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Dyslipidaemias in women using hormonal contraceptives: a cross sectional study in Mulago Hospital Family Planning Clinic, Kampala, Uganda

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ABSTRACT

Objective To determine the prevalence and factors associated with dyslipidaemias in women using hormonal contraceptives.

Design Cross-sectional study

Setting Mulago Hospital, Kampala, Uganda

Participants Three hundred and eighty-four consenting women, aged 18–49 years, who had used hormonal contraceptives for at least 3 months prior to the study.

Study outcome Dyslipidaemias (defined as derangements in lipid profile levels which included total cholesterol ≥200 mg/dL, high-density lipoprotein <40 mg/dL, triglyceride >150 mg/dL or low-density lipoprotein ≥160 mg/dL) for which the prevalence and associated factors were obtained.

Results The prevalence of dyslipidaemias was 63.3% (95% CI: 58.4 to 68.1). Body mass index (BMI) (PR=1.33, 95% CI: 1.15 to 1.54, p<0.001) and use of antiretroviral therapy (ART) (PR=1.21, 95% CI: 1.03 to 1.42, p=0.020) were the factors significantly associated with dyslipidaemias.

Conclusion Dyslipidaemias were present in more than half the participants, and this puts them at risk for cardiovascular diseases. The high-risk groups were women with a BMI greater than 25 Kg/m^2 and those who were on ART. Therefore, lipid profiles should be assessed in women using hormonal contraceptives in order to manage them better.

Strengths and limitations of the study

- This is one of the first studies in Uganda to assess dyslipidaemias in women using hormonal contraceptives, hence providing baseline information.
- Standard approaches were used to carry out the study to ensure repeatability and reproducibility.
- Consecutive non-probability sampling was used so the results may not be generalisable to all hormonal contraceptive users.
- Since this was a cross-sectional study, a causal relationship between hormonal contraceptive use and dyslipidaemias could not be ascertained.
- The results may have been subject to information bias since questionnaires were used to obtain information on some variables based on recall.

INTRODUCTION

Globally, the use of contraception has risen slightly, from 54.7% in 1990 to 64% in 2015.[1] In Uganda particularly, the contraceptive prevalence rate (CPR) is currently 27.2% with hormonal contraceptives (HCs) accounting for 77.9% of the total contraceptive use.[1] Among the HCs used in Uganda, injectables are the most common (72.8%), followed by oral contraceptives (14.3%) and implants (12.9%).[2]

Several researchers have reported the complications and side effects associated with the use of HCs.[3–5] The side effects include nausea and vomiting, headaches, dizziness, breast tenderness and enlargement, irregular bleeding or bleeding between periods, and weight gain. The adverse effects include metabolism impairment, cardiovascular complications, and an increased risk of cancer and liver problems.[3] It has been suggested that some of these complications are a consequence of dyslipidaemias, a potential metabolic impairment effect of long-term use of some HCs.[5] Furthermore, a study by Schueller and colleagues suggested that dyslipidaemias could also arise from the hormones increasing apolipoprotein B-100 synthesis which subsequently increases triglyceride and Low Density Lipoprotein (LDL) levels.[4]

Several factors predispose HC users to dyslipidaemias. The factors include age, race, lifestyle and diseases such as hypertension

and diabetes mellitus. Medications especially ART and steroids also contribute.[5–9] Many of these factors are common in Uganda. For example, 16% of the women in Uganda were found to be obese.[10] Obesity is associated with alterations in lipid profile levels. In the presence of HC use, obesity makes the risk of dyslipidaemias worse.[6 7] In addition, 79% of all women with HIV infection of reproductive age in Uganda are on antiretroviral therapy (ART).[11] Some antiretroviral drugs alter lipid profile levels, hence causing dyslipidaemias.[12 13]

Poorly managed dyslipidaemias can result into cardiovascular diseases such as venous thromboembolism, myocardial infarction and stroke.[14] However, lipid profile levels are not routinely measured in women using HCs in Uganda. Therefore, the objective of this study was to determine the prevalence and factors associated with dyslipidaemias in women using HCs at Mulago Hospital Family Planning Clinic, Kampala in Uganda.

METHODS

Study design, setting and population

This was a cross-sectional study employing both descriptive and analytical techniques carried out from Mulago Hospital Family Planning Clinic in Uganda's Capital City, Kampala from March to April 2017. This clinic receives approximately 320 patients monthly, 215 of whom are on HCs. Using the consecutive sampling procedure, 384 consenting women aged 18–49 years were enrolled into this study. They had to have used HCs for at least 3 months prior to the study. Women who were unable to comprehend either English or *Luganda* (the local language used in Central Uganda) or those physically or mentally unable to adhere to study procedures such as giving of consent and the interview process, were excluded from the study.

Sample size calculation

The Leslie Kish formula[15] was used to estimate the sample size for the prevalence objective. We assumed a prevalence of dyslipidaemias of 33.9% among women on oral contraceptives according to a study by Machado *et al* in Brazil[16] and 95% CIs. This gave a sample size of 345. We also accounted for 10% missing data in the calculation of the sample size. Hence, the final sample size was 380.

For the factors associated with dyslipidaemias, the formula for comparing means in two proportions[17] was used. We assumed an error of 0.05, power of 80% and 95% confidence level; and that 33.9% of women using oral contraceptives would develop dyslipidaemias compared with only 16.9% of those using non-oral contraceptives. We also assumed that the oral CPR in Uganda is 14.3%.[2] This gave a sample size of 384.

Data collection

A questionnaire was administered to collect basic information on age, parity, highest level of education, occupation, type of HC used, duration of use of HCs, use of antiretroviral drugs and history of hypertension. Body mass index (BMI) was determined by measuring weight using the Seca weighing scale and height using a Seca stadiometer. BMI was then computed as weight (in kg)/height (in m^2). Blood samples were aseptically collected from participants after a 6-hour fast and placed in a red top vacutainer without an anticoagulant for the determination of lipid profile levels. The samples were allowed to clot for at least 3 min and centrifuged at 2400 revolutions/min for 5 min. The serum obtained was pipetted into Cobas 6000 caps and taken for analysis using the Cobas 6000 chemistry analyser (Roche Diagnostics, USA). Fasting blood sugar levels were determined using a Freestyle glucometer (Abott Laboratories, Canada) for all the participants 6 hours after their last meal. A sterile single use lancet was used to prick the participant's disinfected finger and a small drop of the blood placed onto the glucometer strip already mounted into the glucometer. The blood sugar level was read off and recorded in mg/dL.

Outcome variable

The outcome variable for this study was dyslipidaemias defined as derangements in lipid profile levels which included a total cholesterol of 200 mg/dL or greater, a high-density lipoprotein cholesterol of less than 40 mg/dL, triglyceride of greater than 150 mg/dL or low-density lipoprotein cholesterol of 160 mg/dL or greater according to the Guidelines for the Diagnosis and Management of Dyslipidemias for Adults.[18] A participant was said to have dyslipidaemias if he/she had any of the lipid profile parameters in ranges stated above. The presence of dyslipidaemias was coded as '1' and its absence as '0'.

Statistical analysis

Data were analysed using STATA V.13.0 (StataCorp. 2013. *Stata Statistical Software: Release 13*) in which all continuous variables were summarised as medians and ranges while the categorical variables were summarised as percentages and proportions. The prevalence of dyslipidaemias was calculated as the percentage of women with dyslipidaemias over the total number of women in the study. The modified Poisson regression model was used to analyse the factors associated with dyslipidaemias in women using HCs. In the multivariate analysis, variables which were significantly associated with dyslipidaemias ($p<0.05$) were used to form two-way product terms that were used in the assessment of interaction using the chunk test. Where necessary, confounding was assessed for. Confounders were retained only if they changed the estimates by greater than or equal to 10%. CIs were presented at 95% level of significance along with the p values. Statistical significance was considered at a p value of less than or equal to 0.05.

Patient and public involvement

Due to patients' experiences and concerns raised about excessive weight gain while on HCs, we felt the need to

determine whether long-term use of HCs (more than 3 months) has an effect on lipid profile levels. Hence, patient experiences informed our research questions and study outcomes.

Patients were involved in the design of the study through their contribution to the refining of the data-collection tool. This was mainly during pretesting or piloting of the questionnaires. Results were disseminated to study participants through the use of text messages and fliers. The fliers, printed both in English and *Luganda,* were issued out at the family planning clinic.

RESULTS

Participants' characteristics

The median age of the 384 participants was 28 years (IQR: 18–49). An estimated 59.1% (227/384) of the participants had attained only up to secondary education, 74.2% (285/384) had at least two or more children and 39.6% (152/384) were self-employed. Only 11 (2.9%) had high fasting blood sugar levels (≥120 mg/dL), 14 (3.7%) had a history of hypertension, 140 (36.5%) had a BMI >25 and 78 (20.3%) were on ART. Most of the participants (48.2%) were using progestin-only injectables, and 219 (57%) had used HCs for over a year (table 1).

Prevalence of dyslipidaemias

The prevalence of dyslipidaemias among the 384 participants was 63.3% (95% CI: 58.4 to 68.1). Dyslipidaemias were higher in women aged above 28 years (68.0%) compared with those who were younger. The prevalence of dyslipidaemias was also higher in participants who had attained up to tertiary education (75%) than those who had acquired lower education. Furthermore, participants who had high fasting blood sugar levels (≥120 mg/dL) had more dyslipidaemias (81.8%) than those who had normal blood sugar levels (table 2).

Factors associated with dyslipidaemias

Variables significantly associated with dyslipidaemias included BMI greater than 25 kg/m^2 (PR=1.33, 95% CI: 1.15 to 1.54, p<0.001) and ART use (PR=1.21, 95% CI: 1.03 to 1.42, p=0.020). These variables were further assessed for interaction between each other and for confounding with other independent variables. However, there was no interaction and the association between dyslipidaemias and these variables was not confounded by any other independent variables. Therefore, BMI and ART use were the only independent factors associated with dyslipidaemias (table 3).

Table 1 Social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March–April 2017

Variable	Number (n=384)	Percentage (%)
Age (categorised at the median)		
18–28	215	56
29–49	169	44
Median (IQR): 28 (18–49)		
Education		
No formal education	14	3.6
Primary	107	27.9
Secondary	227	59.1
Tertiary	36	9.4
Parity		
0–1	99	25.8
Two or more	285	74.2
Fasting blood sugar		
Normal (<120 mg/dL)	373	97.1
High (≥120 mg/dL)	11	2.9
History of hypertension		
No	370	96.3
Yes	14	3.7
Body mass index (BMI)		
≤25	244	63.5
>25	140	36.5
Antiretroviral therapy use		
No	306	79.7
Yes	78	20.3
Hormonal contraceptive used		
Progestin-only pill	5	1.3
Combined oral pill	38	9.9
Progestin-only injectable	185	48.2
Combined Injectable Contraceptive (CIC)	8	2.1
Implant (one rod)	124	32.3
Implant (two rods)	24	6.2
Duration of use of hormonal contraceptive		
<6 months	124	32.3
6–11 months	41	10.7
≥12 months	219	57

DISCUSSION

Dyslipidaemias were present in more than half the participants. This high prevalence of dyslipidaemias could be an overestimate in the general population because of the differences in these populations. This study had a higher prevalence of ART users (20.3%) than what is reported in the general population (less than 5%).[11] Since ART use is associated with dyslipidaemias, the high prevalence obtained could have been as a result of the high percentage on ART.

The presence of dyslipidaemias in HC users has been reported by several other studies which found significant changes in the lipid profile levels of HC users.[5 6 14 19] These

Table 2 Prevalence of dyslipidaemias according to social demographic and clinical characteristics of women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March–April 2017

Variable	Dyslipidaemias present, n (%)	No dyslipidaemias, n (%)	Prevalence ratio (95% CI)	P values
Overall prevalence of dyslipidaemias	243 (63.3)	141 (36.7)	58.4 to 68.1	
Age (categorised at the median)				
18–28	128 (59.5)	87 (40.5)	1	
29–49	115 (68.0)	54 (32.0)	1.14 (0.98 to 1.32)	0.083
Median=28 (18–49)				
Education				
No formal education	6 (42.9)	8 (57.1)	0.68 (0.37 to 1.25)	0.21
Primary	66 (61.7)	41 (38.3)	0.97 (0.81 to 1.16)	0.759
Secondary	144 (63.4)	83 (36.6)	1	
Tertiary	27 (75.0)	9 (25.0)	1.18 (0.96 to 1.46)	0.124
Parity				
0–1	59 (59.6)	40 (40.4)	1	
≥2	184 (64.6)	101 (35.4)	1.08 (0.90 to 1.30)	0.394
Fasting blood sugar				
Normal	234 (62.7)	139 (37.3)	1	
High	9 (81.8)	2 (18.2)	1.30 (0.98 to 1.74)	0.072
History of hypertension				
No	235 (63.5)	135 (36.5)	1	
Yes	8 (57.1)	6 (42.9)	0.90 (0.57 to 1.43)	0.653
Body mass index				
≤25	138 (56.6)	106 (43.4)	1	
>25	105 (75.0)	35 (25.0)	1.33 (1.15 to 1.53)	<0.001
Antiretroviral therapy use				
No	186 (60.8)	120 (39.2)	1	
Yes	57 (73.1)	21 (26.9)	1.20 (1.02 to 1.41)	0.026
Hormonal contraceptive used				
Oral contraceptives	22 (51.2)	21 (48.8)	1.77 (0.57 to 1.05)	0.1
Injectables	128 (66.3)	65 (33.7)	1	
Implants	93 (63.8)	55 (35.2)	0.95 (0.81 to 1.11)	0.508
Duration of use of hormonal contraceptive				
77 (62.1)	47 (37.9)	1		
6–11 months	22 (53.7)	19 (45.2)	0.86 (0.63 to 1.19)	0.366
≥12 months	144 (65.8)	75 (33.6)	1.06 (0.90 to 1.25)	0.504

changes in the lipid profile levels can be attributed to the lipogenic effect of oestrogen in which liver lipogenesis is increased and results in elevated levels of triglycerides and LDL levels.[20] Furthermore, the progestin component of HCs increases hepatic lipase enzyme activity which increases the removal of HDL, hence decreasing the serum HDL levels.[21]

The factors significantly associated with dyslipidaemias in women using HCs were BMI and ART use. Participants who had a BMI greater than 25 kg/m^2 were 33% more likely to have dyslipidaemias compared with those who had a BMI of 25 kg/m^2 or less. This is in line with the findings from a systematic review by Halperin and colleagues in 2011. Halperin *et al*'s study reported that differences in average BMI of women in the individual cohorts explained a portion of the heterogeneity found in High Density LipoproteinCholesterol (HDL-C) levels.[7] These changes can be attributed to BMI independently affecting lipid profile levels as reported by studies which observed a significant association between high BMI and the occurrence of dyslipidaemias.[22 23] A study by Shamai and colleagues reported a significant association between

Table 3 Multivariate analysis of the factors associated with dyslipidaemias in women using hormonal contraceptives at Mulago Hospital Family Planning Clinic in Kampala, March–April 2017

Variable	Prevalence ratio	95% CI	P values
Body mass index			
≤25	1		
>25	1.33	1.15 to 1.54	<0.001
Antiretroviral therapy use			
No	1		
Yes	1.21	1.03 to 1.42	0.02

BMI and both triglyceride and HDL levels which was attributed to insulin resistance.[23]

ART use was the other factor associated with dyslipidaemias in women using HCs. Women who were using ART were 21% more likely to have dyslipidaemias than those who were not. This is one of the first studies to report on dyslipidaemias in ART users on HCs; therefore, there are no studies with which to compare our results. These changes in lipid profile levels can be attributed to some ART regimens exerting distinct alterations in lipid metabolism, hence bringing about dyslipidaemias.[13] A study by Bekolo and colleagues in 2014 demonstrated a high prevalence of dyslipidaemias in patients with HIV infection on first-line ART in Cameroon.[12]

Some of the strengths of this study are: this is one of the first studies assessing dyslipidaemias in women using HCs to be carried out in Uganda. This contributes to further understanding and possibly, better management of dyslipidaemias in women using HCs. In addition, standardised approaches were used when carrying out this study, and this permits the study to be replicated in different areas or over time with an assurance that the results produced will have comparable findings.

We acknowledge the following limitations. The findings of this study may not be generalisable to all HC users because the sample is not representative enough. The sampling procedure used was non-probability, and this does not allow equal opportunity to all women to participate. As this was a cross-sectional study, a causal relationship cannot be established between HC use and dyslipidaemias. Since questionnaires were used for data collection, some of the self-reported information may have been inaccurate, hence affecting some of the results. Finally, information on the physical activity and diet of the study participants was not collected. This information is important since these variables play a significant role in changing lipid profile levels.

In conclusion, more than half the women using HCs had dyslipidaemias and are thus at an increased risk of acquiring cardiovascular diseases. HC users who had a BMI greater than 25 kg/m^2 and/or were on ART were more likely to have dyslipidaemias, and this in the long run increases their risk for cardiovascular disease.

We therefore recommend the Uganda Ministry of Health to formulate policy to better manage women using HCs. The policy should include checking lipid profile levels prior to initiation of HC use and also continued assessment at regular intervals while using contraceptives. The policy should in particular target the high-risk group that includes women whose BMI is greater than 25 kg/m^2 and/or are on ART. Further studies are urgently needed to explore whether the relationship between dyslipidaemias and HC use is causal.

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Contributors RB conceptualised the study, designed it, planned the analysis, did the result interpretation and wrote the manuscript. She is the guarantor and responsible investigator of the study. PB-K planned and supervised the study, interpreted results and reviewed the manuscript. JKT planned the study, contributed in acquisition of funds, interpreted results and revised the manuscript. JNK planned and supervised the study and analysis and interpreted results. GN, IN, GSN and FO: planned the study and contributed in analysis. CK conceptualised, planned and supervised the study, interpreted results and reviewed the manuscript. All authors have read the final manuscript.

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Competing interests None declared.

Patient consent Not required.

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