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Prevalence and Ultrasound Presentations of Polycystic Ovarian Syndrome in Black African Women Presenting with Infertility: A Case of Women in Referral Health Institutions in Bulawayo, Zimbabwe

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Polycystic ovarian syndrome (PCOS) is an endocrine abnormal condition in women of childbearing age with associated health risks, infertility, diabetes mellitus, endometrial hyperplasia and cardiovascular complications. Ultrasound imaging reporting incidences of PCOS

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requires continued exploration and updating as the disease profiles tend to continuously evolve due to fluctuating environmental factors, heterogenous population migration as seen in Bulawayo, Zimbabwe and other parts of the world. There are no known past or recent studies that have described ultrasound imaging of PCOS incidences and the prevalence of PCOS in Bulawayo. This study sought to determine the association between factors contributing to prevalence of PCOS and their association with ultrasound presentations in women with infertility in Bulawayo, Zimbabwe aimed at improving diagnostics algorithms of the disease.

Materials and Methods: Equal invitations to participate in the study were issued at hospital-based study centres. A cross-sectional survey was conducted. Informed and consenting participants from Mpilo Central Hospital, United Bulawayo Hospital and Imagegate Diagnostics Centre, who were presenting with menstrual irregularities, acne, hirsutism and infertility, were recruited. Participants age ranged from 15-45 years. All participants had their demographics collected using questionnaires. Body mass index, waist-hip ration, clinical presentations and pelvic transabdominal ultrasound scan survey were determined.

Results: Participants were grouped into age groups 15-24 years, 25-34 years, 35-44 years. Polycystic ovaries presented as 10 or more 2-9 mm ovarian follicles with mean ovarian volume ≥ 10 cm^3. In establishing the diagnosis of polycystic ovaries, the criterion of 10 or more 2-9 mm ovarian follicles were found to have the highest representation in the 25-34-year age group. The study showed 30.4% of the clients had polycystic ovaries while 46.4% showed other pelvic pathology and the rest, 23.2% had normal pelvis scan results. The prevalence of polycystic ovaries was significantly higher in 25-34 year age sub-group. Acne and hirsutism were significantly associated with positive ultrasound imaging results for PCOS.

Conclusion: The study updated information on PCOS as seen on ultrasound in women in Bulawayo. All women of childbearing age presenting with infertility and clinical signs of hyperandrogenaemia (e.g. hirsutism, acne) should be screened for polycystic ovaries as part of a women wellness program. Furthermore, it is recommended that sonologists and sonographers be aware of the ultrasound criteria for polycystic ovarian syndrome in women of child-bearing age.

Keywords: Ultrasound scanning; polycystic ovarian syndrome; hirsutism; acne; female infertility; Black African women; Bulawayo; Zimbabwe.

1. INTRODUCTION

Women health is complicated and determines the overall perception of world-health as women constitute a critical mass of most populations around the world. Description of the diseases that affect women's cosmetic appearances, their fertility, conception issues, and childbearing, constitute areas of the greatest challenge to health service provision worldwide [1].

The polycystic ovarian syndrome (PCOS) was originally described by Stein and Leventhal in 1935 as consisting of amenorrhea, hirsutism, and obesity. However, lately the perception of PCOS has changed and the emphasis is now on the long-term complications that may ensue [2].

Polycystic Ovarian Syndrome (PCOS) has been observed to constitute a growing concern in women. The PCOS refers to a heterogeneous endocrine and morphological disorder commonly leading to primary/secondary infertility presenting varying incidents among women according to region, race and economic backgrounds [3]. Most often, patients present with body weight complaints, acne, hirsutism, menstrual dysfunction, oligomenorrhea, or infertility; they can also present with a pregnancy-related complication, such as gestational diabetes or spontaneous abortion [4]. Hirsutism or acne could be the patient's primary concern, which can result in profound psychological distress [5]. PCOS is also described as a metabolic disorder as it is associated with insulin resistance having been observed in both White and Mexican women [6]. Association with comorbid conditions [7] which include type 2 diabetes, dyslipidaemia, hypertension, hepatic steatosis, obstructive sleep apnoea, endometrial carcinoma and potentially breast and ovarian cancer, make PCOS a major health concern [8-10]. Indeed, patients with PCOS are at increased risk of spontaneous miscarriages, infertility, obesity, cardiovascular disorders, depression, non-alcoholic fatty liver disease, endometrial hyperplasia and endometrial carcinoma [11] making it imperative that the diseases is diagnosed and confirmed early during the course of its presentation. Ultrasound scanning provides a modality for

visually aided diagnosis of PCOS. Body weight changes and obesity team up to increase the tendency for the diseases which is associated with poor health outcomes for women. These conditions result in increased number of women tending to seek health services more frequently which provides opportunities for them to have ultrasound scanning confirmatory tests done.

PCOS has been found to affect at least 4-8% of women of reproductive age worldwide and this may loosely translate to the level of infertility. In the same vein, incremental changes in the predisposing factors may also mean an increase in the PCOS's. Especially in the younger women, a biopsychosocial understanding of PCOS is paramount to improve knowledge and treatment options emanating from an accurate description of the disease presentation [12,13].

There are different criteria used in the diagnosis and defining of PCOS. Therefore, prevalence of the syndrome varies according to diagnostic consensus used, with estimates ranging from 9% according to National Institutes of Health consensus, up to 18% with the Rotterdam consensus [14,15]. The prevalence is as high as 15%-20% when the European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine criteria are used [16]. This means that there could be an under or over estimation of prevalence rates necessitating regional determination of population-specific ratings. The Rotterdam criteria is currently the most commonly used and as such it was the standard of choice in this study although there has been controversy over its use before [17,18].

While there is a fair mapping of PCOS in the developed world, data is scarce when it comes to the black population of African origin in Zimbabwe and Bulawayo, in particular. There has been a lot of rural-urban migration and life style changes in Zimbabwean of women which negatively impacts on adiposity and metabolic associated conditions predisposing to PCOS as has been observed elsewhere [19].

Early diagnosis of PCOS is of great importance. Effective screening, education, undertaking of suitable preventive measures and treatment may be achieved with reasonable success if the disease or its signs are discovered early enough.

According to routine clinical practice observations, PCOS could not be ascertained to be associated with increased cases of infertility, rural-urban migration, social selection and social causation [20,21]. However, dietary changes instigated by intermittent and sporadic droughts, diminished-alternating-increased food obtainability, rural-to-urban migration induced obesity, urbanisation food type changes may lead to metabolic aberrations that influence weight gain, changes in body mass index and metabolic syndromes [22-24]. The latter are reported to predispose to PCOS [25]. However, there is no concrete evidence linking the various environmental factors, biological changes, clinical presentation and radiological findings to PCOS.

Moreover, in Bulawayo, Zimbabwe, routine practice has reported that the number of women presenting with primary infertility has been steadily increasing. Sub-stimulation of the ova caused by hormonal changes may be a possible cause of the underdevelopment. Dietary and life-style changes have occurred in most women over time and this change may induce PCOS development possibly through obesity and possible hormonal aberrations [26,27].

Hormonal concentrations estimation costs are a barrier to access of this modality for PCOS investigations. However, an ultrasound scan provides a real time visual aid and has ability to identify minute and multiple ovarian cysts in the majority of the clients with this problem at a reduced cost and time.

There has been an upsurge in contraceptive use and it is not clear how this usage may turn out to be with time and its effect on long term fertility in women and how this may be diagnosed with ultrasound. Moreover, the actual associations between ultrasound imaging and development of PCOs with infertility requires stratification in the heterogenous Bulawayo population. The magnitude of PCOs and infertility as shown by ultrasound scanning, the numbers of affected women and the rate of this happening is not well defined or characterized in the study population. Also, for the Bulawayo population, there is limited or scanty data on correlative studies linking ultrasound findings to polycystic ovarian incidence or prevalence. There questions that required to be clarified was, among other investigations, whether health facility location and status would influence prevalence of clients with PCOS reporting to particular facility and

thereby recommend increasing facility type for detection of PCOS in the frequently visited institutions. The current research presents data establishing the incidence and prevalence, ultrasound presentations and clinical findings associated with PCOS in a population of indigenous black Zimbabweans with gynaecological and obstetric complaints. Overall, an updated stratification of PCOS, clinical presentations and ultrasound findings offered here is meant to guide gynaecological and obstetrics health-seeking-client's wholesome management.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Research design and settings

The research design was a prospective cross-sectional study. Participants were complaining infertility and related problems were purposively recruited from consecutive females consulting at the gynaecological clinics of United Bulawayo Hospitals, Mpilo Central Hospital, and Imagegate Diagnostic Centre. Data was collected on the first day of recruitment and on the subsequent visits the clients reported for review during the following period of 6-9 months from August 2017 to April 2018.

2.1.2 Sampling size, sampling techniques

A cohort of 69 women was recruited in the study using a purposive sampling where only those women consulting for gynaecological and infertility were selected and followed up. Women who had read, understood and agreed to participate in the study by signing a consent form were enrolled. Other women who had no characteristics of infertility or being investigated for that were included in the study (n = 16) to serve as a control for particular comparisons and analysis.

2.1.3 Inclusion criteria

Included in the research were females with menstrual irregularities, acne, hirsutism and had agreed to participate in the study by signing a consent form. Menstrual irregularities were defined as chronic anovulation or as amenorrhea of 3 months duration or oligomenorrhea as intermenstrual interval > 35 days. Regular menstruation will be defined as 9-16 cycles of 21-35 days duration within a year and no more than a 4-day difference in duration between cycles.

2.1.4 Exclusion criteria

Excluded from the study were those women on hormonal therapy treatment, those with known diabetes mellitus, thyroid, and adrenal disorders.

2.2 Methods

2.2.1 Participants data collection

Participants who were recruited for the study were either referred by medical practitioners, physicians, specialists' obstetricians, gynaecologists or self-referrals. Questionnaires, accompanied by a research participation consent form, were issued to all participants when the appointment for the scan was made. The questionnaires collected demographic data, clinical history and other pertinent information that was not provided by referring medical practitioners and obstetricians. Other clinical findings were also provided by referring practitioners and obstetricians through patients records which provided clinical features observed in the participants. The participants also had their heights, weights, hip and waist measurements done to enable calculations of their body mass index (BMI) and waist-hip ratio (WHR) [3] used scales shown in Table 1.

Participants' choice of consultation centres was compared among the Imagegate Diagnosis (IGD), Mpilo Central Hospital (MCH) and United Bulawayo Hospitals (UBH).

2.2.2 Ultrasound scans

An ultrasound scanner, Dawei Ultrasound System (Dawei Ultrasound System, China) with a 2D contrast imaging, enhanced tissue harmonics, high-resolution liquid crystal device (LCD) 17-inch monitor, utilizing a 4MHz curved array transabdominal transducer was used to perform pelvic scans or equivalent scanner was used.

The participants had a transabdominal pelvic ultrasound scan with a full bladder to investigate the presence of PCOS. An ultrasound standard technique criterion for abdominal scanning was used. Briefly, the presence of PCOS during ultrasound scanning was defined by the presence of 12 or more 2-9 mm ovarian follicles in a single sonographic plane and an ovarian volume of more than 10 cm^3 [28-30] as guided

by professional Bodies [31,32]. This is the standard method used to diagnose PCOS currently. Improvement in imaging is now done through 3D and 4D ultrasound models with increased advances in ultrasonographic technology. The higher-frequency scanning probes can evaluate the ovary morphological anatomy and volume measurements with highly reproducible precision [33].

All ultrasonic examinations were performed by a single sonographer. Transabdominal ultrasound was performed utilizing a 4 MHz curved-array scanner of the transabdominal transducer. Ultrasound measurements were taken in real-time using a standardized protocol. Gain settings were optimized based on the size of the patient and the amount of pelvic adipose tissue. After identification of the ovaries, the size of the ovary was measured in three dimensions (length, width, and breadth). The highest possible magnification was employed to optimize and enhance follicular detection. The volume of each ovary was calculated using the formula (length x width x breadth x 0.523).

2.3 Data Analysis

Quantitative data was collected for investigation of PCOS prevalence. Statistical comparisons were performed for parametric analysis of percentages and frequency distributions of grouped data using the repeated measures analysis of variance (ANOVA) followed by Tukey's Multiple Comparison Test. Where necessary, the One Sample t test was used as a test for discrepancy between parameters. Percentage means of groups were compared for relative and comparative differences which were considered statistically varied when $P < 0.05$. Data was compared amongst client groups (n = 69) in those with clinical signs of infertility identifying prevalence of PCOS. To serve as a control group for certain analysis, women with normal pelvis or no clinical signs of infertility were included in the study (n = 16). Analysis of data used GraphPad InStat Software (version 5, GraphPad Software, San Diego, California USA).

3. RESULTS

The participants also had their heights, weights, hip and waist measurements done to enable calculations of their body mass index (BMI) and waist-hip ratio scales used in the study as observed from literature review findings [34].

This study was conducted to determine the prevalence of PCOS in women with infertility. The age range of the patients was from 15-45 years and these were drawn from the United Bulawayo Hospital (UBH), Mpilo Central Hospital (MCH) and Imagegate Diagnostics (IGD) which are all located in Bulawayo, Zimbabwe are given in Table 1.

Participating clients showed a relatively higher preference for consulting with Imagegate Diagnostics (Pvt) LTD as compared to either consulting with United Bulawayo Hospitals (1.91 more) and Mpilo Central Hospitals (4.45 more) for infertility and related examinations (IGD > UBH > MCH). In choosing to where to go for infertility investigations, a relatively higher % of clients reported to United Bulawayo Hospitals than to Mpilo Central Hospital during the period of the study (2.33 higher). Overall (1.33 more), clients showed preference for private facilities when consultation for infertility than they did for public hospital despite corresponding ultrasound equipment at all three institutions (57% vs 43% [a]). Also, clients showed a higher (6.6 higher) preferred consulting at urban (IGD) and low density (UBH)-based institutions (88.4%) compared to high density facilities (MCH) [13%]. The Tukey's Multiple Comparison Test for participant's attendance at individual health institutions displayed that "IGD vs UBH" was significantly different (***$P < 0.05$; Mean Difference 28.0, q = 42; 95% CI of diff 24.64 to 31.36), IGD vs Mpilo was significantly different (***$P < 0.05$ Mean Diff 45.0, q = 67.50, 95% CI of diff 41.64 to 48.36), UBH vs Mpilo was significantly different (***$P < 0.05$, Mean Diff 17.00, q = 25.50, 95% CI of diff 13.64 to 20.36) Table 1.

3.1 Scan Report Analysis

Of the 69 patients, 21 (30.4%) were diagnosed with polycystic ovaries (PCO) with a mean age of 33.1 ± 4.7 who had using the ultrasound criteria of 10 or more follicles measuring 2-9 mm. One-way ANOVA with Tukey's Multiple Comparison Test was used to analyze the ultrasound scanning findings, Table 2. Compared with women with normal pelvis investigations, women with other pelvic pathology were significantly over represented at 46.4% with " Non Pelvic disease vs Polycystic ovaries " were significantly different (**$P < 0.05$, Mean diff -5.00, q = 8.660, 95% CI of diff -7.505 to -2.495), while the same respondents were also significantly lower in representation as compared to those with

polycystic ovaries " Polycystic ovaries vs Other Pathology" (***P < 0.05, Mean diff -11.00, q = 19.05, -13.51 to -8.495), "Non Pelvic vs Other Pathology" were significantly different (***P < 0.05, Mean diff -16.00, q = 27.71, 95% CI of diff -18.51 to -13.49). The proportion of women with polycystic ovaries were relatively lower, however, when compared to those with other pelvic pathology (Polycystic ovaries < other pelvic pathology).

Table 3 shows that the age group of 25-34 had a higher prevalence (57.1%) of PCO followed by 35-44 (38.1%) and the lowest being the 15-24 (4.7%) age group. One-way ANOVA prevalence of PCOS among age groups in the study was significantly different among the age groups (***P < 0.0001, F = 2111, R squared = 0.9986).

Respondents with PCOS were distributed according to age groups. The “younger” age group (15-24 years) had the least number of respondents with PCOS. The age group 25-34 years displayed relatively higher members with PCOS as compared to either the 15-24 years and 35-44 years age groups (*** P <0.001 and **P < 0.05, 15-24 < 35-44 < 25-34, respectively). Tukey's Multiple Comparison Test showed that the 15-24 Years vs 25-34 Years were significantly different (***P < 0.05, Mean diff -52.40, q = 90.76, 95% IC of diff -54.91 to -49.89). Moreover, the 25-34 years age group had a relatively higher representation when compared to the 35-44 years age group (**P < 0.05, 34-44 < 25-34 age groups) The 15-24 Years vs 35-44 Years gave ***P < 0.05, Mean diff -33.40, q = 57.85, 95% CI of diff -35.91 to -30.89) [Table 4]. The comparison 25-34 Years vs 35-44 Years was significantly different (***P < 0.05, Mean diff 19.00, q = 32.91, 95% CI of diff 16.49 to 21.51).

Fig. 1 indicates that clients within the 15-24 years age group had the least representation in the number of cysts observed. The age group 25-34 years had significantly higher cysts as compared to their younger age mates (** P <0.05); The 35-44 years age group had the highest representation of number of cysts when compared to the 15-24 years age group and the 25-35 years age groups (** P <0.05 and *** P <0.001, respectively) [Fig. 1].

Table 1. Study participants from United Bulawayo Hospitals, Mpilo Central Hospital and Imagegate Diagnostics (PL) showing the distribution of the study participants according to their institution of origin

Institution	% Study Participants per facility (n = 69)
United Bulawayo Hospitals (UBH)	30 (21) *** (a)
Mpilo Central Hospital (MCH)	13 (9)
Imagegate Diagnostics (Pvt) LTD (IGD)	57 (39) *** (b)
Total	100 (69)

Table 2. Scanning results analysis according to clinical condition (n = 69)

Condition	Number	% of Total
Normal Pelvis	16	23.2 **
Polycystic ovaries	21	30.4 **
Other Pelvic Pathology	32	46.4***
Total (69)	69	100.0

Table 3. Incidence of PCOS patients according to age groups (n = 21)

Age group (Years)	Number of PCO Patients		Percent (%)		p value
15-24	1		4.7		
25-34	12		57.1	***, **	0.001, 0.05
35-44	8	***	38.1		
Total	21		100.0		

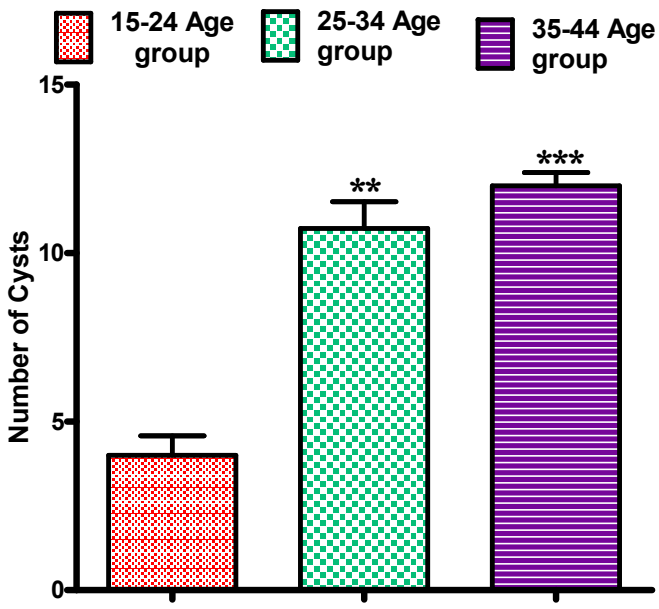

Fig. 1. Number of cysts per age group

*Cysts distribution by age group of clients that had an ultrasound scan done for different complaints. Data presented as mean ± SEM. One-way ANOVA indicated significant difference (***P < 0.004, F = 10.25, R Squared = 0.3981). The age group of 35-44 years had a significantly higher stimulated follicles (cysts) compared to both the 25-34 (1.4-fold higher) and 15-24 (3-fold higher) age groups, [35-44 > 25-35> 15-24]). Tukey's Multiple Comparison Test of 15-24 vs 25-34 was statistically significant (**P < 0.05, Mean diff -6.737, q = 5.586, 95% CI of diff -10.94 to -2.538). The comparison of 15-24 vs 35-44 was statistically significant (***P < 0.05, Mean diff -8.00, q = 6.384, 95% CI of diff -12.36 to -3.637). The 15-24 age group had a significantly lower cyst count (3-fold lower) compared to the 25-34 age group (15-24 < 25-35). [Fig. 1]*

Table 4. Prevalence of PCOS distribution according to Body Mass Index and Type of infertility among the respondents

Average Age of respondents :33.1 ± 4.7			
Body Mass Index and PCOS Prevalence			
< 25	Normal	6 (28.6)	**
25-30	Over-Weight	*** 7 (33.3)	
>30	Obese	8 (38.1)	**
Type of Infertility and PCOS Prevalence			
Primary (gestation = 0)		9 (42.9)	***
Secondary (gestation ≥ 1)		12 (57.1)	

Of the 21 the PCO patients, 12 (57.1%) displayed oligomenorrhea, followed by 10 (47.6%) with Acne, and Amenorrhea showing the lowest number of participants. The clients were further stratified based on their BMI category and type of infertility. Data indicated that 8 clients were obese and 7 were overweight. Prevalence of acne, oligomenorrhea, overweight and obese collectively contributed 71.4% of participants with PCOS. Secondary infertility was also had a high of 57.1% associated with PCOS [Table 5]. Women with acne (47.6%), had oligomenorrhea (57.1%), were overweight (33%), were obese (38.1%), had primary infertility (42.9%) or had secondary infertility (57.1%) had increased potential for PCOS presentations.

Respondents with BMI >30 (obese) were more likely (1.14-fold) to have PCOS when compared to those who were overweight (BMI 25-30) and

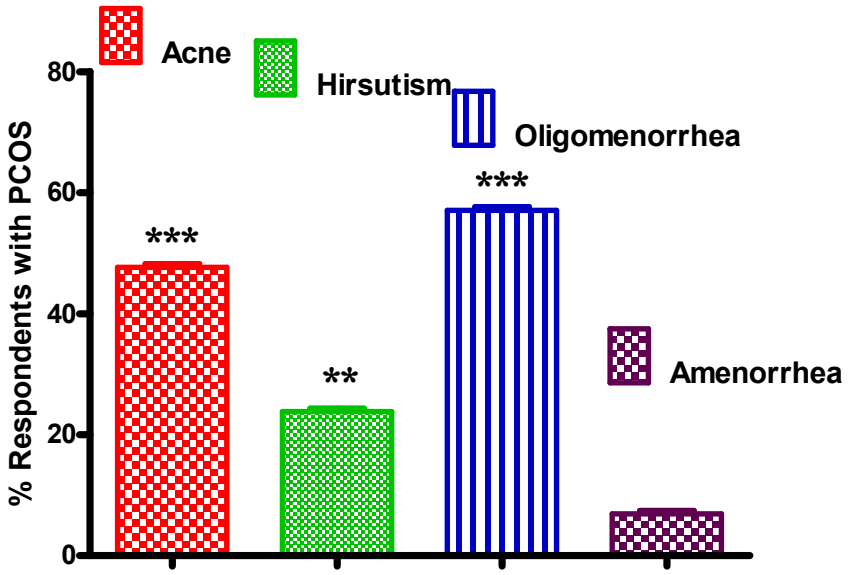

Fig. 2. Distribution of PCOS presentation in respondents with infertility-predisposing conditions

*One-way ANOVA showed significant differences amongst infertility predicting conditions (***P < 0.0001, F = 1557, R squared = 0.9983). Tukey's Multiple Comparison Test showed independent prediction of PCOS amongst the conditions with comparisons of Acne vs Hirsutism being significantly different (***P < 0.05, Mean diff = 23.87, q = 41.32, 95% CI of diff 21.25 to 26.48); Acne vs Amenorrhea being significantly different (***P < 0.05, Mean diff = -9.433, q = 16.33, 95% CI of diff -12.05 to -6.817); Hirsutism vs Oligomenorrhea being significantly different (***P < 0.001, Mean diff = -33.30, q = 57.65, , 95% CI of diff -35.92 to -30.68); Hirsutism vs Amenorrhea being significantly different (***P <0.05, Mean diff = 16.90, q = 29.26, 95% CI of diff 14.28 to 19.52) and Oligomenorrhea vs Amenorrhea being significantly different (***P < 0.05, Mean diff 50.20, q = 86.91, 95% CI of diff 47.58 to 52.82). [Fig. 2]*

Table 5. Ultrasound scan findings for Polycystic ovaries (PCO) as descriptors associated with PCOS prevalence

Parameter	Category	Number of Patients	Percent	
Follicles in a single sonographic plane (FSSP)	9-11 follicles	10	47.6	**
	12 or more follicles	11	52.6	
	Total	21	100	
Ovarian Volume	<10cm^3	4	19.0	***
	≥10cm^3	17	81.0	
	Total	21	100	

*Key: Cysts considered for diagnosis of PCO was 2-9 mm in size in single sonographic plane. Normal ovarian volume is <10 cc. The number of cysts in a FSSP differentiated PCOS prevalence according to either 9-11 follicles or > 12 follicles with >12 follicles being 1.1-fold higher. A comparison of 9-12 follicles vs > 12 follicles per FSSP showed a relatively significant difference between the means of the categories using Unpaired t test (**P = 0.0018, One-tailed, t = 6.124, df = 4, Difference between means = -5.000 ± 0.8165, 95% confidence interval -7.267 to -2.733, R squared = 0.9036). Fig. 6. As an ultrasound scan biomarker for PCOS prevalence in the study sample, ovarian volume was comparatively over represented in those with ≥10 cm^3 volume as shown in Fig. 6. Overall, more women (81%) had larger ovarian volumes with sparsely populated cysts per single sonographic plane showing increased follicular growth in infertility. Women with infertility had a 4.25-fold of having an ovarian volume of ≥10cm^3 when compared to those with an ovarian volume of ≤10 cm^3. An Unpaired t test analysis confirmed significant different of means when making a comparison between Ovarian volume <10cm3 vs Ovarian volume > 10 cm^3 (***P < 0.0001, One-tailed, t = 75.93, df = 4, Difference between means = -62.00 ± 0.8165, 95% confidence interval -64.27 to -59.73, R squared = 0.9993). [Table 5]*

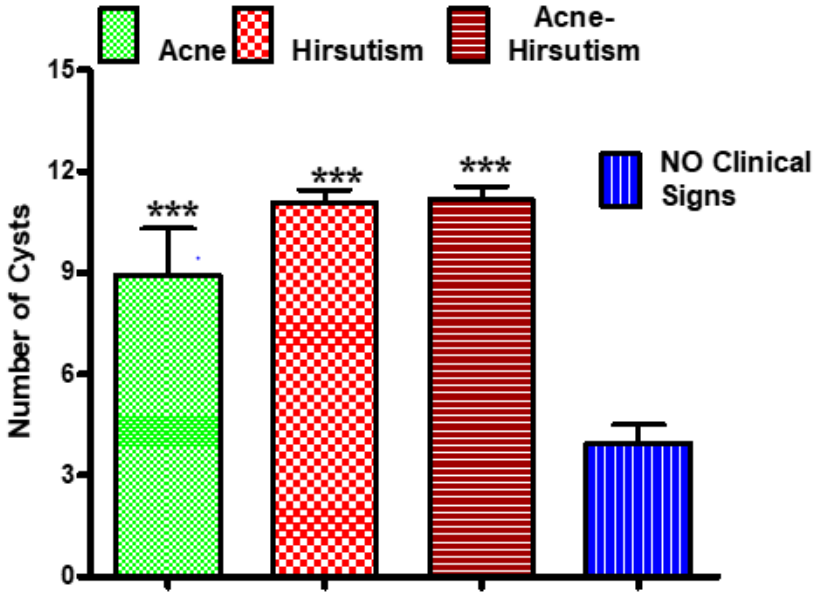

Fig. 3. The number of cysts per signs clients presented with at ultrasound scan examination as indicators of PCOS prevalence

The number of cysts observed in the population under study by the underlying clinical picture show the PCOS prevalence at >9-10 cyst per ovary

1.3-fold more as well to those with normal BMI of <25. One-way analysis of variance showed that all means were significantly. different between those with PCOS and BMI < 25 (Normal), BMI 25-30 (Over-weight), BMI >30 (Obese) [***P < 0.0001, F = 67.69, R squared = 0.9576). The BMI categories predicted PCOS prevalence independently with each other with Tukey's Multiple Comparison Test for < 25 (Normal BMI) vs 25-30 (Over-Weight) being significantly different (**P < 0.05, Mean diff = -4.700, q = 8.141, 95% CI of diff -7.205 to -2.195), < 25 (Normal BMI) vs >30 (Obese) being significantly different (***P < 0.05, Mean diff = -9.500, q = 16.45, 95% CI of diff -12.01 to -6.995) and 25-30 BMI (Over-Weight) vs >30 BMI (Obese) being significantly different (**P < 0.05, Mean diff -4.800, q = 8.314, 95% CI of diff -7.305 to -2.295) [Table 5].

Primary (gestation = 0) and secondary (gestation ≥ 1) infertility independently predicted PCOS prevalence with Unpaired t test comparison of Primary vs secondary infertility showing significant difference between them (***P < 0.0001, One-tailed, t = 17.39, df = 4, Difference between means = -14.20 ± 0.8165, 95% confidence interval = -16.47 to -11.93, R squared = 0.9869) [Table 4].

Clients with acne had a higher number of cysts compared to the control that had no signs. Compared to the clients without clinical signs, clients with hirsutism had significantly higher cyst count. The number of cysts or activated follicles was twice as many in women with either acne or hirsutism when compared to women who had no clinical signs of infertility.

One-way ANOVA indicated that the means of the number of cysts in the clinical groups were significantly different (**P = 0.0012, F = 6.223, R squared = 0.2843). Bartlett's test for equal variances gave a corrected Bartlett's score of 21.98 (***P < 0.0001). Tukey's Multiple Comparison Test for Acne vs NO Acne-Hirsutism and for Acne-Hirsutism vs NO Acne-Hirsutism gave significant differences (***P < 0.05, Mean diff = 4.994, q = 5.924, 95% CI of diff "1.821 to 8.167") and (***P < 0.05, Mean diff 7.219, q = 6.105, 95% CI of diff 2.768 to 11.67), respectively. Also, Hirsutism vs NO Acne-Hirsutism differed significantly (***P < 0.05, Mean diff = 7.136, q = 7.664, 95% CI of diff 3.631 to 10.64) [Fig. 3].

Menstrual cycle duration and clinical conditions predicted prevalence of PCOS. Clients PCOS and hirsutism were more likely to be having a 35-day menstrual cycle as compared to those with a

regular (28 Day cycle) and those with amenorrhea Fig. 4A. Clients with a 35-day long menstruation cycle had a significantly higher chance to have acne amongst those with PCOS as compared to those with a regular cycle (28 days) and with amenorrhea Fig. 4B.

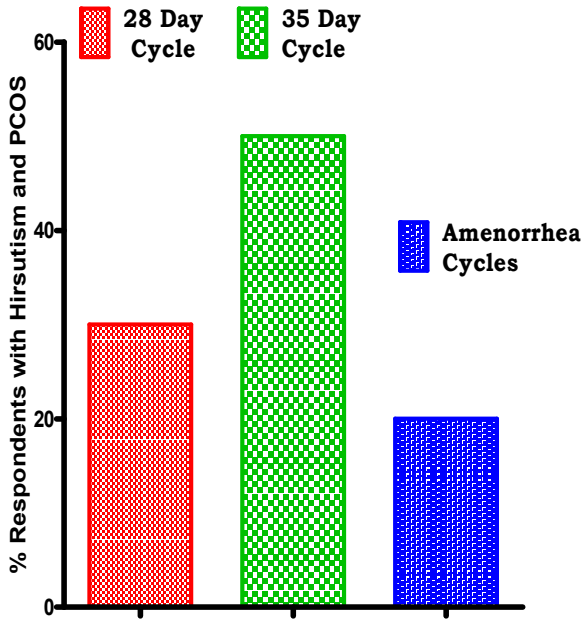

Fig. 4A. Comparison of menstrual duration and Hirsutism in respondents with PCOS
The 35-day menstrual cycle predicted presence of hirsutism in respondents with PCOS

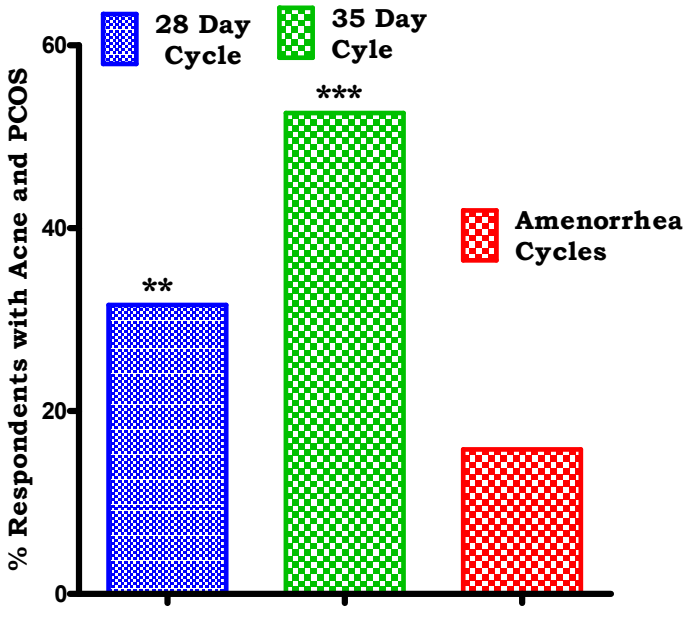

Fig. 4B. Comparison of menstrual duration and acne in respondents with PCOS
Acne was associated with PCOS in clients with a 35-day menstrual cycle as compared to either those with 28-day cycle or amenorrhea

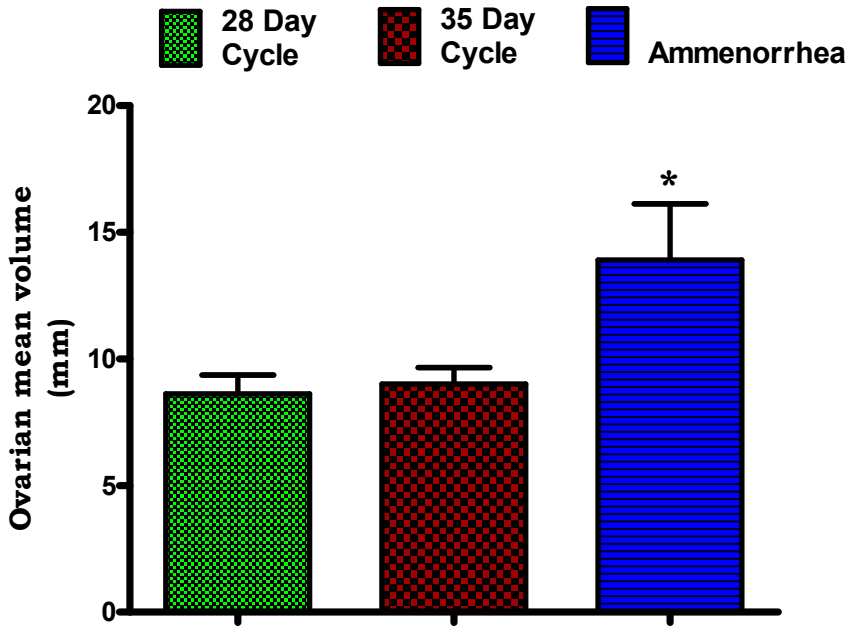

Fig. 5. Comparison of mean ovarian volume with menstrual cycle duration as a disaggregation of PCOS prevalence. PCOS were associated with higher ovarian volume seen amenorrhoea

One-way analysis of variance for comparisons made showed that menstrual cycles durations predicted PCOS prevalence in respondents with hirsutism independently at statistically significant levels (***P < 0.0001, F = 700.0, R squared = 0.9957). Tukey's Multiple Comparison Test of respondents with hirsutism showed groups to be significantly different in predicting PCOS prevalence when comparing the 28 Day Cycle vs 35 Day Cycle (***P <0.05, Mean diff = -20.00, q = 34.64, 95% CI of diff -22.51 to -17.49), the 28 Day Cycle vs Amenorrhea Cycles (***P < 0.05, Mean diff 10.00, q = 17.32, 95% CI of diff 7.495 to 12.51), and the 35 Day Cycle vs Amenorrhea Cycles (***P < 0.05, Mean diff = 30.00, q = 51.96, 95% CI of diff 27.49 to 32.51).

One-way analysis of variance for comparisons made showed that menstrual cycles durations predicted PCOS prevalence in respondents with acne independently at statistically significant levels (***P < 0.0001, F = 1022, R squared = 0.9971). Tukey's Multiple Comparison Test of respondents with acne showed groups to be significantly different in predicting PCOS prevalence when comparing the 28 Day Cycle vs 35 Day Cycle (***P < 0.05, Mean diff = -21.00, q = 36.37, 95% CI of diff -23.51 to -18.49), 28 Day Cycle vs Amenorrhea Cycles (***P < 0.05, Mean diff = 15.80, q = 27.37, 95% CI of diff 13.29 to 18.31) and 35 Day Cycle vs Amenorrhea Cycles (***P < 0.05, Mean diff = 36.80, q = 63.74, 95% CI of diff 34.29 to 39.31) Fig. 4B.

On the question of which menstrual cycle is associated with a higher PCOS prevalence, amenorrhea had significantly higher chances of having significantly high ovarian volume when compared to clients with either a 28-day or 35-day menstrual cycle duration, clients with Fig. 5. Mean ovarian volumes predicted the prevalence of PCOS with high volumes most likely to indicate the presence of the disease as shown in clients with amenorrhea in the study. One-way ANOVA showed that a comparison of the means for PCOS clients with 28, 35 Days and amenorrhea menstrual cycles were significantly different (*P < 0.05, F = 4.188, R Squared = 0.1055). Tukey's Multiple Comparison Test of groups showed independent prediction for PCOS by menstrual cycles for 28 Day Cycle vs Amenorrhea (*P <0.05, Mean diff = -5.284, q = 4.024, 95% CI of diff -9.737 to -0.8313) and (*P < 0.05, Mean diff = -4.888, q = 3.807, 95% CI of diff -9.242 to -0.5343).

On evaluating whether the uterine lining definition was associated with the ovarian volume to describe prevalence of PCOS in the study, the fibrotic uterine lining and the fibrotic uterine lining was associated with increased ovarian volume. Increased ovarian volume was

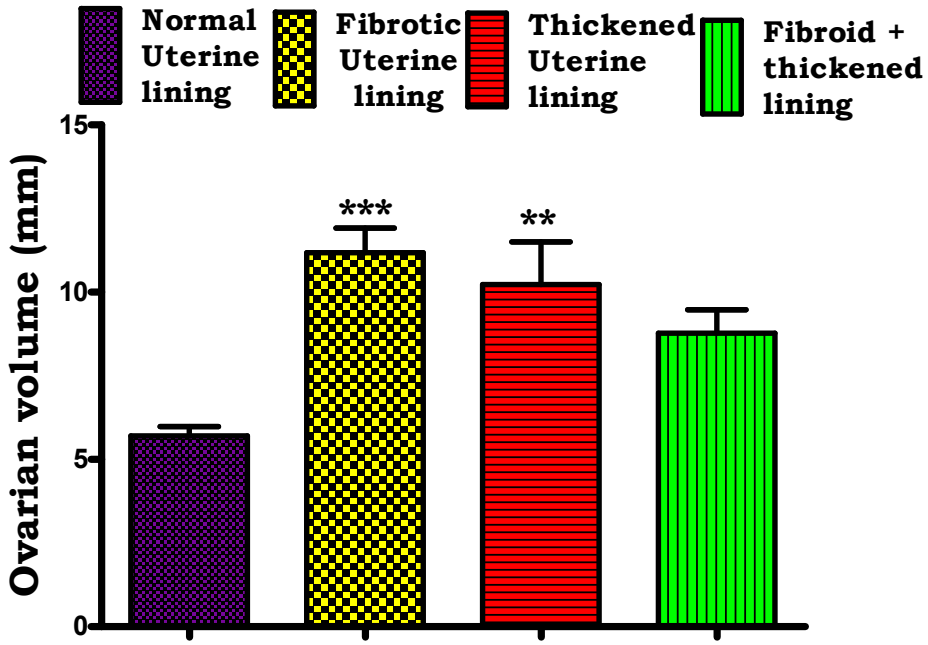

Fig. 6. Uterine findings compared to ovarian volume as predictors of PCOS prevalence

associated with prevalence of PCOS. The fibrotic uterine line displayed a significant higher representation in influencing or being influenced by a larger ovarian volume when compared to normal uterine lining, thickened uterine or both thickened and fibrotic during ultrasound investigations. One-way ANOVA for the ovarian volume in different uterine line showed significant difference in the study (***P < 0.0001, F = 16.68, R squared = 0.4312, Corrected Bartlett's statistic = 24.64 [***P < 0.0001 for significantly different variances]). Tukey's Multiple Comparison Test showed significantly different variance between uterine linings representation and ovarian volume as a biomarker for PCOS prevalence. Normal uterine lining vs Fibrotic uterine lining was significantly different for PCOS prevalence prediction (***P < 0.05, Mean diff = -5.478, q = 9.758, 95% CI of diff -7.573 to -3.383). Normal uterine lining vs Thickened uterine lining was significantly different for PCOS prevalence prediction (**P < 0.05, Mean diff = -4.525, q = 5.401, 95% CI of diff -7.652 to -1.399).

4. DISCUSSION

Client distribution according to centre of consultation and/or management showed an increased number of clients reporting to Imagegate Diagnostics (Pvt) LTD. At this centre, clients were able to receive a same-day-all-round service as compared to other two centres where clients were referred from one unit to the other possibly over periods exceeding days or weeks. Results turn-around-time, reduced waiting times and same day services, which describe quality of service, are some of the preferred determinants used by clients on deciding where they choose to seek health services and consultations [35-37]. Also, the penchant for private medical institutions as compared to public medical institutions requires further investigation. Private medical facilities tend to charge higher consultation fees in general although with a higher service efficiency, higher confidentiality and discretion. The dichotomous nature of sampling tended to influence PCOS prevalence determination that brought a wholesome picture as most cases of PCOS were possibly captured.

In this prospective study, 69 women between the ages of 15-45 years were assessed for incidence of PCOS using ultrasound imaging and associated clinical manifestations. The overall prevalence was found to be 30.4% which is higher than the worldwide prevalence of 5-10% [38]. The inclusion of 15-year-olds in study arises from the observation that teenagers as young as 14 years are presenting with pelvic area complaints which PCOS have been found emanating from pelvis inflammatory diseases. While illegal, under age pregnancies and fertility

issues are a common occurrence necessitating extending research to this group of "children mothers" [39].

The reason for the high prevalence may be due to high incidence of acne, oligomenorrhea, overweight and obesity which were observed in 71.4% of the participants as this was a health institution obtained sample. These clinical presentations have an established association with PCOS and also the sample used in the study may yield different results than an unselected sample [40]. While the selection criteria were based on primary or secondary infertility complaints by the clients, the high prevalence of clinical finings associated with PCOS in the current study may be putting emphasis on these parameters as first line screenings and guidelines for the diagnosis of the disease. What it may allude to is that algorithms for PCOS diagnosis need to include these as well. Similarly, a study conducted on 29-43-year-old Saudi female patients with a diagnosis of PCOS showed a high prevalence of obesity (64.5%) and overweight (24.2%). Of note, women with overt or known metabolic syndromes, like diabetes type 2 were not included in the study as a measure to eliminate bias in the study and improve quality control.

The prevalence of acne and hirsutism in the current study may be masked or not shown as high as in other researches because of the increase and availability of cosmetic treatments for these which brings a bias to the results. Visual observational studies as well as questionnaires were used to obtain information on the presence of acne and hirsutism in the clients. However, the clients were not apt to disclose for reasons of embarrassment associated with the conditions which the client will have resorted to hiding by using facial cosmetics. Transabdominal ultrasound scan of the pelvis was used to evaluate the ovaries for polycystic manifestations as well as to exclude androgen producing ovarian tumors and developmental abnormalities [17] to optimise PCOS prevalence detection. Of note, clients did not complain of acne or hirsutism *per se* for they seemed to cope with this by cosmetic applications.

Assessed were the number of ovarian cysts per clinical sign per single longest sonographic plane. Clients with acne had significantly higher number of cysts compared to the control that had no signs indicating that acne could be a signal towards identification clients with PCOS's. Also, compared to the clients without clinical signs, clients with hirsutism had significantly higher cyst count. Overall, acne and hirsutism combined displayed a higher preponderance towards increased ovarian cysts content as seen by ultrasound scan.

Number of cysts or follicles per ovary per age group showed significant variations showing that PCOS prevalence could follow the same pattern. Cysts distribution by age group of clients tended to be different according the complaints clients presented with. Clients within the 15-24 years age group (which were the youngest group by age) had the least representation in the number of cysts observed and lower PCOS prevalence. This is expected as gynaecological complaints tend to be fewer in this age group. Also, at the15-24 years age group consulting for fertility issues is not common and PCOSs are discovered incidentally during investigation for amenorrhea or other menstrual irregularities. However, due to other religious and marriage practices, adolescents of 14 years are reporting for gynaecological examination more frequently as 32% of girls in Zimbabwe are married before the age of 18 and 4% are married before their 15th birthday [41,42]. Moreover, increased follicles numbers above a certain threshold (>10 are also associated with PCOSs even when the evaluating criteria has been revisited to improve diagnostic specificity [43]. Intriguingly, despite legislation against women at 15-18 years becoming pregnant, there is a tendency of females as young as 15 years falling pregnant in the population [44,45] with possibilities of infertility complaints. Indulging in sex before or after age of consent or falling pregnant during date rape is are criteria for a girl to be married in Zimbabwe increasing opportunities for ultrasound scan fertility investigations likely increase PCOS prevalence.

The age group 25-34 years had significantly higher cysts as compared to their younger age mates. The 35-44 years age group had the higher representation of cysts when compared to the 15-24 years age group and the 25-35 years age groups. Polycystic ovaries development is linked with subfertility in this age group necessitating a need to investigate the condition earlier or when acne and hirsutism is observed or suspected or anticipated [3,38].

Despite the tendency of the 35-44 years age group towards frequent medical consultation with

fertility complaints, the significantly higher cyst count indicates a higher prevalence of PCOSs in this age group as a possible cause of infertility. As age proceeds, fertility inversely decreases, and feminine hormonal activities follow the same pattern going towards menopause. This is also associated with reduced ovary volume reserve which show reduced capacity for fertile ovulation cycles in certain racial/ethnic groupings [46,47].

Comparison of menstrual duration and hirsutism showed that clients with hirsutism were more likely to be having a 35-day menstrual cycle as compared to those with a regular (28 Day cycle) and those with amenorrhea. Increased menstrual cycle may result from delayed ovulation due to failure of follicles to release the ovum which invariably shows low follicle stimulation and luteinisation. As a result, increased immature cysts (both in size and or number) that will not reach maturity or cease to grow in situ will be observed. Cysts, therefore, may remain underdeveloped and persist into the next intervening menstrual cycle resulting on PCOS's as a disease. Being biologically active, ovarian cysts continue to synthesize other feminine and androgenic hormones at different levels. This may confirm the association of hirsutism with the presence of PCOS in this category of women who may have elevated androgen hormones triggering a vicious cycle of more hirsutism yielding more androgens, *ad infinitum*, until treatment intervention.

Comparison of menstrual cycle differences in clients with acne showed a higher prevalence of acne in clients with a 35-day cycle as compared to regular, irregular (oligomenorrhea) and amenorrhea mensuration cycles. The association of acne and a longer menstrual cycle may indicate decreased follicle stimulation and androgen hormones increase that may derange lipid metabolism and cause fat distribution the skin layers. Visual observation of client presentation and acne may thus be used a predictor of PCOS's especially in clients where intervention against acne has not been affected.

Mean ovarian volumes and menstrual cycle duration were compared among clients with 28- and 35- day cycles. Clients with amenorrhea showed a tendency towards higher ovarian mean volume which may be attributed to increase in the number of immature ova resulting from anovulation. Accumulation of these immature cysts can cause associated ovarian enlargement. Uterine findings compared to ovarian volume showed that the number of clients with fibroid uterus displayed a significant tendency towards a larger ovarian volume when compared to other signs observed during ultrasound investigations. However, further investigations may be needed to ascertain the possible association of the fibrotic uterus and the PCO development.

5. CONCLUSION

The combined data showed an increased prevalence of PCO ultrasound presentation in women with infertility in the 35-44 years age group as compared to 25-34 years and the 15-24 age groups. The overall prevalence was found to be 30.4% which is higher than the world prevalence for the disease at prevalence of 5-10%. A notable high percentage of clients with ovarian cysts and a higher count per single sonographic plane was observed in the 35-44 years age group as well. A significant correlation between patient clinical presentations of acne, hirsutism and obesity with polycystic ovarian ultrasound findings was also presented.

Association of amenorrhea with increased ovarian volume and activated follicles allows a predictive ability for PCOS development.

6. RECOMMENDATIONS

Detections, diagnosis and prognosis of PCOS should made based on the ultrasound findings in association with the clinical picture if the client and algorithms formulated within frequent time lines as the prevalence of the disease seem to be increasing in urban areas. At a prevalence of 30.4%, the disease seems to be relatively higher than has been reported in other studies at 8-10%.

Further research is recommended using a larger sample, 3D ultrasound function to improve follicular count as well as to include the hormonal assessment of the patients found to have polycystic ovaries.

7. STUDY LIMITATION

The study sample was small therefore limiting the level of generalization of the results.

The use of the transabdominal ultrasound as opposed to the more accurate transvaginal method due to the less acceptability of the former

method by clients, lessened the amount of pelvic information obtained especially where the client was obese.

Also, the study was a clinical area-based study.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Written ethical approvals were sought, obtained from the Research Council Zimbabwe (MRCZ/B/1667) and respective participating medical facilities Research Ethical Review Boards. Letters of approval to conduct the study were obtained from the respective Hospital Chief Executives of United Bulawayo Hospitals (UBH), Mpilo Central Hospital and Imagegate Diagnostics (PL). All participants gave their written informed consent to be enrolled. The consent form clearly stated what to expect during the study as well notifying them of their right of refusal to participate in the study as well as the right to pull out of the study at any stage. A clear explanation was given to the participants concerning safety of the investigations, that is, ultrasound scan examinations.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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