The Journal of Obstetrics and Gynaecology

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Journal of Obstetrics and Gynaecology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ijog20

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To cite this article: Essam El Mahdi, Nabil Fekry, Mohamed Ahmed & Kebreab Ghebremeskel (2023) Testosterone, sex hormone-binding globulin and dehydroepiandrosterone levels and cervical length of Egyptian women with a history of recurrent miscarriages, polycystic ovary syndrome and without the conditions at three stages of pregnancy, Journal of Obstetrics and Gynaecology, 43:1, 2163625, DOI: 10.1080/01443615.2022.2163625

To link to this article: https://doi.org/10.1080/01443615.2022.2163625

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JOURNAL OF OBSTETRICS AND GYNAECOLOGY
2023, VOL. 43, NO. 1, 2163625
https://doi.org/10.1080/01443615.2022.2163625

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ORIGINAL ARTICLE

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Testosterone, sex hormone-binding globulin and dehydroepiandrosterone levels and cervical length of Egyptian women with a history of recurrent miscarriages, polycystic ovary syndrome and without the conditions at three stages of pregnancy

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ABSTRACT

Total testosterone (TT), sex hormone-binding globulin (SHBG), dehydroepiandrosterone (DHEA) levels, and cervical length (CL) were investigated in pregnant Egyptian women with polycystic ovary syndrome (PCOS, $n = 38$), history of miscarriages (RM, $n = 40$) and without the conditions (HC, $n = 40$). At week 8, the RM had lower levels of TT ($p = 0.000$) and free androgen index (FAI) ($p = 0.000$) and higher SHBG ($p = 0.000$) and DHEA ($p < 0.05$) than the PCOS. Compared with the HC, they had elevated SHBG ($p < 0.05$) and DHEA ($p = 0.001$) and reduced CL ($p = 0.000$). TT ($p = 0.001$) and FAI ($p = 0.000$) were higher and SHBG ($p = 0.000$) and CL ($p = 0.001$) lower in the PCOS than in the HC group. At week 16, TT ($p = 0.000$) and FAI ($p = 0.000$) were higher, and SHBG ($p = 0.000$) and CL ($p < 0.05$) lower in PCOS than in RM and HC. The PCOS had elevated FAI than the RM ($p = 0.000$) and HC ($p = 0.001$) at week 20. The DHEA, SHBG and CL abnormalities in PCOS and RM may compromise pregnancy outcomes.

IMPACT STATEMENT

- **What is already known on this subject?** Hyperandrogenaemia, low sex hormone-binding globulin (SHBG), shortened cervical length (CL) and polycystic ovary syndrome (PCOS) are the most cited risk factors for recurrent miscarriages (RM). However, the published data are inconsistent, perhaps because of the confounding effects of ethnicity and nutritional milieu.
- **What do the results of this study add?** The study's findings comprising ethnically and socially homogenous women demonstrate that PCOS and RM are characterised by elevated dehydroepiandrosterone (DHEA) and shortened CL, and PCOS by reduced SHBG. These abnormalities would be expected to have an adverse impact on pregnancy outcomes.
- **What are the implications of these findings for clinical practice and/or further research?** Twenty-weeks DHEA and CL values have the potential to predict outcome risk in women with a history of RM and PCOS. Further research on other population groups is required to validate the current study's findings.

ARTICLE HISTORY
Received 30 April 2022
Accepted 17 December 2022

KEYWORDS
Polycystic ovary syndrome; recurrent miscarriage; total testosterone; sex hormone binding globulin; dehydroepiandrosterone; cervical length

Introduction

Recurrent miscarriage (RM), also known as recurrent pregnancy loss, is commonly defined as the loss of ≥2 (ESHRE – The European Society of Human Reproduction and Embryology 2017, Van Dijk *et al*. 2020, ASRM – The American Society for Reproductive Medicine 2020) or ≥ 3 (RCOG – The Royal College of Obstetricians and Gynaecologists 2011, HSE – Health Service Executive, Ireland 2016, Huchon *et al*. 2016) consecutive pregnancies before 20 weeks of gestation. RM affects 1–2% (Hennessy *et al*. 2021), 2–4% (Stephenson and Kutteh 2007) and 7.46% (Patki and Chauhan 2016) of reproductive-age women. These prevalence variations could reflect the RM definition used, the ethnicity of the populations investigated (Patki and Chauhan 2016) and lifestyle factors (Ng *et al*. 2021). Besides, there is some evidence that the incidence of RM has increased over the last decades (Rossen *et al*. 2018). This increase may be due to the obesity epidemic since there is an association between body mass index and RM (Eapen *et al*. 2021, Ng *et al*. 2021)

The established risk factors of RM include chromosomal and genetic (Turki *et al*. 2016), uterine anatomical (Venetis *et al*. 2014, Gabbai *et al*. 2018), endocrine (Kaur and Gupta 2016, El Hachem *et al*. 2017) and immune system (Li *et al*.

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/01443615.2022.2163625.

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2021, Vomstein *et al*. 2021) abnormalities, blood clotting disorders (Di Prima *et al*. 2011, Nassour-Mokhtari *et al*. 2020), infection (Nigro *et al*. 2011), obesity (Eapen *et al*. 2021, Ng *et al*. 2021), maternal age (Magnus *et al*. 2019) and lifestyle factors – smoking and alcohol consumption (Sharma *et al*. 2013, Ng *et al*. 2021). However, the cause of about 50% of RM (Diejomaoh 2015, Vomstein *et al*. 2021) remains unknown.

Although the reported incidence rates are variable (Cocksedge *et al*. 2009, Ashaq *et al*. 2017), polycystic ovary syndrome (PCOS) is thought to be associated with RM (Cocksedge *et al*. 2008, Mayrhofer *et al*. 2020). Hyperandrogenism and hyperinsulinemia (Tian *et al*. 2007, Maryam *et al*. 2012) and hyperhomocysteinemia (Chakraborty *et al*. 2013) have been implicated in PCOS-related pregnancy loss.

The pathological mechanism of the established risk factors of RM in women with and without PCOS is yet to be fully elucidated. However, there is evidence that a reduction of sex-hormone-binding globulin (SHBG) level and a concomitant hyperandrogenaemia (elevation of testosterone) (Dendana *et al*. 2018) shortens the endocervix (Papastefanou *et al*. 2016) and subsequently causes miscarriage. Perhaps paradoxically, dehydroepiandrosterone (DHEA), a precursor of steroid hormones including testosterone, supplementation has been shown to reduce miscarriage rates in women with diminished ovarian reserves (Gleicher and Barad 2011).

There is a scarcity of rigorous investigations that compared androgens and endocervix length in women with RM and PCOS.

Aim

This study investigated the changing pattern of testosterone, sex hormone-binding globulin, dehydroepiandrosterone levels, and cervical length during pregnancy in women with polycystic ovary syndrome, a history of RM, and women without the conditions.

Subjects, diagnosis and methods

Subject and diagnosis

Women aged 23 to 40 years, with PCOS ($n = 38$), history of RM ($n = 40$) and healthy control group ($n = 40$) were recruited during their first antenatal visit to Al-Agoza Hospital, Cairo, Egypt. The exclusion criteria were – age above 40, genetic (Sickle cell disease (SCD) and thalassaemia, etc.) or non-genetic chronic (diabetes, high blood pressure) diseases, thyroid issues, physical disability restricting access to food or eating, malnutrition and inability to provide informed consent for participation in the study. Detailed demographic, obstetric and medical history data were meticulously documented. Five ml of blood samples were collected at weeks 8, 16, and 20 of pregnancy. The study was approved by the Ethics Committee of Al-Agoza Hospital, Cairo, Egypt, and informed and signed consent was obtained from all participants. This study was conducted in line with the human experimentation guidelines of the Helsinki declaration (second revision, 1983).

Diagnosis and measurement

Pregnancy was diagnosed based on an immunometric analysis of serum beta-human chorionic gonadotropin and an ultrasound dating scan.

Hormonal evaluation (follicle-stimulating hormone, luteinising hormone, oestradiol, etc.), ultrasonography (enlarged ovaries with thickened sclerotic capsules and an abnormal number of follicles) and clinical presentation (menstrual dysfunction, anovulation, hirsutism, acne, androgenic alopecia, etc.) were used to diagnose polycystic ovary syndrome (Rotterdam Criteria – The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group) 2004).

Based on the Royal College of Obstetricians and Gynaecologists guidelines (RCOG 2011), women with a history of loss of three or more consecutive pregnancies before 24 weeks from the last menstrual period were diagnosed with RM.

Cervical length, the distance between the external and internal os along the endocervical canal (Berghella *et al*. 1997), was measured at eight, sixteen and twenty gestation weeks using a transvaginal ultrasound (Voluson™ E8 ultrasound system, USA).

Methods

Weight was measured with a Seca Electronic Scale 890 (UNISCALE, Seca, Birmingham, UK), and height was assessed using a height–length measuring board (Schorr, Weight and Measure, LLC, Olney, Maryland, USA).

Serum testosterone, dehydroepiandrosterone and sex hormone and binding globulin, and urine beta-human chorionic gonadotropin were measured by immunometric methods using an advanced automated immunoassay analyser (ADVIA Centaur® XPT Immunoassay System, Siemens Healthineers, Healthcare GmbH, Germany).

Data analyses

The data are expressed as mean ± standard deviation (±sd), and the level of statistical significance is set at $p < 0.05$. The demographic and obstetrics data were tested for normality and homogeneity of variance and analysed with a one-way analysis of variance (ANOVA). The post hoc test Fisher's Least Significant Difference (LSD) was conducted when ANOVA indicates significance. Statistical analyses were performed using IBM SPSS, version 25 (International Business Machines Corporation, New York, USA).

Results

Demographic data of the women with a history of RM, PCOS and healthy control group (HC) are presented in Table 1. There was no difference in ages or body mass index between the three groups ($p > 0.05$). The PCOS women were lighter and shorter than the RM ($p < 0.05$). Similarly, the women with RM were shorter than their healthy counterparts ($p < 0.001$).

Table 1. Anthropometric data (mean ± sd) of women with a history of recurrent miscarriages (RM, $n = 40$), polycystic ovary syndrome (PCOS, $n = 38$) and healthy control group (HC, $n = 40$) at week eight of pregnancy.

	PCOS	RM	HC
Age (year)	30.5 ± 3.8	30.9 ± 3.8	29.5 ± 3.7
Height (cm)	1.44 ± 0.09[a]	1.50 ± 0.09[e]	1.57 ± 0.06[c]
Weight (kg)	57.0 ± 9.4[a]	64.0 ± 11.4[d]	65.6 ± 8.3[b]
Body Mass Index	27.4 ± 3.0	28.1 ± 3.2	26.6 ± 2.5

[a] $p < 0.05$ (PCOS vs. RM).
[b] $p = 0.001$, [c] $p = 0.000$ (PCOS vs. HC).
[d] $p < 0.05$, [e] $p = 0.001$ (RM vs. HC).

Levels of total testosterone (TT), sex hormone-binding globulin (SHBG), dehydroepiandrosterone (DHEA), free androgen index (FAI) and cervical length (CL) of the HC women and women with RM and PCOS at week eight, sixteen and twenty are shown in Table 2.

At week eight of pregnancy, the women with RM had lower levels of TT ($p = 0.000$) and FAI ($p = 0.000$) and higher SHBG ($p = 0.000$) and DHEA ($p < 0.05$) than those with PCOS. Besides, compared with their HC counterparts, they had elevated concentrations of SHBG ($p < 0.05$) and DHEA ($p = 0.001$) and reduced CL ($p = 0.000$). The values of TT ($p = 0.001$) and FAI ($p = 0.000$) were higher and SHBG ($p = 0.000$) and CL ($p = 0.001$) lower in the PCOS than in the HC group.

At week sixteen of pregnancy, the concentrations of TT ($p = 0.000$) and FAI ($p = 0.000$) were higher, and SHBG level ($p = 0.000$) and CL length ($p < 0.05$) lower in the PCOS than in the RM and HC women. DHEA ($p = 0.000$) and SHBG ($p = 0.001$) concentrations were elevated CL length ($p = 0.000$) reduced in the women with RM compared with the HC.

At week twenty of pregnancy, the HC women had higher TT ($p = 0.000$) and CL ($p = 0.000$) and lowered DHEA ($p = 0.000$) than the other two groups. The PCOS group had an elevated level of FAI compared with those of the RM ($p = 0.000$) and HC ($p = 0.001$) women.

Table 3 depicts changes in levels of testosterone (TT), sex hormone-binding globulin (SHBG), dehydroepiandrosterone (DHEA), free androgen index (FAI) and cervical length (CL) of the three groups of women between pregnancy week eight and twenty.

Table 2. Mean (±sd) cervical length (CL, mm) and total testosterone (TT, mmol/L), sex hormone-binding globulin (SHBG, mmol/L) dehydroepiandrosterone (DHEA, mmol/L), free androgen index (FAI) levels of women with a history of recurrent miscarriages (RM, $n = 40$), polycystic ovary syndrome (PCOS, $n = 38$) and healthy controls (HC, $n = 40$) at three stages of pregnancy.

Gestation weeks		PCOS	RM	HC
Eight	TT	1.96 ± 0.53[c]	1.37 ± 0.30	1.48 ± 0.28[d]
	SHBG	44.0 ± 11.6[c]	99.8 ± 18.0[f]	89.05 ± 13.4[e]
	DHEA	4.04 ± 1.17[a]	4.82 ± 0.75[g]	3.7 ± 0.52
	FAI	4.83 ± 1.88[c]	1.42 ± 0.39	1.68 ± 0.38[e]
	CL	34.7 ± 5.2	33.7 ± 4.6[h]	40.7 ± 3.5[d]
Sixteen	TT	2.42 ± 0.34[c]	1.9 ± 0.25	2 .0 ± 0.26[e]
	SHBG	73.5 ± 18.1[c]	123.5 ± 22.9[g]	105.3 ± 15.9[e]
	DHEA	6.27 ± 1.08	6.63 ± 0.84[h]	4.52 ± 0.44[e]
	FAI	3.52 ± 1.14[c]	1.59 ± 0.36	1.48 ± 0.19[e]
	CL	27.3 ± 9.7[a]	29.8 ± 9.1[h]	39.8 ± 2.9[e]
Twenty	TT	2.52 ± 0.26[a]	2.29 ± 0.34[h]	3.07 ± 0.42[e]
	SHBG	86.1 ± 13.5[c]	134.2 ± 19.4[g]	120.2 ± 14.9[e]
	DHEA	6.48 ± 0.83	6.71 ± 0.80[h]	3.09 ± 0.54[e]
	FAI	2.95 ± 0.57[c]	1.76 ± 0.36[h]	2.59 ± 0.45[d]
	CL	22.1 ± 7.6	24.3 ± 9.1[h]	37.5 ± 3.7[e]

[a] $p < 0.05$, [b] $p = 0.001$, [c] $p = 0.000$ (PCOS vs. RM).
[c] $p < 0.05$, [d] $p = 0.001$, [e] $p = 0.000$ (PCOS vs. HC).
[f] $p < 0.05$, [g] $p = 0.001$, [h] $p = 0.000$ (RM vs. HC).

Table 3. Mean (±sd) changes of cervical length (CL, mm) and total testosterone (TT, mmol/L), sex hormone-binding globulin (SHBG, mmol/L) dehydroepiandrosterone (DHEA, mmol/L), free androgen index (FAI) levels of women with a history of recurrent miscarriages (RM, $n = 40$), polycystic ovary syndrome (PCOS, $n = 38$) and healthy controls (HC, $n = 40$) with the progress of pregnancy.

		Week 8	Week 16	Week 20
TT	PCOS	1.96 ± 0.53[c]	2.42 ± 0.34	2.52 ± 0.26[e]
	RM	1.37 ± 0.30[c]	1.90 ± 0.25[h]	2.29 ± 0.34[e]
	HC	1.48 ± 0.28[c]	2.0 ± 0.26[h]	3.07 ± 0.42[e]
SHBG	PCOS	44.0 ± 11.6[c]	73.5 ± 18.1[g]	86.1 ± 13.5[e]
	RM	99.8 ± 18.0[c]	123.5 ± 22.9[f]	133.4 ± 19.6[e]
	HC	89.1 ± 13.4[c]	105.3 ± 15.9[h]	120.2 ± 14.8[e]
DHEA	PCOS	4.04 ± 1.17[c]	6.27 ± 1.08	6.48 ± 0.83[e]
	RM	4.82 ± 0.75[c]	6.63 ± 0.84	6.73 ± 0.80[e]
	HC	3.7 ± 0.52[c]	4.52 ± 0.44[h]	3.09 ± 0.54[e]
FAI	PCOS	4.83 ± 1.88[b]	3.53 ± 1.14	2.95 ± 0.58[e]
	RM	1.42 ± 0.39	1.59 ± 0.36	1.76 ± 0.36[d]
	HC	1.68 ± 0.38[a]	1.48 ± 0.19[h]	2.59 ± 0.45[e]
CL	PCOS	34.7 ± 5.2[b]	27.3 ± 9.7[g]	22.1 ± 7.6[e]
	RM	33.7 ± 4.6[a]	29.8 ± 9.1[g]	24.3 ± 9.1[e]
	HC	40.7 ± 3.5	39.8 ± 2.7[f]	37.5 ± 3.7[d]

[a] $p < 0.05$, [b] $p = 0.001$, [c] $p = 0.000$ (8 vs. 16 week).
[d] $p = 0.001$, [e] $p = 0.000$ (8 vs. 20 week).
[f] $p < 05$, [g] $p = 0.001$, [h] $p = 0.000$ (16 vs. 20 week).

The week eight TT, SHBG and DHEA levels of the PCOS group, respectively, were lower than that of weeks sixteen ($p = 0.000$, $p = 0.000$ & $p = 0.000$) and twenty ($p = 0.000$, $p = 0.000$ & $p = 0.000$). In contrast, the group had higher FAI and CL values in weeks sixteen ($p = 0.000$, $p = 0.000$) and twenty ($p = 0.000$ & $p = 0.000$) than in week eight.

The women with RM had reduced concentrations of TT, SHBG, DHEA and FAI in weeks sixteen ($p = 0.000$, $p = 0.000$ & $p = 0.000$, $p > 0.05$) and twenty ($p = 0.000$, $p = 0.000$, $p = 0.000$ & $p = 0.001$) than in week eight of pregnancy. Conversely, compared to week eight, they had higher CL levels in week sixteen ($p < 0.05$) and twenty ($p = 0.000$).

Compared with week eight of pregnancy, the TT, SHBG and DHEA values of the HC women were higher in week sixteen ($p = 0.000$, $p = 0.000$ & $p = 0.000$) and twenty ($p = 0.000$, $p = 0.000$ & $p = 0.000$). Besides, compared with week twenty, the HC group had a lower FAI concentration ($p = 0.000$) and higher CL length ($p = 0.001$) in week eight.

Twenty-eight (74%) of PCOS, thirty-four (85%) of RM, and none of the control groups miscarried. Nine (26%, mean gestation week 27.7 ± 2.3) of PCOS, five (15%, mean gestation week, 28.2 ± 2.1) of RM and four (10%, mean gestation week 34.3 ± 2.9) of the control women delivered before date (gestation week 37). One of the PCOS (gestation week 38), one of the RM (gestation week 37) and 36 of the control (gestation week 39.4 ± 2.9) women gave birth at term.

Discussion

Previous communications have reported that obesity is a common phenomenon in women with polycystic ovary syndrome (PCOS) both before (Vanky and Lovvik 2020, Liu *et al.* 2021) and during (Kakoly *et al.* 2017) pregnancy. However, in the current study, inconsistent with the reports mentioned above, the women with PCOS compared with the other two groups (RM and HC) had a lower mean body weight. This

reflected the intensive dietary and lifestyle counselling given to women with PCOS Al-Agoza Hospital to help enhance their ability to conceive and prevent maternal and foetal morbidity (Figure 1).

Hyperandrogenism (Ashraf *et al*. 2019, Valdimarsdottir *et al*. 2021) and lower blood SHBG concentrations (Deswal *et al*. 2018, Qu and Donnelly 2020) have been reported in women with PCOS. Consistent with these findings, the PCOS group in our study had higher TT (Supplementary Figure 1) and FAI (Supplementary Figure 2) and lowered SHBG (Figure 2) levels on weeks eight, sixteen and twenty. There is evidence that higher levels of TT and FAI in women with the disorder indicate enhanced production of ovarian androgen (Ashraf *et al*. 2019) and impaired synthesis and secretion of SHBG, which is the primary testosterone binder (Dunn *et al*. 1981), respectively. The reason for the reduced level of SHBG in women with PCOS is yet to be fully elucidated. However, obesity and body fat distribution (Zain and Norman 2008, Qu and Donnelly 2020), low levels of HDL-cholesterol (Chen *et al*. 2006), hyperinsulinemia (Lin *et al*. 2015, Tawfeek *et al*. 2017) and hepatic lipogenesis (Qu and Donnelly 2020) have been implicated.

It is postulated that a reduction in SHBG expression resulting from SHBG gene polymorphism increases the risk of RM by inducing hyperandrogenaemia (Dendana *et al*. 2018). Similarly, Hogeveen *et al*. (2002) have suggested that a low plasma SHBG concentration resulting from variations of the SHBG gene is associated with recurrent pregnancy loss. Indeed, it has been reported that a low SHBG level and PCOS-related complications in women with the condition could be ameliorated with SHBG treatment (Deswal *et al*. 2018).

In this study, the Egyptian women with a history of RM did not have elevated TT and FAI or lower SHBG levels, unlike their counterparts with PCOS. In contrast, other investigators have reported hyperandrogenaemia (Cocksedge *et al*. 2008) and reduced SHBG (Spencer *et al*. 2005) in miscarrying women in Europe. The reason behind these contradictory findings is not evident. There is evidence that blood levels of sex hormones and sex hormone-binding globulin are influenced by dietary habits (Moran *et al*. 2016, Huang *et al*. 2018). Therefore, differences in dietary habits between the population studied (Egyptians and Europeans) might have contributed to the conflicting observations.

The levels of DHEA in the women with PCOS and RM compared with that of the control group were higher by 9 and 30% on week eight, 38 and 47% on week sixteen and 83 and 117% on week twenty (Figure 1). Similarly, a meta-analysis of case-control studies undertaken by Benjamin *et al*. (2021) revealed women with PCOS have elevated concentrations of DHEA. Excess adrenal precursor androgen production (DHEAS, DHEA) was also reported in women with PCOS (Goodarzi *et al*. 2015, Moran *et al*. 2015). Besides, reproductive abnormalities similar to that observed in women with PCOS was exhibited in rats treated with DHEA (Seow *et al*. 2018). Regardless, the aetiology of excess DHEA production and its obstetric and clinical implications are unclear and require further investigations.

The cervix lengths (CL) of the PCOS and RM groups, respectively, were shorter than their healthy counterparts by 9 and 30% at eight, 38 and 47% at sixteen and 83 and 117% at twenty weeks of pregnancy (Figure 3). At twenty weeks, the CL of the PCOS was 22.1 mm and the RM 24.3 mm. A short CL, conventionally defined as shorter than 25 mm, measured during the second trimester, predicts the risk of spontaneous delivery before the due date (Berghella *et al*. 1997, O'Hara *et al*. 2015). However, Bortoletto *et al*. (2021) have questioned using a single cut-off point to diagnose cervical competence. They contend that it is necessary to identify different CL curves and cut-off values that reflect cervical length variations of varying population groups. Regardless, CL is an effective predictor of spontaneous preterm birth for singleton (Hernandez-Andrade et al. 2012, Wulff *et al*. 2018) and twin (Souka *et al*. 2011) pregnancies.

The conventionally accepted cut-off point of cervical competence suggests that the women with PCOS and RM who

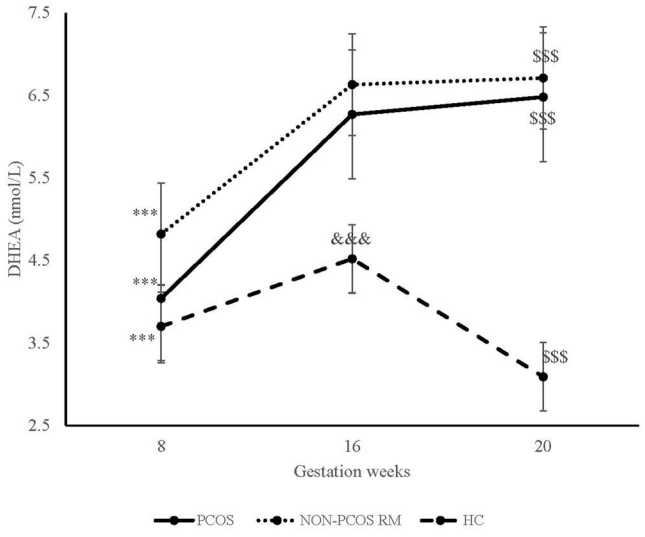

Figure 1. Changes in mean (±se) dehydroepiandrostrone (DHEA) concentration of women with recurrent miscarriages, polycystic ovary syndrome, and healthy control group between pergnancy week 8 and 20.
Notations – $^{a}p = 0.000$(8 vs. 16 week); $^{b}p = 0.000$ (8 vs. 20 week);$^{c}p = 0.000$ (16 vs. 20 week).

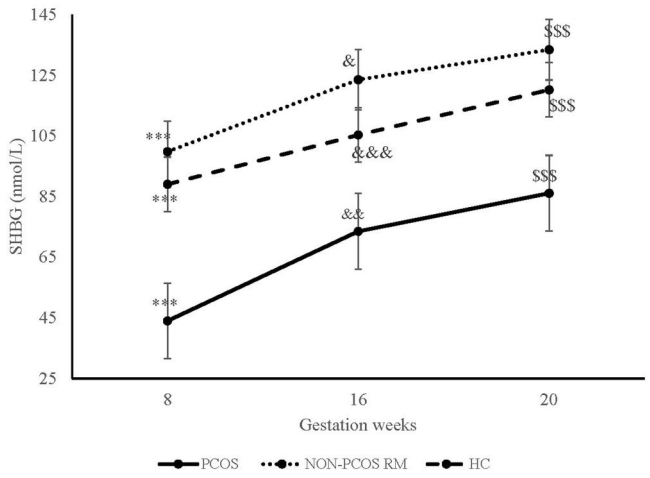

Figure 2. Changes in mean (±se) sex hormone binding globulin (SHBG) concentration of women with recurrent miscarriages, polycystic ovary syndrome, and healthy control group between pergnancy week 8 and 20.
Notations – $^{a}p = 0.000$(8 vs. 16 week); $^{b}p = 0.000$ (8 vs. 20 week); $^{c}p < 0.05$, $^{d}p < 0.001$, $^{e}p < 0.000$, (16 vs. 20 week).

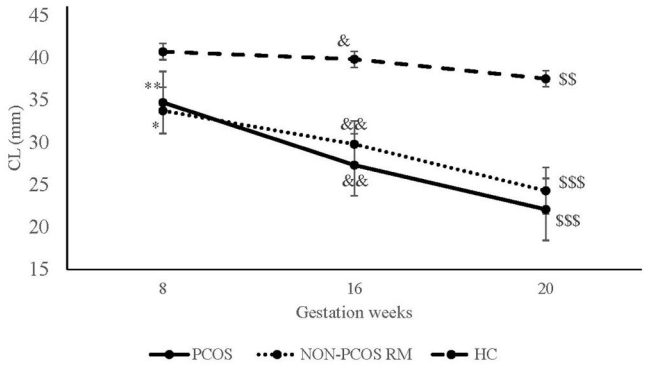

Figure 3. Changes in mean (±se) cervical length of women with recurrent miscarriages, polycystic ovary syndrome, and healthy control group between pergnancy week 8 and 20.
Notations – [a]$p < 0.05$, [b]$p < 0.001$ (8 vs. 16 week); [c]$p = 0.001$, [c]$p = 0.000$ (8 vs. 20 week); [d] $p < 0.05$ [e]$p = 0.001$ (16 vs. 20 week).

had a mean CL of 22.1 and 24.3 mm, respectively, were at higher risk of delivery before date or miscarrying. The question is, why was the CL of the two groups significantly shorter compared to that of the healthy control women. It is hypothesised that hyperandrogenism plays a role in the shortening (Lovvik *et al*. 2015) and remodelling and ripening of the cervix (Naver *et al*. 2014). The HC women had a higher total testosterone concentration than the other two groups at week twenty. Similarly, their FAI was higher than the RM group (2.59 vs 1.76). Hence, TT or FAI on its own would not have influenced the shortening or ripening of the cervix. However, the DHEA levels of the PCOS and RM groups which were almost 1.4 (week sixteen) and 2.0 (week twenty) times higher than that of the HC women, on its own or in concert with TT, may have been the driving factor behind cervical shortening. The elevated DHEA levels in the PCOS and RM groups without the concomitant increase in testosterone on weeks sixteen and twenty suggests its conversion to testosterone may be impaired.

The study's findings comprising ethnically and socially homogenous women demonstrate that PCOS and RM are characterised by elevated DHEA and shortened cervical length and PCOS by reduced SHBG. These abnormalities would be expected to have an adverse effect on pregnancy outcomes. Also, the findings suggest that the twenty-week DHEA and cervical length values can potentially predict outcome risk in this population.

The outcome of pregnancy, blood lipid parameters, biomarkers of insulin resistance, dehydroepiandrosterone sulphate were not assessed because of financial and logistic constraints. These limitations will be addressed in the study that will be undertaken shortly.

Acknowledgement

Very sincere thanks are due to the women who graciously consented to participate in the study, and the obstetrics and gynaecology team and the pathology laboratory technicians at Al-Agoza Hospital for their contributions to the data collection and collection and processing of blood specimens, respectively.

Author contributions

EEM and NF conceptualised and conducted the study, and collected the laboratory data, KG, MA and EEM analysed the data, and KG and EEM wrote the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

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