



Association Between Serum Free Testosterone Levels and Preeclampsia from 20 to 40 Weeks of Gestation

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Abstract

Background: Preeclampsia remains a leading global cause of maternal and perinatal morbidity, disproportionately affecting low-and middle-income countries like Bangladesh where its rising prevalence necessitates identifying hormonal risk factors such as elevated serum free testosterone for improved early detection and prevention.

Aim: To determine the relationship between serum free testosterone levels and the occurrence of preeclampsia in pregnant women between 20 and 40 weeks of gestation.

Materials and Methods: This case-control study was conducted at the Bangladesh Medical University (BMU), Dhaka, from September 2021 to August 2022. It included 39 primigravid women with preeclampsia and 39 gestational age-matched normotensive controls (20-40 weeks), selected via purposive sampling. Data was collected through interviews and clinical assessments. Proteinuria was measured from midstream urine, and serum free testosterone was analyzed using the Diagnosis Related Group (DRG) Enzyme-Linked Immunosorbent Assay (ELISA) kit at BMU. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 26.

Results: Among 78 pregnant women, high serum free testosterone levels were more prevalent in the preeclampsia group 48.7% than in controls 41.0%, with a significant association observed $p = 0.030$. Preeclampsia cases had higher rates of obesity 56.4%, moderate to severe edema 41.0%, and primigravida status 79.5%. Educational level, income, and employment diversity were lower in the case group. Proteinuria was more severe among cases, with 48.7% showing ++ or +++ levels compared to 35.9% in controls.

Conclusion: Elevated serum free testosterone levels were significantly associated with preeclampsia, suggesting a potential role for androgens in its pathogenesis and utility as an early biomarker in pregnancy risk assessment.

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Introduction

Preeclampsia, a major contributor to maternal and perinatal morbidity and mortality, presents a significant global health challenge, with a disproportionate impact on low- and middle-income countries like Bangladesh [1,2]. The

rising incidence of hypertensive disorders of pregnancy in Bangladesh underscores the urgent need to identify early predictive factors [3]. While the pathophysiology of preeclampsia is multifactorial [4], hormonal imbalances are increasingly implicated [5]. Beyond the well-established role of the renin-angiotensin system, the involvement of androgens, including testosterone, is gaining attention [5]. Specifically, free testosterone, the biologically active fraction, may be altered in preeclamptic pregnancies [6,7]. Studies from various regions, including the Indian subcontinent and Russia, have explored the association between androgens and preeclampsia [8,9,12,14]. Furthermore, research has examined the broader role of androgens in both normal pregnancy and preeclampsia [13,15]. Studies conducted in India have specifically reported on maternal testosterone levels in preeclampsia [8,9]. Clinical guidelines from international organizations emphasize the importance of understanding the pathophysiology of preeclampsia for improved management [10,11]. This study aimed to determine the relationship between serum free testosterone levels and the occurrence of preeclampsia in pregnant women between 20 and 40 weeks of gestation at a tertiary care hospital in Dhaka, Bangladesh.

Materials and Methods

This case-control study was conducted at the BMU, Dhaka, Bangladesh, from September 2021 to August 2022. It included 39 primigravid women with preeclampsia and 39 normotensive controls, matched for gestational age (20–40 weeks), selected via purposive sampling.

Cases met criteria for blood pressure $\geq 140/90$ mmHg (on at least two occasions, four hours apart), proteinuria ≥ 0.3 g/L, or systemic signs of preeclampsia. Controls were normotensive primigravid women with singleton pregnancies. Exclusion criteria included pre-existing hypertension, systemic diseases, prior antihypertensive or hormone use, hormonal disorders (e.g., polycystic ovary syndrome), psychotic conditions, and smoking.

After informed consent, socio-demographic, anthropometric, and obstetric data were collected via questionnaire. Blood pressure was measured in the supine position, and BMI was calculated. Midstream urine samples were tested for proteinuria, and 5 mL venous blood samples were analyzed for serum free testosterone levels using the DRG free Testosterone ELISA kit at BMU.

Data analysis was performed using International Business Machines Corporation IBM SPSS Statistics version 26, employing descriptive and inferential statistical tests.

Results

The study included 78 pregnant women, equally divided into preeclampsia (cases) and control groups. Urban residency was more common among 87.2% than controls 69.2%. Age distribution was similar, with slightly more women aged 40+ in the control group 43.6% vs. 33.3%. Higher education (higher secondary or above) was lower in cases 20.5% compared to controls 51.3%. Most cases were housewives 82.1% versus 53.8% in controls, who had more service holders 23.1% and businesswomen 17.9%. Family income above 50,000 BDT was reported by fewer cases 7.7% than controls 28.2%.

Data processing plan

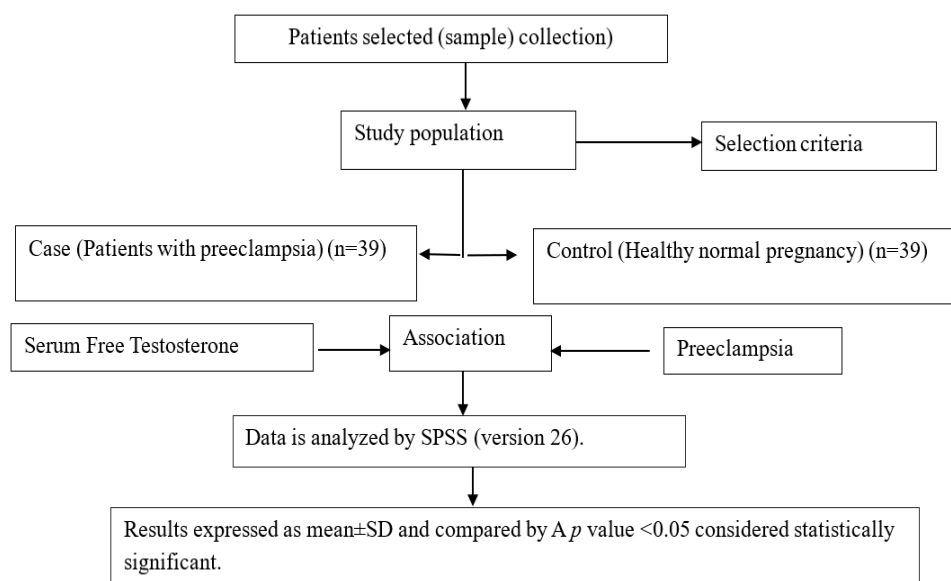


Figure 1: Data processing plan.

Obesity was more frequent in cases 56.4% than controls 46.2%. Moderate to severe edema was more common in cases 41.0% than controls 23.1%. Primigravida and primipara status were higher in the case group 79.5% and 82.1% compared to controls 41.0% and 61.5%. Gestational age was mostly 30–36 weeks in cases 56.4% and 36–40 weeks in controls 66.7%.

Medical history showed that hypertension 7.7%, prior preeclampsia 5.1%, family history of hypertension 12.8%, and preeclampsia 2.6% were less frequent in cases than controls (20.5%, 12.8%, 23.1%, and 10.3%, respectively). Gestational diabetes was also lower in cases 15.4% than controls 25.6%.

Vitamin D supplementation was higher in cases 64.1% than controls 51.3%. Sunlight exposure over 30 minutes was more common in cases 41.0% than controls 28.2%, while 15–30 minutes was higher in controls 43.6%. Moderate physical activity was more frequent among cases 53.8% and mild activity among controls 59.0%. Dairy intake was evenly distributed among cases; controls had a slightly higher proportion reporting low intake 38.5%.

Proteinuria was more severe in cases, with 33.3% showing ++ and 15.4% +++ levels, compared to 23.1% and 12.8% in controls. Negative results were lower in cases 17.9% than in controls 28.2%. Similar trends were seen in urine protein status.

A significant association was found between serum free testosterone levels and preeclampsia ($p = 0.030$), with high levels in 48.7% of cases versus 41.0% of controls.

Table 1: Socio-demographic characteristics of respondents by group classifications (Case vs Control).

Group Classification	Residence	Frequency	Percent
Case	Urban	34	87.2
	Rural	05	12.8
	Total	39	100
Control	Urban	27	69.2
	Rural	12	30.8
	Total	39	100
Age group			
Case	19-30	15	38.5
	30-40	11	28.2
	40+	13	33.3
	Total	39	100
Control	19-30	11	28.2
	30-40	11	28.2
	40+	17	43.6
	Total	39	100

Education Level			
Case	No formal education	02	5.1
	Primary	10	25.6
	Secondary	19	48.7
	Higher Secondary	06	15.4
	Graduate or above	02	5.1
	Total	39	100
Control	No formal education	03	7.7
	Primary	03	7.7
	Secondary	13	33.3
	Higher Secondary	14	35.9
	Graduate or above	06	15.4
	Total	39	100
Occupation			
Case	Housewife	32	82.1
	Service holder	04	10.3
	Businesswoman	03	7.7
	Total	39	100
Control	Housewife	21	53.8
	Service holder	09	23.1
	Businesswoman	07	17.9
	Other	02	5.1
	Total	39	100
Monthly Family Income (BDT)			
Case	<30,000	10	25.6
	30,000–50,000	26	66.7
	>50,000	03	7.7
	Total	39	100
Control	<30,000	06	15.4
	30,000–50,000	22	56.4
	>50,000	11	28.2
	Total	39	100

Table 1 shows among women with preeclampsia (Case), 87.2% resided in urban areas compared to 69.2% of controls. Age distribution was similar, though 43.6% of controls were aged 40+ versus 33.3% in cases. Educationally, only 20.5% of cases had higher secondary or above, compared to 51.3% of controls. Most cases were housewives (82.1%), while controls had more service holders (23.1%) and businesswomen (17.9%). Family income was lower among cases, with 25.6% earning <30,000 BDT and only 7.7% earning >50,000 BDT, compared to 15.4% and 28.2% in controls, respectively.

Table 2: Distribution of Health and Obstetric Profile of Respondents by Group Classification (Preeclampsia vs. Control).

Group Classification	BMI	Frequency	Percent
Case	Normal	14	35.9
	Overweight	03	7.7
	Obese	22	56.4
	Total	39	100
Control	Normal	16	41
	Overweight	05	12.8
	Obese	18	46.2
	Total	39	100
Presence of edema			
Case	None	05	12.8
	Mild	18	46.2
	Moderate	09	23.1
	Severe	07	17.9
	Total	39	100
Control	None	09	23.1
	Mild	21	53.8
	Moderate	04	10.3
	Severe	05	12.8
	Total	39	100
Gravida			
Case	Primi Gravide	31	79.5
	Multigravide	08	20.5
	Total	39	100
Control	Primi Gravide	16	41
	Multigravide	23	59
	Total	39	100
Parity			
Case	Primipara	32	82.1
	Multipara	07	17.9
	Total	39	100
Control	Primipara	24	61.5
	Multipara	15	38.5
	Total	39	100
Current gestational age (weeks)			
Case	20-30 weeks	07	17.9
	30-36 weeks	22	56.4
	30-40 weeks	10	25.6
	Total	39	100
Control	20-30 weeks	05	12.8
	30-36 weeks	08	20.5
	30-40 weeks	26	66.7
	Total	39	100

Table 2 illustrates obesity was more common among pre-eclampsia cases at 56.4% than controls 46.2%, while normal BMI was slightly higher in controls 41.0% vs. 35.9%. Edema severity was greater in cases, with only 12.8% showing no edema compared to 23.1% in controls, and 17.9% of cases had severe edema versus 12.8% in controls. Most cases were primigravida 79.5% and primipara 82.1%, in contrast to 41.0% and 61.5% in the control group, respectively. Gestational age at data collection was mostly 30–36 weeks in cases 56.4%, while 66.7% of controls were in the 36–40 weeks range.

Table 3: Distribution of Respondents by Previous Medical and Family History (Preeclampsia vs. Control).

Group Classification	Variables	Frequency	Percent
History of hypertension			
Case	Yes	03	7.7
	No	36	92.3
	Total	39	100
Control	Yes	08	20.5
	No	31	79.5
	Total	39	100
History of preeclampsia			
Case	Yes	02	5.1
	No	37	94.9
	Total	39	100
Control	Yes	05	12.8
	No	34	87.2
	Total	39	100
Family history of hypertension			
Case	Yes	05	12.8
	No	34	87.2
	Total	39	100
Control	Yes	09	23.1
	No	30	76.9
	Total	39	100
Family history of preeclampsia			
Case	Yes	01	2.6
	No	38	97.4
	Total	39	100
Control	Yes	04	10.3
	No	35	89.7
	Total	39	100
History of gestational diabetes			
Case	Yes	06	15.4
	No	33	84.6
	Total	39	100
Control	Yes	10	25.6
	No	29	74.4
	Total	39	100

Table 3 displays a smaller proportion of pre-eclampsia cases had a history of hypertension 7.7% compared to controls 20.5%. Similarly, history of preeclampsia 5.1% vs. 12.8% and family history of both hypertension 12.8% vs. 23.1% and preeclampsia 2.6% vs. 10.3% were all less common among cases than controls. The history of gestational diabetes was also lower in 15.4% than in controls 25.6%.

Table 4: Laboratory Investigation Findings (Proteinuria) Among Respondents by Group Classification.

Group Classification	Proteinuria	Frequency	Percent
Case	Negative	07	17.9
	Trace	09	23.1
	+	04	10.3
	++	13	33.3
	+++	06	15.4
	Total	39	100
Control	Negative	11	28.2
	Trace	09	23.1
	+	05	12.8
	++	09	23.1
	+++	05	12.8
	Total	39	100

Urine protein status			
Case	1+	05	12.8
	2+	01	2.6
	Negative	22	56.4
	Trace	11	28.2
	Total	39	100
Control	1+	03	7.7
	2+	03	7.7
	Negative	24	61.5
	Trace	09	23.1
	Total	39	100

Figure 2 displays vitamin D supplementation was slightly more common among cases 64.1% than controls 51.3%. Sunlight exposure over 30 minutes daily was higher in the case group 41.0% than in controls 28.2%, though controls had more in the 15–30-minute range 43.6% vs. 35.9%. Physical activity levels were similar, with more moderate activity in cases 53.8% and more mild activity in controls 59.0%. Dairy intake was evenly distributed among cases 33.3% across all frequencies), while controls had a slightly higher percentage reporting low intake 38.5% and fewer consuming dairy more than 5 times weekly 28.2%.

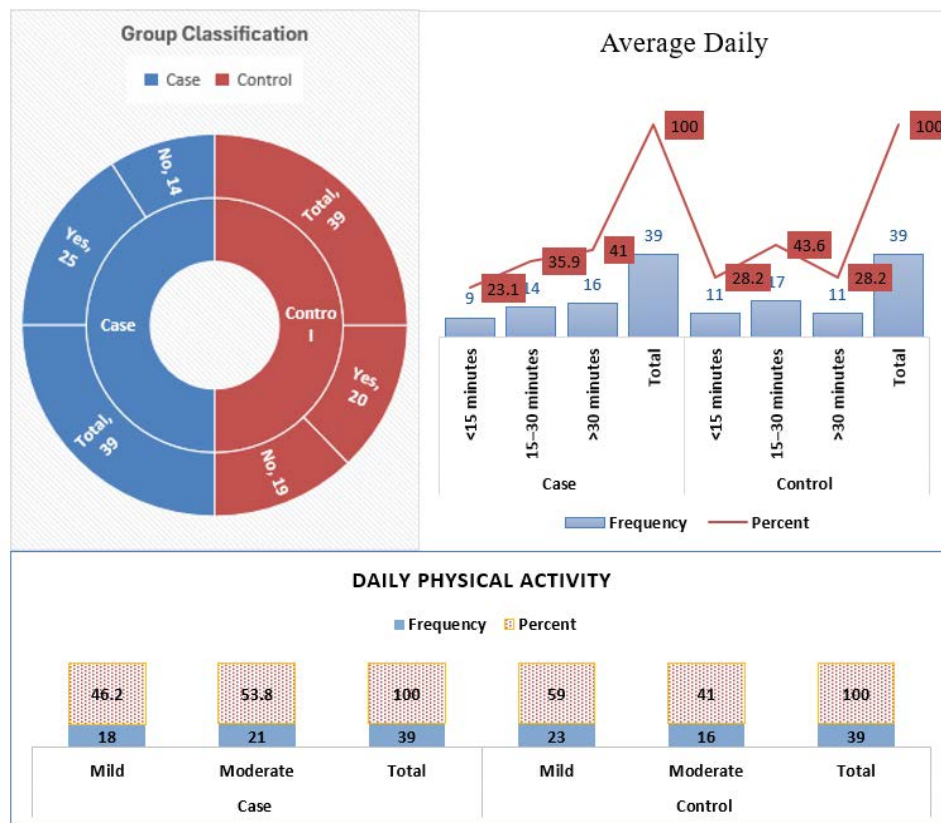


Figure 2: Behavioral Characteristics of Respondents by Group.

Table 4 shows proteinuria severity was higher among preeclampsia cases, with 33.3% showing ++ and 15.4% +++, compared to 23.1% and 12.8% in controls, respectively. Fewer cases were negative for proteinuria 17.9% versus controls 28.2%. In urine protein status, 12.8% of cases had 1+ and 2.6% had 2+, while 56.4% tested negative and 28.2% had trace amounts. Among controls, 61.5% were negative, 23.1% had trace, and 7.7% each had 1+ and 2+, indicating milder proteinuria in the control group.

Table 5: Association between Serum Free Testosterone Levels and preeclampsia.

Group Classification	Serum Free Testosterone Levels		p-value
	Normal	High	
Case	23	19	0.030*
Control	16	20	
Total	39	39	

* χ^2 test was done. *Level of significance $p < 0.05$ at 95% CI.

Table 5 demonstrates high serum free testosterone levels were more prevalent among women with preeclampsia 48.7% compared to controls 41.0%, with a statistically significant association observed between testosterone levels and preeclampsia $p = 0.030$, suggesting a potential hormonal link to the condition.

Discussion

This study demonstrated a statistically significant association between elevated serum free testosterone levels and the occurrence of preeclampsia ($p = 0.030$), with a greater proportion of affected women exhibiting high levels compared to normotensive controls. These findings align with previous studies from the Indian subcontinent and other regions, including a recent meta-analysis that supports a hormonal contribution to preeclampsia pathogenesis [8,9,20]. Venkatesha et al. [8] and Jain et al. [9] reported elevated maternal total testosterone levels in preeclamptic women, reinforcing our observation that the biologically active free testosterone fraction may play a more direct role in disease development.

Free testosterone, as measured in our study, represents an unbound, physiologically active form capable of exerting vascular and placental effects. Previous research has highlighted its influence on endothelial function and trophoblast invasion key mechanisms in preeclampsia pathophysiology [6,7]. Moreover, a growing body of evidence supports the interplay between the androgen pathway and angiogenic imbalance in preeclampsia, complementing the traditionally emphasized roles of the renin-angiotensin system and anti-angiogenic factors [5,15].

The high burden of preeclampsia in low- and middle-income countries, particularly in Bangladesh and across

the Indian subcontinent, underscores the need for locally relevant biomarkers and early predictors [2,3]. Our findings contribute to this understanding by providing evidence from a Bangladeshi cohort, aligning with national studies that have also reported elevated free testosterone levels in preeclamptic pregnancies [18,19]. These results suggest the potential of free testosterone as a biomarker for early identification of preeclampsia risk in resource-limited settings.

Additionally, socio-demographic differences observed in our study such as higher rates of urban residency, lower educational attainment, and lower income among preeclampsia cases are consistent with known risk factors for adverse pregnancy outcomes [16,17]. While our primary focus was the hormonal association, future research should explore how these social determinants may interact with endocrine pathways, including androgen metabolism, in the development of preeclampsia.

Conclusion

This study identified a significant association between elevated serum free testosterone levels and the occurrence of preeclampsia among primigravid women in Bangladesh. The findings support growing evidence that androgens, particularly free testosterone, may contribute to the pathophysiology of pre-eclampsia by influencing vascular and placental function. Given the high burden of hypertensive disorders in pregnancy in low- and middle-income countries, serum free testosterone may serve as a promising biomarker for early identification and risk stratification of preeclampsia. Future large-scale, prospective studies are recommended to validate these findings and explore their clinical utility in maternal health interventions.

Declaration of Interest

The authors declare no competing interests.

Conflict of Interest

The authors have no conflicts of interest to disclose related to this study.

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