

## Risk Factors of Pre-Eclampsia: A Case-Control Study

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### Abstract

*Introduction:* The risk factors of pre-eclampsia have to be identified early in order to prevent eclampsia, placental abruption and other life-threatening complications to mother and newborn. *Objectives:* 1. To find association between psychological stress and pre-eclampsia. 2. To study the risk factors of pre-eclampsia among pregnant women admitted for delivery in a district hospital. *Methodology:* This case-control study recruited 100 pregnant women diagnosed with pre-eclampsia and 200 gestational age-matched controls. Age of the mother, parity, diet, previous abortion, pre-pregnancy BMI, gestational diabetes, family history of hypertension and multiple gestation were assessed. Psychological stress was assessed using Cohen's PSS-10 instrument. Crude and adjusted odds ratios were calculated. *Results:* Median PSS score was 14 among cases and 13 among controls. (P value = 0.045). Being a homemaker (aOR = 2.67; 1.32-5.38), first pregnancy (aOR = 3.13; 1.771-5.534), history of previous abortion (aOR= 1.61; 1.23-9.53), oral contraceptive pill use within one year of pregnancy (aOR= 7.88; 1.66-37.40) and BMI > 23 kg/m<sup>2</sup> (aOR = 2.40; 1.35-4.29) showed significant association with pre-eclampsia. *Conclusion:* Interventions to manage emotional stress during pregnancy may be helpful in preventing the development of pre-eclampsia. Antenatal care should focus on these risk factors and prevent complications of pre-eclampsia.

**Keywords:** Antenatal Care; Cohen's Perceived Stress Scale; Hypertensive Disorders of Pregnancy; Maternal Health; Pre-Eclampsia; Psychological Stress.

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### Background

Chronic hypertension, preeclampsia-eclampsia,

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**Received on** December 13, 2016

**Accepted on** December 28, 2016

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preeclampsia superimposed on chronic hypertension, and gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy) are the four conditions included under hypertensive disorders of pregnancy [1]. They are an important cause of maternal and child mortality, complicating up to 8% of all pregnancies [2]. The most frequently encountered hypertensive state is pre-eclampsia, seen in 4-7% of all pregnant women in developing and developed countries [3]. Almost 5% of maternal mortality in India is attributed

to hypertension [4]. Developing countries like India contribute more than one half of the global burden of maternal deaths.

The pathogenesis of pre-eclampsia has been explained by several theories which incriminate immune-based and environmental factors in the causation [2]. Pregnancy at above 30 years of age and primigravid status, having a history of hypertensive disorders during pregnancy in self or family and having coexistent diabetes, chronic hypertension and renal diseases are shown to place the mother at an increased risk of developing pre-eclampsia [5-10]. Similar suspicions have been seen in studies from India and other countries, but there is lack of uniformity and consistency in the findings [8,11-13].

Few systematic reviews have raised questions about the reliability of the findings from these studies from across the world [14-20]. Pre-eclampsia and gestational hypertension are situations with high corticotrophin-releasing hormone and sympathetic activity, which correlate well with psychological stress [21]. Psychological stress, as a risk factor, is amenable to interventions. Efforts to manage stress can improve maternal and foetal outcomes.

This study sought to find out the risk factors of pre-eclampsia and the association of perceived emotional stress with pre-eclampsia with a case-control design.

## Methodology

Present study was undertaken in the antenatal clinic of Mc Gann Teaching Hospital, a tertiary care hospital attached to Shivamogga Institute of Medical Sciences in Shivamogga. Pregnant women with hypertension and proteinuria after the 20th week of gestation qualified for enrolment as cases. Diagnosis was made by the consulting obstetrician. Controls were pregnant women matched against cases for gestational age. Deliveries in private hospitals and nursing homes and home deliveries were not a part of this study. Ethical clearance was obtained from Institutional Ethics Committee of Shivamogga Institute of Medical Sciences. Subjects were interviewed only after obtaining their informed consent.

In order to detect a minimum odds ratio of 3, with power 80% and confidence level 95%, we enrolled 100 cases and 200 controls. We could enrol the required number of cases of pre-eclampsia during a time period of six months from February to June 2015 from the antenatal clinic. Pregnant women from the same day's out-patient consultation were enrolled as

controls through random sampling. For every case, we selected two controls of the same gestational age as of cases. We recorded information on sociodemographic factors such as age, religion, education and occupation from the cases and controls using a pretested and semi-structured questionnaire.

Body-mass index (BMI) was studied for its association with presence of pre-eclampsia. BMI was calculated by dividing weight of the subject in kilograms divided by square of the height in metres. Height and weight measurements made during the first antenatal visit were recorded for calculating BMI. For classifying and comparing BMI groups, BMI cut-offs for Asian population were used [22].

Perceived emotional stress was measured using Cohen's Perceived Stress Scale (PSS-10). PSS-10 is an internationally used questionnaire to measure perceived emotional stress across various population groups [23]. Psychological stress is defined as the extent to which people perceive that their demands exceed their ability to cope [24]. Cases and controls were administered the PSS-10 instrument after piloting with Kannada-translated questions from the original scale, as Kannada is the local language. Interviewers were trained in the Kannada version of this scale and were blinded to case-control status of the study participants. There are 10 items in the PSS-10 instrument, each having a sub-score from zero to five. Total scores above 20 are considered as high stress.

Various proportions were compared with the  $\chi^2$  test for which a p-value of less than 0.05 was considered to be statistically significant. Crude and adjusted odds ratios with their 95% confidence intervals were calculated. SPSS software version 20 (IBM Corporation, USA) was used for statistical analysis.

## Results

We analysed the data from a total of 300 subjects, which comprised of 100 cases of pre-eclampsia and 200 controls matched by gestational age. Majority of the study participants belonged to the age group of 21 to 25 years. Cases and controls were comparable as regards age, residence and religion. Working women constituted 14% of cases and 36% of controls (crude OR=3.2; 1.71-6.14). Sociodemographic characteristics of the subjects are displayed in Table 1.

Pre-eclampsia was found to be 2.85 times common in the first pregnancy (*primigravid*) compared to second and higher order pregnancies (crude OR = 2.85; 1.74-4.67). Any number of abortions in the past

was recorded as a positive history of abortion. History of an abortion was present in 28% of cases and 7.5% of controls (crude OR = 4.98; 2.42-9.50).

Among cases of pre-eclampsia, 70% had BMI more than 23 kg/m<sup>2</sup>, while 53% of the controls had BMI less than 23 kg/m<sup>2</sup>. Only 28% of the cases had a normal BMI of 18-22.9 kg/m<sup>2</sup>.

Among women with second and higher order pregnancies, history of hypertension in the previous pregnancy was present in 17% of the present cases of pre-eclampsia, whereas only 7% of the controls had such a history. Recurrence of pre-eclampsia was found to be 2.88 times common among women with hypertension in their previous pregnancy compared to controls (crude OR = 2.88; 1.01-8.29).

**Table 1:** Socio-demographic characteristics and parity of cases and controls

Sl. No.	Characteristics	Cases (Total = 100)	Controls (Total = 200)	P-value*
1.	<b>Age (years)</b>			
	≤20	20 (20%)	19 (9.5%)	
	21-25	43 (43%)	144 (72%)	
	26-29	22 (22%)	01 (0.5%)	
	≥30	15 (15%)	36 (18%)	
	Median age	23	24	0.09
2.	<b>Residence</b>			
	Rural	57 (57%)	124 (72%)	0.45
Urban	43 (43%)	76 (28%)		
3.	<b>Religion</b>			
	Hindu	79 (79%)	158 (94%)	1.00
Muslim	21 (21%)	42 (6%)		
4.	<b>Occupation</b>			
	Homemaker	86 (86%)	132 (66%)	<0.001
Working	14 (14%)	68 (34%)		
5.	<b>Parity</b>			
	First pregnancy	60 (60%)	69 (35%)	<0.001
Second and above	40 (40%)	131 (65%)		

\*p-value less than 0.05 was considered to be statistically significant.

**Table 2:** Comparison of Perceived Stress Scale (PSS) scores of cases and controls

Parameters	Cases (100)	Controls (200)	p-value*	OR (95% CI)
Median	14	13	0.045	1.294 (0.646-2.593)
IQR	7	5		
Scores < 20	85	176		
Scores ≥ 20	15	24		

\*p-value less than 0.05 was considered to be statistically significant.

**Table 3:** Multivariate analysis of risk factors of pre-eclampsia

No.	Characteristics	Adjusted OR (95% CI)	Comparison	p-value*
1.	<b>Occupation</b>			
	Homemakers	2.669 (1.324-5.378)	Working women	0.006
Working women				
2.	<b>Parity</b>			
	First pregnancy	3.131 (1.771-5.534)	Second and higher	0.45
Second and higher				
3.	<b>Previous abortion</b>			
	Yes	1.612 (1.229-9.527)	No abortion	0.01
No				
4.	<b>OCP use</b>			
	Yes	7.881 (1.661-37.402)	Not used OCP	0.009
No				
5.	<b>BMI</b>			
	> 23 kg/m <sup>2</sup>	2.406 (1.350-4.286)	BMI < 23 kg/m <sup>2</sup>	0.003
≤ 23 kg/m <sup>2</sup>				

\*p-value less than 0.05 was considered to be statistically significant.

Among cases, 13% of women reported having taken oral contraceptive pills (OCPs) in the past one year, whereas only 1% of the controls used OCPs in the past one year (crude OR = 4.83; 1.78-13.13).

#### *Perceived Stress Scale (PSS) Scores*

The median PSS score among cases was found to be 14, while the median PSS score among controls was found to be 13. Statistically significant difference was observed between the scores of cases and controls when the medians were compared by Mann-Whitney U Test. Details are tabulated in Table 2.

All independent variables were included in multivariate logistic regression. The adjusted Odds ratios are displayed in Table 3. Not working (being a homemaker), first pregnancy, history of previous abortion, BMI more than 23 kg/m<sup>2</sup> and OCP use within past one year showed retained significant association with pre-eclampsia.

### **Discussion and Conclusion**

The ideal setting for studying the risk factors would have been the homes of the women. We undertook this study in the district hospital where a large proportion of all deliveries in Shivamogga take place. Information required on several variables in this study is not routinely available from the antenatal record entries of the women. Direct interviews helped collect all the required exposure information. However, the exposure assessment is not free from recall and selection biases.

Cases and controls did not differ systematically and thus, were mutually comparable. Our findings are similar to the findings from several studies from India and other countries [8]. Pre-eclampsia was seen to occur significantly in the first pregnancies. In the subsequent pregnancies, maternal-foetal HLA sharing results in a state of histo-incompatibility and consequently, successful pregnancy.<sup>25</sup> Homemakers were more likely to have pre-eclampsia compared to working women, which was also observed in a study by Ghojazadeh *et al* among Iranian women, and contrary to the finding by Klonoff-Cohen *et al* that working women had higher risk of pre-eclampsia compared to housewives [26,27]. Spontaneous abortions are often accompanied by other conditions like infertility that increase the risk of pre-eclampsia. A large cohort study on Norwegian mothers did not find any differences in risk among cases and non-

cases with respect to history of previous abortion, which is contrary to our finding. However, both studies did not differentiate between spontaneous and induced abortions [28]. The unanimous finding has been that a history of term pregnancy (> 37 weeks) offers substantial protection against developing pre-eclampsia in subsequent pregnancies [29].

As seen in the present study, a systematic review had shown that pre-pregnancy body mass index determines the risk of development of pre-eclampsia and recommended pre-pregnancy weight-reduction measures to prevent the same [30].

Our study showed that cases of pre-eclampsia had higher levels of perceived emotional stress compared to controls. Kurkiet *al* had similar findings, suggesting that stress reduction measures can protect against pre-eclampsia [31,32]. Distress conditions during pregnancy increase cortisol levels, thereby causing endothelial dysfunction [33]. The findings in a case-control study by Rossi *et al* contradicted this theory and stated that pressor reactivity in pre-eclampsia could not be attributed entirely to psychological stress [34].

A prospective cohort study would help in accurate sketching of the role of risk factors in pre-eclampsia and in assessing the pregnancy outcomes. Present study, however, identifies a set of determinants which can be easily identified among women during antenatal registration. Evidence of biological mechanisms of emotional stress as an agent of pre-eclampsia are substantial. Interventions to manage emotional stress during pregnancy may be helpful in preventing the development of pre-eclampsia. The findings from this study takes forward the discussion on early identification of high-risk conditions by healthcare workers at the district level. Community level workers can identify these conditions are play a significant role in averting complications and thus, ensuring a healthy mother and child at the end of pregnancy [35].

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