INTRODUCTION

Polycystic ovary syndrome (PCOS) is a long-term recognized complex and heterogeneous disorder that affects reproductive-aged women and presents with varying degrees of gynecological, reproductive, endocrine, metabolic, and various organ-specific aberrations. The disorder is characterized by chronic ovulatory dysfunction, hyperandrogenism, and polycystic ovaries on ultrasound. It was in 1935 that Irving F. Stein and Michael L. Leventhal first described the clinical, macroscopic, and histological characteristics of the disorder and its association with hirsutism and amenorrhea. Its reported global prevalence among reproductive-aged women is about 10%, however, the prevalence varies with races and ethnicities. A recent study had reported a 12.2% prevalence of the disorder among Nigerian women with the syndrome. The syndrome is common in Nigeria occurring in approximately one in six infertile Nigerian women.

The etiopathogenesis of PCOS is ill-defined and very obscure. However, several theories had been suggested as possible favored factors in the evolution of the disorder. Currently, the interaction of certain genes with various environmental factors is the most accepted
pathophysiologic event in the evolution of the syndrome.9,9 Due to the varied clinical features of the syndrome, it is usually defined and phenotyped based on either the 1990 National Institute of Health, the 2006 Androgen Excess Society, or the 2003 Rotterdam International Consensus criteria.10,12 Over the decades since it was first described in the literature, numerous evidence from various epidemiological reports had noted that the disorder is associated with distinct metabolic aberrations including obesity, insulin resistance, type 2 diabetes mellitus, hyperinsulinemia, hyperandrogenism, and dyslipidemia.13

Dyslipidemia is the most persistent and prevalent metabolic aberration observed among women with the syndrome.14 These lipid aberrations had been ascribed to various metabolic perturbances such as obesity, insulin resistance, and hyperandrogenemia associated with the syndrome which enhances the risk of adverse cardiovascular events in women with the syndrome in various studies.15 However, many of these studies are all confined to western populations with paucity of data in our region. Therefore, this study was designed to investigate the pattern of dyslipidemia among adult reproductive-aged women with PCOS in Port Harcourt, Nigeria. The specific objectives of the present study were to determine the prevalence of dyslipidemia among the study population, to determine the variants of dyslipidemia among the study population, to determine the pattern of dyslipidemia in various age groups of the study population, and to compare the findings from this study with similar reports around the world.

METHODS

Study Area and location

This present study was carried out in the Department of Chemical Pathology and Metabolic Medicine of the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria. UPTH is one of the tertiary care hospitals situated in the Niger Delta region of Nigeria. The hospital serves as a referral center for all the primary and secondary health centers in the region and the neighboring states. The Department of Chemical Pathology and Metabolic Medicine of the hospital carries out routine and complex clinical chemistry analysis and also has an attached Metabolic Clinic where patients with uncomplicated metabolic disorders, including PCOS, are referred to from different points within the hospital.

Study design and structure

The study is a retrospective, descriptive, and cross-sectional study of laboratory variables including age, plasma total cholesterol (Tc), plasma high density cholesterol (HDL-c), plasma low density cholesterol (LDL-c), and plasma triglycerides (Tg) of all patients with diagnosed PCOS irrespective of phenotype who presented for fasting plasma lipid profile in the Department of Chemical Pathology and Metabolic Medicine of the University of Port Harcourt Teaching hospital (UPTH) from different points within the hospital between 1st January, 2008 to 31st December, 2017. All the patients with PCOS had been diagnosed by the specialist gynecologist in UPTH based on the Rotterdam International consensus criteria which is defined as the presence of any two of the following three features of the syndrome15:

- Chronic oligo-ovulation/anovulation evidenced biochemically by a mid-luteal phase (day 21-23) menstrual cycle serum progesterone of less 10ng/ml (32nmol/l) or clinically by oligomenorrhea/amenorrhea.
- Hyperandrogenism evidenced either clinically (hirsutism, acne, and androgenic alopecia) or biochemically (serum total testosterone level of greater than 2.8 nmol/l)
- Polycystic ovaries on transvaginal ultrasound scan (presence of twelve or more follicles measuring 2-9mm in diameter and/or at least one enlarged ovary measuring more than 10 cm³).

Inclusion criteria

- Records of fasting lipid profile of patients more than 18 years of age with any phenotype of PCOS.

Exclusion criteria

- Records of fasting lipid profile of PCOS patients who are either pregnant, on lipid-lowering medications, with established diabetes mellitus, with androgen excess disorders, hyperprolactinemia, thyroid disorders including those with incomplete data.

Specimen collection, processing, and laboratory analysis

During the period under study, fasting venous whole blood specimen were collected from each patient by phlebotomy through the antecubital vein while adhering to the basic universal safety precautions. All collected specimen were emptied into ethylenediaminetetraacetic acid (EDTA) specimen collection tubes and subsequently processed accordingly.

Laboratory analysis for plasma Tc, HDL-c, and and Tg were all carried out through the enzyme-catalyzed colorimetric methods with same brands of laboratory reagents including three levels (levels 1, 2, and 3) of commercial quality control sera sourced from Randox Laboratories, United Kingdom.

While the plasma LDL-c were calculated using the following Friedewald formula.16

\[ \text{Tc} - \text{HDL-c} - \frac{\text{Tg}}{2.2} \]
All parameters in the Friedewald formula were all in mmol/l unit.

The Friedewald formula was only applied if fasting plasma triglyceride (Tg) level was less than 4.5 mmol/l.

**Data Collection, stratification, and definitions**

All records from laboratory result sheets and case notes of each PCOS patient were collected, reviewed and entered into Statistical Package for Social Sciences (SPSS) version 20. Records collected were demographic data (age), clinical diagnosis (PCOS), total cholesterol (Tc) in mmol/l, high-density cholesterol (HDL-c) in mmol/l, triglycerides (Tg) in mmol/l and the calculated low-density lipoprotein (LDL-c) in mmol/l.

Age of study cohorts was arbitrarily stratified in four groups as follows: < 20 years, 20 – 30 years, 30 – 40 years, and > 40 years.

Dyslipidemia was defined in this study based on the National Cholesterol Education Program-Adult Treatment Panel 111 (NCEP-ATP 111) as the presence of any of the following plasma lipid profile:

- Total cholesterol of greater than 5.17 mmol/l
- High-density cholesterol less than 1.3 mmol/l
- Triglycerides greater than 1.7 mmol/l
- Low-density lipoprotein greater than 3.36 mmol/l

Therefore, based on the NCEP-ATP 111 criteria, Tc was stratified as normal (< 5.17 mmol/l) or abnormal (>5.17mmol/l), HDL-c stratified as normal (> 1.3 mmol/l) or abnormal (< 1.3 mmol/l), Tg stratified as normal (1.7 mmol/l) or abnormal (> 1.7 mmol/l), and the calculated LDL-c stratified as normal (< 3.36 mmol/l) or abnormal (> 3.36 mmol/l).

**Statistical analysis**

All the acquired data were entered into the SPSS version 20 software. Subsequently, the data were all reviewed, coded, and properly validated. The non-Gaussian distributed data were logarithmically transformed prior to statistical analysis. Analysis was done using Shapiro-Wilk test, descriptive statistics, Chi-square test, and Fisher’s exact test. Probability value of less than 0.05 were regarded as statistically significant.

**RESULTS**

During the 10-year period (1st January 2008 to December 2017), two hundred and thirty-four (234) patients with PCOS presented to the Department of Chemical Pathology and Metabolic Medicine for fasting lipid profile investigations using fasting plasma Tc, HDL-c, and Tg lipid panels. Among the plasma lipid panels of these 234 patients who presented during that period under study, the data of 226 (which is 96.6% of the total) of these patients met the inclusion criteria of the present study and were recruited for the present study.

**Table 1: Characteristics of study variables.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>Range</th>
<th>Mean±2SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>226</td>
<td>18-42</td>
<td>28.40±5.75</td>
</tr>
<tr>
<td>Plasma Tc (mmol/l)</td>
<td>226</td>
<td>3.0-5.7</td>
<td>4.34±0.65</td>
</tr>
<tr>
<td>Plasma HDL-c (mmol/l)</td>
<td>226</td>
<td>0.5-1.7</td>
<td>1.10±0.34</td>
</tr>
<tr>
<td>Plasma Tg (mmol/l)</td>
<td>226</td>
<td>1.5-6.7</td>
<td>3.40±1.58</td>
</tr>
<tr>
<td>Plasma LDL-c (mmol/l)</td>
<td>166</td>
<td>1.1-4.8</td>
<td>1.90±0.65</td>
</tr>
</tbody>
</table>

**Table 2: Age distribution of the study population.**

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>N</th>
<th>%</th>
<th>Fisher’s Exact</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>19</td>
<td>8.4</td>
<td>164.903</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>20-30</td>
<td>125</td>
<td>55.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-40</td>
<td>78</td>
<td>34.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>4</td>
<td>1.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant

The mean of the plasma HDL-c concentration among the study population was decreased as adjudged by NCEP-ATP 111 definition. The mean plasma level of the Tg was also high among the study population based on the NCEP-ATP 111 definition.

**Table 3: Prevalence of dyslipidemia among study population based on the national cholesterol education program-adult treatment panel 111 criteria.**

<table>
<thead>
<tr>
<th>Dyslipidemia</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>45</td>
<td>19.9</td>
</tr>
<tr>
<td>Positive</td>
<td>181</td>
<td>80.1</td>
</tr>
</tbody>
</table>

Chi-square = 13.897; p-value = < 0.001
The plasma level of Tg of sixty (n = 60) of the study population was more than 4.5 mmol/l, hence only those (n = 166) with plasma Tg level less than 4.5 mmol/l had their LDL-c calculated using the Friedewald formula in this study. In table 2, the majority of the study population are within the age group 20-30 years (55.3%) with the least study population (1.8%) within the age group of more than forty years. In Table 3, majority (80.1%; n = 181) of the study population had defined dyslipidemia based on the NCEP-ATP 111 criteria.

In Table 4, based on the NCEP-ATP 111 plasma lipid limits, there were significant difference between those with normal and abnormal plasma lipid levels of Tc, HDL-c, Tg, and LDL-c.

### Table 4: Stratification of plasma lipid levels of study population based on the national cholesterol education program-adult treatment panel 111 limits.

<table>
<thead>
<tr>
<th>Lipid variables</th>
<th>Based on NCEP-ATP 111 Criteria</th>
<th>Chi-square</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal n (%)</td>
<td>Abnormal n (%)</td>
<td></td>
</tr>
<tr>
<td>Plasma Tc (mmol/l)</td>
<td>186 (82.3)</td>
<td>40 (17.7)</td>
<td>94.319</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma HDL-c (mmol/l)</td>
<td>88 (38.9)</td>
<td>138 (61.1)</td>
<td>10.195</td>
</tr>
<tr>
<td>Plasma Tg (mmol/l)</td>
<td>55 (24.3)</td>
<td>171 (75.6)</td>
<td>15.735</td>
</tr>
<tr>
<td>Plasma LDL-c (mmol/l)</td>
<td>142 (85.5)</td>
<td>24 (14.5)</td>
<td>97.097</td>
</tr>
</tbody>
</table>

*Statistically Significant; NCEP-ATP 111 = National Cholesterol Education Program-Adult Treatment Panel 111; Tc = Triglycerides; HDL-c = High Density Lipoprotein Cholesterol; Tg = Triglycerides; LDL-c = Low Density Lipoprotein Cholesterol.

However, the most common lipid abnormality is elevated Tg (75.6%) followed by decreased HDL-c (61.1%). While the least lipid abnormality was elevated Tc (17.7%) and elevated LDL-c (14.5%). In Table 5, dyslipidemia was observed more (51.9%) within the study population of age group 20-30 years.

### Table 5: Distribution of dyslipidemia based on each age group of the study population.

<table>
<thead>
<tr>
<th>Status of Dyslipidemia</th>
<th>Age groups (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 20</td>
</tr>
<tr>
<td>Negative n (%)</td>
<td>9 (20%)</td>
</tr>
<tr>
<td>Positive n (%)</td>
<td>10 (5.5%)</td>
</tr>
<tr>
<td>Fisher Exact; p-value</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### DISCUSSION

PCOS had historically been characterized as a disorder of the female reproductive function and that of fertility. This assumption stem from the report in 1935 by Stein and Leventhal who had described the syndrome as a triad of hirsutism, amenorrhea, and polycystic ovaries. However, with the decade-long intense research on its varied clinical features, etiology, pathophysiology coupled with the improved diagnostic capabilities of the disorder, the syndrome has gained prominent attention as a rather multi-complex disorder with various gynecological, reproductive, endocrine, and metabolic consequences. It has been linked to the increased risk of obesity, insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus, metabolic syndrome, non-alcoholic fatty liver disease, hypertension, and dyslipidemia. However, the most frequent metabolic aberration observed among women with the syndrome in recent time is dyslipidemia. In this present study, we had evaluated the pattern of lipid and lipoprotein pattern among adult PCOS patients based on the NCEP-ATP 111 criteria and observed 80.1% incidence of dyslipidemia which is in agreement with the 80% incidence of dyslipidemia reported recently from Pakistan. Moreover, the high incidence of dyslipidemia obtained in this study is almost in accord with the 76.7% incidence of dyslipidemia observed among patients with PCOS using the NCEP-ATP 111 criteria in a similar study. However, some other authors had reported lower frequencies of dyslipidemia among women with PCOS. It has been reported that young adult women with PCOS are more at risk of dyslipidemia than their older counterparts due to the increased incidence of obesity, insulin resistance, and the androgen excess state inherent in these young adult women with PCOS. These reports are all in accord with this study where dyslipidemia was found to be more frequent (55.3%) among the young adult women within the age group of 20-30 years.

Although multiple studies have demonstrated an increased incidence of dyslipidemia among women with PCOS in recent time, however, the specific pattern of these lipid disorders varies among these studies. Some studies had reported an increased level of LDL-c as the most lipid abnormality, some had documented only low HDL-c cholesterol as the only abnormality observed in women while others have reported elevated Tc as the only abnormality. However, the most consistent lipid abnormality reported in most studies is the increased Tg level associated with low HDL-c level. The finding in
this study is in agreement with most of these studies in support of the high Tg and low HDL-c levels among the majority of women with PCOS. Using the NCEP-ATP 11 criteria in this study, most (75.7%) of the study population had elevated Tg levels while 61.1% had low HDL-c levels. The conflicting variations of the pattern of dyslipidemia among these studies could be related to genetic and environmental factors which influences plasma lipid levels in women with PCOS.28

Reproductive-aged women with PCOS harbor clusters of metabolic factors such as obesity, insulin resistance and hyperandrogenism which all act in concert to increase the risk of these adverse cardiovascular events in this group of women compared with the general population.29 Cardinal to the development of these adverse cardiovascular events is the formation of atherosclerosis which is ultimately enhanced among women in presence of dyslipidemia.28–30 Patients with PCOS have a higher prevalence of atherosclerosis and an estimated sevenfold increased likelihood of myocardial infarction which are pathological events linked to dyslipidemia.31 This factor underscores the expert-suggested need for regular assessment for dyslipidemia among these patients with PCOS.32 The pathogenesis of dyslipidemia in PCOS has been ascribed to various metabolic consequences of the syndrome. However, there is some form of uniformity of its involvement with insulin resistance and that of hyperandrogenism among most researchers.13–16

CONCLUSION

The findings of this study are suggestive of high incidence of dyslipidemia among women with PCOS, especially the young adult women. Therefore, regular assessment for dyslipidemia among patients with PCOS should be mandatory as part of their management modalities to mitigate the long-term consequences of dyslipidemia.

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17. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment

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