Original Article

Thyroid function patterns in Ghanaian women using depo-medroxyprogesterone acetate

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ABSTRACT

Background: The main hormonal contraceptives of choice for most women in Ghana are progestin-only injectables, norethisterone enanthate and depot-medroxyprogesterone acetate (DMPA). As more women adopt these short-to-medium-action injectable contraceptives, over time, they may develop a disruption in their body's metabolic processes, which may result in dyslipidaemia and glucose intolerance or may impact thyroid hormone function. In Ghana, limited knowledge exists regarding the effects, biosynthesis and activity of thyroid hormones among users of progestin-only injectables.

Aims: The aim is to evaluate thyroid function among women on progestin-only injectable contraceptives and those who are not.

Materials and Methods: Two hundred women of reproductive age (18–45 years) were recruited for this study. Of these, 100 women were on the depot medroxyprogesterone, and 100 women had no history of taking hormonal contraceptives and served as controls. Sociodemographic and clinical information was obtained from recruits using a standard questionnaire. Each participant had venous blood samples taken and analysed for levels of free thyroxine (FT4), free triiodothyronine (FT3) and thyroid-stimulating hormones (TSH).

Results: The DMPA group had significantly higher levels of FT4 ($P = 0.001$) and considerably lower levels of TSH ($P = 0.011$) than the non-DMPA group. Results also showed that fifteen women in the DMPA group had overt hyperthyroidism (low TSH and high FT4), seven had a diagnosis of subclinical hyperthyroidism (normal TSH and high FT4) and four had isolated high FT3 (normal TSH, normal FT4 and high FT3).

Conclusions: The use of DMPA can lead to changes in thyroid hormone levels and hyperthyroidism.

Keywords: Contraception, depot medroxyprogesterone, hyperthyroidism, injectable, thyroid hormone

INTRODUCTION

The thyroid gland plays a crucial role in the production of thyroxine (T4) and triiodothyronine (T3), the primary hormones produced by the thyroid gland. T3 is the most active form of thyroid hormone and is created in the tissues by deiodination of thyroxine. T3 and T4 are largely protein-bound to thyroxine-binding globulin (TBG) and a tiny fraction is biologically active.[1-3] Some external factors, such as drugs, may compete with thyroid hormones for binding sites, thus lowering the TBG concentration.[1,2]

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Hyperthyroidism and hypothyroidism are conditions in which there is a high or reduced synthesis of thyroid hormones, respectively. There is a connection between the thyroid profile and the gonadal hormonal picture of an individual. The roles of exogenous and endogenous oestrogens or progestins in altering thyroid hormones cannot be overstated, as they primarily target the unbound, free fractions that transport thyroid hormones in the bloodstream,[3,4] which may increase or decrease the plasma concentrations of the thyroid hormone-binding proteins.[4]

The effects of reproductive hormones on thyroid function have shown conflicting results. Some studies have revealed that combination therapy (progestins and oestrogen) does not alter serum TBG concentrations. However, this change may be oestrogen induced if it occurs rather than due to the progestin component.[4-7] Increased oestrogen production or administration of synthetic oral contraceptives (OCs) is one of the most common causes of high TBG levels.[4,7] Some studies have also shown the effects of either progesterone-only or estrogen-only on thyroid physiology.[6] A recent study showed that plasma FT4 significantly increased when progestin depot medroxyprogesterone acetate (DMPA) was administered, more than other contraceptives that were used.[7] In addition, increased FT4 and decreased thyroid-stimulating hormone (TSH) levels were observed with the use of micronised progesterone in therapy,[8] suggesting that progestins play a significant role in affecting thyroid function during the administration of OCs.

Recently, there has been a marginal increase in the rate of contraceptive use in Ghana and most parts of Southern Africa.[9,10] Currently, injectables still stand as the most common hormonal contraceptive methods patronised among females.[11] MPA and norethisterone enanthate (NET-TEN) are the main synthetic hydroxyprogesterones used in therapeutics owing to their progestin-like properties as well as glucocorticoid and androgen activity. Administration of this type of injectable contraceptive has been shown to cause dyslipidaemia in Ghanaian women and women in other parts of the world,[12-14] which may result in an increase in weight as well as the development of some heart-related conditions, especially in prolonged usage.[15,16] Contraceptives in general have also been shown to have effects on certain sex hormones in the body, such as prolactin and sex hormone-binding globulin.[17] Studies have also shown that progestin-only contraceptives increase thyroxine levels but reduce TSH by modulating its secretion.[18,19] The use of DMPA significantly increases thyroxine levels compared to the use of other forms of contraceptives.[8] In addition, even in smaller mammals, the administration of anabolic steroids has been shown to increase the metabolism of thyroid hormones and thus has a high proliferative effect on thyroid cells.[20]

Hyperthyroidism induced by contraceptive administration can result in irregular menstrual bleeding, usually anovulatory cycles and acne.[21,22] A recent study identified the effect of progestins on TSH secretion[8] and the subsequent increase in free T4 production. To date, no study has been published on the impact of progestin-only hormonal contraceptives on thyroid function in Ghana. This study sought to establish the effects of progestin-only contraceptives on thyroid function among Ghanaian women.

MATERIALS AND METHODS

Study design and settings

This comparative cross-sectional study was conducted at Ho Teaching Hospital and the Sogakope Planned Parenthood Association of Ghana Clinic in the Volta Region of Ghana.

Participant recruitment and selection

A total of 200 women of reproductive age (18–45 years) were recruited for this study. Of these, 100 women were on the depot medroxyprogesterone, and 100 women with no history of taking hormonal contraceptives served as controls. All of these were obtained using the convenience sampling method. Women outside the age range and those on any other form of hormonal or steroid therapy, thyroid medications or therapy and those with previous thyroid surgery or disorder were excluded from the study.

Data collection and measurement of parameters

A standard questionnaire was used to collect socio-demographic and clinical information of the study participants. The data obtained included ethnicity, occupation, income level, duration of contraceptive use, parity, marital status, educational status and other relevant factors.

An Omron HEM-712 CLC automatic blood pressure monitor (Omron Healthcare, Inc., Vernon Hills, IL, USA) with appropriate cuffs was used to measure diastolic and systolic blood pressure and the mean values were used in the analysis. The weights and heights of participants were measured using a Seca stadiometer (Seca, Germany) and recorded to the nearest 0.1 kg and 1 cm, respectively. Body mass index (BMI) in kg/m^2 was computed by dividing the individual's body weight (in kilograms) by the square of their height (in meters).

The circumferences of the waist and hips were measured using a non-stretch tape measure. All measurements were estimated to the nearest 0.1 cm. Three measurements were performed and the mean was calculated as the actual value. The waist-to-hip ratio (WHR) was computed by dividing the waist circumference by the hip circumference.[23]

Four millilitres (4 mL) of the venous blood sample (fasting independent) were collected from each of the study participants into serum separator gel tubes. Samples were then allowed to stand for 30 min to clot. The clotted samples were spun at 3500 rpm for 15 min to obtain serum. Measurements of free T4, free T3, TSH, total protein, albumin and globulin were carried out on the serum by the use of Vitros® 5600 Integrated System (Ortho Clinical Diagnostics, Mexico), a fully automated chemistry analyser.

Ethical considerations

The study was approved by the Ethical and Protocol Review Committee (EPRC) of the College of Health Sciences, University of Ghana (ID: CHS-Et/M.7–P 5.8/2022-2023) and the Institutional Review Board of the Ho Teaching Hospital. Before initiating the study, the participants were required to sign an informed consent form. This form provided detailed information about the study's aims, duration, potential benefits, materials used for sample collection and any risks associated with the sampling process.

Statistical analysis

Data collection and coding were performed using Microsoft Excel 2016 (Microsoft Corporation, 2016, Redmond, Washington, USA). The analysis was performed using SPSS version 25 (IBM SPSS Statistics Version 25.0, 2017, Armonk, New York, USA). For analysis, the study was divided into four groups based on the duration of injectable use: Group 1 (1–12 months), Group 2 (13–24 months), Group 3 (>25 months) and the control group of non-users. A *t*-test for non-paired data was used to determine any difference between the control group and the study group, and one-way analysis of variance was performed to analyse the differences in means between the case groups and controls. Pearson's Chi-square test was used for categorical data. For all analyses, $P < 0.05$ was considered statistically significant.

RESULTS

Socio-demographic and clinical characteristics

In this comparative cross-sectional study, 200 women voluntarily participated in the survey; 50% ($n = 100$) were women using progestin-only contraceptives, and 50% ($n = 100$) were women not using any form of contraception (control group). The mean age of the study participants was 29.42 ± 6.7 years in the DMPA group and 28.2 ± 6.9 years in the control group. The majority of study participants were from the Ewe tribe. In addition, the majority (40.0%) of patients in the DMPA group were married, whereas 22.0% of patients in the control group were married. It was found that 87 (87.0%) of the controls and 94 (94.0%) of the DMPA group were Christians. The majority were employed and earning a decent income, with 86 (86.0%) in the DMPA group and 83 (83.0%) in the control group. However, the majority of the control group (37.0%) and the DMPA group (61.0%) earned an income of less than GHC 599. The dominant occupation among both groups was trading/hawking ($n = 45$, 45.0% of controls vs. $n = 66$, 66.0% of cases).

It was also found that at least 61% of the DMPA users had basic education (Junior High School) and that only 4% had no formal education and were illiterate. The details are illustrated in Table 1.

Anthropometric characteristics of the study participants

The weight, height and BMI of the DMPA group did not differ significantly from those of the control group.

Analysis of systolic and diastolic blood pressure showed a significant difference between these women on contraceptives and those who were not. Further information is presented in Table 2.

Parity and menstrual cycle history of study participants

The study found a significant difference ($P < 0.001$) in the number of children a mother had and their use of DMPA. A total of 85 (85.0%) of the DMPA group had at least one child, while 65 (65.0%) of the control group had given birth previously. The highest age of menarche observed in the DMPA and control groups was 15 years or older (40.0%) and 14 years (27.0%), respectively. In their response to whether they had regular menstrual cycles, 78 (78.0%) of the control group reported having regular menstrual cycles and could monitor their flow very well (77%). In contrast, only 33 (33.0%) patients in the DMPA group experienced regular menses. They also could not indicate the time of their next menses, thus having an abysmal track record of their menses (59%). Additional information regarding the parity and menstrual cycle of the study participants is shown in Table 3.

Contraceptive history of depot-medroxyprogesterone acetate users

Among the participants using contraception, 51 (51.0%) had previously used other hormonal contraceptives before switching to DMPA for one reason or another, and most were on implants (36.0%). None of the participants reported the use of vaginal rings or skin patches. The duration of DMPA use indicated that 58 (58.0%) out of the 100 DMPA subjects had been on the therapy for 1–12 months, followed by those who had been on the treatment for 13–24 months (25%). The study participants who had been on therapy for the longest duration (≥25 months) recorded the lowest number (17%). Moreover, 95 (95.0%) of the DMPA users had discovered a change in their menstrual cycle and flow from the time they

Table 1: Socio-demographic characteristics of the study participants

Features	Control group (n=100), n (%)	DMPA group (n=100), n (%)	χ^2	P
Age (years), mean±SD	28.2±6.9	29.4±6.7		0.185
Age distribution (years)				
18–24	34 (34.0)	26 (26.0)	5.011	0.286
25–34	47 (47.0)	53 (53.0)		
35–45	19 (19.0)	21 (21.0)		
Tribe				
Akan	29	7	38.115	<0.001*
Ga	17	4		
Ewe	46	78		
Northern	6	8		
Non-Ghanaians	2	3		
Facility				
HTH	94 (94.0)	21 (21.0)	0.814	0.367
PPAG Sogakope	6 (6.0)	79 (79.0)		
Marital status				
Single	46 (46.0)	36 (36.0)	142.668	<0.001*
Married	22 (22.0)	40 (40.0)		
Separated/divorced	4 (4.0)	2 (2.0)		
Cohabiting	28 (28.0)	22 (22.0)		
Religion				
Christianity	87 (87.0)	94 (94.0)	35.223	<0.001*
Islam	13 (13.0)	6 (6.0)		
Employment status				
Employed	83 (83.0)	86 (86.0)	43.738	<0.001*
Unemployed	17 (17.0)	14 (14.0)		
Occupation type				
Education/teaching	10 (10.0)	6 (6.0)	222.310	<0.001*
Healthcare	26 (26.0)	10 (10.0)		
Trading/hawking	45 (45.0)	66 (66.0)		
Civil service	2 (2.0)	4 (4.0)		
Unemployed	17 (17.0)	14 (14.0)		
Monthly income				
Less than GHC 599	37 (37.0)	61 (61.0)	163.524	<0.001*
GHC 600–GHC 999	28 (28.0)	16 (16.0)		
GHC 1000–GHC 1599	5 (5.0)	3 (3.0)		
GHC 1600–GHC 1999	7 (7.0)	4 (4.0)		
GHC 2000 and above	6 (6.0)	2 (2.0)		
No fixed income/unemployed	17 (17.0)	14 (14.0)		
Formal education/literacy				
Yes	93 (93.0)	96 (96.0)	54.804	<0.001*
No	7 (7.0)	4 (4.0)		
The highest form of formal education				
Junior high	45 (45.0)	61 (61.0)	183.476	<0.001*
Senior high	27 (27.0)	21 (21.0)		
Tertiary	21 (21.0)	14 (14.0)		
No formal education	7 (7.0)	4 (4.0)		

*The significance threshold was set at P<0.05. PPAG: Planned Parenthood Association of Ghana, HTH: Ho teaching hospital, SD: Standard deviation, DMPA: Depot medroxyprogesterone acetate, GHC: Ghana cedis

started the use of this form of progestin-only contraceptive, and this was seen in about 59.0%, indicating that they had irregular bleeding episodes as a side effect of DMPA.

When asked about any non-hormonal contraceptives they preferred as an adjunct to DMPA, 45 (45.0%) of this category indicated that they preferred condoms to the other methods/agents. 29 (29.0%) responded that they would stick only to DMPA and not use any other methods. The satisfaction rate in the DMPA was 52.0% for those who were extremely satisfied and 44.0% for those who were satisfied but had some reservations. Table 4 illustrates

the details of the contraceptive history of the DMPA study group.

Levels of thyroid hormones among various groups of depot-medroxyprogesterone acetate users and non-depot-medroxyprogesterone acetate users (controls)

Among participants who had been on DMPA for up to 12 months, 13–24 months and more than 25 months, no significant difference existed in their mean FT3 levels ($P = 0.603$), FT4 levels ($P = 0.694$) and TSH levels ($P = 0.121$), respectively. However, the FT4 and TSH levels of the cases were significantly different ($P = 0.001$ and $P = 0.011$, respectively) from the mean values of the controls [Table 5]. Regarding protein parameters, the total protein and globulins showed significant differences among the various DMPA administration groups ($P = 0.012$ and $P = 0.005$, respectively).

Table 2: Clinical characteristics of the study participants (mean±standard deviation)

Features	Control group ($n=100$)	DMPA groups ($n=100$)	*P*
Weight (kg)	66.0±11.4	67.3±15.0	0.473
Height (m)	1.6±0.1	1.7±0.3	0.111
BMI (kg/m^2)	24.5±3.7	24.5±6.6	0.974
Waist–hip ratio	0.80±0.1	0.84±0.18	0.004*
Systolic BP (mmHg)	108.9±8.7	115.3±9.8	<0.001*
Diastolic BP (mmHg)	74.9±4.8	79.3±10.0	<0.001*

*The significance threshold was set at $P<0.05$. BP: Blood pressure, DMPA: Depo-medroxyprogesterone acetate, BMI: Body mass index

Thyroid dysfunction patterns between depot-medroxyprogesterone acetate users and non-depot-medroxyprogesterone acetate users (controls)

Out of the hundred women on DMPA therapy, fifteen had overt hyperthyroidism (low TSH and high FT4), seven women had subclinical hyperthyroidism (normal TSH and high FT4) and four had isolated high FT3 (normal TSH, normal FT4 and high FT3). None of the DMPA participants were diagnosed with overt or subclinical hypothyroidism [Figure 1]. Comparatively, among non-DMPA users, four had isolated high FT3, one had overt hypothyroidism (high TSH, low FT4) and six had

Table 3: Parity and menstrual cycle history of participants

Features	Control group ($n=100$), *n* (%)	DMPA group ($n=100$), *n* (%)	χ^2	*P*
Parity				
1 Child	23 (23.0)	37 (37.0)	346.520	<0.001*
2 Children	16 (16.0)	20 (20.0)		
3 Children	13 (13.0)	15 (15.0)		
4 Children	10 (10.0)	11 (11.0)		
5 or more children	3 (3.0)	2 (2.0)		
Nulliparous	35 (35.0)	15 (15.0)		
Years of menarche				
11 years	13 (13.0)	2 (2.0)	145.355	<0.001*
12 years	9 (9.0)	8 (8.0)		
13 years	24 (24.0)	15 (15.0)		
14 years	27 (27.0)	26 (26.0)		
15 years and above	23 (23.0)	40 (40.0)		
Cannot remember	4 (4.0)	9 (9.0)		
Regular menses				
Yes	78 (78.0)	33 (33.0)	15.865	<0.001*
No	22 (22.0)	67 (67.0)		
Track of menses				
Very well	77 (77.0)	20 (20.0)	45.898	<0.001*
Satisfactory	16 (16.0)	21 (21.0)		
Very bad	7 (7.0)	59 (59.0)		
Duration of engaging in physical activity (h/day)				
1–2	3 (3.0)	14 (14.0)	50.224	<0.001*
3–5	28 (28.0)	32 (32.0)		
>5	69 (69.0)	54 (54.0)		
Tobacco consumption				
Yes	0	0	-	-
No	100 (0.0)	100 (0.0)		
Alcohol consumption				
Yes	12 (12.0)	17 (17.0)		
No	88 (88.0)	83 (83.0)	66.576	<0.001*

*The significance threshold was set at $P<0.05$. DMPA: Depo-medroxyprogesterone acetate

Table 4: Contraceptive history of depo-medroxyprogesterone acetate users

Features	DMPA group (n=100), n (%)
Previously using hormonal contraceptives	
Yes	51 (51.0)
No	49 (49.0)
Type of hormonal contraceptives previously used	
Oral contraceptives	9 (9.0)
Implants	36 (36.0)
IUD	6 (6.0)
Vaginal rings	0
Skin patches	0
Was not using any	49 (49.0)
Duration of DMPA usage (months)	
1–12	58 (58.0)
13–24	25 (25.0)
≥25	17 (17.0)
Changes in the menstrual cycle since the start of DMPA	
Yes	95 (95.0)
No	5 (5.0)
Side effects of using DMPA	
Weight loss	9 (9.0)
Weight gain	19 (19.0)
Irregular bleeding	59 (59.0)
No observed weight loss/gain	9 (9.0)
Others (headache, acne, reduced libido)	4 (4.0)
Reasons for the choice of DMPA	
Prefer injections	39 (39.0)
Cannot remember	24 (24.0)
Does not want a partner to know	7 (7.0)
Other methods not working properly	25 (25.0)
Injectables have minimal side effects	4 (4.0)
To treat dysmenorrhea	1 (1.0)
Non-hormonal contraceptives preferred aside from DMPA	
Condom	45 (45.0)
Spermicide	1 (1.0)
Tubal ligation	2 (2.0)
Rhythm method	2 (2.0)
Copper IUD	13 (13.0)
LAM	6 (6.0)
Coitus interruptus	2 (2.0)
None	29 (29.0)
Source of contraceptive information	
Family planning unit of the facility	60 (60.0)
Media (print and electronic)	8 (8.0)
Relatives and friends	26 (26.0)
Medical professionals	6 (6.0)
Level of satisfaction	
Very satisfied	52 (52.0)
Satisfied	44 (44.0)
Not satisfied	4 (4.0)
Do you recommend DMPA	
Yes	86 (86.0)
No	14 (14.0)
Consent from spouse	
Yes	62 (62.0)
No	38 (38.0)

DMPA: Depot medroxyprogesterone acetate, IUD: Intra-uterine device, LAM: Lactational amenorrhoea method

subclinical hyperthyroidism. Eighty-five were biochemically euthyroid, and none had either subclinical hypothyroidism or overt hyperthyroidism.

DISCUSSION

This study aimed to evaluate the levels and patterns of thyroid hormones in women on progestin-only injectable contraception. The study found significantly higher mean serum concentrations of free thyroxine (FT4) and lower TSH levels among women using DMPA compared to those who did not use it. These findings align with those of a similar study conducted in Brazil that assessed the effects of progestins on thyroid function. Although their study was longitudinal, thyroid hormone levels were measured after 1 year.[24] The study is also consistent with a placebo-controlled trial, which found that both FT4 and TSH values are significantly affected when progesterone-only contraceptives are administered over time.[8] This could be explained by the fact that progestins increase the gene expression of thyroid cells and may be mediated through their nuclear receptors.[21] In addition, there is a possibility that progestins may stimulate the release of TSH by the pituitary.[21,25] However, it is believed that complex mechanisms around these processes exist and could be investigated further. However, the work done by Kivelä *et al.*[6] did not prove consistent with the findings of this study. They found no significant difference in thyroid hormone levels when progestin-only contraceptives were administered to female subjects. This was because, although progestins were assessed in their study, DMPA was not administered, but rather levonorgestrel and desogestrel, which may have unique metabolic pathways.

Concerning the effect of the duration of the administration of progestin-only contraceptives, it was generally observed that key changes occurred in the group who had been on the DMPA for close to 2 years. The thyroid dysfunction patterns of women who were on DMPA showed that although the majority of them had been euthyroid, 15% were diagnosed with hyperthyroidism and 6% had subclinical hyperthyroidism based on their serum TSH and FT4 levels. None of the patients was reported to have overt or subclinical hypothyroidism based on the criteria used. This outcome is also consistent with

Table 5: Comparison of levels of thyroid hormones, albumin, total protein and globulin levels among users of depot medroxyprogesterone acetate and controls (mean±standard deviation)

Duration of DMPA use	1–12 months (*n*=58)	13–24 months (*n*=25)	>25 months (*n*=17)	*F*	*P*	Mean levels	Control group (*n*=100)	*P*
FT3 (pmol/L)	6.14±1.22	6.38±1.14	6.14±1.33	0.509	0.603	6.21±1.21	6.24±1.48	0.831
FT4 (pmol/L)	16.8±2.25	17.2±2.39	16.6±2.56	0.366	0.694	16.82±2.32	14.02±3.05	0.001*
TSH (mIU/L)	1.23±1.00	0.86±0.83	1.18±0.69	2.158	0.121	1.13±0.94	1.42±0.79	0.011*
Total protein (g/l)	70.28±7.53	75.08±12.17*	66.81±7.84	4.626	0.012*	70.90±9.27	70.81±5.55	0.942
Albumin (g/l)	41.87±87	42.13±7.67	39.86±5.56	0.660	0.519	41.59±6.86	41.24±3.7	0.661
Globulin (g/l)	28.41±6.94	32.95±6.41*	26.95±5.02	5.536	0.005*	29.22±6.82	29.57±6.62	0.774

*The significance threshold was set at $P<0.05$. DMPA: Depo medroxyprogesterone acetate, FT3: Free triiodothyronine, FT4: Free thyroxine, TSH: Thyroid-stimulating hormone

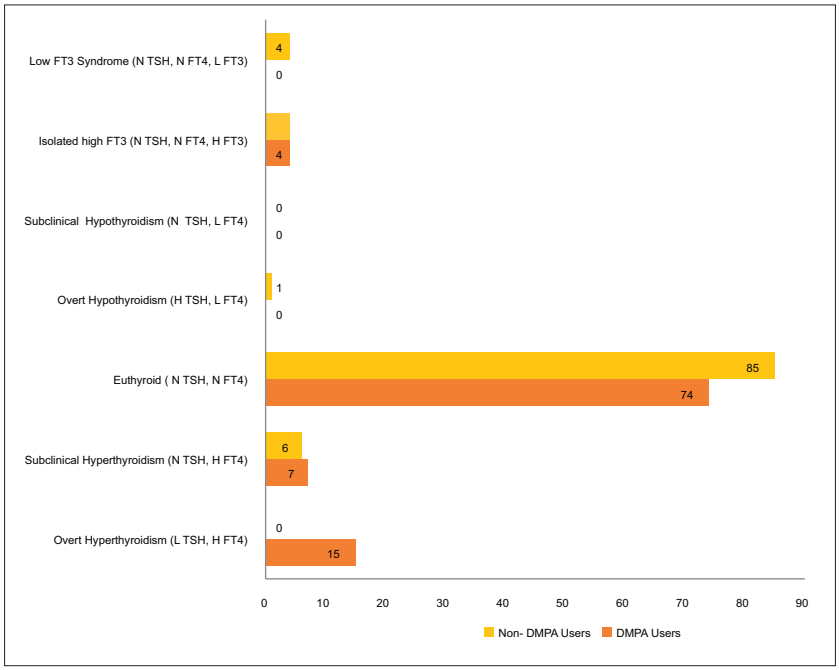

Figure 1: Thyroid dysfunction patterns among Depot medroxyprogesterone acetate (DMPA) and non-DMPA users. N: Normal, L: Low, H: High, FT4: Free thyroxine, FT3: Free triiodothyronine, TSH: Thyroid stimulating hormone

that of a placebo-controlled trial that found that progestins resulted in increased levels of FT4.[8] It also agrees with the comparative study, which found that DMPA therapy increased the FT4 levels of participants after a year of administration.[24]

The increased transcription of genes responsible for thyroid cell production upon progestin administration may also have led to increased levels of FT4 in these women.[21] The opposing effects of progesterone on oestrogens may have also contributed to the reduced levels of TBG, thereby increasing free thyroxine levels. Oestrogens cause hypothyroidism by increasing plasma TBG through increased sialylation of TBG. This complex reduces TBG clearance in the liver.[4] In addition, the isolated high FT3 levels observed in a few women in the DMPA group confirmed the minimal activity of deiodinases in converting FT4 into FT3 in women undergoing prolonged progestin therapy. This outcome aligns with the findings of a prospective study conducted in Brazil.[24]

The study also found no significant difference in the mean BMI between women using progestin-only injectables and non-DMPA users. The non-significance of BMI in the DMPA group compared with that in the non-DMPA group, as found in this study, is inconsistent with a similar study conducted in Ethiopia.[12] However, a significant change in BMI was observed in another group of study participants in Brazil who had been on DMPA for 1 year as compared to those who had not.[24] The waist–hip ratio of the DMPA group was higher than that of the control group, indicating a statistically significant difference, as reported in this study. In both cases, the increase in visceral fat could not be attributed to increased thyroid metabolism. The DMPA-associated increase in visceral fat may be attributed to its glucocorticoid-like activity, which leads to the upregulation of appetite and energy expenditure. Another study also discovered that, generally, there are increasing weight changes among DMPA users and those using other

hormonal contraceptives.[26] This finding was inconsistent with the results of this study.

However, the blood pressures (systolic and diastolic) in the DMPA group were significantly higher than those in the control group. The significantly high difference observed in this study is consistent with a study conducted in another Ghanaian community that assessed the effect of various hormonal contraceptives on blood pressure.[13] The findings in this study are also similar to those in Ethiopia, where blood pressure values (systolic and diastolic) were significantly higher among users than among non-users.[12] Nonetheless, several studies have established progestins to be a safer alternative to oestrogen, which induces high cardiovascular disease risks.[13,17,27] Oestrogens are relatively potent activators of the renin–angiotensin–aldosterone system (RAAS) compared to progestins. Thus, eliciting this pathway leads to vasoconstriction and subsequent volume retention, thereby increasing the blood pressure.

The study participants on DMPA complained of irregular and reduced menstrual flow as the main side effect of the use of DMPA, which is a common finding in most contraceptive studies and has been expanded upon in a review done by Schindler *et al.*[28] It may be due to increased levels of progesterone which suppresses the hypothalamic-pituitary-gonadal axis by inhibiting the activity of gonadotropin-releasing hormone.[29] This results in thinning of the endometrium and induction of hypothalamic amenorrhoea;[30] however, regular menstrual cycles return after discontinuation of DMPA use. This outcome is consistent with other studies by Chane *et al.*[31] and Bertoni *et al.*,[21] which also reported menstrual abnormalities among their study participants.

Limitations

As a cross-sectional study, we could only establish associations, but not causal relationships, between DMPA use and thyroid hormone dysfunction. This study is a 2-site localised study, and the generalisability of the findings must be done with caution. Nonetheless, this study provides valuable insights into the current understanding of thyroid hormone dysfunction and DMPA use. In addition, it allows for larger studies and the management of women on hormonal contraceptive therapy.

CONCLUSION

The DMPA group was found to have reduced TSH and increased FT4 levels compared to the non-DMPA group. The study also revealed that thyroid hormone levels increased approximately 1 year after DMPA administration. Prolonged use of DMPA therapy appears to be associated with a shift towards hyperthyroid states in a subset of women, warranting further longitudinal investigations.

This study has also shown that the WHR and systolic and diastolic blood pressures of women on DMPA are relatively higher than those of women who are not on DMPA.

A larger, multi-site prospective study will be conducted to build on existing knowledge and gain a better understanding of DMPA's effects on thyroid hormones in a broader group of Ghanaians.

Availability of data and materials

All data generated or analysed during this study are included in this published article

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We believe that the requirements for authorship have been met and that each author believes that the manuscript represents honest work.

Authors contributions

JCO and EY, HA-N, EKO, ENYN, CGD, GOM and NEA conceived the study, participated in its design, data collection, data analysis and drafted the manuscript. EY and JCO collated all drafts. All authors read and approved the final version of the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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