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Association between Pre-Eclampsia and Spontaneous Prelabour Rupture of Membrane (Prom) in Pregnancy

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Abstract **Original Research Article**

Background: Pre-eclampsia and other hypertensive disorder in pregnancy are among the top causes of maternal and perinatal death globally. About 10% of all pregnancies have pre labor (premature) rupture of membranes (PROM), of which 7%–8% occur after 37–42 weeks. The objective of the study was to observe if pre-eclampsia is associated with spontaneous PROM. ***Method:*** Eighty (80) eligible pregnant women with gestational age ≥20 weeks were included in this study. They were divided into 2 equal case and control groups; 40 pregnant women with Pre-eclampsia and 40 pregnant women with normal blood pressure. The association of the risk of spontaneous PROM was assessed among these groups. ***Results:*** In this study 87.5% of the Pre-eclampsia case group and 75% of the normotensive control group were primigravida. There was a significant association between the gestational age of 82.5% of the Pre-eclampsia group and 70% of the normotensive group being full term (p=0.034). In the Pre-eclampsia group, there were 29(72.5%) PROM with a significant association (p=0.010), whereas in the normotensive group, there were 4 (10%) PROM with no significant association. The risk of PROM was found among Pre-eclampsia patients. ***Conclusion:*** In this study, we concluded that Pre-eclampsia is associated with the risk of spontaneous PROM.

Keywords: Pre-eclampsia, Spontaneous Pre-labor rupture of membrane.

INTRODUCTION

Pre-eclampsia is defined as new hypertension presenting after 20 weeks with one or more new-onset features, including significant proteinuria or maternal organ dysfunction, such as renal insufficiency, liver involvement, neurological complications or haematologicalcomplications [1]. It affects 5% to 7% of all pregnant women but has the highest morbidity and mortality that result in more than 700,000 maternal fatalities and 50,000 fetal deaths annually across the globe. In addition, it is a significant contributor tocesarean section, critical care hospitalizations, and preterm labor in the United States [2, 3]. Prelabor (premature) rupture of membranes (PROM) is the fetal membranes rupture at term prior to the onset of labor, but labor fails to start [4]. About 10% of pregnancies are affected by PROM, with 7%– 8% of cases occurring beyond 37 weeks (Term PROM) and 2% occurring between 24- 37 weeks (Preterm PROM) [5]. Mothers and newborns may have a number of negative effects as a result of PROM, including respiratory distress syndrome, intraventricular hemorrhage, infection, and even death [6]. Association of many risk factors including Gestational hypertension and pre-eclampsia with PROM were explored in some studies from abroad with different observations [7-9].

In Bangladesh, diseases associated to eclampsia are the second highest direct cause of obstetric mortality and account for 24% of all maternal

deaths [10]. As in many low- and middle-income nations, the majorities of pregnant women in Bangladesh who develop Pre-eclampsia are never identified nor treated [11]. Moreover there are not much studies conducted on both Pre-eclampsia and PROM. So this study was carried out to investigate the association between Pre-eclampsia and spontaneous PROM in pregnancy.

METHOD

This Case-control study was conducted between August 2021 and July 2022 in the department of Obstetrics and Gynaecology, Shahabuddin Medical College Hospital, Gulshan- 2, Dhaka and Gulshan Maa-O-Shishu Clinic, Progati Sarani Road, Dhaka. Eighty (80) pregnant women with a gestational age ≥20 weeks who met the selection criteria were included in the study. Women between 16 to 39 years of age with a singleton pregnancy, gestational age 24- 41 weeks and parities of 1 to 7 were included. Women with Multiple pregnancy, polyhydramnios, congenital uterine anomalies, vaginal spotting or bleeding, urinary tract infections, chorioamnionitis and other medical conditions (such as chronic hypertension, diabetes mellitus, chronic kidney disease and cardiovascular disease) were excluded from the study. They were informed of the purpose of the investigation, and their verbal agreement was obtained. A custom-designed questionnaire was used to gather the data. Forty (40) pregnant women diagnosed with Pre-eclampsia at a gestational age ≥ 20 weeks were in the case group A. Group B, the control group, consisted of 40 pregnant women with normal blood pressure. For each woman a through obstetric and gynaecological history as well as social history, previous medical history and family history were documented. In cases with PROM, a history of visualizing a large flow of clear vaginal fluid or a constant trickle of fluid before to the commencement of labor was usually sufficient to make the diagnosis. The length of fluid leaking, whether there was a history of lower abdomen discomfort or vaginal bleeding, and if there was a history of prior prelabor rupture of membranes were noted. Then each woman had a complete physical examination including BMI calculation and blood pressure measurements twice with a 5 minutes rest interval. Abdominal exam was done to determine the symphysio-fundal height, the fetal heart rate and the frequency of uterine contractions. Sterile per- speculum examination was done to confirm PROM. Necessary biochemical tests for management and confirmation of Pre-eclampsia were done along with abdominal ultrasounds for pregnancy profile.

STATISTICAL ANALYSIS

Using the statistical program SPSS 23, data analysis was done (Statistical Packages for Social Sciences, version 23). Simple frequency, percentage, mean, standard deviation, and range calculations were used to show the data. The significance of the difference between two independent means or the difference between the three separate means (quantitative data) was examined using the Students*t* test or the ANOVA *t* test, respectively. Whenever necessary, the Fisher exact test was used in conjunction with the Pearson chi-square test ($\chi 2$ test) to determine the significance of the differences between various percentages (qualitative data). The P value was regarded as significant if it was ≤ 0.05.

ETHICAL CONSIDERATION

The study was carried out in accordance with the ethical standards set out in the Helsinki Declaration. Before a sample was obtained, it was done with the patient's informed verbal consent. This permission was obtained after a local ethics committee evaluated and approved the research protocol, subject information, and consent form.

RESULTS

The mean maternal age of patients in the 2 groupswas 20.3±5.2 for those with Pre-eclampsia, 26.4±5.8 for normotensive group. There were more patients in the Pre-eclampsia group who aged <25 years (n = 32, 87.5%) than in the normotensive group (27, 67.5%), which showed a significant difference (P = 0.016). There was no significant difference between the groups and level of education (p=0.139). The prevalence of maternal BMI of 18.5-23.9 was 33 (82.5%) for Pre-eclampsia group and 3 (85%) for normotensive group, with no significant difference among both the groups (P = 0.734). In regards to gestational age, 82.5% of the Pre-eclampsia group and 70% of the normotensive group was of full term. There was significant association between both the group and gestational week (P = 0.034).There was significant difference among study groups and parity (P = 0.012); 87.5% in the Pre-eclampsia group and75% in the normotensive group were primigravida.

Tale 1: Socio-demographic characteristics of study group

Characteristics	Normotensive n= 40 (%)	Pre-eclampsia n=40 (%)	P value
Age			
16-25	27 (67.5)	32 (87.5	
26-35	11 (7.5)	8 (25)	**0.016**
≥36	2 (5)	-	
Mean ± SD	26.4±5.8	20.3±5.2	

Level of Education Primary/Secondary High school/college Diploma/Graduate	 2 (5) 25 (62.5) 13 (32.5)	 6 (15) 20 (50) 15 (37.5)	 **0.139**
BMI <18.5 18.5-23.9 ≥24	 4 (10) 34 (85) 2 (5)	 4 (10) 33 (82.5) 3 (7.5)	 **0.734**
Gestational week <37 ≥ 37 **Mean ± SD**	 12 (42.5) 28 (70) 23.6±2.2 (20–29)	 7 (17.5) 33 (82.5) 23.9±2.8 (19–31)	 **0.034**
Parity 1 ≥ 2	 30 (75) 10 (25)	 35 (87.5) 5 (12.5)	 **0.012**

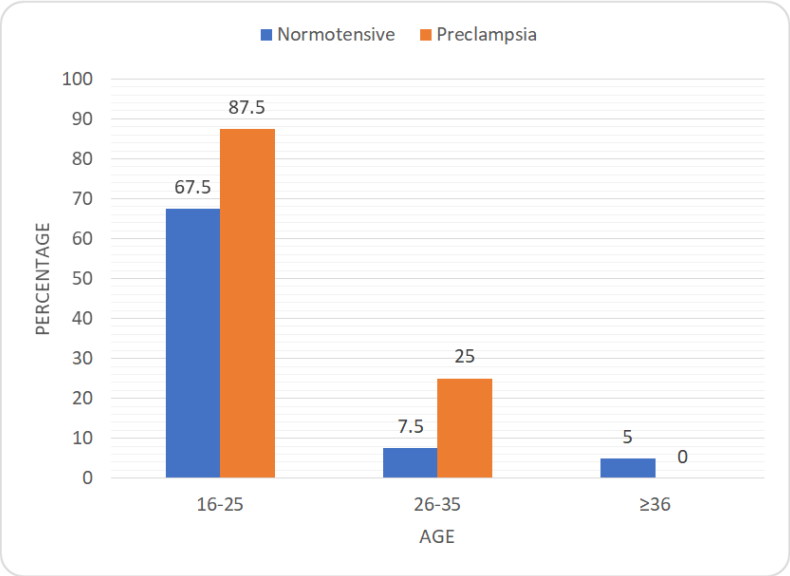

Fig. 1: Distrubution of groups according to age

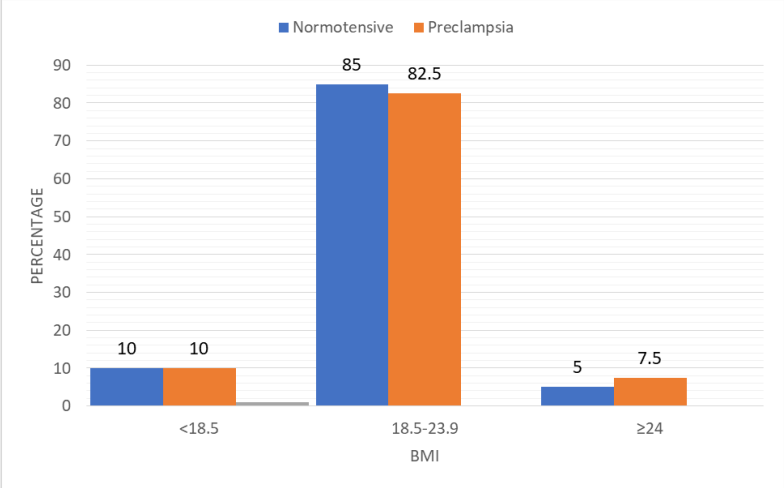

Fig. 2: Distribution of groups according to BMI

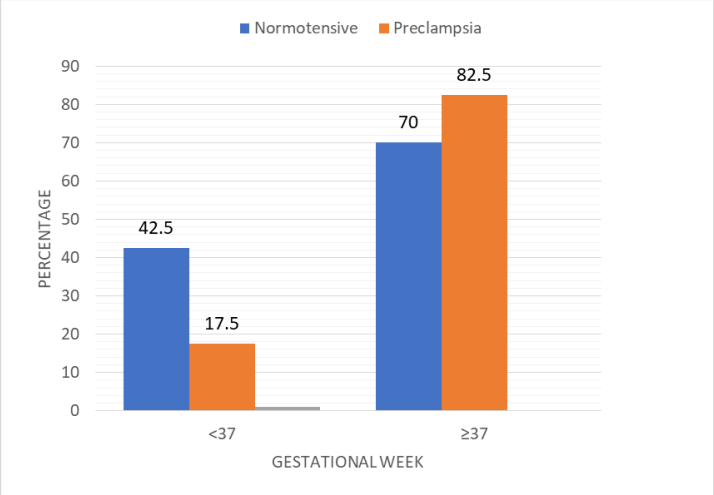

Fig. 3: Distribution of groups according to gestational week

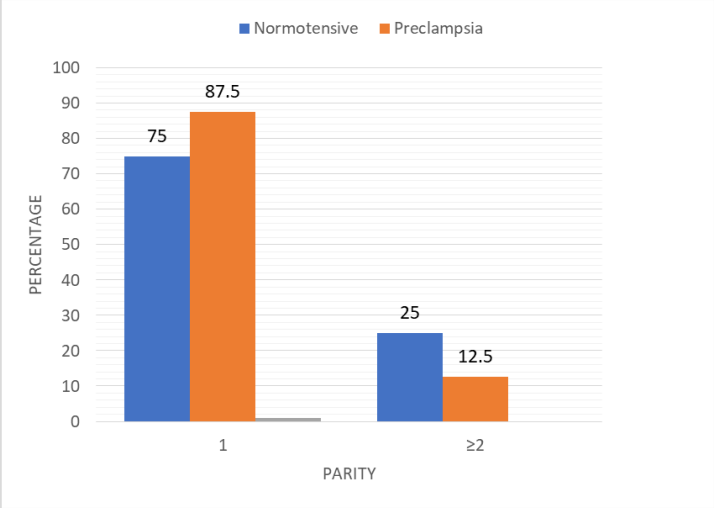

Fig. 4: Distribution of groups according to parity

Table 2: Association of spontaneous PROM and Pre-eclampsia and normotensive patients

Study group	PROM		P value
	Yes	No	
	n (%)	n (%)	
Pre-eclampsia	29 (72.5)	11(27.5)	**0.010**
Normotensive	4 (10)	36 (90)	**0.124**

In the Pre-eclampsia group, 29 (72.5%) of 40 patients with PROM show a significant association (P = 0.010), but in the normotensive group, 4 (100%) of 40 patients with PROM had no significant association (P = 0.124).

DISCUSSION

Pre-eclampsia of pregnancy and other hypertensive diseases are among the top causes of maternal and perinatal death globally [12]. It complicates 3%–5% of all pregnancies [13]. On the other hand Pre-labour Rupture of Membranes (PROM) is also an important cause of maternal and fetal morbidity and increased rate of cesarean section delivery [14]. In this study, we analyzed Pre-eclampsia patients with normotensive patients to determine the association between spontaneous PROM and Pre-eclampsia after omitting possible confounding variables such as multiple pregnancy, polyhydramnios, congenital uterine anomalies, vaginal spotting or bleeding, urinary tract infections, chorioamnionitis and other medical conditions. In the present study there was a statistically significant association between Pre-eclampsia and the mean maternal age of patients in each study group. There were more patients in the Pre-eclampsia group (n = 32, 87.5%) aged <25 years than in the control group. Although it is generally known that advanced maternal age (35 years or older) is associated with an increased risk of Pre-eclampsia but our

observation was similar to other studies by Wenas *et al.,* (2022) [15], Tebeu *et al.,* (2011) [16] and Adeyinka *et al.,* (2010) [17] who also observed that Pre-eclampsia and other hypertensive disorders of pregnancy are more common in younger patients.

Primigravida made up 87.5% of the Pre-eclampsia group in our study compared to the normotensive 75% in the control group. This supports the fact that nulliparous women have a higher chance of developing Pre-eclampsia [18, 19]. Majority of our patients with PROM were at term. This finding also coincides with the finding of the study by Wenas *et al.,* (2022) [15]. At term, the expression of the relaxin gene is enhanced, which increases MMP-3 and MMP-9 activities in the fetal membrane, resulting in the degradation of collagen and the ruptures of membrane [20].

In this study, 29 (72.5%) of the 40 patients in the Pre-eclampsia case group had PROM, which was statistically significant (p=0.010) compared to the 4 (10%) in the normotensive control group. The study by Wenas *et al.,* (2022) [15] concluded that gestational hypertension is associated with the risk of PROM and Pre-eclampsia is not associated with the risk of PROM. But the study by Liu *et al.,* (2019) [7] concluded that both gestational hypertension and pre-eclampsia were associated with an increased risk for PROM.

Though pre-eclampsia has been linked to PROM, the exact mechanism is yet unknown. Through the stimulation of oxidative stress and elevation of associated cytokines, chemokines, and molecules, hypertension may maintain the body in a low-grade inflammatory state [21]. Once an infection or inflammation has taken place, the host will react by causing the fetal membranes to produce prostaglandins, which may lead to uterine irritability and collagen breakdown inside the membranes. As a result, the fetal membranes may be vulnerable and simple to rupture. Additionally, the buildup of inflammatory molecules in the uterus, membranes, and placenta might result in irregular uterine contractions, which could ultimately result in membrane rupture [22].

CONCLUSION

In this study, we concluded that Pre-eclampsia is associated with the risk of spontaneous PROM.

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