient position is adjusted and contrast to be injected slowly under fluoroscopic monitoring. Films are taken with the patient in the supine position after injection of about 5 ml of contrast to demonstrate the cavity of the uterus and after injection of another 5 ml to demonstrate free spillage into the peritoneal cavity. Patients are actively informed that vaginal bleeding may occur for one to two days following the procedure (Toufig et al., 2020).

2.4.5 Hysterosalpingo-contrast sonography(HyCoSy)

Hysterosalpingo-contrast sonography (HyCoSy) is the favored method in the assessment of the tubal patency in women specially with the secondary subfertility , with a history of previous abdominal surgery and also in the cases of primary subfertility where laparascopy is not necessary. Unlike HSG, HyCoSy does not involve the use of ionising radiation and iodine-based contrast media (Lee, 2010).

It uses ultrasound to view the uterus, tubes, and adnexa before and after transcervical injection of echogenic contrast media. It is a safe, well-tolerated, quick and easy method for obtaining information on tubal status, the uterine cavity, the ovaries, and the myometrium using conventional ultrasound.

The procedure is usually done as an outpatient procedure. The patients vulva and vagina are cleaned and speculum inserted into the vagina under aspectic conditions. A ballon catheter is inserted into the vagina through the cervix and into the uterine cavity. Once the catheter is in the satisfactory position, the balloon is inflated to make sure the catheter is secured and then the speculum is removed. The endocavitary probe is then inserted into the vagina. The echocontrast agent is injected about 1-2 mls at a time slowly, and the fallopian tubes are filled intermittently. The ultrasound is maneuvered to visualize the different areas of interest. A fallopian tube is then considered to be patent if the intratubal flow can be visualized using the B-mode scanning for at least 5-10 seconds. Shahid et al found it to be a useful screening test and an effective alternative for laparoscopy (Shahid et al., 2005).

2.4.6 Saline infusion sonohysterography

Saline infusion sonohysterography is a procedure in which saline is instilled into the uterine cavity through the cervix to get enhanced endometrial visualization by doing a TVUS. The technique helps in sonographic detection of main pathologies of endometrium like for example-polyps, hyperplasia, carcinoma, leiomyomas, and adhesions. Moreover, it can avoid invasive diagnostic procedures and help triage patients who may need therapeutic intervention. The procedure can be easily performed in less time, cost-efficient, and usually well tolerated by the patients and has minimal complications (Uptodate).

The contraindications of the procedure are pregnancy, pelvic inflammatory disease and the presence of the intrauterine contraceptive device.

Mild cramping and spotting can be caused by the procedure as complications.

The technique of the procedure is as follows:

The study is usually scheduled for the days 4-7 of the menstrual cycle.

The patients is put in the lithotomy position and with the help of the speculum, the cervix is identified and prepped with iodine. The catheter used is flushed with saline to remove any bubbles of air and then it is introduced into the uterine cavity through the os of the cervix and the ballon of the catheter is inflated after passing through the cervix.

Then the pre-warmed saline in quantity of 5-30 mls is injected slowly under the guidance of the ultrasound of the uterus. And then the imaging is carried out in the coronal and sagittal planes and the volumes are measured using the 3D ultrasound. Some technicians leave the speculum in place during the procedure but it may hinder the visualization of the endocavitary probe (Radiopeadia).

2.4.7 Hysteroscopy

It is the ‘gold standard’ in the diagnosis of intrauterine pathologies. It’s the definitive method for the evaluation of abnormalities of the endometrial cavity and also offers the opportunity for treatment at the time of diagnosis (Gillespie & Nichols, 1994).

The indications for the hysteroscopy in subfertility are as follows:

1. Abnormal HSG
2. Abnormal uterine bleeding
3. Suspected intrauterine pathologies
4. Unexplained cases of subfertility
5. History of pregnancy wastages
6. Targeted biopsies

Hysteroscopy provides an excellent mode of evaluation and therapeutic method in cases of post –intrauterine surgery such as for intrauterine adhesions, uterine septations and myomectomy(submucous).

The best time to perform the procedure is in the early follicular phase so as to avoid the increased thickness of the endometrium and mucus which can hinder the proper visualization. Though diagnostic hysteroscopy can be combined with the laparoscopy procerdure and should be performed in the luteal phase of the menstrual cycle but care should be taken to avoid unnecessary trauma to the endometrium.

The limitations of the procedure are that it requires special instrumentation and expertise with cost aslo being high. Also the tubes cannot be evaluated like HSG (Metello, 2017).

In a study done by Hadra et al at Kenyatta National Hospital on Causes and types of subfertility amongst couples, it was shown that the most common cause of subfertility was a tubal peritoneal factor (83.6%), with those having bilateral tubal blockage (60.6%). Endocrine causes were identified in 16.4% of the female subfertile partners, polycystic ovarian syndrome (PCOS) had 11.5% and hyperprolactinemia (4.9%) (Hadra, 2015).

CHAPTER THREE: METHODOLOGY

3.1 Study Setting

The study was conducted at the Radiology and Imaging department at Moi Teaching and Referral Hospital (MTRH). The Hospital is in Eldoret town, which is 350 Kilometers northwest of the capital Nairobi. MTRH is a tertiary (level 6) health facility serving as a teaching hospital for Moi University School of Medicine, Public health, and Dentistry. Others include Kenya Medical Training Center (KMTC), Eldoret and University of Eastern Africa Baraton School of Nursing. MTRH is also a training centre for medical, clinical, and nursing officer interns. It is the referral hospital for the Western part of Kenya and North rift and has a catchment population of approximately 24 million people. The facility has several departments, including Surgery, Pediatrics and Radiology and Imaging, among others.

3.2 Study Design

The study was a cross-sectional descriptive study design conducted over a period of one year.

3.3 Study Population

All adult female clients, presenting at MTRH radiology department for ultrasound examination with a diagnosis of subfertility.

3.4 Sample size and Sampling Procedures

3.4.1 Sampling technique

Patients with subfertility referred to the MTRH radiology unit, which met the study's inclusion criteria, were consecutively recruited after consenting.

3.4.2 Sample size determination

To be able to estimate the proportion of leiomyoma among the TVUS findings, we used a sample size formula described by Fisher et al(1998),

$$n = \frac{z2p(1-p)}{d2}$$

n = desired sample size

Z= standard normal variance equivalent to 1.96

p= estimated prevalence rate of leiomyoma=7.5% (Cook, Ezzati, Segars, & McCarthy, 2010)

d= desired level of significance (0.05)

When this formula was applied at d=0.05, z=1.96 and p=0.075

$$n = \frac{(1.96)2 \times 0.083(1-0.083)}{(0.05)2} = 100$$

Therefore n = 100.

The expected minimum sample size was 100 patients.

3.5 Eligibility Criteria

3.5.1 Inclusion criteria

1. Female patients with subfertility referred by medical specialists for transvaginal ultrasound examination.

3.5.2 Exclusion criteria

1. Female patients on hormonal therapy.
2. Female patients on treatment/follow up for subfertility.

RECRUITMENT SCHEMA

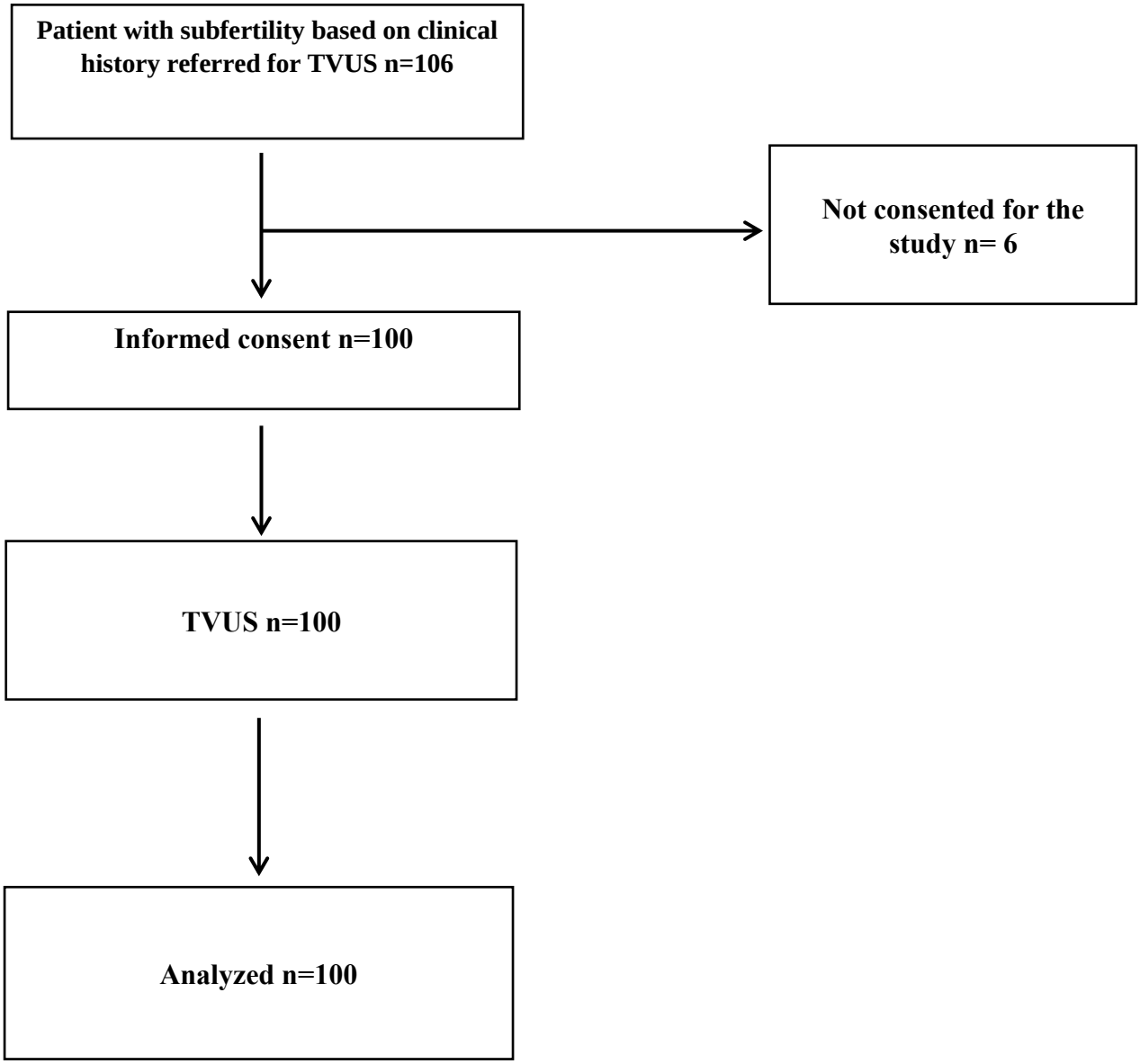

Figure 7: Recruitment Schema

3.6 Study Procedure

Clinicians in radiology and gynaecology clinics were sensitized prior to the study.

All patients presenting for TVUS examination and who meet the inclusion criteria were explained to in a language they understood about the purpose, risks and benefits of the study and given a chance to consent to be part of this study. All their details were retrieved from their records and recorded. All this data was recorded in a questionnaire. Those who consented were subjected to a TVUS**.** All the TVUS examinations were performed by the principal investigator or by a trained assistant using the available ultrasound machine in MTRH.

The TVUS procedure was done as per the protocol mentioned below:

Through the aseptic technique and gloved, the endovaginal probe covered with condom and lubricated with gel was introduced through the vagina. The uterus, endometrium, ovaries, adnexal structures and pouch of Douglas were scanned in both long and short axial planes, any pathologies noted, and images were produced sequentially.

Image interpretation was done by the principal investigator and later reviewed by at least two consultant radiologists. Data was obtained through a structured questionnaire, and all data and images collected were kept confidential.

3.7 Data Collection and Management

3.7.1 Data Collection

Data was collected between May 2019 and April 2020. Entry was made in the questionnaires and later transferred to a computer database. Double entry was used to ensure the accuracy of the data. All patient details were kept confidential, and data was only available to the investigator and the supervisors via a password-protected database. Patients had access to a copy of their results and had autonomy over who else can be disclosed. Serial numbers were used in order to protect patients' identity. At the end of each day, data collection forms were verified for completeness.

3.7.2 Quality control

The images were reviewed by the principal investigator and verified by two consultant radiologists. Preliminary reports were then sent to the referring clinician, and the reports also entered in the data collection forms by research assistants for later analysis.

3.7.3 Data Analysis

Data was imported into STATA/MP version 13, coded and cleaned before analysis was done. Descriptive statistics were done to explore and summarize the variables; for categorical variables- frequencies and proportions were reported in tables. For continuous variables, histograms and box plots were plotted to shows distributions, means (standard deviations) or medians (interquartile range) were computed where applicable and presented in tables.

Fischer's exact test was used to assess the relationship between the transvaginal ultrasound findings and subfertility types. A p-value of less than 0.05 was considered significant.

3.8 Ethical considerations

Ethical approval of the research proposal was granted by the Moi University/MTRH Institutional Research and Ethics Committee (IREC), and permission to conduct the study was obtained from the CEO of MTRH. Written consent was obtained from the patients who were included in the study. The nature, purpose and risks of the study were explained to each participant in details before consenting. No participants were coerced or enticed to participate. Confidentiality of the patients' data was maintained by de-identifying the collected data using codes and storing the data securely in a lockable cabinet for hard copy questionnaires and on a password-protected laptop for the soft copies.

3.9 Data Dissemination Plan

The research findings will be presented to the Department of Radiology and Imaging Moi University and Hospital's management and for use as necessary. It will also be made available to the Moi University Library. The results of this research shall be availed for publication in a reputable journal of medicine for use in improving the diagnosis and management of female subfertility.

CHAPTER FOUR: RESULTS

4.1 Introduction

In this chapter, the findings of the study are presented. The chapter is organized into four sections. The first section is on the demographic information of the participants; the second section is on types of subfertility. The third section is on transvaginal ultrasound patterns, while the last section is on the relationship between transvaginal ultrasonography and subfertility type.

4.2 Results

4.2.1 Demographic profiles of women with subfertility who underwent transvaginal ultrasound

The mean age of the patients included in the study was 35.3 ±5.1 years. The youngest participant was 24 years while the oldest was 45 years.

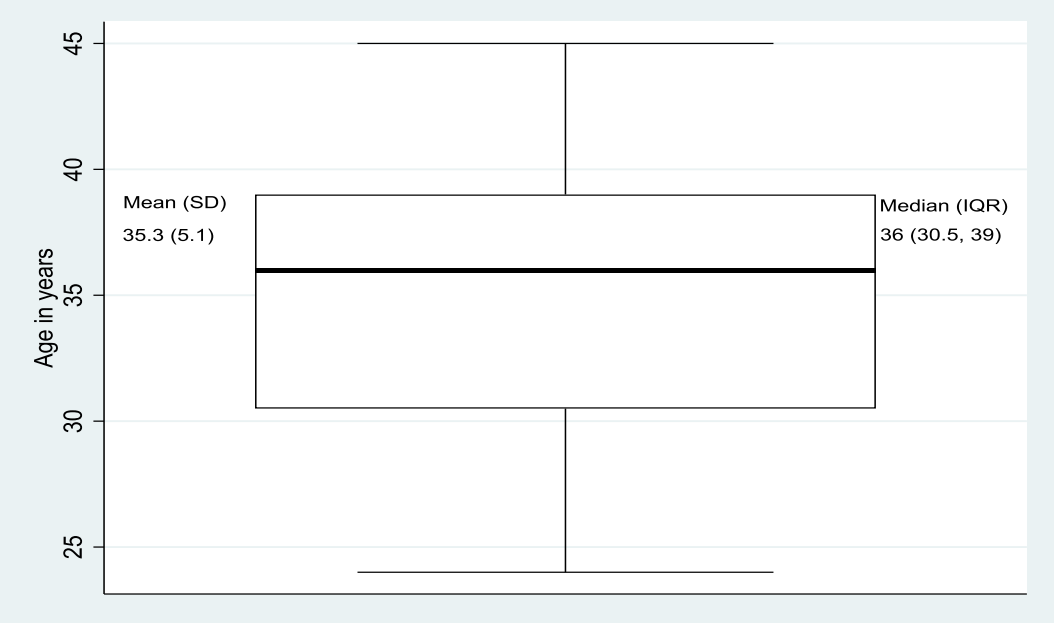

Figure 8: Age distribution

A majority (97; 97.0%) were married while 3 (3.0%) were single. Among them, 37 (37.0%) had university or college level of education, 29 (29.0%) primary school level of education, 27 (27.0%) secondary school level of education, and 7 (7.0%) had no formal education.

Table 1: Demographic information

Variable	Category	Frequency	Percentage
Marital status	Married	97	97.0
	Single	3	3.0
Level of education	None	7	7.0
	Primary school	29	29.0
	Secondary school	27	27.0
	College/University	37	37.0

4.2.2 Proportions of primary and secondary subfertility among women referred for transvaginal ultrasonography

Of the 100 patients, 80 (80.0%) had primary subfertility, while 20 (20.0%) had secondary subfertility.

Table 2: Type of subfertility

Variable	Category	Frequency (n)	Per cent (%)
Types of subfertility	Primary subfertility	80	80.0
	Secondary subfertility	20	20.0

The duration of subfertility was more than five years for 37 (37.0%) participants, 4-5 years for 34 (34.0%) and 2-3 years for 29 (29.0%) participants.

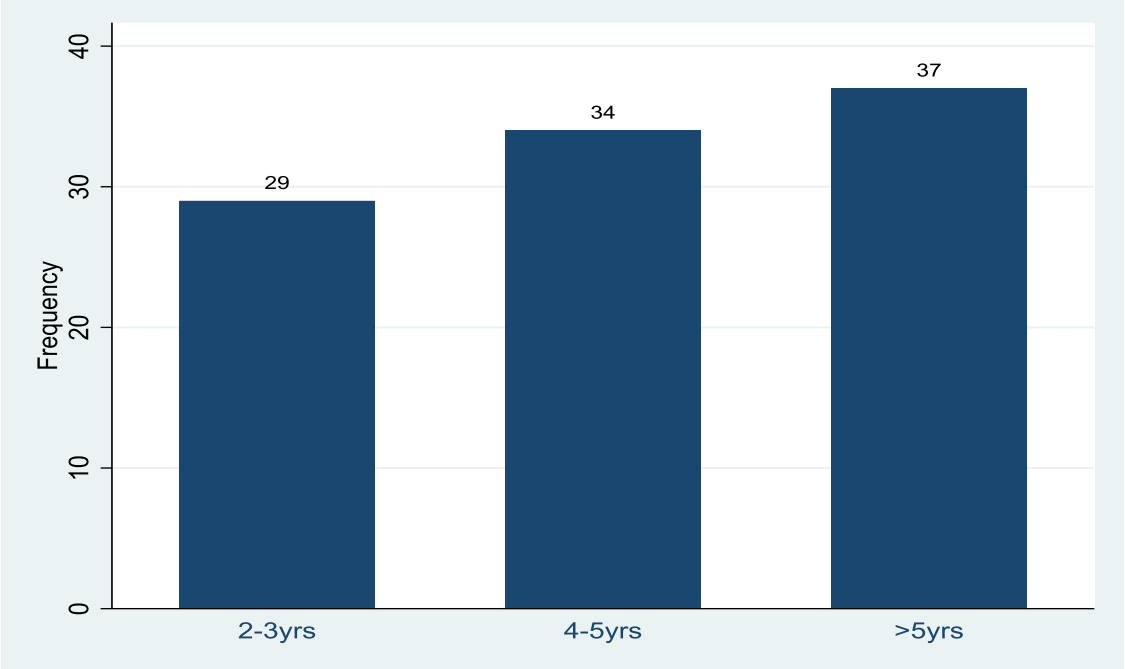

Figure 9: Duration of subfertility

4.2.3 Patterns of transvaginal ultrasonographic findings among women with subfertility

On the patterns of transvaginal ultrasonographic findings, 40 (40.0%) had normal ultrasound findings, 14 (14.0%) had leiomyoma, 13 (13.0%) polycystic ovaries, 8 (8.0%) free pouch of Douglas fluid, 6 (6.0%) ovarian cysts, 6 (6.0%) adenomyosis, 5 (5.0%) hydro-salpinx, 3 (3.0%) bicornuate uterus, 3 (3.0%) endometrioma, 1 had tubo-ovarian mass and 1 hydro-salpinx, ovarian cyst.

Table 3: Transvaginal ultrasonographic findings

Findings	Frequency	Per cent
Normal	40	40.0
Leiomyoma-submucosal/intramural	14	14.0
Polycystic ovaries	13	13.0
Free POD fluid	8	8.0
Ovarian cysts	6	6.0
Adenomyosis	6	6.0
Hydro-salpinx-bilateral	5	5.0
Bicornuate uterus	3	3.0
Endometrioma	3	3.0
Tubo-ovarian mass	1	1.0
Hydro-salpinx, ovarian cyst	1	1.0

4.2.4 The relationship with the patterns of transvaginal ultrasonographic findings and subfertility subtypes

There was no statistically significant association between the subfertility types and the patterns of TVUS findings.

Table 4: Association between subfertility subtypes and transvaginal ultrasound findings

Ultrasound findings	Subfertility		p-value
	Primary (n=80)	Secondary (n=20)	
Normal	31(38.7)	9(45.0)	0.610[c]
Leiomyoma	9(11.2)	5(25.0)	0.147[f]
Polycystic ovaries	12(15.0)	1(5.0)	0.456[f]
Free pod fluid	7 (8.7)	1(5.0)	>0.99[f]
Ovarian cysts	3(3.7)	3(15.0)	0.092[f]
Adenomyosis	6(7.5)	0	-
Hydrosalpinx	4(5.0)	1(5.0)	>0.99[f]

[c] Chi-Square Test, [f] Fishers Exact Test

SAMPLE IMAGES

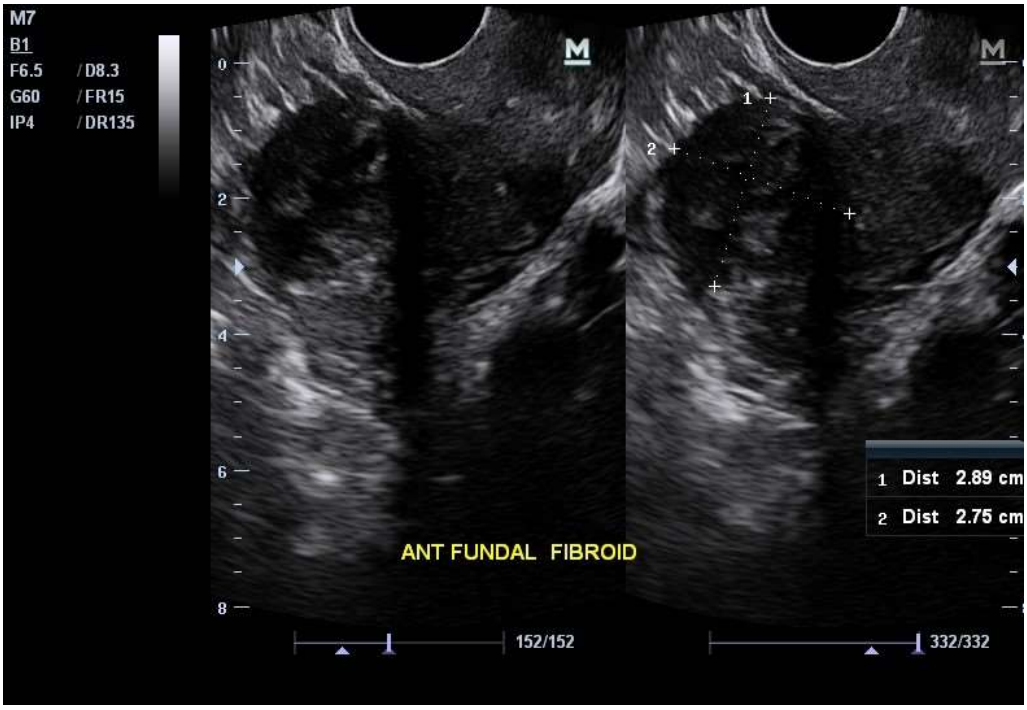

Figure 10: Shows an anterior fundal fibroid- patient with primary subfertility.

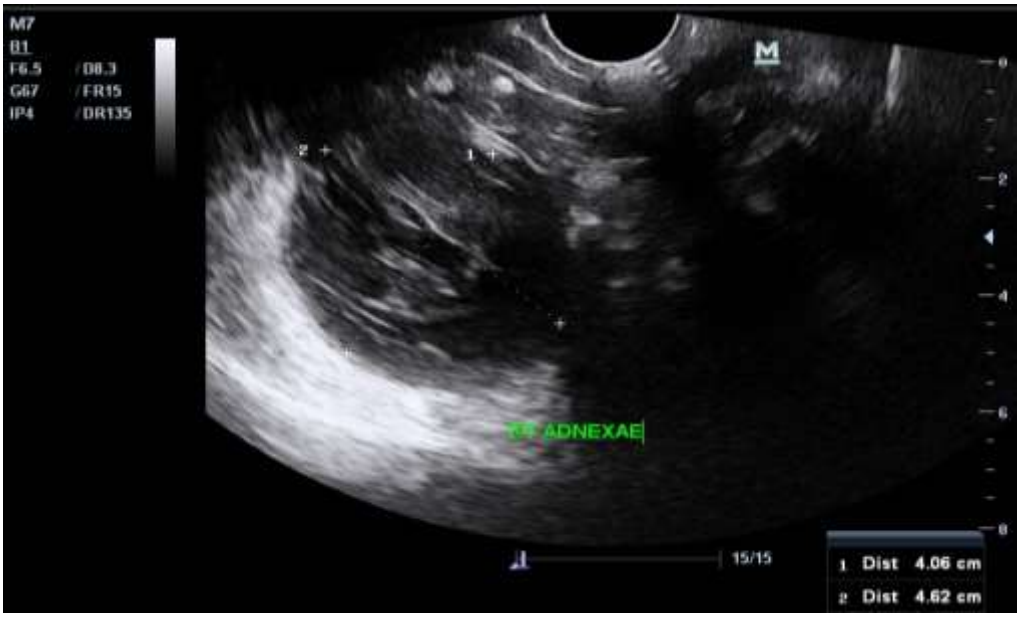

Figure 11: shows a right adnexal complex mass- with solid and cystic components in a patient with primary subfertility.

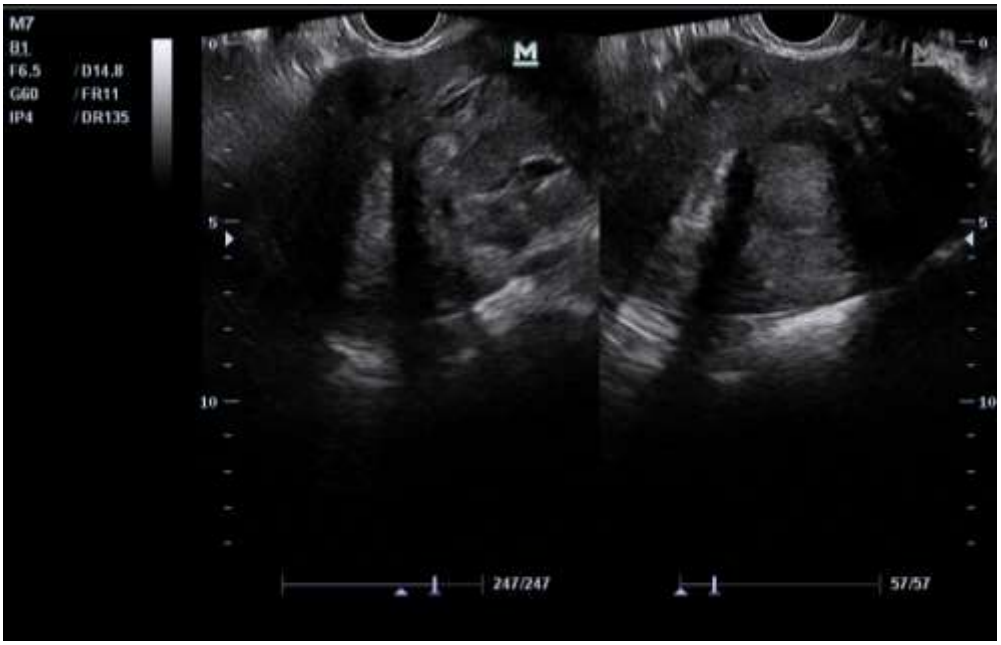

Figure 12: shows multiple intramural fibroids in a patient with primary subfertility.

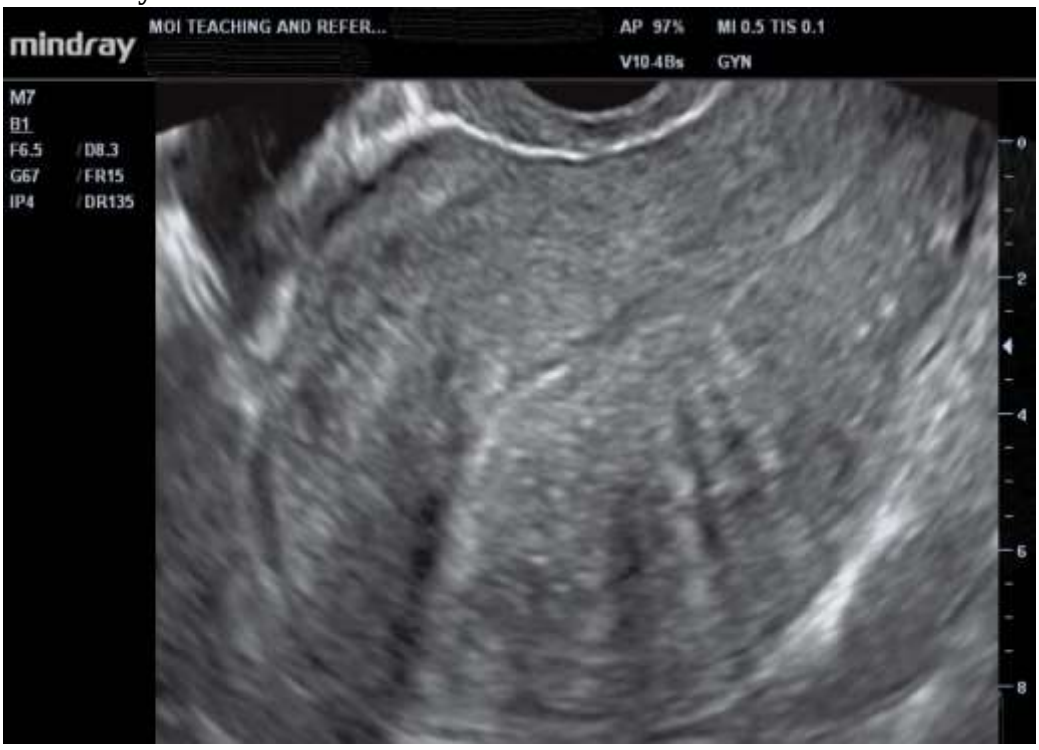

Figure 13: coarsened myometrial echotexture in a bulky uterus with loss of myometrial and endometrial interface - Adenomyosis in a patient with secondary subfertility.

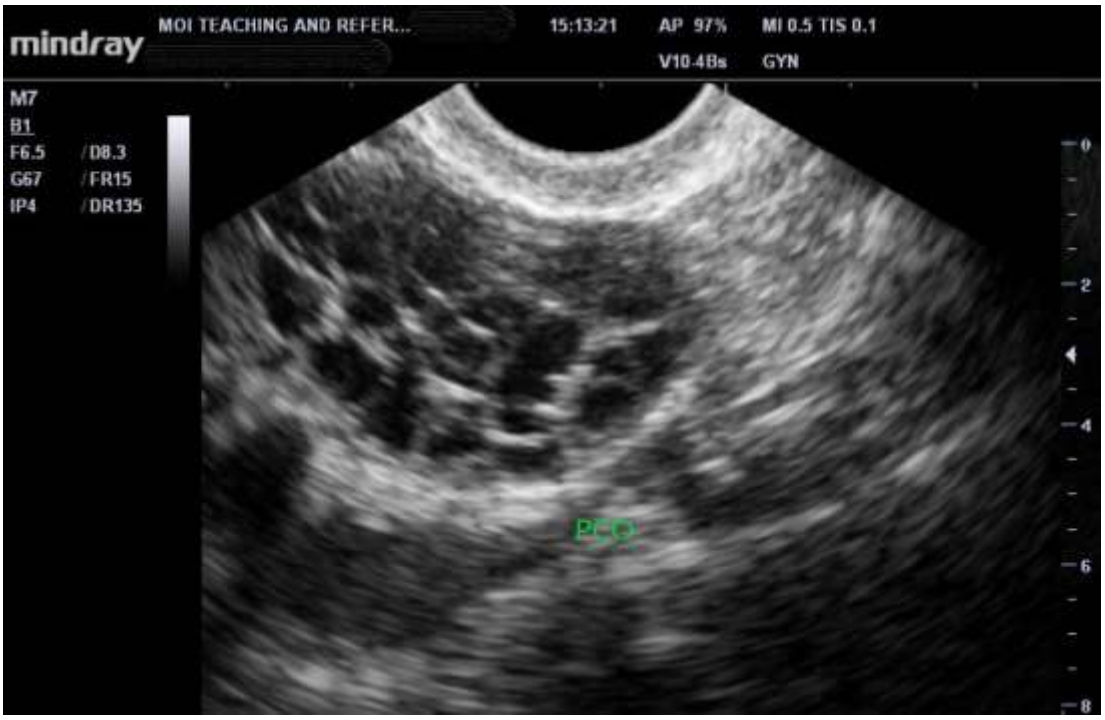

Figure 14: patient with polycystic ovaries- presented with primary subfertility.

CHAPTER FIVE: DISCUSSION

5.1 Introduction

In this chapter, the study results are compared to what had been reported in previous studies, and the findings are put into perspective.

5.2 Discussion

5.2.1 Demographic profiles of women with subfertility

The mean age of the patients in the study was 35.3 years, an indicator that most of them were young adults below 40 years, at the prime of their reproductive age.
The result compares well with Cabrera, et al in Spain, who found a mean age of 38.7 years (Cabrera-León et al., 2015).

According to the Kenya Demographic Health Survey (KDHS), menopause was reported to start early in some women, with menopause prevalence being 5% in women 30-34 years of age, 6.1% in those aged 35-39 years, 9.1% in those 40-41 years, increasing with age to 45% among women age 48-49 years (National Bureau of Statistics-Kenya and ICF International, 2015).

Similarly, a review of national, regional, and global trends in subfertility prevalence, reported cases of subfertility among women as young as 20 years, indicating that it is a problem affecting even young women (Mascarenhas et al., 2012). Hence, subfertility of women younger than 35 years is something that is becoming common and not surprising.

An alternative explanation is that many young couples are delaying childbearing until they are well established, socially, economically, and career-wise; hence the high mean age of those with subfertility as increasing age results in decreased fertility (Sartorius GA et al., 2009).

Most of the women in the study (37%) had a university or college level of education, with only 7% having no formal education. Unlike this study, a community-based study conducted in Spain found a high proportion of 6 months subfertility (45.8%) in women with primary school and below the level of education compared to a lower ratio among those with university education (Cabrera-León et al., 2015).

This being a facility-based study, it is likely that women who sought fertility-related care are those with a high level of education. Hence it might be that cases of subfertility in women who do not seek hospital care services are rarely documented. A community-based fertility study can help capture this group.

Most of them (97.0%) were married, highlighting the importance placed on the marriage institution and family.

5.2.2 Proportion of primary and secondary infertility

A total of 80% of the participants in this study had primary subfertility. In comparison, 20% had secondary subfertility, as was the case in a facility-based study in Bangladesh, where 75% of the included women with subfertility had primary subfertility (75%) (Hussain, 2017).

While the proportion of those with primary subfertility was higher than that of secondary subfertility, primary subfertility has previously been found to be low in Sub-Saharan Africa, with a proportion of 2% in Kenya and a highest of 6% in the Central African Republic and Cameroon. Similarly, the highest secondary subfertility was reported in Cameroon and the Central African Republic among women aged 20 to 44 years, with a prevalence of 20% and 25%, respectively. Kenya had a secondary subfertility estimate of 15% (Larsen, 2000).

Contrary to this study findings, a population-based study conducted in Huelva, Spain, found a high prevalence of secondary subfertility than primary subfertility, 11.33% and 6.12%, respectively. The prevalence of subfertility was noted to reduce with the 6-month subfertility being 19.98%, 12-month subfertility being 11.21%, reducing to 4.36% at 24 months (Cabrera-León et al., 2015).

The high number of primary subfertility than that of secondary subfertility in this study could be explained by that the secondary subfertility not being a considered a health problem as these women have already given birth before compared to those with primary subfertility hence forcing many of those with primary subfertility to seek medical attention.

5.2.3 Patterns of transvaginal ultrasonographic findings among women with subfertility and its association with the subfertility types

Most patients in our study had normal transvaginal ultrasound findings, which accounted for 40%. This is in contrast with a study that found normal findings in about 80% of their patients presenting with subfertility (Ali et al., 2020).

This could be explained by the fact that the most common cause of subfertility in Africa is bilateral tubal occlusion which was found to be three times more in Africa compared to the other developing countries, with 85% being an infectious aetiology and pelvic inflammatory disorder was found in 15% of those women presented with subfertility (A Meheus, J Reniers, 1986).

Thus the normal findings on TVUS can be justified because HSG is best in detecting tubal blockages (Phillips et al., 2015), given the fact that tubal occlusion is more common in our region.

Among the subfertile women in this study, 14% had leiomyoma, which was the most common cause of subfertility. Likewise, the proportion reported in this study, leiomyomas, have been previously reported to occur in 9.1% of women with subfertility. The data had suggested the high prevalence of leiomyoma associated subfertility in blacks. However, approximately 50% of subfertile women with leiomyoma become pregnant after myomectomy (Buttram & Reiter, 1981). The likely reason being generally the African race, obesity and genetic predisposition.

The proportion of subfertile women with Polycystic ovaries was 13%. It compares to the low proportion of PCO of 12.2% in a study done in southern Nigeria on prevalence of PCO (Ogueh et al., 2014). This contrasts with a study in Bangladesh that found 69% of the women with subfertility in their study to have PCO on TVUS (Hussain, 2017). The differences could be explained probably due to geographical differences and Hussain et al did a retrospective study. Elsewhere, PCO has also been reported to be the leading cause of medically treatable subfertility causing approximately 70% of anovulatory subfertility cases (Hamilton-Fairley & Taylor, 2003). Women who have PCO have been found to have increased ovarian gonadotrophins responsiveness hence increased risk of ovarian hyperstimulation syndrome (Agrawal et al., 1998). This is associated with high mortality (Delvinge & Rozenberg, 2002). Ultrasonography helps with the diagnosis of PCO, which is essential in guiding the clinician to develop an appropriate ovarian stimulation protocol for improved patient outcomes (Hart, 2008).

The percentage of adenomyosis found to be 6% in this study. It compares well with a study done in Egypt found 7.5% of adenomyosis prevalence in subfertile women (Abu Hashim et al., 2020). And contrasts with a study done by Margit *et al* found a

high percentage of adenomyosis at 21% (Margit *et al*., 2001). This could be explained by the fact that Margit *et al* used both TVUS and MRI for the diagnosis of adenomyosis.

While we found the percentage of endometrioma to be 3%, a study in Brazil found a slightly higher proportion of 7.8% among 334 women in the study with 1-4 years of subfertility (Chamié et al., 2012). Contrary to the low proportion in our study, previous studies have reported endometriosis as prevalent in approximately 40% of women with subfertility issues (Kinkel et al., 2006) which is higher than what was found in this study. The explanation could be due to a bigger sample size used for a longer duration.

The proportion of bicornuate uterus was found to be 3% in our study. In contrast, in a study done by Gruszka, M., Wilczyński, J, et al on the prevalence of uterine malformations and its impact on subfertility found its proportion to be 46.7% which could be explained by the fact that they conducted the study for 13 years (Gruszka et al., 2012).

However, as was the case in this study, a low proportion of patients with adenomyosis (5%), endometrioma (4%), ovarian masses (2%) and tubo ovarian masses (2%) were found in Bangladesh on TVUS evaluation of women with subfertility (Hussain, 2017). Similar trend and features were noted in a study in Iran where both hysteroscopic examination and TVUS were utilized. TVUS had high specificity in the range of 79%-100% in the detection of the different features (Maryam Niknejadi et al., 2010). The TVUS has been shown to have high sensitivity in detecting endometrial changes and uterine bleeding with histopathology as reference (Anjali Singh, Saroj Singh, Veena Mathur, 2001).

Transvaginal ultrasound has also been demonstrated to be nearly 99.7% sensitive in the diagnosis of hydrosalpinx with a specificity of up to 84.6% (Walker et al., 2007). Hence, it is likely that TVUS could detect most of the conditions that the women with subfertility in our study had.

When transvaginal ultrasound is utilized, uterine and ovarian changes can be instantly evaluated. Abnormalities, such as cysts, tumours, fibroids, endometriomas, hydrosalpinx, and congenital anomalies, can be visualized easily, as was the case in this study to allow for appropriate therapeutic actions early in the care of the subfertile couple (Itskovitz et al., 1990).

Ultrasound, especially TVUS, has become vital in the screening, diagnosis, and management of women with fertility issues, as demonstrated in this study. It is also useful in women on assisted reproductive treatment. It also helps the delivery of safe and effective treatment leading to an increased conception probability. It has replaced more invasive modes in subfertility investigation and can be considered part of standard subfertility care. It enables the evaluation and visualization of ovarian and uterine abnormalities, including fibroids, congenital disorders and cyst, to inform therapeutic decisions (D Chizen, 2010).

Regarding the association between the TVUS ultrasound findings and the subfertility types, no statistically significant association was found between the ultrasound findings and subfertility type. On the contrary, David et al in United States found adenomyosis to be associated with secondary subfertility as the more common cause of uterine disease in women over 30 (Redwine, 2002). This could be attributed by the fact that Davis et al used a larger sample size.

A study done by Gupta et al in India found polycystic ovaries to be associated with primary subfertility followed by tubal causes (Gupta, 2019).

5.3 Limitations

1. This study was a hospital-based study hence leaving out many subfertility cases that exists in the community.
2. As female subfertility is a multifactorial disease, some patients might not afford imaging, thus would have missed out on patients referred for ultrasound.
3. Poor assessment of tubal blockage by using TVUS.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

Mean age of the patients in the study was 35 years. Most of the women in the study had university or college level of education and married. The proportion of primary subfertility was higher than that of secondary subfertility. Leiomyoma and PCO were the main identified causes among the women with subfertility on TVUS. There was no significant association found between the transvaginal ultrasound findings and subfertility subtypes. In general, TVUS proved to be a useful non-invasive diagnostic modality for evaluating subfertility causes of pelvic organs in women.

6.2 Recommendations

6.2.1 Policy recommendations

The subfertility treatments are complicated, uncomfortable and painful medical procedures for women. So, TVUS can play a huge role in the initial

workup of female subfertility.

TVUS thus should be used as a first resort in evaluating the different pathologies associated with subfertility and encouraging more practice of it in the management of the same by sensitization of the clinicians and sonographers/radiologists.

6.2.2 Recommendation for further research

Well-designed large cohort or randomized studies are needed to understand the association between clinical and ultrasound findings in patients with subfertility.

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APPENDICES

Appendix I: Consent Form

English Version

Investigator: My name is Dr. Lajja Dhiren Parikh. I am a qualified doctor registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Masters degree in Radiology and Imaging at Moi University. I would like to recruit you for my research which is to study patterns of transvaginal ultrasonographic findings in subfertile women at MTRH.

Purpose: This study will seek to describe the findings of transvaginal ultrasonography in subfertile women.

Procedure: Women presenting with subfertility referred for an ultrasound will be recruited for the study after the consent has been obtained. They will be interviewed by using a structured questionnaire, and an ultrasound will be performed. Data will be collected on data collection forms. Data collecting material will be kept in a locked cabinet in the office of the principal investigator during the study period.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded the same quality of management as non-study subjects

Risks: There are no anticipated risks to the participants attributable to this study.

Confidentiality: All information obtained in this study will be treated with the utmost confidentiality and shall not be divulged to any unauthorized person

Rights to Refuse: Participation in this study is voluntary. There is the freedom to decline to take part or withdraw at any time. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study

Patient: …… Investigator: …….. Date:

Swahili Consent Form

Mtafiti: Jina langu ni Dkr Lajja Dhiren Parikh. Mimi ni daktari aliyestahili, amesajiliwa na Waziri wa Matibabu wa Kenya na Bodi ya Madaktari wa meno. Kwa sasa ninafuatilia shahada ya uzamili katika Radiolojia na Imaging katika Chuo Kikuu cha Moi. Ningependa kukuajiri katika utafiti wangu ambao ni kujifunza ruwaza za matokeo ya ultrasonograf transvaginal katika wanawake wanaojitokeza katika MTRH.

Kusudi: Utafiti huu utatafuta kuelezea matokeo ya ultrasonograf ya transvaginal katika wanawake waliona shida ya uzazi.

Utaratibu: Wanawake walio na shida ya uzazi watatayarishwa kwa ajili ya utafiti baada ya idhini ya kupatikana. Watashughulikiwa kwa kutumia dodoso la muundo na ultrasonograf itafanyika. Takwimu zitakusanywa kwenye fomu za kukusanya data. Takwimu za kukusanya data zitahifadhiwa katika baraza la mawaziri limefungwa katika ofisi ya mpelelezi mkuu wakati wa utafiti.

Faida: Hakutakuwa na manufaa ya moja kwa moja ya kushiriki katika utafiti huu. Masomo ya kujifunza yatapewa ubora wa usimamizi kama masomo yasiyo ya kujifunza

Hatari: Hakuna hatari inayotarajiwa kwa washiriki inayotokana na utafiti huu.

Usiri: Taarifa zote zilizopatikana katika somo hili zitatambuliwa kwa usiri mkubwa na hazitafunuliwa kwa mtu yeyote asiyeidhinishwa

Haki za Kuepuka: Kushiriki katika utafiti huu ni kwa hiari, kuna uhuru wa kupungua kushiriki au kuondoka kwa wakati wowote. Utafiti huu umekubalika na Kamati ya Utafiti na Maadili ya Taasisi (IREC) ya Chuo Kikuu cha Moi / Chuo cha Mafunzo na Hospitali ya Moi.

Ishara au ufanye alama ikiwa unakubali kushiriki katika utafiti

Mgonjwa: ..... Mtafiti: .... Tarehe:

Appendix II: Data Collection Form
PART 1: DEMOGRAPHIC DATA

1. Date of birth _____
2. Residence _____

3. County of referral _____

4. Marital status of the mother/study subject

Single (never married) [ ] Married [ ] Divorced [ ] Widowed [ ]
Separated [ ] other specify _____

9. Level of education of the mother
None [ ] primary [ ] secondary [ ] college/university [ ]

PART 2: GYNAECOLOGICAL HISTORY

Last menstrual period _____

Parity _____

Duration in years since last delivery _____

Subfertility type primary [ ] secondary [ ]

Duration of subfertility 1 yr [ ] 2-3 yr [ ] 4-5 yr [ ] >5 yr [ ]

PART 3: RADIOLOGICAL/IMAGING HISTORY AND FINDINGS

Number of times investigations done once [ ] more than once [ ]

If more - results of initial exam _____

Results of examination_____

Uterus _____

Endometrial thickness_____

Ovaries _____

Cervix_____

Adnexae _____

The questionnaire has come to an end. Thank you very much for your participation.

Appendix III: Procedure for Doing Transvaginal Ultrasound(TVS)
Patient preparation

- Inform the patient about the procedure
- Seek consent
- The bladder should be empty
- Chaperon must be available, especially if the sonographer is a male
- Maintain confidentiality and privacy

Equipment required

Gloves, lubricating gel, probe cover, 7.5- 10 MHZ probe

Positioning

-Patient wears a hospital gown

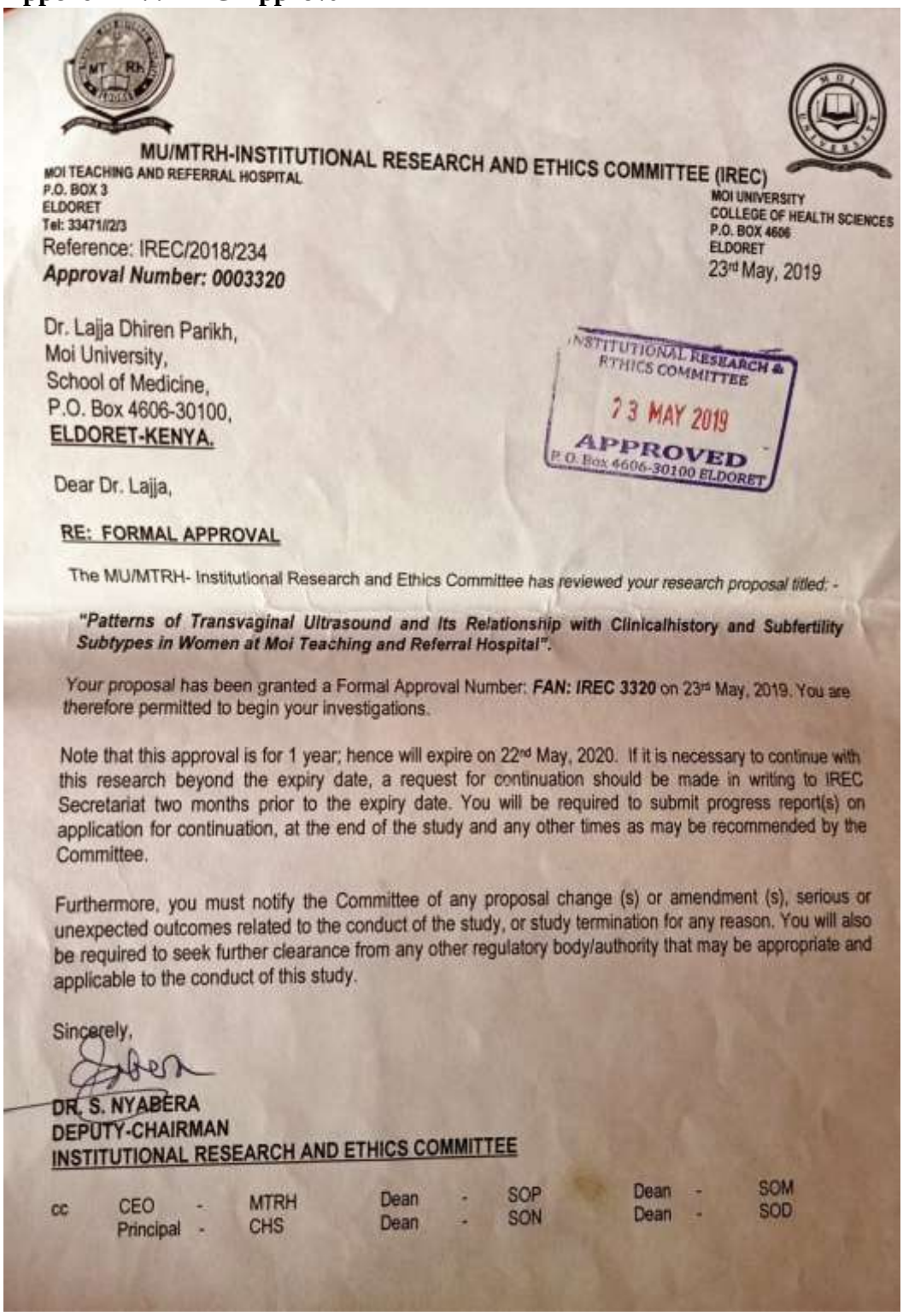
- patient in a supine lithotomy position

-expose from the waist downwards

Imaging procedure

Through the aseptic technique, the ultrasound probe, which is covered and lubricated, is introduced through the vagina, and the uterus is scanned in both long and short axial planes. Any abnormalities are noted, and images are produced sequentially

Appendix IV:IREC Approval



MU/MTRH-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2018/234
Approval Number: 0003320

23rd May, 2019

Dr. Lajja Dhiren Parikh,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
23 MAY 2019
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Lajja,

RE: FORMAL APPROVAL

The MU/MTRH- Institutional Research and Ethics Committee has reviewed your research proposal titled: -

"Patterns of Transvaginal Ultrasound and Its Relationship with Clinicalhistory and Subfertility Subtypes in Women at Moi Teaching and Referral Hospital".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 3320*** on 23rd May, 2019. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; hence will expire on 22nd May, 2020. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date. You will be required to submit progress report(s) on application for continuation, at the end of the study and any other times as may be recommended by the Committee.

Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. You will also be required to seek further clearance from any other regulatory body/authority that may be appropriate and applicable to the conduct of this study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix V: IREC Approval letter

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.keldirectorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

28th May, 2019

Dr. Lajja Dhiren Parikh,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Patterns of Transvaginal Ultrasound and Its Relationship with Clinicalhistory and Subfertility Subtypes in Women at Moi Teaching and Referral Hospital".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

MOI TEACHING AND REFERRAL HOSPITAL
C E O
APPROVED
28 MAY 2019
SIGN.....
P. O. Box 3 - 30100, ELDORET

28/05/2019

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - Senior Director, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM