PREVALENCE OF POLYCYSTIC OVARY SYNDROME AMONG WOMEN PRESENTING WITH AMENORRHEA AND OLIGOMENORRHEA AT THE KENYATTA NATIONAL HOSPITAL

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Dissertation submitted as partial fulfillment of the requirements for the award of degree of Masters of Medicine in Obstetrics and Gynaecology, University of Nairobi.

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DECLARATION

I declare that this dissertation is my own work done under the guidance of my supervisors. It has not been accepted for the award of a similar or any other degree or diploma at the University of Nairobi or any other educational institution.

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DEDICATION

This book is dedicated to me, and all the women with Polycystic Ovary Syndrome.

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LIST OF ABBREVIATIONS

AE-PCOS	Androgen Excess –Polycystic Ovary Syndrome Society
ASRM	American Society of Reproductive Medicine.
BMI	Body Mass Index
DHEAS	Dehydroepiandrosterone Sulphate
ESHRE	European Society for Human Reproduction
GOPC	Gynecology Outpatient Clinic
HPO	Hypothalamo Pituitary Ovarian axis.
KNH	Kenyatta National Hospital
LH	Luteinising Hormone
NIH	National Institute of Health
NICHHD	National Institute of Child Health and Human Development
PCOM	Polycystic Ovary Morphology
PCOS	Polycystic Ovary Syndrome
RIA	Radioimmunoassay
U/S	Ultrasound

OPERATIONAL DEFINITIONS

Amenorrhea Absence of menses for more than 6 months in a reproductive age woman

Androgenaemia Increased blood androgen levels

Anovulation Failure of release of an oocyte from the ovary during the menstrual cycle, leading to lack of ovulation

Fertility The capacity to conceive or induce conception

Hirsutism The presence of terminal coarse hairs in females in a male like distribution

Hyperandrogenism The clinical signs related to the biological actions of androgens

Irregular menses Unpredictable inter menstrual period.

Oligomenorrhea Fewer than 6 cycles annually or a cycle length longer than 35 days.

Polycystic ovary morphology More than 12 follicles of 2-9mm in diameter and ovarian volume more than 10ml(2004 revised 2003 consensus on diagnostic criteria and long term health risks related to PCOS. Fertil Steril 81: 19-25)

Syndrome A group of signs and symptoms that occur together and characterize a particular abnormality or condition

ABSTRACT

Background: Polycystic Ovary Syndome is the commonest endocrinological condition associated with anovulatory infertility in women of reproductive age. It is also associated with morbidities like type 2 diabetes, cardiovascular diseases and endometrial carcinoma. Lowered quality of life from mood changes, low sexual satisfaction, increase in weight, acne on the skin and hair loss have also been reported. Majority of PCOS patients have ovarian dysfunction, with 70%-80% of women with PCOS presenting with menstrual irregularities (oligomenorrhea/amenorrhea) which forms the basis for this study.

Objectives: To determine the prevalence of polycystic ovary syndrome among women presenting with amenorrhea and oligomenorrhea at the Kenyatta National Hospital.

Methodology: This was a descriptive cross sectional study. The study population comprised of 131 patients recruited at Kenyatta National Hospital gynecology department. Those enrolled, gave an informed consent, filled a questionnaire, had their anthropometric measurements taken, then underwent a pelvic ultrasound scan and a blood sample for serum free testosterone levels was taken. PCOS was determined using the Rotterdam criteria, therefore the participants whose results reflected the presence of 2 out of the 3 criteria were considered to have PCOS.

Results: A total of 49 (37.4%) was diagnosed with PCOS using the Rotterdam criteria in this study. Their mean age was 25.9+/-3.8, mean BMI of 25.9+/-5.6 and twenty one women (42.9%) of those with PCOS had testosterone levels higher than the upper limit of normal.

Conclusion: Prevalence of PCOS in special populations like among women with amenorrhea and oligomenorrhea is higher than that of the general population.

Polycystic ovary syndrome should rank highly in the differential diagnosis when evaluating a woman with oligomenorrhea or amenorrhea as evidenced by the high prevalence.

Key words

Poly cystic ovary syndrome, Oligomenorrhea, Amenorrhea.

CHAPTER ONE: INTRODUCTION

1.1 Definition and historical background.

Polycystic ovary syndrome (PCOS) is a common endocrine disorder of women, characterized by a heterogeneous presentation of hyperandrogenism and ovulatory dysfunction. Ovulatory dysfunction may manifest as oligomenorrhea, amenorrhea and infertility. The cause is not known, however it has significant future health implications due to its association with type 2 diabetes, cardiovascular disease (2) and endometrial carcinoma (3). Lowered quality of life from mood changes, low sexual satisfaction, increase in weight, acne on the skin and hair loss have also been reported (26). Considering the aforementioned, this syndrome is a important public health concern in society, which therefore indicates a need to accurately identify the proportion of women affected.

The syndrome was first described by Irving F. Stein and Michael L. Leventhal in 1935 as a symptom complex associated with anovulation. Stein and Leventhal described seven patients (four being obese) with amenorrhea, hirsutism, and enlarged, polycystic ovaries. They reported that all seven resumed regular menses and that two became pregnant after bilateral ovarian wedge resection, involving the removal of one-half to three-fourths of each ovary (1)**.** Stein and Leventhal developed the wedge resection procedure after observing a resumption of menses following ovarian biopsy in several patients with amenorrhea.

Over the years, a lot of knowledge has been gained about the disordered hormonal interplay and insulin and androgen metabolism and the possible effects of genetics and environmental influences that eventually lead to the features of PCOS.

1.2 Epidemiology

According to the 1990 National Institute of Health Criteria, Poly cystic ovary syndrome is the commonest endocrine disorder in women within the reproductive age group affecting approximately 6.6% of unselected women. It is also the number one cause of female infertility in

the West. The estimated prevalence of PCOS in the general population is variable ranging from 2.2% to 26% (7, 10, 11, 12, 13) despite it being the commonest endocrine disorder in women of reproductive age (7, 8, 9)

The high variability in the prevalence range can be attributed to the multiplicity of diagnostic criteria, that is, the NIH 1990, The Rotterdam 2003 and the AE-PCOS 2009, therefore leading to differences in prevalence rates depending on the criteria used (14)

According to a retrospective study by Wendy A. March et al 2010, in a community sample whereby the prevalence of PCOS was assessed under contrasting criteria, it was noted that under the NIH criteria, 8.7 +/- 2.0% had PCOS. Under the Rotterdam Criteria, 11.9+/- 2.4% which rose to 17.8+/- 2.8% with attributed data had PCOS and Under the AE-PCOS criteria, it was 10.2+/- 2.2% which rose to 12.0+/-2.4% with imputation (14). The same study also established that out of those that had PCOS, 68-69% had not been diagnosed prior. This means that a number of PCOS patients actually miss out on accurate diagnosis.

Ninety to ninety five percent of women seeking treatment for anovulatory infertility have PCOS (16) and the average time a woman takes to get pregnant is prolonged in PCOS (15) compared to normal ovulating women. In the United States, the PCOS prevalence of 4-12% was reported (7) with up to 10% of women are diagnosed with PCOS during gynecology visits (17). In Spain, the prevalence of PCOS on an unselected population of Caucasian women has been reported to be 6.5-8% (18). Fransisco Alvarez-Blasco et al also described the prevalence of PCOS in a population of obese women in Spain, and the findings were 28.3% had PCOS (30).

In Africa, PCOS occurred in approx 1 in 6 infertile Nigerian women (19) and 32% of infertile women in Tanzania were diagnosed with Poly cystic ovary morphology(25).

There are no Kenyan studies on the prevalence of poly cystic ovary syndrome in any population, hence no data on the same.

1.3 Pathophysiology of PCOS

Poly cystic Ovary Syndrome can be considered a complex heterogenous metabolic syndrome initiated or promoted by a combination of inheritable genetic susceptibilities and environmental risk factors. Women with PCOS have two major genetic alterations in androgen synthesis and in insulin action and a higher incidence of different gene polymorphisms (27)

1.4 FLOW CHART OF PATHOPHYSIOLOGY

Genetics, Obesity, Sedentary lifestyle

? Intrauterine androgen exposure

↙ ↘

Increased GnRH pulsatile release **Insulin resistance**

↓ ↓

Increased LH:FSH ratio **Hyperinsulinemia**

↘ ↙

ANDROGEN EXCESS

Hirsutism ↙ ↘

Acne, Alopecia **Arrest in antral follicle development**

Commorbid Depression ↙ ↘

ANNOVULATION **POLYCYSTIC OVARIES**

↓Progesterone release ↙ ↓ ↘ **(string of pearls on U/S,↑ ovary vol)**

↓ **Oligo/amenorrhea** **Subfertility**

Unopposed estrogen **annovulatory bleeds**

↓

Increased risk of endometrial hyperplasia

and endometrial cancer

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

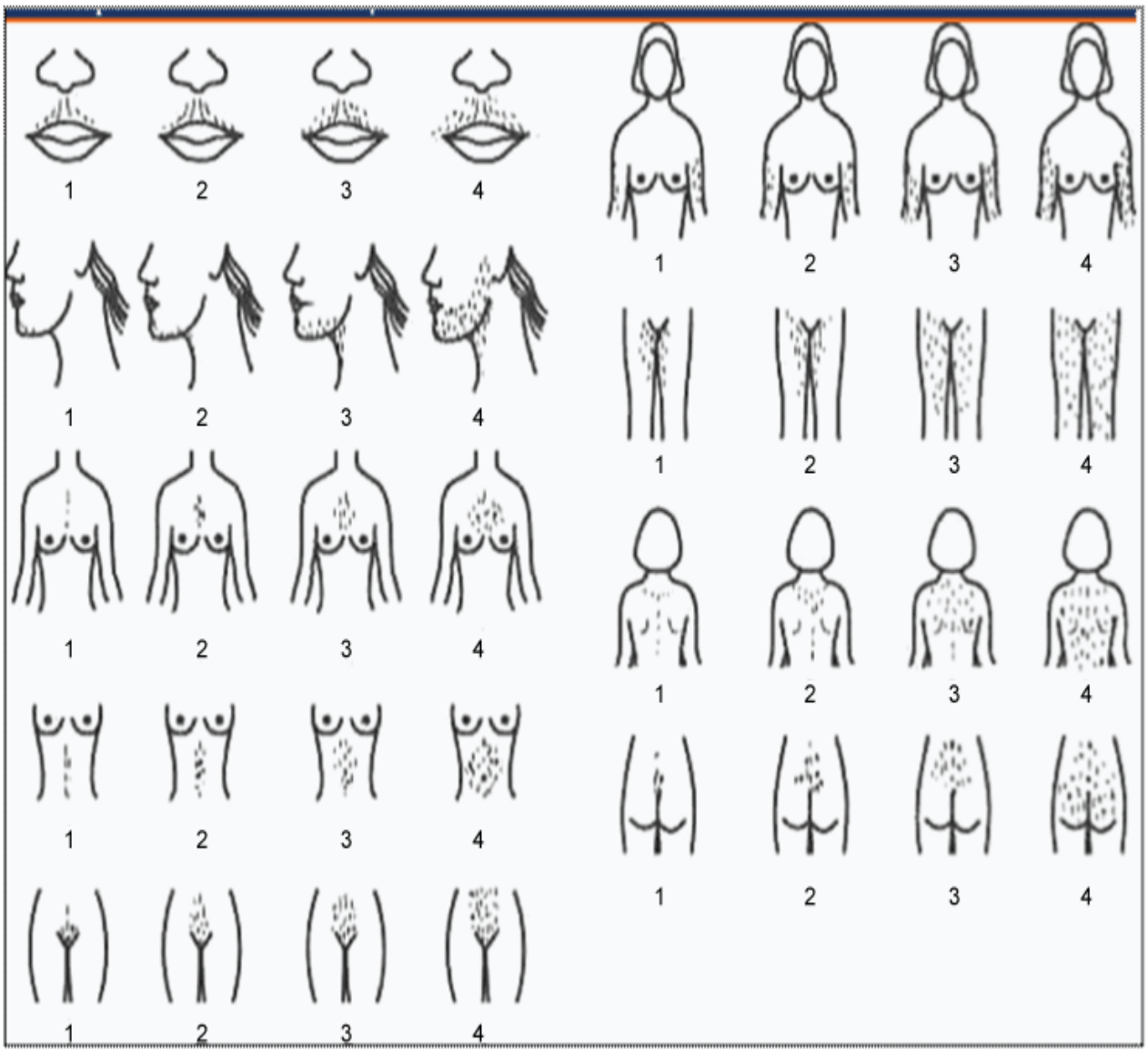
Polycystic Ovary Syndrome is a heterogenous disorder that affects 1 in 15 women worldwide, making it the single most common endocrine abnormality of women of reproductive age (7) First reported in 1935 (1) and considered the commonest cause of oligo ovulatory infertility (20). These patients are at higher risk for developing infertility, dysfunctional uterine bleeding and endometrial carcinoma, and a number of metabolic disorders, including insulin resistance, diabetes mellitus, hypertension, dyslipidemia, cerebrovascular and cardiovascular morbidity (2 , 3, 21, 22 , 23). The metabolic abnormalities occasioned by PCOS may result in an increased risk of obstetric complications like gestational diabetes, pregnancy induced hypertension and pre eclampsia (24).

Polycystic Ovary Syndrome can be directly interpreted as the presence of multiple cysts within the ovary, with increased ovarian stroma together with the associated syndrome of menstrual changes and hyperandrogenaemia/androgenism (4). The 2003 Rotterdam diagnostic criteria was arrived at after a consensus of European Society of Human Reproduction and Embryology and American Society of Reproductive Medicine(ESHRE-ASRM) and is based on the presence of two out of three of the following cardinal features (4)

1. Polycystic Ovarian Morphology, characterized by either detection of 12 or more subcapsular follicular cysts or an ovarian volume of at least 10ml.

2. Biochemical or physical evidence of hyperandrogenism with hirsutism score of 6 or more using the Ferriman Gallwey hirsutism scoring system. (See table 1)

3. Oligo/amenorrhea, less than 6-9 cycles annually or inter menstrual intervals of 35 days or more.



The Ferriman Gallwey hirsutism score.

Figure 1

The modified Ferriman Gallwey score grades 9 body areas from 0(no growth of terminal hair) to 4 (extensive hair growth) in each of the 9 locations. The score may therefore range from a minimum of 0 to a maximum of 36. A score of 6 or more is indicative of hirsutism in the Rotterdam 2003 criteria (4).

Due to the complexity of this syndrome, there has been several attempts to come up with an all inclusive diagnostic criteria, in order to capture all the major characteristics of the syndrome. (See table 2)

The three available diagnostic criteria for the diagnosis of Polycystic cystic ovary are shown on table 2 below.

NIH 1990 Both criteria met.	**ROTTERDAM 2003** 2 out of 3 criteria met.	**AE-PCOS 2006** Both criteria met after excluding androgen excess or related disorders.
1.Chronic anovulation 2.Clinical and/or biochemical signs of hyperandrogenism with exclusion of other aetiologies	1.Oligo ovulation and/or anovulation 2.Clinical and /or biochemical signs of hyperandrogenism 3.Polycystic ovaries	1.Clinical and/or biochemical signs of hyperandrogenism 2.Ovarian dysfunction (oligo-anovulation and or polycystic ovarian morphology.

Table 1: criterias for diagnosis of PCOS.

The National Institute of Health (NIH) criteria of 1990 defined PCOS as the presence of chronic anovulation (which manifests as irregular menses) together with clinical and/or biochemical signs of hyperandrogenism with the exclusion of other aetiologies. The Androgen excess -PCOS (AE-PCOS) Society taskforce defines PCOS as the presence of hyperandrogenism (clinical and/or biochemical) and ovarian dysfunction (oligo/annovulation and/or polycystic ovaries.) with the exclusion of related disorders (5).

The evidence based methodology workshop on Polycystic Ovary Syndrome recommends maintaining the diagnostic criteria of Rotterdam 2003 which includes the NIH and AE-PCOS criteria while specifically identifying the phenotype(6).

Notwithstanding the significant reproductive, endocrine, and metabolic morbidity of PCOS, little is known of its prevalence in the general population, particularly in Africa due to lack of prevalence studies. The prevalence of PCOS, like that of any other complex multifactorial disorder, greatly depends on which criteria are used to define it. The majority of PCOS patients have ovarian dysfunction with 70%-80% of women with PCOS presenting with oligomenorrhea or amenorrhea, and among those with oligomenorrhea, 80%-90% will be diagnosed with PCOS (28).

Oligo ovulation and anovulation presents as menstrual cycle irregularity, and the type of menstrual cycle abnormality might represent a useful tool for identifying a more severe metabolic profile in PCOS (29)

For purposes of this study, the all inclusive 2003 Rotterdam diagnostic criteria was used, which is based on the presence of two out of three of the following cardinal features;

1. Poly Cystic Ovarian Morphology, characterized by either detection of 12 or more subcapsular follicular cysts or an ovarian volume of at least 10ml.

2. Biochemical OR physical evidence of hyperandrogenism with hirsutism score of 6 or more using the Ferriman Gallwey hirsutism scoring system.

3. Oligo/amenorrhea, less than 6 cycles annually or intermenstrual intervals of more than 35 days.

1.5 CONCEPTUAL FRAMEWORK

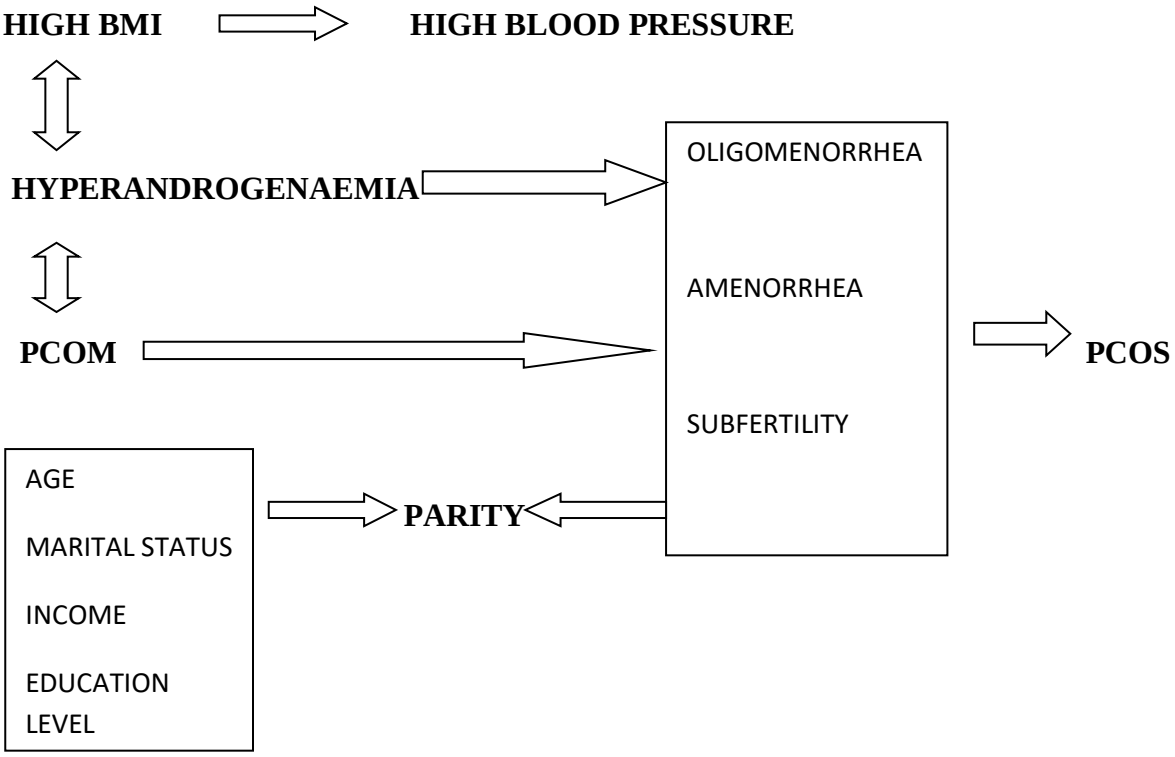


Figure 2: Conceptual framework.

Figure 2 demonstrates the inter relationship of factors in the development of polycystic ovary syndrome. High blood pressures positively correlates to high BMI in the pathophysiology of metabolic syndrome X which is a known late sequel of polycystic ovary syndrome(2) . High BMI through insulin resistance and hyperinsulinemia results to hyperandrogenaemia and vice versa. Hyperandrogenaemia may cause polycystic ovary morphology due to arrest of antral follicular morphology(17).A woman's age, marital status, income and education level affects her parity, which is also affected by her ovulatory status (that manifests as oligomenorrhea and or amenorrhea) that is part of the PCOS syndrome.

2.2 Problem statement

Polycystic Ovary Syndrome remains an important cause of anovulatory infertility presenting with menstrual irregularities like oligomenorrhea / amenorrhea and hirsutism thereby necessitating frequent gynecological and dermatological consultations. The associated health risks of hypertension, diabetes and insulin resistance, metabolic syndrome X, dyslipidemias, obesity and cardiovascular disorders further enhances the need to early diagnosis, follow up and management to identify, delay and mitigate the sequelae

2.3 Justification

Due to the association of Polycystic Ovary Syndrome with long term health risks, and the documented delay from the time of first presentation to the actual diagnosis, this study will bring to our attention the local prevalence rates and will also sensitize the health care givers of this common yet largely under diagnosed condition. Amenorrhea and oligomenorrhea is one of the clinical presentations of PCOS that necessitates gynecological visits, hence the choice of this population for this study.

Timely and accurate diagnosis will enable the health care providers to identify and manage the PCOS patient and institute lifestyle modification that delay the onset and mitigate severity of the sequelae of PCOS. Provision of local population specific data on prevalence, clinical and biochemical features may be used to influence on screening and follow up.

2.4 Research Question

What is the prevalence of polycystic ovary syndrome among women presenting with amenorrhea and oligomenorrhea at the Kenyatta National Hospital in the year 2018?

2.5 Broad Objective

To determine the prevalence of polycystic ovary syndrome among women presenting with amenorrhea and oligomenorhea in Kenyatta National Hospital.

2.6 Specific Objectives

1. To determine the prevalence of polycystic ovary syndrome at Kenyatta National Hospital
2. To compare the socio demographic and anthropometric characteristics of women with Polycystic Ovary Syndrome and those without at the Kenyatta National Hospital.
3. To describe the clinical and biochemical features of Poly cystic ovary syndrome at Kenyatta National Hospital.

CHAPTER THREE: METHODOLOGY

3.1 Study design

This was a hospital based descriptive cross sectional study whereby 131 patients with amenorrhea and oligomenorrhea were recruited.

3.2 Study site

The study was carried out at the acute gynaecology room 8 at the Accidents and Emergencies department and at the GOPC clinic 18 at Kenyatta National Hospital. These are the areas within the hospital that receive gynaecology patients.

The KNH is a national teaching and referral hospital located 4 kilometers away from the Central Business District in Kenya's capital, Nairobi. It serves as the teaching hospital for the University of Nairobi- Medical School and the Kenya Medical Training college. It is also a centre for many medical researches due to its richness in patient diversity and uniqueness of presentations.

The KNH has 50 wards, 24 operating theatre, 22 out-patient clinics, and a busy Accident and Emergency Unit. It boasts a bed capacity of 1800 and an ongoing development of a state of the art day surgery centre.

3.3 Study setting

The hospital runs GOPC from Tuesday to Thursday, handling approximately 75 general gynecology patients per week translating to an average of 3000 patients annually, and a special fertility clinic on Fridays that handles approximately 20 patients weekly. KNH was chosen for this prevalence study because the condition of interest poses a diagnostic challenge and therefore, as a National Teaching and Referral Hospital it received a large number of patients from all over the country from whom an appropriate sample was selected. It also has patients with a varied socio- demographic background.

The KNH Diagnostic Imaging and Radiology department is where the imaging was carried out. This department is managed by highly trained and qualified staff and the ultrasound machines therein are of good quality and regularly serviced.

Laboratory tests were done at the Kenyatta National Hospital laboratory. This laboratory supports the diagnostic functions of the whole hospital departments and hence is well supported by endocrinologists, pathologists, cytologists, clinical chemists and highly trained laboratory technologists.

3.4 Study population

Women aged between 18-45 years attending the gynecology clinic at the KNH with history of irregular menstrual cycles.

Set inclusion and exclusion criteria applied.

3.5 Selection and enrolment of study participants

Identification

All patients attending the KNH acute gynecology room 8 or the gynecology clinic 18 with complaints of oligomenorrhea and or amenorrhea were subjected to a pre enrollment questionnaire (annex 6) in order to select those eligible for the study.

Sampling

All patients with oligomenorrhea and or amenorrhea, found eligible after being subjected to a pre enrollment questionnaire, were considered for the study.

Informed consent

Informed consent (annex 2) was obtained from the eligible patients and an interviewer guided questionnaire (annex 3) administered to those that accept to participate in the study.

3.5.1 Inclusion criteria

1. Women aged between 18 and 45 years.
2. Women who give informed consent to participate in the study.

3.5.2 Exclusion criteria

1. Women on contraception that affects the regularity of the menstrual cycle.

3.6 Sampling method

All patients presenting with a history of oligomenorrhea and or amenorrhea were considered for the study. Consecutive screening and enrolment of all women meeting the inclusion criteria was done until the desired sample size was reached.

3.7 Sample size calculation

$$N = \frac{z^2_{1-\alpha/2} \times p(1-p)}{d^2} \quad (35)$$

α=Level of significance (0.05)

$Z_{1-\alpha/2}$= Standard normal deviate at 95% confidence interval (1.96)

p= Proportion in the target population with specific characteristics = 32% (25)

d=margin of error allowed= 0.08

Therefore **N =** 131

3.8 Study Procedure

Upon enrollment, the questionnaire was filled, the anthropometric parameters, laboratory tests and ultrasound performed same day according to the procedure outlined below.

Anthropometric measurements

The Healthometer Scale for weight and height was used as it is the one that is available at the GOPC clinic and the Accidents and Emergencies department. BMI was calculated from this. The scale was calibrated weekly to ensure accuracy of measurements.

Blood pressure measurement was taken using the Omron automated BP machine that was checked weekly to ensure good working quality. All the measurements were taken and documented by the research assistant stationed at the clinic.

Procedure for blood collection

The patient sat for approximately 15 minutes. The procedure was explained to the patient and verbal consent obtained. Thereafter a tourniquet was applied approximately 3 to 4 cm above the median cubital vein of the non dominant hand. Protective gloves were worn by the study assistant. Antiseptic was used to wipe the cubital fossa and thereafter left to dry. A blue (23 gauge) needle was attached to a 5 ml syringe for the blood collection. Five milli litres of blood was drawn and immediately transferred to a plain red top (non additive tube) bottle. The bottle bore the study participants details including their unique identification number. The tourniquet was removed, firm pressure applied on the venepuncture site for 10min and thereafter the patient thanked and allowed to leave. The collected blood was transported to the laboratory within 1 hour, having been stored in a coolant with ice packs at 4 degrees celcius. Laboratory assay of the serum total testosterone was done at the Kenyatta National Hospital laboratory.

Standard operating procedure for the serum total testosterone assay

Blood samples, upon reception in the laboratory, were centrifuged within 1 hour and serum aliquots removed into a different bottle for further analysis, as outlined in the schema below (Figure 3)

The lower limit of testosterone was 0.084ng/ml while the upper limit was 0.481ng/ml according to the testing kit that was used.

SCHEMA FOR MEASUREMENT PROCEDURE FOR

TOTAL TESTOSTERONE IN SERUM BY RADIOIMMUNOASSAY

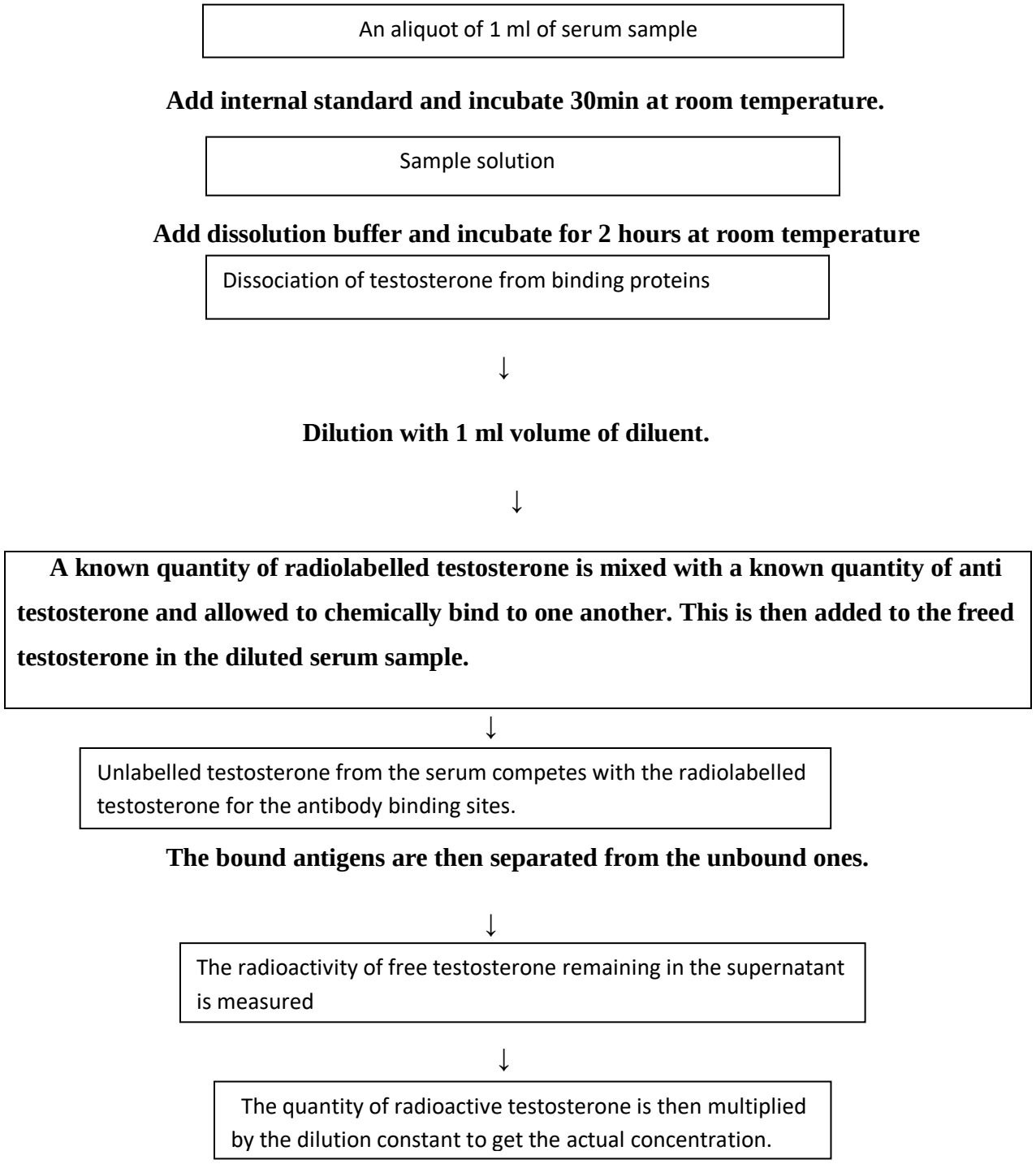


Figure 3: Schematic representation of the laboratory assay of testosterone**.**

Ultrasonography

Ultrasonography was done at the KNH radiology department. Imaging was trans abdominal for all the study subjects for standardization purposes and its general acceptability because it is non invasive. All efforts were made to ensure minimal inter operator differences in reporting by availing an ultrasound reporting checklist (annex 7) which accompanied the request form.

The specific Toshiba Ultrasound machine was used. It is the machine widely in use at the Kenyatta National Hospital radiology department.

Cost

The cost of the laboratory investigation and ultrasound was borne by the Kenyatta National Hospital research and programs department. The study subject was not required to pay for any procedure while participating in the study from the time of recruitment to the end of the participation.

3.9 Study flow chart

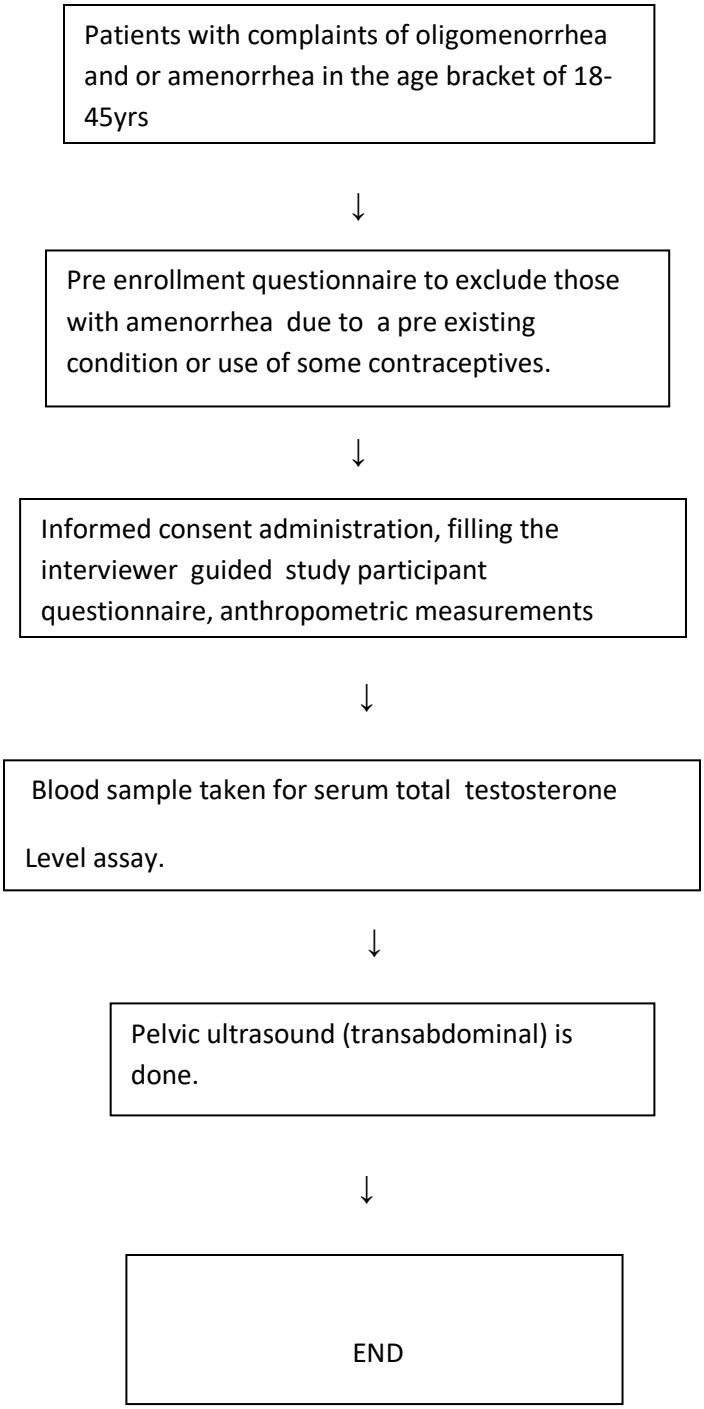


Figure 4: Study flow chart

3.9 Data collection

Participants bio data and anthropometric parameters was recorded on the first part of the questionnaire, which bore unique participant specific number for identification purposes. The participant was then guided through filling the questionnaire by the research assistant. Once the questionnaire is fully filled, the participant's blood sample was drawn and taken to the laboratory for the biochemical tests. The participant was then taken to the imaging department where the ultrasound was performed.

The laboratory results and the ultrasound reports were obtained same day and the information entered into a preformed data entry form (annex 5) which was attached at the back of each questionnaire. The collected data was then checked on a daily basis before being entered into an excel sheet for further analysis.

3.10 Variables

The variables for this study were as shown below (Table 2)

The variable included dependent variables like irregular menses and independent variables which is presence of poly cystic ovaries and hyperandrogenaemia. The indicators, data source and study instrument are as shown below.

3.10.1 Table of variables

VARIABLE	INDICATOR	DATA SOURCE	INSTRUMENT
DEPENDENT -Oligomenorrhea / amenorrhea	-Cycle >35 days apart -Amenorrhea of >3-6 months(in absence of pregnancy)	Study participant	Questionnaire
INDEPENDENT -Poly cystic ovary morphology -Hyperandrogenaemia	-U/S evidence of ovary vol >10cm3 - >12 small peripheral placed follicles. -Elevated serum free testosterone levels	Ultrasonography report Laboratory report	Ultrasound machine Laboratory hormonal assay

Table 2

3.11 Research Training

Research assistants were sourced from the nursing and clinical officer health workers cadres. They underwent a short training at the GOPC on study participant selection, use of the pre enrollment questionnaire, administration of the study participant questionnaire, obtaining of anthropometric information and how to enter the raw data. They were then assessed by way of a trial run.

3.12 Data management and analysis

Data on pre-defined patient attributes extracted from the patient records (file/card) was entered into the data analysis table. More data was obtained from the questionnaire filled by the study subjects, together with the laboratory test results and the imaging reports.

Categorical data was tabulated and summarized as proportions on a pie chart while continuous variables was reported as means, with standard deviations or medians, with inter-quartile ranges as appropriate. The primary outcome, women with PCOS and the clinical and biochemical features, was computed as a proportion along with a 95% confidence interval.

3.13 Quality Control

The study participants was each assigned a unique identification code that was borne on all the participants results. Quality control systems to check data (questionnaires filled and laboratory results and ultrasound results) as soon as they are received, looking for completeness, correctness and logical consistency. Weekly status reports for constant monitoring of the study process was conducted and findings availed to the supervisors.

3.14 Control of biases and errors

Detailed history taking and questionnaire filling to pick only those that have oligomenorrhea and amenorrhea not attributable to other factors.

One laboratory technologist working in the same laboratory using the same equipment and reagents was responsible for the assay.

Every effort was made to have one sonographer (with a higher diploma in Ultrasonography) perform all the ultrasounds using the same machine, all scans were transabdominal and the reporting done according to the checklist (annex 7) for standardized reporting.

3.15 Study limitations

Pre-selection of Kenyatta National Hospital as the study site, as this introduced selection bias since KNH is a National Teaching and Referral Hospital.

Random total serum testosterone level was assayed, with no regard to the diurnal or circadian changes that are typical of reproductive hormones.

Due to resource limitation, only the main androgen Testosterone was assayed. Testosterone is the major ovarian androgen. Other important androgenic hormones like Dehydroepiandrosterone, Dehydroepiandrosterone sulfate (DHEAS), androstenedione and dihydrotestosterone(DHT) were not assayed. DHEA, DHEAS and androstenedione are predominantly adrenal androgens.

3.16 Ethical considerations

Permission was sought from the Kenyatta National Hospital and Kenyatta National Hospital/University of Nairobi Ethics and Research Committee to carry out this study as part of the thesis dissertation. Copies of this protocol, the informed consent form as well as any modifications that arose were presented to this committee for written approval prior to commencing the study. The study was fully explained to the study participants prior to obtaining consent to participate in the study.

No extra cost or risk was passed to the study participant. The study participant was at liberty to stop her participation in the study without any prejudice or negative effect on the quality of care they received. The participant was informed of the results of their biochemical tests and imaging.

In the event that an abnormality was noted in the participants test result, the participant was referred appropriately for intervention.

CHAPTER 4: RESULTS

One hundred and thirty one women with complaints of oligomenorrhea and or amenorrhea attending the gynaecology clinic were recruited to the study. Polycystic ovary Syndrome was diagnosed in 49(37.4%).

Table 5: Sociodemographic and anthropometric parameters of the study population, n=131

Characteristic		Frequency (n)	Percentage (%)
Age in years	18-21	13	9.9
	22-25	55	42.0
	26-29	28	21.4
	30-33	25	19.1
	34-45	10	7.6
Marital status	Single	78	59.5
	Married	53	40.5
Education level	Primary	1	0.8
	Secondary	12	9.2
	Post secondary	118	90.1
Income (Ksh)	None	54	41.2
	Up to 50,000	61	46.6
	>50,000	16	12.2
BMI	<18.5	4	3.1
	18.5-24.9	70	53.4
	25-29.9	31	23.7
	>30	26	19.8
Parity	Nulliparous	105	80.2
	Ever been pregnant	26	19.8
Systolic Blood Pressure	<120	64	48.9
	120-140	63	48.1
	>140	3	2.3
Diastolic Blood Pressure	<80	61	46.6
	80-90	53	40.5
	>90	16	12.2

*KSH= Kenya Shillings

One hundred and twenty six of the participants were of African descent while five were Asians. Eighty three (63.4%) of the study participants were between the ages of 22-29 years with a median age of 25 years and an inter quartile range of 7 years (Table 5). Seventy eight (59.5%) of them were single and 90.1% of all the participants had post secondary education. Seventy (53.4%) of the study participants had a normal BMI with 23.7% being overweight and 19.8% being obese. The median BMI was 24.2 with an inter quartile range of 5.9 (Table 5)

The nulliparous participants accounted for 80.2% while 19.8 % reported having ever been pregnant, regardless of the outcome. Fifty four (41.2%) of the participants had no income while 61(46.6%) earned up to Kenya shillings 50,000. Nineteen participants were hypertensive from a single blood pressure reading (Table 5)

The prevalence of polycystic ovary syndrome using the Rotterdam 2003, the NIH 1990 and AE-PCOS 2006 criteria.

The prevalence of PCOS was determined using the Rotterdam criteria, as earlier outlined in the study protocol. The other criterias were also considered for comparison purposes.

Table 6: Prevalence of polycystic ovary syndrome using the three criteria.

Criteria	n=/ 131	%
National Institute of Health 1990	26	19.8%
Rotterdam 2003	49	37.4%
Androgen Excess-Polycystic Ovary Syndrome 2006	15	11.5%

The prevalence of PCOS was **37.4%** using the Rotterdam 2003 criteria. Under the AE-PCOS 2006 criteria it was 11.5% and under the NIH 1990 criteria it was 19.8% (Table 6)

Table 7: Comparison of the Socio-demographic and anthropometric characteristics of women with and without PCOS

Characteristic		Women with PCOS n=49		Women without PCOS n=82		Odds ratio (CI-95%)	P value
		n	%	n	%		
Age yrs(median)	18-21 (19.5)	4	8.2	9	11.0	0.7 (0.2-2.5)	0.776
	22-25 (23.5)	25	51.0	30	36.6	1.8 (0.9-3.7)	0.105
	26-29 (27.5)	10	20.4	18	22.0	0.9 (0.4-2.2)	0.835
	30-33 (31.5)	9	18.4	16	19.5	0.9 (0.4-2.3)	0.872
	34-45 (39.5)	1	2.0	9	11.0	0.2 (0.0-1.4)	0.089
Marital status	married	16	32.7	30	36.6	0.8 (0.4-1.8)	0.648
	Single	33	67.3	52	63.4		
Education	primary	0	0.0	1	1.2		1.000
	Secondary	3	6.1	9	11.0	0.5 (0.2-2.1)	0.533
	Post secondary	46	93.9	72	87.8	2.1 (0.6-8.1)	0.369
Income (Ksh)	none	19	38.8	35	42.7	0.9 (0.4-1.8)	0.660
	Up to 50,000	27	55.1	34	41.5	1.7 (0.3-3.5)	0.130
	>50,000	3	6.1	13	15.9	0.3 (0.1-1.3)	0.100
BMI	<18.5	1	2.0	3	3.7	0.5(0.1-5.4)	1.000
	18.5-24.9	28	57.1	42	51.2	1.3 (0.6-2.6)	0.511
	25-29.9	7	14.3	24	29.3	0.4 (0.2-2.1)	0.051
	>30	13	26.5	13	15.9	1.9 (0.8-4.6)	0.138
Parity	nulliparous	45	91.8	60	73.2	4.1 (1.3-12.8)	0.010
	Ever been pregnant	4	8.2	22	26.8		
Systolic	<120	24	49.0	40	48.8	1.0 (0.5-2.0)	0.982
Blood	120-140	23	46.9	40	48.8	0.9 (0.5-1.9)	0.838
Pressure	>140	1	2.0	2	2.4	0.8 (0.1-9.4)	1.000
Diastolic	<80	23	46.9	38	46.3	1.0 (0.5-2.1)	0.947
Blood	80-90	19	38.8	34	41.5	0.9 (0.4-1.8)	0.762
Pressure	>90	6	12.2	10	12.2	1.0 (0.3-2.9)	0.993

Kshs Kenya shilling

Fifty one percent of the women with PCOS were aged between 22-25 years, 32.7% married with 93.3 % having attained post secondary education. Fifty seven point one percent had a normal BMI with 50.8% being overweight and obese. An income level of up to 50,000 Kshs monthly was reported in 51.1%. Ninety one point eight percent were nulliparous.

Age, BMI, parity, education level, income, blood pressure and marital status were not statistically different among women with and without PCOS (Table 7).

Table 8: Comparison of the clinical and biochemical features of women with and without PCOS

Characteristic	PCOS (n=49)		No PCOS (n=82)		P value
	Mean	SD	Mean	SD	
Right ovary volume in Cm^3	17.7	8.6	8.3	3.7	<0.001
Left ovary volume in Cm^3	15.8	6.4	9.6	6.9	<0.001
Testosterone in ng/ml	0.43	0.21	0.19	0.15	<0.001

All the participants were subjected to a pelvic ultrasound in order to determine the ovarian size, follicular cyst arrangement and stromal echotexture. Adjustment for obvious causes of significant ovarian enlargement like hemorrhagic cysts was done.

The mean ovary size of the study participants with PCOS was noted to be significantly larger, the right ovary being $17.7cm^3$+/-$8.6cm^3$ and the left ovary being $15.8cm^3$+/-6.4 cm^3 in women with PCOS compared to a mean right ovarian size of $8.3cm^3$+/-3.7 cm^3 and left ovarian size of $9.6cm^3$+/-$6.9cm^3$ in those without.

In the PCOS subgroup, total serum testosterone levels was significantly higher in women with PCOS (0.43+/-0.21) ng/ml compared to the women without (0.19+/-0.15) ng/ml.

CHAPTER 5: DISCUSSION

The results of this study showed that slightly over a third of the women with complaints of amenorrhea and oligomenorrhea who were seen at the gynaecology clinic during the study period had polycystic ovary syndrome using the Rotterdam Criteria. This prevalence is comparable to a study by B. Husein and S. Alalaf who found a prevalence of PCOS of 33% among infertile women attending the IVF infertility centre (37). Fransisco Alvarez-Blasco et al. also described the prevalence of PCOS of 28.3% in a population of obese women in Spain (30).

The obese and infertile populations are not exactly the same as the population of women with amenorrhea and oligomenorrhea. They are however a specific population at a higher probability of having PCOS than the general population just as the oligomenorrheic and amenorrheic women, and therefore the comparison of the prevalence rates is reasonably justified. Pembe A.B et al in Tanzania also found that 32% of infertile women had PCO (25). This shows that the PCO prevalence among specific populations of women tends to go higher than the prevalence in the general population due to the pre existing pre disposition.

We compared the prevalence of PCOS using the different criteriae, the all inclusive Rotterdam 2003 criteria yielded the highest prevalence of 37.4% followed by the NIH 1990 criteria with a prevalence of 19.8% and AE-PCOS 2006 criteria with a prevalence of 11.5%. These results compares to the findings by Wendy A. March et al, whereby in the determination of prevalence of polycystic ovary syndrome in a community sample under contrasting criteria, the highest prevalence rates were recorded when the Rotterdam 2003 criteria was used, compared to the NIH 1990 and AE-PCOS 2006 criteriae (14) possibly because the Rotterdam criteria for diagnosis focuses on the presence of 2 out of 3 symptoms as opposed to the NIH 1990 and AE-PCOS criteria which are stricter and require the patient to have both symptoms outlined in the criteria in order to be diagnosed with PCOS (14)

In our study, it was apparent that there was a high number of post secondary educated participants which can be ascribed to the timing of the study that coincided with the university holiday period, hence many were available for check up, which also positively correlates with the number of single and nulliparous participants. There was, however, no statistically significant

difference in the socio demographic and anthropometric characteristics of the study participants with PCOS and those without. Similar findings were reported by Pembe A.B et al (25)

In our study we focused upon the ovarian size for diagnosis because we performed trans abdominal ultrasounds. Although transvaginal ultrasound is superior in determination of the ovarian morphology and better diagnosis of PCOS (31), trans abdominal scans can be used reasonably for the same, as a study by Farquhar CM et. al showed no difference in the prevalence of PCOS diagnosed by trans abdominal or transvaginal ultrasound in a group of randomly selected women (36).

The average ovarian size of the women with PCOS was significantly larger than the ovarian sizes of the women without, and which is deducible in the pathophysiology of PCOS (17) and which also compares to the findings of Farquhar CM. et al (36). A statistically significant difference was noted in the sizes of the ovaries of participants with PCOS compared to those without. This finding is similar to a study by Y. Chen et al 2008 (34) who also noted a statistically significant difference in the ovary volume and follicular number between PCOS patients and controls.

The ovarian volume in this study was correlated with serum concentrations of total testosterone (32), as the women with PCOS had a significantly larger ovarian volume and significantly elevated levels of total testosterone. This finding is also in keeping with the ovarian changes in the pathophysiology of PCOS (17)

There was also a statistically significant difference in the total serum testosterone levels in the participants with PCOS compared to those without PCOS (Table 8). Elevated serum testosterone, as part of hyperandrogenaemia, is one of the diagnostic criteria of PCOS according to the Rotterdam 2003 criteria (4).

A possible noteworthy limitation was on the type of ultrasound performed. The ultrasound performed on the study participants was trans abdominal as opposed to the trans vaginal ultrasound that best characterizes the ovarian morphology. Trans abdominal ultrasound was preferred because of its widespread acceptability, non invasiveness and low chances of study participant declining the procedure. No validity issues arose (36)

It was not possible to consider the cycle and circadian changes that are expected to influence reproductive hormone levels, since sample collection for this study was random (33), however, the difference does not have a significant impact on the clinical value of circulating androgens (10).

CONCLUSION

Polycystic ovary syndrome is common among women attending the Kenyatta National Hospital with amenorrhea and oligomenorrhea.

RECOMMENDATION

Poly cystic ovary syndrome should rank highly in the differential diagnosis when evaluating a woman with oligomenorrhea or amenorrhea as evidenced by its prevalence.

Development of an algorithm to guide the management of patients with oligomenorrhea and amenorrhea will have an impact on timely diagnosis of PCOS as evidenced by its prevalence.

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CHAPTER 7: ANNEXES

5.1 Annex 1: Study budget

ITEM	DESCRIPTION	QUANTITY	UNIT PRICE	TOTAL
STATIONERY				
1	Biro pens	10	20	200
2	Pencils	5	10	50
3	Box files	4	150	600
4	Spring files	4	100	400
5	White out pen	1	150	150
6	Stapler	1	500	500
7	Paper punch	1	600	600
8	Staple remover	1	250	250
9	Notebook	1	150	150
10	Printing	50	10	500
11	Photocopying	3000	3	9000
12	Binding	100	3	300
13	Final proposal booklet	4	1000	4000
14	Final dissertation booklet	4	1000	4000
15	Poster presentation	4	2500	10000
TOTAL				20,750

OTHERS

1	**Communication**		**10000**	**10000**
2	**Research assistants**	**4**	**10000**	**40000**
3	**Statistician**	**1**	**40000**	**40000**
	TOTAL			**90,000**

INVESTIGATIONS

1	**Red top blood collection tube**	**200**	**10**	**2000**
2	**Cotton wool+spirit +gloves**			**500**
3	**10ml syringes**	**200**	**5**	**1000**
4	**Ultrasound**	**131**	**1800**	**235800**
5	**Lab test for serum total testosterone**	**131**	**700**	**91700**
Total				**331,000**

GRAND TOTAL Kshs 441,750

5.2 Annex 2: STUDY PARTICIPATION CONSENT FORM

STUDY TITLE: PREVALENCE OF POLYCYSTIC OVARY SYNDROME AMONG WOMEN PRESENTING WITH AMENORRHEA AND OLIGOMENORRHEA AT THE KENYATTA NATIONAL HOSPITAL

Participant's study number:

Principle investigator: Dr. Odera Freda

Institution: University of Nairobi

Department: Obstetrics and Gynaecology

Registration no.: H58/74774/2014

Contacts: 0724451697

This research project is done as a part of the requirements for the award of the masters degree in Obstetrics and Gynecology at the University of Nairobi.

Supervisors;

Professor Joseph Karanja – Associate Professor in the Department of Obstetrics and Gynaecology/ UON

Dr Kireki Omanwa– Consultant in Obstetrics and Gynecology , Lecturer UoN.

Dr John Kinuthia- Consultant in Obstetrics and Gynecology, KNH, Honorary lecturer, Dept. of Infectious and Tropical Diseases UoN, and Dept of Obstetrics and Gynecology, UoN.

Investigator's statement.

I am inviting you to participate in this research study. This consent form is intended to give you information about the study that will help you make a decision on whether to participate in the study or not.

This study has the approval of the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol number P733/12/2017

Introduction

Polycystic ovary syndrome is a common endocrinological condition of reproductive age women with important immediate and long term health implication. It is often under diagnosed and therefore under managed.

Purpose of study

This study will help us estimate the local prevalence rates together with the clinical and biochemical characteristics of this important gynecological condition among women with oligomenorrhea and amenorrhea with a view of creating awareness and possibly informing policy on timely diagnosis and subsequent follow up.

Voluntary participation

Your participation in this research study is voluntary. Any participant willing to withdraw from the study will be free to do so at any stage without being penalized or victimized. Your participation will involve filling the questionnaire, having your weight and height taken, providing us with a blood sample for the biochemical tests and undergoing pelvic ultrasound imaging.

Your participation in the study will not cost you anything.

Risks:

There are no short or long term risks associated with participation in this study.

Potential benefits:

Participants will benefit by having a pelvic ultrasound scan and total serum testosterone level test at no extra cost.

The findings of the tests will be communicated to the patients and appropriate management as per the existing protocols will be instituted at the GOPC.

Protection of confidentiality

Only those involved in the study will be allowed access to any data collected. True participant's identity will not be revealed in data analysis or in any publication resulting from this study. Only their unique coded numbers will be used. The blood sample availed will be used only for the investigations described in the study. The images obtained will only be used for the intended purposes in the study.

Contact information

Please contact Dr. Odera on 0724 451697 if you have any questions or concerns about the study. In case of any questions concerning your rights as a research subject you can contact the Secretary/Chairperson, Kenyatta National Hospital-University Of Nairobi Ethics& Research Committee on telephone number 2726300-9 Ext 44102

Consent by Participant:

I have read this consent form, understood it fully, was given the opportunity to ask questions and assured of confidentiality. I voluntary give my informed consent to participate in this study.

Participants name_____

Participant's signature_____ Date:_____

Person conducting the consenting process:

I have provided the required information and ensured that the participant understood the study as described in this consent form.

Signature_____ Date:_____

Role in the study_____

Study participants will be given a copy of this consent form.

5.3 Annex 3: Questionnaire

Serial number: Blood pressure

Date of birth: Occupation

Parity: Marital status

Weight: Education level

Height: Residence

BMI (to be calculated): Average monthly income

1.What is the average length of your menstrual cycle?

---

2. Have you ever missed your menstrual periods for more than your normal cycle? (*mark as appropriate in the box against your choice.*

□Yes

□ No

3. Have you ever used any form of Family planning?

□ Yes

□No

4. If yes (In Q 3) which ones?

□Pills

□DMPA(Depo provera) 3 monthly injection

□IUCD (coil)

□Implant

□Others (specify)

5. Do you have hair in your body which you consider not normal or not feminine?

□ Yes

□ No

6. Do you have hair in any of these body parts?

□Chin (beards)

□upper lip

□around the nipples

□chest

□abdomen

□extension of pubic hair to the umbilicus

□hands

□thighs

□upper back

□lower back

7. Have you ever had a pelvic or a transvaginal ultrasound (scan)?

□Yes

□ No

8. If yes (In Q 5) what was the reason for it?

□Abnormal menstrual periods/ bleeding

□Pelvic pains

□Fertility concerns

□Others (specify)

9. Do you have any other known medical condition for which you may or may not be on follow up?

□ Yes

□No

10. If yes (In Q6) which ones?

□ Diabetes

□ High blood pressure

□ Skin condition (pimples/acne)

□Dyslipidemia (high cholesterol)

11. Do you have difficulty conceiving/ getting pregnant ?

□Yes

□No

12. If yes in Q8 , For how long have you been trying or (ever tried) to conceive?

---

13. If Yes In Q 8, have you used any of the following fertility enhancing medication?

□ Clomid (clomiphene citrate)

□ Letroz/ Femara (Letrozole)

□ Herbal medicine

□Others (specify)

Annex 4: Study Timelines

Proposal development	June –Oct 2017
Proposal presentation	Nov 2017
Ethical board review	Dec 2017- April2018
Data collection	July-Oct 2018
Data analysis	Nov 2018
Thesis writing	Nov 2018
Results presentation	Nov 2018

5.5 Annex 5: Data entry forms (raw data)

Anthropometric data

	Serial no.	**Age**	**Height**	**Weight**	**Blood pressure**	**BMI**	**Parity**

Laboratory findings

Serial no		**Total serum testosterone level**
1		
	PCOS STATUS	

Imaging findings

	Serial no.	**Ovary volume**		**No. of Cysts**		**General comments**
1		**Left ovary**	**Right Ovary**	**Left ovary**	**Right Ovary**	
	PCOS STATUS					

5.6 Annex 6: Pre enrollment Checklist

Please confirm that the study participant meets the following criteria

1. Age (18-45)

2. Has reported irregular menstrual cycles (amenorrhea and or oligomenorrhea) in the history or as a chief complaint.

3. Not been pregnant in the last 6 months.

4. Not been on Depo provera or Mirena within the last 6 months.

5. Is not on follow up for any known Gynecological or endocrinological conditi

Annex 7: Note to sonographer

PCOS PREVALENCE STUDY

Dear Radiologist/Sonographer

The PCOS prevalence study 2018 is a prospective cross sectional study by Dr Freda Odera, SHO Obstetrics and Gynecology, Tel No. 0724 451697. Part of it involves information reported by the Radiologist/ Sonographer on the pelvic ultrasound report of the study participant.

Kindly report on the following:

1. The Left and Right Ovary volume in cm3.
2. The presence and distribution of the follicular cysts in each ovary and where possible, the number of cysts.
3. Please provide an image of each ovary attached to the report.
4. Report on any other findings of importance within the pelvis, eg fibroids, hydrosalpinges etc.