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Risk Factors of Pre-Eclampsia: A Hospital Based Case Control Study

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ABSTRACT

Introduction: Hypertension, complicating 5 to 7% of all pregnancies, is a leading cause of maternal and fetal morbidity, particularly due to pre-eclampsia, pre-eclampsia contributes about 8 to 10% of maternal deaths in India.

Methodology: Hospital based case control study; cases were women in post-natal period within 2 days of delivery suffering from pre-eclampsia Controls were Women in post-natal period within 2 days of delivery not suffering from pre-eclampsia of same age (±2 years) as that of cases.

Results: Significant independent risk factors of pre-eclampsia. found were first degree relative with HTN (OR = 5.0; 95% CI 3.2 – 8) ;Twin gestation (OR = 4; 95% CI 1.3 - 12.2) ,Family history of pre-eclampsia (OR = 3.7; 95% CI 1.2 - 11.2), Absence of essential obstetric care (OR = 3; 95% CI 1.8 – 5), History of PIH in previous pregnancy (OR = 2.8; 95% CI 1.5 – 5.0), History of abortion in previous pregnancy (OR = 2.8; 95% CI 1.3 - 5.9), Pre pregnancy BMI (OR = 2.7; 95% CI 5.1 –1.4)

Conclusion: If greater awareness of the associated risk factors leads to earlier diagnosis and improved management, there may be scope for reducing a proportion of the morbidity and mortality from preeclampsia.

Keywords: Preeclampsia, risk factors, case control study, PIH

INTRODUCTION

Preeclampsia is a multisystem disorder of unknown aetiology characterized by development of hypertension to the extent of 140/90 mm Hg or more with proteinuria after 20 weeks in previously normotensive and nonproteinuric patient.[1] Hypertension, complicating 5 to 7% of all pregnancies, is a leading cause of maternal and fetal morbidity, particularly when the elevated blood pressure (BP) is due to pre- eclampsia, either alone (pure) or "superimposed" on chronic vascular disease.[2]

Pre-eclampsia is a major cause of pre- term birth and an early marker for future cardiovascular and metabolic diseases, whereas preterm delivery is associated with immediate neonatal morbidity and has been linked to remote cardiovascular and metabolic disease in the newborns. [2]

Incidence of pre-eclampsia 2.8% of live births for developing countries and 0.4% of live births in developed countries.[3] Pre-eclampsia contributes about 8 to 10% of maternal deaths in India and 5 to 10% of maternal deaths in western countries.[4] Though the cause for pre-eclampsia is unknown, there does appear to be certain risk factors associated with the condition. The factors that have been postulated to influence the risk of pre-eclampsia among the mothers include diabetes, renal disease, obesity, multiple pregnancy, primiparity, age above 30 years, personal or family history of pre-eclampsia, and chronic hypertension.[5]

Is it possible, therefore, to prevent pre-eclampsia and eclampsia? Eclampsia is almost always preventable. Good antenatal care will identify pre-eclampsia in the early stages and effective man-

agement will prevent a woman from developing complications.[6]

In developing countries, evidence on the association between these factors and pre-eclampsia is scarce. There are many studies in developed and some developing countries to assess the association between these factors and pre-eclampsia.[5]

Those that have been conducted have often had an inadequate control and lack of statistical power, resulting in inconclusive evidence for determinants of pre-eclampsia in developing countries.[5] In this context, a case-control study was conducted to elucidate some of the major risk factors for pre-eclampsia.

METHODS

This present hospital based case control study was conducted to study risk factors of pre-eclampsia at regional tertiary care center from January 2013 to August 2014. Institutional ethical committee of the tertiary care center approved the study.

The study population consisted of post-natal women admitted in the regional tertiary care center. The cases consisted of all postnatal women who were suffering from pre-eclampsia; diagnosed between 20 weeks of gestation to 48 hours after delivery. Study participants were interviewed within 2 days of delivery.

The diagnosis of pre-eclampsia had been made by obstetricians on the basis of blood pressure >140/90 mm of Hg and proteinuria of >300mg/24 hour urine sample.

Women in post-natal period within 2 days of delivery not suffering from pre-eclampsia were selected as control. Controls were of same age (±2 years) as that of cases.

The respondent was interviewed after obtaining consent. The predesigned and pretested proforma was used for interview. The respondent was free to leave the study at any stage without any explanation. The questions were asked in a language and manner that the respondent understood. Adequate time was given in-between the questions to think, understand and answer. Privacy was maintained throughout the interview. Queries, if any, were answered to ensure participant's complete understanding and satisfaction.

The interview consisted of socio demographic history, obstetric history and anthropometric measurement, mental stress measured by using Perceived Stress Scale [7]

The sample size was estimated using the formula for proportions difference assuming the ratio of controls to cases as 1:1 with the level of significance 0.05 and power 0.8 using OpenEpi version- 3 open source calculator. Considering the proportion of women with multiparity (risk factor with least OR) among women with preeclampsia as 37% and proportion of women with multiparity among women without preeclampsia as 27 %, the sample size was estimated to be 360 cases and 360 controls.[5]

Statistics- The data of respondents was collected, compiled and then entered in MS Excel 2008 worksheet. It was analyzed using SPSS (Statistical Package for Social Sciences) version 20.All the statistical tests were considered statistically significant whenever $p < 0.05$.

Further statistical analysis by multivariate analysis (i.e. Binary logistic regression) was done to calculate regression coefficient β, odds ratio with their 95% confidence intervals (CI), SE β, Z values of regression coefficients and p values by SPSS (Statistical Package for Social Sciences) version 20 to analyze independent risk factors associated with pre-eclampsia.

RESULTS

Age distribution in present study ranged from 18-38 years with mean age of cases and controls 23.19 ± 4.12 and 23.28 ± 4.05 years respectively. There was no significant difference between cases and control according to religion, area of residence, occupation, socio economic status, type of family, past history of tobacco addiction. (Table-1) There was significant difference among cases and controls with respect to education, family history of pre-eclampsia, history of HTN ,DM in first degree relative, history of PIH in previous pregnancy, history of GDM in pregnancy, Absence of essential antenatal care, parity, Twin gestation, Increase in BMI.

DISCUSSION

The present case control study was conducted in a Tertiary care centre; Our study showed that maximum cases of pre-eclampsia were having maternal age < 20 years as similarly observed in other study. [8]

There was no significant difference between cases and control according to religion.

This finding was similar to the findings observed by Shamsi U et al.[9] while studies like Manandhar BL et al. (2013)[10] showed increased risk of pre-eclampsia in non-Hindu women.

Table -1 Distribution of participants according to socio-demographic factors with univariate analysis-

Socio-demography	Cases (n=360) (%)	Controls (n=360) (%)	Total (n=720) (%)	p value	OR(CI)
Religion					
Hinduism	139 (38.6)	154 (42.8)	293 (40.7)	> 0.05	Ref
Islamic	165 (45.8)	142 (39.4)	307 (42.6)		0.7(0.56 to 1.1)
Buddhist	56 (15.6)	64 (17.8)	120 (16.7)		1.03(0.67 to 1.59)
Residence					
Urban	163 (45.3)	159 (44.2)	322 (44.7)	> 0.05	Ref
Rural	197 (54.7)	201 (55.8)	398 (55.3)		1.04 (0.78-1.40)
Education					
Illiterate	46 (12.8)	37 (10.3)	83 (11.5)	<0.05	Ref
Primary	25 (6.9)	18 (5.0)	43 (6.0)		0.9(0.42 to 1.88)
Middle	89 (24.7)	91 (25.3)	180 (25.0)		1.3(0.75 to 2.14)
High School	110 (30.6)	142 (39.4)	252 (35.0)		0.8(0.5-1.3)
Intermediate	66 (18.3)	66 (18.3)	132 (18.3)		0.8(0.5-1.3)
Graduate	24 (6.7)	6 (1.7)	30 (4.2)		3.2(1.2-8.7)
Occupation					
Housewife	299 (83.1)	289 (80.3)	588 (81.7)	> 0.05	Ref
Laborer	45 (12.5)	38 (10.6)	83 (11.5)		1.1(0.7-1.8)
Farmer	9 (2.5)	24 (6.6)	33 (4.6)		0.4(0.5-0.8)
Own business	3 (0.8)	4 (1.1)	7 (1.0)		0.7(1.6-3.2)
Employed	4 (1.1)	5 (1.4)	9 (1.2)		0.77(0.2-2.9)
Socio-economic status					
I	8 (2.2)	3 (0.8)	11 (1.5)	> 0.05	Ref
II	95 (26.4)	86 (23.9)	181 (25.1)		0.4(0.1-1.6)
III	105 (29.3)	111 (30.8)	216 (30.0)		0.35(0.09-1.4)
IV	127 (35.4)	143 (39.8)	270 (37.6)		0.33(0.08-1.3)
V	25 (6.7)	17 (4.7)	42 (5.8)		0.5(0.12-2.3)
Type of Family					
Joint	264 (73.3)	263 (73.1)	527 (73.2)	p > 0.05	Ref
Nuclear	96 (26.7)	97 (26.9)	193 (26.8)		1.01 (0.72 – 1.41)

Agrawal AS, Walia GK (2007) [11] from cross sectional survey showed increase risk in Islam and Christian women. We didn't found significant difference in urban and rural population as similarly observed by Minire A et al. (2013)[12]. Agrawal AS, Walia GK (2007)[11] data from a cross sectional survey showed rural–urban variation, women residing in rural areas showed this discrepancy in results may be because of geographical variation

There was significant difference among cases and controls with respect to education similar with Agrawal AS, Walia GK (2007)[11] who observed that the prevalence odds of pre-eclampsia was also higher among educated. In present study occupation of postnatal women among cases and controls did not differ significantly, as observed by Shamsi U et al.[9]

In class I, 8 were cases and 3 were controls but there was no significant difference found between cases and controls according to socioeconomic status, similarly observed with Shamsi U et al. (2010)[9].

Out of 360 cases 4 (1.1%) had past history of hypertension and none of the controls had past history of hypertension, this difference was not statistically significant. But past history of hypertension was significantly associated with pre-eclampsia as shown in other study. [11] H/O DM was not significantly associated with pre-eclampsia; while other studies[5,9] showed significant association between history of diabetes and risk of pre-eclampsia/eclampsia. These disparities in results with other studies may be because other studies showed combined risk with pre-eclampsia or eclampsia and age distribution of study participants.

Family history of preeclampsia in first-degree relative was a significant risk factor for preeclampsia in our study , as similarly observed in study by Cincotta, R (1998).[13]

History of hypertension in first-degree relative found statistically significant as observed in previous studies.[5,9,12] This results suggest that family history of hypertension reflects genetic and behavioral factors whereby women may be predisposed to an increased pre-eclampsia risk.

History of diabetes in first-degree relative was a significant risk factor for preeclampsia in our study. This positive association between family history of diabetes, hypertension and pre-eclampsia risk was consistent with other studies. [15]

Table-2 Distribution of study participants according to risk factors with univariate analysis

Risk factors	Cases (n=360) (%)	Controls (n=360) (%)	Total (n=720) (%)	p value	OR(CI)
Past H/O HTN					
Present	4 (1.1)	0 (0.0)	4 (0.6)	> 0.05	_
Absent	356 (98.9)	360 (100.0)	716 (99.4)		
Past H/O DM					
Present	3 (0.8)	0 (0.0)	3 (0.4)	> 0.05	_
Absent	357 (99.2)	360 (100.0)	717 (99.6)		
Past H/O Tobacco addiction					
Present	1 (0.3)	4 (1.1)	5 (0.7)	> 0.05	0.24 (0.02-2.22)
Absent	359 (99.7)	356 (98.9)	715 (99.3)		
Family H/O Pre-eclampsia					
Present	23 (6.4)	5 (1.4)	28 (3.9)	< 0.01	4.84 (1.82 - 12.89)
Absent	337 (93.6)	355 (98.6)	692 (96.1)		
First degree relative with HTN					
Present	130 (36.1)	32 (8.9)	162 (22.5)	< 0.01	5.79 (3.7 – 8.83)
Absent	230 (63.9)	328 (91.1)	558 (77.5)		
First degree relative with DM					
Present	48 (12.3)	17 (4.7)	65 (9.0)	p< 0.001	3.1(1.7 - 5.5)
Absent	312 (86.7)	343 (95.3)	655 (91.0)		
Age at menarche					
11-13 years	182 (50.5)	171 (47.5)	353 (49.0)	p>0.05	
14-16 years	173 (48.1)	177 (49.2)	350 (48.6)		0.9(0.7-1.2)
17-19 years	5 (1.4)	12 (3.3)	17 (2.4)		0.4(0.13-1.13)
History of PIH in previous pregnancy					
Present	53 (14.7)	26 (7.2)	89(12.4)	< 0.05	2.2 (1.3 – 3.6)
Absent	307 (85.3)	334 (92.8)	631(87.6)		
History of GDM					
Present	10 (2.8)	2 (0.6)	12 (1.7)	< 0.05	5.11 (1.11 – 23.5)
Absent	350 (97.2)	358 (99.4)	708 (98.3)		
Essential obs care					
Absent	70 (19.4)	34 (9.4)	104 (14.4)	< 0.05	2.3 (1.49 – 3.59)
Present	290 (80.6)	326 (90.6)	616 (85.6)		
Parity					
Primiparity	202 (56.1)	143 (39.7)	345 (47.9)	< 0.05	1.94 (1.14 – 2.6)
Multiparity	158 (43.9)	217 (60.3)	375 (52.1)		
Gestation					
Twin	16 (4.4)	5 (1.4)	21 (2.9)	< 0.05	3.3 (1.19 – 9.11)
Singleton	344 (95.6)	355 (98.6)	699 (97.1)		
Abortion					
Present	37 (10.3)	13 (3.6)	50 (6.9)	< 0.01	3.05 (1.59 – 5.85)
Absent	323 (89.7)	347 (96.4)	670 (93.1)		
H/O Contraceptive use					
No contraceptive	312 (86.7)	315 (87.5)	627 (87.0)	> 0.05	
OC Pill	21 (5.8)	20 (5.6)	41 (5.7)		0.06(0.56-1.99)
Condom	19 (5.3)	16 (4.4)	35 (4.9)		1.2(0.6-2.4)
IUCD	8 (2.2)	9 (2.5)	17 (2.4)		0.9(0.3-2.35)
Mental stress					
Low Acuity	141 (39.1)	231 (64.2)	372 (51.7)	< 0.05	
Moderate Acuity	136 (37.8)	98 (27.2)	234 (32.5)		2.3(1.6-3.2)
High Acuity	83 (23.1)	31 (8.6)	114 (15.8)		4.4(2.7-6.9)
Pre-pregnancy BMI					
>25BMI	60 (16.7)	19 (5.3)	79 (11.0)	< 0.05	3.58(2.09 – 6.15)
<25 BMI	300 (83.3)	341(94.7)	641 (89.0)		

History of PIH in previous pregnancy increases the risk of pre-eclampsia as observed in previous studies.[8,16] The result of our study showing a relationship between pre-eclampsia and diabetes was also consistent with previous findings.[9,17] Increases the risk of pre-eclampsia, was also consistent with previous findings.[10,17] This results are comparable with other studies which shows primiparity as a risk factor for pre-eclampsia.[8,10,14,16,17] These results were comparable with other studies [5,18] which found that twin gestation was risk factor for pre-eclampsia. History of abortion in past pregnancy was found as significant risk factor for preeclampsia as similarly observed in previous studies.[10,18] In present study we found that there was no significant difference among cases and control with re-

spect to contraceptive use; Manandhar BL et al. (2013)[10] use of modern contraceptive methods decreases the risk. Kashanian M, Baradaran HR, Bahasadri S, Alimohammadi R (2011) [8] oral contraceptive pills were protective for pre-eclampsia. Increase in mental stress associated with increased risk of preeclampsia as observed in other study[9] Increase in BMI (>25) was associated with increased risk of preeclampsia as similarly observed by other studies.[5,17]

Table-3 Multivariate Analysis

Risk factors	Sig.	Exp(B)	95% CI. For EXP(B)	
			Lower	Upper
Family h/o PE	.022	3.7	1.2	11.2
First degree relative with HTN	.000	5.0	3.2	8.0
First degree relative with DM	.071	1.9	0.95	3.7
History of PIH in previous pregnancy	.001	2.8	1.5	5.0
GDM	.721	0.6	0.05	8.5
Absence of essential obstetric care	.000	3.0	1.8	5.0
Primiparity	.000	2.5	1.8	3.6
Twin gestation	.014	4.0	1.3	12.2
Mental stress	.000	2.4	1.7	3.4
Prepregnancy BMI (>25 kg/m^2)	.002	2.7	1.4	5.1
Abortion	.009	2.8	1.3	5.9

Factors found to be significant in univariate analysis viz. family history of pre-eclampsia, first degree relative with HTN, first degree relative with DM, history of PIH in previous pregnancy, history of GDM, essential obstetric care, parity, type of gestation, mental stress, pre pregnancy BMI, history of abortion in previous pregnancy were subjected to Multivariate analysis to study independent association of each factor with pre-eclampsia. Out of total 11 factors 9 were found to be significant independent risk factors of pre-eclampsia. These includes first degree relative with HTN (OR = 5.0; 95% CI 3.2 – 8; similarity found with other studies[5,9,14]); twin gestation (OR = 4; 95% CI 1.3 - 12.2; similarity found with other study[5]); family history of pre-eclampsia (OR = 3.7; 95% CI 1.2 - 11.2); absence of essential obstetric care (OR = 3; 95% CI 1.8 – 5; similarity found with other study[14]); history of PIH in previous pregnancy (OR = 2.8; 95% CI 1.5 – 5.0; similarity found with other study[14,16]); history of abortion in previous pregnancy (OR = 2.8; 95% CI 1.3 - 5.9; similarity found with other study[14]); and pre pregnancy BMI (OR = 2.7; 95% CI 5.1 –1.4; similarly found with other studies[5]).

CONCLUSION

Preeclampsia is a multifactorial disease. If greater awareness of the associated risk factors leads to earlier diagnosis and improved management, there may be scope for reducing a proportion of the morbidity and mortality from preeclampsia.

All the findings of the studies show the importance of gaining a comprehensive medical history from the women early in the pregnancy. Based on history, the screening should begin early to detect and treat the condition before it threatens the survival of mother and fetus.

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