International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2024; 8(3): 36-42
Received: 02-04-2024
Accepted: 05-05-2024

Most. Ayesha Siddika
Emergency Medical Officer (Obstetrics and Gynecology), 250 Bed General Hospital, Pabna, Bangladesh

Sharmin Akthar
Assistant Surgeon, Department of Obstetrics and Gynecology, Sheikh Hasina National Institute of Burn & Plastic Surgery, Dhaka, Bangladesh

Masuma Nargish Urmee
Assistant Registrar, Department of Obstetrics and Gynecology, Colonel Malek Medical College Hospital, Manikgan, Bangladesh

Mst. Nurjahan Khatun
Medical Officer (Obstetrics and Gynecology), 250 Bed General Hospital, Jashore, Bangladesh

Safa Mohsin Chowdhury
Medical Officer (Obstetrics and Gynecology), 300 Beded Hospital Khanpur, Narayngonj, Bangladesh

Md. Yousuf Ali
Junior Consultant (ENT), Shaheed Ahsan Ullah Master General Hospital, Tongi, Gazipur, Bangladesh

Lotifa Khatun
Assistant Surgeon (Obstetrics and Gynecology), Bandor Upazila Health Complex, Bandor, Narayanganj, Bangladesh

Corresponding Author:
Most. Ayesha Siddika
Emergency Medical Officer (Obstetrics and Gynecology), 250 Bed General Hospital, Pabna, Bangladesh

Association of serum free testosterone with preeclampsia

Most. Ayesha Siddika, Sharmin Akthar, Masuma Nargish Urmee, Mst. Nurjahan Khatun, Safa Mohsin Chowdhury, Md. Yousuf Ali and Lotifa Khatun

DOI: https://doi.org/10.33545/gynae.2024.v8.i3a.1450

Abstract
Background: Preeclampsia is a pregnancy specific disorder characterized by hypertension and proteinuria or new onset of hypertension and significant end organ disfunction with or without proteinuria after 20 weeks of gestation. Preeclampsia is associated with reduction of utero-placental blood flow, which is reflected in high blood pressure and proteinuria during the second half of pregnancy. Hyper-androgenism may be implicated in the pathogenesis of preeclampsia, if so, there should be a difference between the levels of testosterone in pregnant women complicated with preeclampsia and those without this complication.
Objective: To determine association of serum free testosterone with preeclampsia.
Methods: This case control study was conducted in the department of Obstetrics & Gynaecology of Institute of Child & Mother Health (ICMH), Matuail, Dhaka during September 2021 to August 2022. Patient complicated by preeclampsia and patient without preeclampsia attending Obstetrics and Gynecology Department was included in this study by consecutive sampling. All of them were briefed regarding the study. After that they were included by eligibility criteria and patients were classified into two groups. A total of 80 participants during second half of pregnancy were enrolled and among them 40 patient complicated by preeclampsia was considered as case and 40 patients without preeclampsia was considered as control. A written consent was obtained. Data were analysed by using Statistical Packages for Social Sciences (SPSS-26). The significance test was done by unpaired t test and Chi square test. P value less than 0.05 was considered statistically significant.
Results: The mean age of the cases was 23.6±3.66 years and the mean age of the control was 24.25±4.91 years. In both group maximum study subjects were secondary education 40% and 45% in case and control group respectively. Maximum patients 52.5% and 42.5% were 31-35 gestational weeks in case and control group respectively. The mean gestational age 32.1±2.92 weeks in preeclamptic group and 32.4±3.53 weeks in control group. Data analysis revealed no statistically significant difference between two groups patients in terms of sociodemographic parameters ($p>0.05$). The mean free serum testosterone was 2.91±0.62 in preeclampsia group and 1.19±0.49 in healthy normal pregnancy group. Analysis revealed that mean free serum testosterone was significantly increased among the preeclampsia group than the healthy normal pregnancy group ($p<0.001$). It was confirmed that the serum free testosterone levels were considerably high in the preeclamptic participants than the participants without preeclampsia.
Conclusion: The levels of free testosterone is higher in patients with preeclampsia compared to normotensive pregnant women during the second half of pregnancy. This difference could indicate an involvement of testosterone in the pathophysiology of preeclampsia and stimulates research in the potential role of anti-androgens in the management of preeclampsia.

Keywords: Association, Serum Free Testosterone, Preeclampsia

Introduction
Preeclampsia is a multisystem disorder of unknown etiology characterized by development of hypertension to the extent of 140/90 mmHg or more with proteinuria after the 20th week of gestation in a previously normotensive and nonproteinuric woman. In the absence of proteinuria additional features contribute to diagnosis (i.e., thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, cerebral or visual symptoms) [1]. Preeclampsia is classified into mild preeclampsia and severe preeclampsia. Severe preeclampsia is characterized by severe hypertension (≥160/110 mmHg) or endorgan injury. Women who met criteria of preeclampsia but not severe preeclampsia are diagnosed as mild preeclampsia. The threat of severe

preeclampsia to mothers and infants is more serious than that of mild preeclampsia. A gradual increase in its prevalence has been observed worldwide. It is estimated that the prevalence of preeclampsia globally is 4.6% with 95% CI, 2.7%–8.2% [2]. Preeclampsia and related hypertensive disorders of pregnancy impact 5-8% of all births in the United States. Incidence rates for preeclampsia alone-in the United States, Canada and Western Europe, range from 2-5%. In the developing world, severe forms of preeclampsia and eclampsia are more common, ranging from a low of 4.0% of all deliveries to as high as 18% in parts of Africa. The incidence of severe preeclampsia is about 5/1,000 maternities. Pregnancy induced hypertension complicates about 10.0% of pregnancies, but there is a widespread geographic variation in its incidence. Bangladesh is a developing country where higher (about 16.0%) incidence of preeclampsia was reported [3, 4]. Although the identification of underlying risk factors for preeclampsia is different but some identified risk factors are documented like nulliparity, family history, preeclampsia in previous pregnancy, multiple gestation, and pregestational diabetes mellitus, chronic hypertension, chronic renal disease and some auto immune diseases [5]. Preeclampsia is associated with morbidities or complications which are well established. If not diagnosed or treated, it increases the risk of abruptio-placenta, acute renal failure (ARF) disseminated intravascular coagulation (DIC), HELLP (H: haemolysis, EL: Elevated liver enzyme and LP: Low Platelet count) syndrome, cerebral haemorrhage and maternal death [6]; intrauterine growth retardation (IUGR), preterm delivery, low birth weight and neonatal death are common perienatal outcome associated with preeclampsia [7]. Similarly, high testosterone in women with polycystic ovary syndrome augments the risk and incidence of preeclampsia in future pregnancy [8]. Therefore, it is possible that testosterone may play a potential role in the pathogenesis of preeclampsia through modulation of vascular reactivity and endothelial functions through activation of platelet aggregations and renin-angiotensin system [9]. Besides, preeclampsia is associated with high free androgen index and total testosterone that induce vasoconstriction through the reduction of vasodilator prostacyclin and increase of vasoconstrictor thromboxane A2 [10]. In human male the peripheral aromatization of testosterone to estradiol (E2) account for 80% of the production of the latter. In female, adrenal androgens are important substrates, since as much as 50.0% of the estradiol E2 produced during pregnancy comes from the aromatization of androgens [11]. Aromatase activity is present in adipose cells and also in liver, skin and other tissues. Increased activity of this enzyme may contribute to the estrogenization that characterizes such disease as cirrhosis of the liver, hyperthyroidism and obesity [12]. Therefore, the aim of the present study will be to find the association between serum free testosterone levels and preeclampsia.

Materials and Methods

Study design: Case control study.

Place of study: Department of Obstetrics and Gynaecology Department of ICMH, Dhaka, Bangladesh.

Study participants: Women with preeclampsia was one group (case) and healthy pregnant women were another group (control) attending in the department of Obstetrics and Gynaecology, ICMH, Dhaka, Bangladesh.

Period of study: September 2021 to August 2022.

Sample size determination

To calculate sample size for case control study the comparison between two means, the following formula was followed:

$$n = \frac{(Z_\alpha + Z_\beta)^2 \times (\sigma_1^{\ 2} + \sigma_2^{\ 2})}{(\mu_1 - \mu_2)^2}$$

Hoque et al. [13]
Sample size= 40 (in each group).
All values were taken from Salamalekis et al. [14].
Therefore, total targeted sample size was 80 (40×2).

Selection criteria

Inclusion criteria for case

a) Primigravida in 20 completed weeks to 40 weeks.
b) Age of all subjects within 18-35 years.
c) Blood pressure ≥140/90 mm of Hg observed at least on two occasions 4 hours apart.
d) Proteinuria: Dipstick reading and or >1+ and or severe features.
e) Singleton gestation.

Inclusion criteria for control

a) Normotensive primigravida between 20 completed weeks to 40 weeks.
b) Age of all subjects within 18-35 years.
c) Singleton gestation.
d) Proteinuria: Dipstick reading ≤ 1 + or nil.

Exclusion criteria for case and control

a) History of hypertension and proteinuria before 20 weeks of gestation of before gestation associated with any systemic diseases (Diabetes mellitus, chronic renal disease, essential hypertension, liver disease, autoimmune disease, heart disease, epilepsy, coagulation disorder.
b) Patients with antihypertensive.
c) Patients with hormone treatment.
d) Any condition resulting in hormone disorder like PCOS etc.
e) Psychotic patients.
f) Smoker.

Study Procedure

This study consists of 20 weeks to 40 weeks of pregnancy with preeclampsia in 40 cases (Case) and 40 case of healthy normal pregnancy without preeclampsia (control). This was done over a period of 12 months (September 2021 to August 2022). All the cases that was available up to the study period have been taken for the purpose of study. For all the selected cases, detailed history was taken and complete examination was done. The previous obstetric records and ultrasound reports were reviewed. The demographic and anthropometric variables were age, socio-economic status, weight, and height. The obstetrical variables were gestational age, gravida, parity and biochemical parameters that included free testosterone. Data were collected using a structured questionnaire containing all the variables of interest and by interview, clinical examination and laboratory investigations and recorded on the pre-designed data collection sheet. All information was keep confidential. Purpose and procedure of the study was discussed with the patients who fulfilled the inclusion criteria. Written consent was taken from those who agreed to be included in the study. A clean urine container was given to each of them with proper instructions to collect midstream urine for the study.

An immediate dipstick test was performed using Multistix reagent strips. 5 ml of blood was collected from every patient with all aseptic precaution by a disposable syringe for free serum testosterone. Serum was separated, stored under -20^{0}c in department. After completion of sample collection, assay was carried out in Microbiology Department of BSMMU by the DRG free Testosterone ELISA kit. Relevant investigations were also done in necessary cases.

Data Analysis: Statistical analyses were carried out by using the Statistical Package for Social Sciences version 26 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ±standard deviation, and categorical variables as frequencies and percentages n (%). Chi-square test used to analyze the categorical variables and shown in cross tabulation. The mean difference between groups were analyzed by unpaired t-test for continuous variables. P values <0.05 considered as statistically significant.

Results

Table 1: Sociodemographic characteristics between case and control group (n=80)

Sociodemographic characteristics	Case (n=40)		Control (n=40)		p value
	No.	%	No.	%	
Age in years					
18- 25	27	67.5	22	55.5	
26-35	13	325	18	45.0	
Mean± SD (Years) Range (years)	23.6±3.66 18-35		24.25±4.91 18-35		0.488
Level of education					
Primary	8	20.0	4	12.0	0.445
Secondary	16	40.0	18	45.0	
Higher Secondary	10	25.0	8	20.0	
Graduate or higher	6	15.0	10	25.0	
Occupation					
Housewife	28	70.0	27	67.5	0.530
Service	9	22.5	7	17.5	
Student	3	7.5	6	15.0	
Socioeconomic status					
Affluent class	6	15.0	7	17.5	0.766
Lower middle class	20	50.0	22	55.0	
Lower class	14	35.0	11	27.5	

Case- Preeclampsia, Control- Healthy normal pregnancy, p value reached from unpaired student's t test for quantitate data and Chi-square test for qualitative data

Table-1 showed that the mean age of the cases was 23.6±3.66 years and the mean age of the control was 24.25±4.91 years. Data showed that the highest percentage of the patients 67.5% and 55.5% in age group below 26 years in case and control group respectively. Maximum study subjects were secondary education 40% and 45% in case and control group respectively. Above table showed that proportion of housewife 70.0% in cases group and in control group in 67.5%. Maximum patients (50.0%) were came from lower middle class family followed by lower class 35.5% in case group and in control group 55.0% patients came from lower middle class family followed by 27.5% in lower class. Data analysis revealed no statistically significant difference between two groups patients in terms of sociodemographic characteristics (p>0.05).

Table 2: Distribution of the study subjects by gestational age (Weeks) in two groups (n=80)

Gestational age (Weeks)	Case (n=40)		Control (n=40)		p value
	No.	%	No.	%	
20-25	1	2.5	1	2.5	
26-30	13	32.5	14	35.0	
31-35	21	52.5	17	42.5	
36-40	5	12.5	8	20.0	
Total	40	100.0	40	100.0	
Mean±SD	32.1±2.92		32.4±3.53		0.655

Case- Preeclampsia, Control- Healthy normal pregnancy, p value reached from unpaired student's t test

Above table showed that maximum patients (52.5%) were 31-35 gestational weeks followed by 32.5% patients gestational age 26-30 weeks in cases group and in control group 42.5% patients gestational age 31-35 weeks followed by 35.0% patients had gestational age 26-30 weeks. Data analysis revealed no statistically significant difference between two groups patients in terms of gestational weeks (p>0.05).

Table 3: Distribution of the study subjects by BMI in two groups (n=80)

BMI (kg/m^2)	Case (n=40)		Control (n=40)		p value
	No.	%	No.	%	
Underweight (<18.5)	1	2.5	3	7.5	
Normal weight (18.5-24.9)	28	70.0	31	77.5	
Overweight (>25)	11	27.5	6	15.0	
Total	40	100.0	40	100.0	
Mean ±SD	24.1±2.40		23.9±2.92		0.139

Case- Preeclampsia, Control- Healthy normal pregnancy, p value reached from unpaired student's t test

Above table showed that maximum patients (70%) had normal weight in case group and 77.5% in control group. Overweight was found in 27.5% and 15.0% in case and control group respectively. Data analysis revealed no statistically significant difference between two groups patients in terms of BMI (p>0.05).

Table 4: Distribution of the study subjects by proteinuria in two groups (n=80)

Proteinuria	Case (n=40)		Control (n=40)		p value
	No.	%	No.	%	
Nil	3	7.5	37	95.5	<0.001*
+	4	10.0	3	7.5	
++	23	57.5	0	0.0	
+++	9	22.5	0	0.0	
++++	1	2.5	0	0.0	
Total	40	100.0	40	100.0	

Case- Preeclampsia, Control- Healthy normal pregnancy, p value reached from chi square test

In the group with pre-eclampsia, 57.5% of patients had proteinuria 2+, 22.5% patients had proteinuria 3+ levels were significantly higher in the preeclamptic group than in the control group (p<0.001).

Table 5: Comparison of blood pressure between two groups (N=80)

Blood pressure	Case (n=40) Mean± SD	Control (n=40) Mean± SD	p value
Systolic BP (mmHg)	158.4±9.23	119.6±8.83	<0.001*
Diastolic BP (mmHg)	103.87±4.40	74.0±6.62	<0.001*

Case- Preeclampsia, Control- Healthy normal pregnancy, p value reached from unpaired student's t test

In Table-5 showed the comparison of mean blood pressure between two group. The mean SBP 158.4±9.23 in case group and 119.6±8.83 in control group. The mean DBP was 103.87±4.40 in case group and 74.0±6.62 in control group. The mean SBP and DBP significantly in preeclamptic group compare to healthy normal pregnancy (p<0.001).

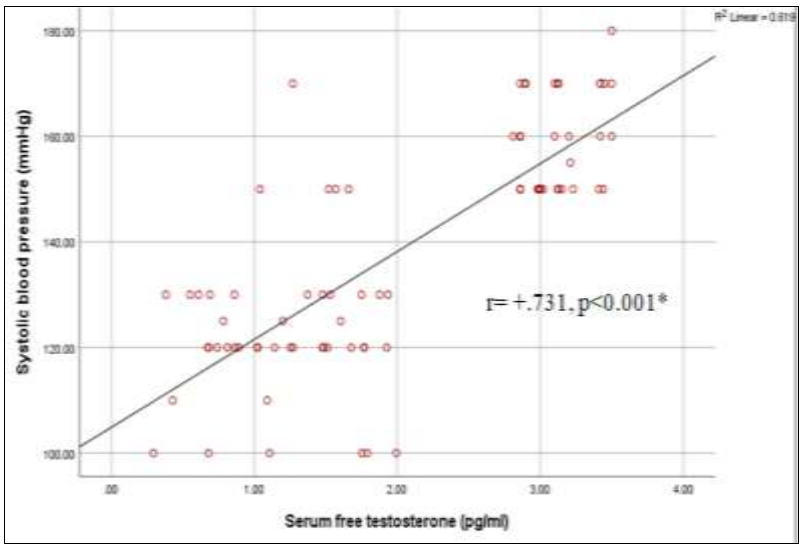

Fig 1: Scatter diagram showing the correlation the serum free testosterone with systolic blood pressure.

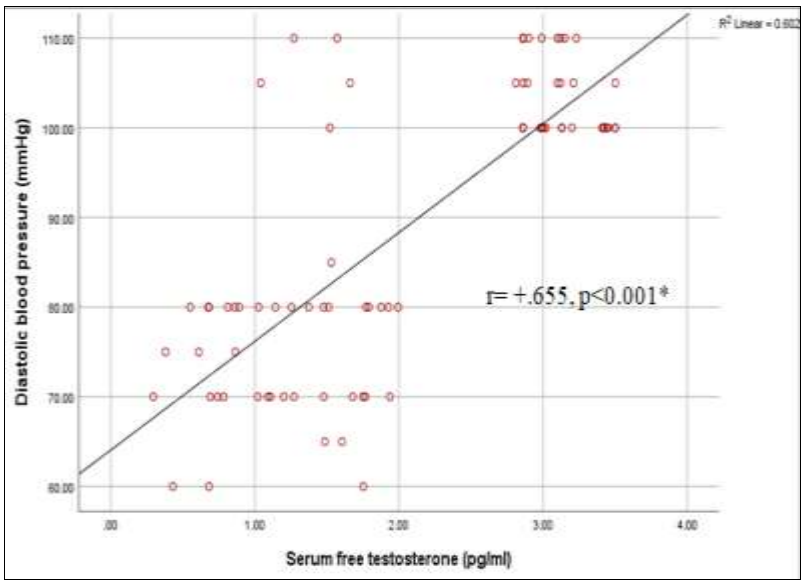

Fig 2: Scatter diagram showing the correlation the serum free testosterone with diastolic blood pressure.

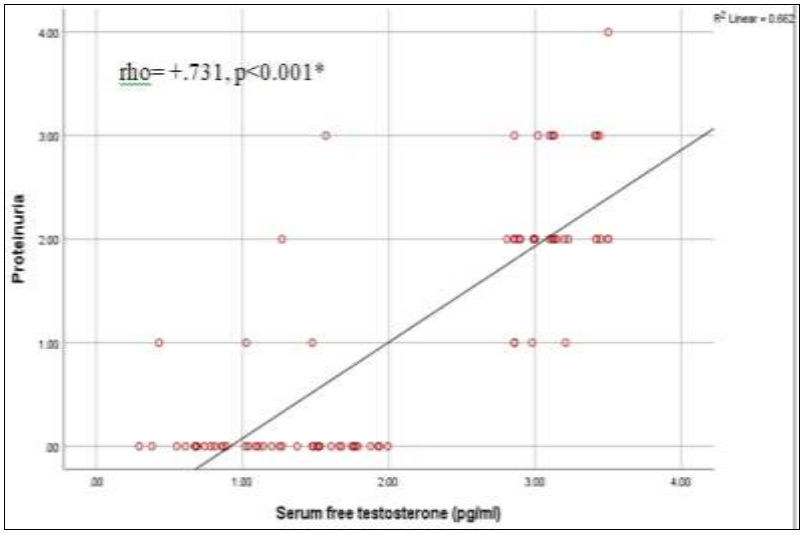

Fig 3: Scatter diagram showing the correlation the serum free testosterone with proteinuria.

Table 6: Comparison of free serum testosterone between case and control group (n=80)

Parameter	Case (n= 40)	Control (n= 40)	p value
Free mean Serum Testosterone (pg/ml)	2.91±0.62	1.19±0.49	*p*<0.001*

Values depicted are mean ±SD, p-value obtained from unpaired student's 't' test, *significant, Case- Preeclampsia, Control- Healthy normal pregnancy

Table-6 showed the comparison of free serum testosterone between two groups. The mean free serum testosterone was 2.91±0.62 in case group and 1.19±0.49 in control group. Analysis revealed that mean free serum testosterone was significantly increased among the preeclampsia group than the healthy normal pregnancy group (*p*<0.001).

Table 7: Distribution of study subjects by serum free testosterone level between two groups (n=80)

Free serum testosterone	Case (n=40) No. (%)	Control (n=40) No. (%)	OR 95% CI	p value
Elevated (>2.85 pg/ml)	35 (87.5%)	9 (22.5%)	24.11 (7.3-79.7)	<0.001*
Normal (0.50-2.85 pg/ml)	5 (12.5%)	31 (77.5%)		
Total	40 (100.0%)	40 (100.0%)		

*significant, p value reached from Chi square test

Data analysis revealed that the percentage of free serum testosterone above normal was found to be high among the preeclampsia group (87.5%) whereas normal pregnancy group (22.5%) and the difference was statistically significant (*p*<0.001) between case and control having OR=24.11 with 95% CI.

Discussion

This was a case control comparative study carried out in the Department of Obstetrics and Gynaecology of ICMH, Dhaka from September 2021 to August 2022. A total of 40 women with preeclampsia was case group and 40 healthy pregnant women were control group between 20 weeks to 40 weeks with primigravida singleton gestation aged within 18-35 years. In present study showed that the mean age of the cases was 23.6±3.66 years and the mean age of the control was 24.25±4.91 years. In both group maximum study subjects were secondary education 40% and 45% in case and control group respectively. Maximum patients (52.5%) were 31-35 gestational weeks followed by 32.5% patient's gestational age 26-30 weeks in cases group and in control group 42.5% patients gestational age 31-35 weeks followed by 35.0% patients had gestational age 26-30 weeks. The mean gestational age 32.1±2.92 weeks in preeclamptic group and 32.4±3.53 weeks in control group. Data analysis revealed no statistically significant difference between two groups patients in terms of sociodemographic parameters (p>0.05) but about 80% patients both case and controlled group come from lower and lower middle class family. In accordance with Chowdhury et al. [15] reported the mean age and socio-economic condition of the participants with or without preeclampsia were 27.1±5.2 years and 25.8±4.5 years, respectively (p=0.271) and 53.3 and 72.9% belonged to the middle class. The body mass index of 46.7% from the experimental group and 41.7% from the control group were ≥25 kg/m2, respectively. The differences between the two groups were not statistically significant (p=0.665). In terms of gestational age, 86.7% in the experimental group and 72.9% in the control group were preterm (<37 weeks of gestation) (p=0.152). In this study showed that the mean free serum testosterone was 2.91±0.62 in preeclampsia group and 1.19±0.49 in healthy normal pregnancy group. Analysis revealed that mean free serum testosterone was significantly increased among the preeclampsia group than the healthy normal pregnancy group (*p*<0.001). It was confirmed that the serum free testosterone levels were considerably high in the preeclamptic participants than the participants without preeclampsia. In a similar study by Acromite et al. [16] on 16 pre-eclamptic women, they showed a higher level of serum free and total testosterone in these women in comparison with normotensive women but no significant difference for SHBG and DHEA-S, which is in agreement with the present study. Agreement with present study Serin et al. [17] revealed that in the third trimester of preeclamptic participants, the total and free testosterone levels were markedly high compared to participants without preeclampsia. Wan et al. [18]

also reported that total and free testosterone levels of preeclamptic participants were considerably high than the participants without preeclapmsia. In preeclamptic women [19], also found that the free testosterone level was higher than the normotensive women. In present study showed that significant strong positive correlation of serum free testosterone with SBP (r=+.731, p<0.001), DBP (r=+.655, p<0.001), proteinuria (r=+.731, p<0.001). Akram et al [20] reported strong positive correlation between serum free testosterone with systolic (r=+.887, p<0.001) and diastolic blood pressure (r=+.892, p<0.001) and protein over creatine ratio (r=+.863, p<0.001). The study showing the percentage of free serum testosterone above normal was found to be high among the preeclampsia group (87.5%) whereas below normal level of serum testosterone was found among the normal pregnancy group (12.5%) and 24 times more risk for preeclampsia (OR 24.11, 95%CI 7.3-79.7, p<0.001) compare to healthy normal pregnancy. In accordance this findings Keya et al. [21] reported high serum free testosterone was found in 74.3% preeclampsia patients and in 7.5% healthy pregnant patients. The difference was statistically significant (p<0.05) having OR=35.63 with 95% CI. Another similar study by Ghorashi and Sheikhvatan et al. [22] reported free testosterone levels were significantly higher in the pre-eclamptic group (mean = 1.97, SD = 0.58, median = 1.90 ng/dL) than in the control group (mean = 0.58, SD = 0.29, median=0.50 ng/dL) (p<0.001). They concluded that an increase in serum free testosterone concentration may be considered an important risk factor for pre-eclampsia and might be implicated in the pathogenesis of pre-eclampsia. Consistently Sharifzadeh et al [23] reported free testosterone (1.28 ± 0. 17 vs. 0. 74 ± 0.07 pg/ml, p=0.01) was higher in the pre-eclamptic women. Akram et al [20] reported serum free testosterone was significantly higher among women with preeclampsia compared with control 5.00±0.72 versus 1.28±0.97, p<0.001. In addition, some other studies have shown that hypertension is associated with high levels of androgen in non-pregnant healthy women [24, 25, 26]. The exact mechanism underlying preeclampsia is still to be defined despite extensive research. Until preeclampsia pathogenesis is well-defined, effective preventive strategies are unlikely to be developed.

Conclusion

The study result showed the level of free testosterone was significantly higher in patients with preeclampsia compared to normotensive pregnant women during the second half of pregnancy. This difference indicate an involvement of testosterone in the pathophysiology of preeclampsia and in future it would be possible to prevent preeclampsia by using androgen receptor blocker.

Limitations

1. This study included a small number of patients, so the results were not all consistent with similar large studies.
2. Time and resources were limited. A longer study period could have allowed more time for recruitment of more patients.
3. Our patients primarily came to single tertiary center which could not demonstrate the true population of preeclampsia.
4. The patients in control group enrolled before term, lack of follow up as they developed preeclampsia or not in later period.
5. In all study subjects baseline sex hormone binding globulin level was not done.

Recommendation

The following recommendations can be suggested based on the present study:

- A large population based and multi-centres study should be under taken.
- Subjects should be selected by random sampling to avoid biasness.
- Serum free testosterone should be routinely examined in all pregnant women in second half of pregnancy.
- Further research about the potential role of anti-androgen in the management of preeclampsia.
- To evaluate the association of low level of progesterone in preeclamptic women, further randomized control studies are required.

Conflict of Interest

Not available.

Financial Support

Not available.

References

1. Henderson JT, Thompson JH, Burda BU, Cantor A. Preeclampsia screening: Evidence report and systematic review for the US Preventive Services Task Force. Jama. 2017 Apr 25;317(16):1668-1683.
2. Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: A systematic review. Eur. J Obstet. Gynecol. Reprod. Biol. 2013 Jan;170(1):01-07.
3. Rudra P, Basak S, Patil D, Latoo MY. Recent advances in management of pre-eclampsia. BJMP. 2011;4(3):433-441.
4. Sultana R, Ahmed S, Sultana N, Karim SF. Iron status in pre-eclampsia: A case-comparison study. Bangladesh J Med Biochem. 2012;5(2):53-55.
5. Vousden N, Shennan AH, Jauniaux E, Bhide A, Burton GJ, Hirst JE, et al. Fetomaternal Medicine. In: Oxford Textbook of Obstetrics and Gynaecology. Oxford: Oxford University Press; c2019. p. 107.
6. Cunningham WA, Johnson MK, Gatenby JC, Gore JC, Banaji MR. Neural components of social evaluation. J Pers. Soc. Psychol. 2003 Oct;85(4):639.
7. Lyell DJ. Hypertensive disorders of pregnancy: Relevance for the neonatologist. Neo Reviews. 2004 Jun;5(6):240-246.
8. Xia H, Zhang R, Sun X, Wang L, Zhang W. Risk factors for preeclampsia in infertile Chinese women with polycystic ovary syndrome: A prospective cohort study. J Clin. Hypertens (Greenwich). 2017 May;19(5):504-509.
9. Verdonk K, Saleh L, Lankhorst S, Smilde JI, Van Ingen MM, Garrelds IM, et al. Association studies suggest a key role for endothelin-1 in the pathogenesis of preeclampsia and the accompanying renin–angiotensin–aldosterone system suppression. Hypertension. 2015 Jun;65(6):1316-23.
10. Hanson AE, McKenna JM, Garcia NW, Perusquia M, Stallone JN. Preeclampsia alters the role of nitric oxide in androgen metabolite-induced vasorelaxation of rat uterine artery. FASEB J. 2018 Jan; 32:584-588.
11. Murray-RK, Granner-DK, Mayes-PA, Rodwell-VW. Harper's Illustrated; c2011.
12. Ojeda NB, Grigore D, Yanes LL, Iliescu R, Robertson EB, Zhang H, et al. Testosterone contributes to marked elevations in mean arterial pressure in adult male intrauterine growth restricted offspring. Am. J Physiol. Regul. Integr. Comp Physiol. 2007 Feb;292(2): R758-763.

13. Hoque M. ABC of research methodology and biostatistics. 2nd edition. Dhanmondi: Sultana P; c2014.
14. Salamalekis E, Bakas P, Vitoratos N, Eleptheriadis M, Creatsas G. Androgen levels in the third trimester of pregnancy in patients with preeclampsia. Eur. J Obstet. Gynecol. Reprod. Biol. 2006 Jan;126(1):16-19.
15. Chowdhury S, Ferdous J, Nahar KN, Mahmood S. Maternal serum progesterone level in preeclampsia. Bangabandhu Sheikh Mujib Med Univ. J. 2020;13(1):09-12.
16. Acromite MT, Mantzoros CS, Leach RE, Hurwitz J, Dorey LG. Androgens in preeclampsia. Am. J Obstet. Gynecol. 1999 Jan;180(1):60-63.
17. Serin İS, Kula M, Başbuğ M, Ünlühizarci K, Güçer Ş, Tayyar M. Androgen levels of preeclamptic patients in the third trimester of pregnancy and six weeks after delivery. Acta Obstet Gynecol Scand. 2001 Nov;80(11):1009-1013.
18. Wan J, Hu Z, Zeng K, Yin Y, Zhao M, Chen M, et al. The reduction in circulating levels of estrogen and progesterone in women with preeclampsia. Pregnancy Hypertens. 2018 Apr; 11:18-25.
19. Laivuori H, Kaaja R, Rutanen EM, Viinikka L, Ylikorkala O. Evidence of high circulating testosterone in women with prior preeclampsia. J Clin. Endocrinol. Metab. 1998 Feb;83(2):344-347.
20. Akram W. Association between preeclampsia and hyperandrogenemia. Mustansiriya Med J. 2014;13(2):1.
21. Keya SL, Khanam NN, Chowdhury AA, Ripon R, Tasnim T, Sharmin A. Relationship between Free Testosterone and Preeclampsia. Mymensingh Med J. 2019;28(3):574-581.
22. Ghorashi V, Sheikhvatan M. The relationship between serum concentration of free testosterone and pre-eclampsia. Endokrynol Pol. 2008;59(5):390-392.
23. Sharifzadeh F, Kashanian M, Fatemi F. A comparison of serum androgens in pre-eclamptic and normotensive pregnant women during the third trimester of pregnancy. Gynecol Endocrinol. 2012 Oct;28(10):834-836.
24. Nahar K, Islam F, Khan NA. Relationship between severity of hypertension and renal impairment in preeclampsia. Bangabandhu Sheikh Mujib Med. Univ. J. 2018;11(3):213-217.
25. Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. Semin Perinatol. 2012 Feb;36:56-59.
26. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet. 2008 Jan 5; 371(9606):75-84.

How to Cite This Article
Siddika A, Akthar S, Urmee MN, Khatun N, Chowdhury SM, Md. Ali Y, Khatun L. Association of serum free testosterone with preeclampsia. International Journal of Clinical Obstetrics and Gynaecology 2024; 8(3): 36-42.