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Original Article

Risk Factor Assessment for Pre-eclampsia: A Case Control Study

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ABSTRACT

Background: Knowledge and identification of risk factors for preeclampsia will help in estimating each woman's individualized risk and possibly reduce the recurrence risk of preeclampsia. So this study was conducted to assess and compare the socio-demographic profile of women with and without preeclampsia and to determine the risk factors associated with preeclampsia. **Methodology:** This Hospital based Case control analytical study was conducted among 180 preeclampsia case and 180 control subjects at Mahila chikitsalaya, Jaipur, from June 2014 to May 2015. **Results:** Bivariate analysis found that preeclampsia was significantly associated with rural residence (p=0.033), joint family type (p=0.025), low education of head of family(p=0.007), young age at menarche (11-12years) (p<0.001) Anemia (P=0.034) and primiparity (p<0.001), Family history of preeclampsia (p<0.001) and hypertension (p=0.007) and Non veg. diet (p=0.042). Preeclampsia was not found to be significantly associated with history of previous abortion, inter pregnancy period and sex of last child of multiparous women and ANC characteristics, TT immunization, IFA tablets, twin pregnancy or gestational diabetes. In the multiple regression analysis, Age >30 years, Preobese (BMI=25-29.9), obese (BMI≥30 Kg/m2), Primiparity, age of menarche at 12 years and rural residence were found to be independent risk factors associated with Preeclampsia. **Conclusion:** Age>30 years, Preobese, Obese, Primiparity, early age of menarche (12 years) and Rural residence were found as significant predictor for development of Preeclampsia. Most of these factors are non modifiable, but can be used to screen women during antenatal visits to identify those at higher risk of Preeclampsia.
Key words: Preeclampsia, Risk Factor, Pregnancy.

INTRODUCTION

Hypertensive disorders of pregnancy are one of the most common causes of maternal and fetal morbidity and mortality accounting for more than 40,000 maternal deaths worldwide annually.[1] In developing countries, it causes about one third of maternal mortality.[2] India accounted for 19% of maternal deaths worldwide.[3] Five percent of maternal deaths in India are due to Hypertensive disorder.[4]

Preeclampsia (PE) has remained a significant public health threat in both developed and developing countries,[5] however, the impact of the disease is felt more severely in developing countries, where treatment may be ineffective due to late presentation of cases. Although pre-eclampsia is not a totally preventable condition, its early detection and proper treatment can prevent severity,[6] Unclear etiology and the unpredictable nature of the disease further worsen the situation.[5] The incidence of PE ranges from 2% to 10%.[4-7] WHO estimates the incidence of preeclampsia to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%).[8] Pre-eclampsia has been associated with increased risk of adverse fetal, neonatal and maternal outcomes including Antepartum and Postpartum haemorrhage, Acute renal and Hepatic failure, eclamptic seizures, stroke, Placental abruption, HELLP syndrome Heart failure, DIC, Multiple organ failures and Maternal death.[9-12] Fetal complications include Fetal distress, Intrauterine growth retardation, Preterm birth, Stillbirth, Perinatal death and Neonatal asphyxia.[11-15] The factors that have been postulated to influence the risk of pre-eclampsia in various studies include Diabetes and Gestational Diabetes,[12-14-16-18] Obesity,[19] Multiple pregnancy.[17,18] Personal and family history of pre-eclampsia,[20] chronic infections,[21] UTI,[2] First pregnancy and Older maternal age or Younger than 20 years age,[2] Renal disease and autoimmune disorder,[16,17] prolonged interval between pregnancies[2-18] and History of abortion [8] and maternal diet.[22]

Rationale: Knowledge and identification of socio-demographic and clinical risk factors for PE will help in estimating each woman's individualized risk and allow antenatal surveillance to be directed at these women and guide the healthcare providers for counseling of such women and possibly reduce the recurrence risk of PE if some modifiable risk factors (like obesity) are present.

While most studies have been undertaken in high-income settings, some inconsistencies exist, especially in developing settings where pre-eclampsia risk factors have been explored less. Furthermore, conditions such as severe anaemia and lack of antenatal care that

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are more prevalent in less developed regions require further investigation and validation of findings.

Aims and *objectives* were to assess and compare the socio-demographic profile of women with and without preeclampsia and to determine the risk factors associated with preeclampsia.

METHODOLOGY

This Hospital based Case control analytical study was conducted at Mahila chikitsalaya, Jaipur, from June 2014 to May 2015. 180 preeclampsia case and 180 control subjects were included in the study. Sample size was calculated at alpha error 0.05 and power 80%, taking the expected Odds ratio for family History of Hypertension as a risk factor of preeclampsia as 5.48 and proportion of control subjects with Family History of Hypertension as 0.02.[23]

Case group: Woman admitted to post natal ward who delivered during preceding 2 days, who in the antenatal period or before going to labor was diagnosed by a doctor as having preeclampsia.

Control Group: Women admitted to post natal ward who delivered during preceding 2 days and did not had Preeclampsia during pregnancy.

Pre-eclampsia (ICD-10 code 014) was defined as a diastolic blood pressure of at least 90 mmHg on two or more consecutive occasions 24 hours apart or a diastolic blood pressure of at least 110 mmHg on any one occasion plus proteinuria (one 24-hour urine collection with a total protein excretion of at least 300 mg or two 1+ on a urine dipstick).[24]

Study subjects were selected from three post Natal wards of Mahila Chikitsalaya, Jaipur after getting ethical clearance from research review board. Each day all delivered women fulfilling the criteria for Preeclampsia case were enrolled into the study. Same no of controls were then selected each day by random selection of remaining beds. Case and control were enrolled within 2 days of delivery and informed consent was taken. Matching among cases and controls was not performed because many of the socio-demographic parameters are suspected risk factors for PE. Information was collected from hospital case sheet of the women and by interviewing the Study subject herself. In case, a patient was comatose after delivery, the history was taken when she regained consciousness or from relatives who accompanied her. Women, who delivered before 20 week of gestation irrespective of the outcome, were excluded from study. Anaemia was defined as Hemoglobin < 11g/dl. A women was considered non vegetarian if she took any non vegetarian dish (excluding egg), at least once a week in the last one month.

All the information was collected using a Predesigned, semi-structured study Performa to eliminate recording bias. Potential risk factors for study were selected on the basis of literature review and biological plausibility for an association with both the exposure and outcome.

Statistical analysis: Data obtained from study Performa was entered in MS Excel to figure Master Chart. Continuous variables were summarized as mean and standard deviation while categorical variables were summarized as proportion (%). Unpaired t-test was used for comparison of continuous variable while Chi-square test was used for analysis of Categorical variable. Risk was assessed by calculation of Odds Ratio in Bivariate analysis. Step wise Multiple Logistic Regression analysis was done to find out predictors of Preeclampsia. All variables, found significantly associated with Preeclampsia, were entered in Regression model. Probability of independent variable in retaining Regression model was kept<0.05 while that of removal as >0.10. All statistical calculations were done by using Med Calc.14.2.1.0 software. P<0.05 was taken as significant.

RESULT

Present study included 180 preeclampsia cases and 180 controls. Most of the study population belonged to 21–30 years of age. More preeclampsia women (25%) belonged to ≤20 years as compared to controls (17.8%). Both groups did not differ significantly in relation to education, religion, occupation and socio-economic status. Bivariate analysis found that preeclampsia was significantly associated with rural residence (p=0.033), joint family type (p=0.025), low education of head of family(p=0.007), primiparity (p<0.001), young age at menarche (11-12years) (p<0.001), Anemia (P=0.034), Family history of preeclampsia (p<0.001) and hypertension (p=0.007) and Non veg. diet (p=0.042). (Table 1-4). There was 1.22 times more risk in joint family in bivariate analysis. Similarly illiterate, middle and graduate mothers were having 1.05, 1.30 and 1.25 times more risk. 1.33 times more risk was found when the age at conception was between 21 to 25 years. Rh positive mothers were having 2.7 times more risk and mothers having family history of hypertension were found to be at 2.8 times more risk of developing preeclampsia. Likewise non vegetarian mothers have 1.63 times risk of preeclampsia.

Young age at menarche (11-12 years) was significantly more among preeclampsia (46%) as compared to controls (23%). Women with menarche at 11 &12 years had more than thrice the risk of preeclampsia as compared to those with menarche at 14 years. Preeclampsia was also significantly associated with primiparity. The risk of preeclampsia in primipara was more than twice (OR=2.39; 1.23-4.65) as compared to those with third parity. Preeclampsia was not found to be significantly associated with history of previous abortion, inter pregnancy period and sex of last child of multiparous women (Table-2). Anaemia was found to be associated with preeclampsia (P=0.034), however no association was found between preeclampsia and ANC characteristics, TT immunization, IFA tablets, twin pregnancy or gestational diabetes (Table-3). Personal history of preeclampsia and Family history of hypertension were also significantly associated with preeclampsia (table 4). Non veg. diet was found to be significantly more among Preeclampsia cases (37.2%) as compared to controls (26.7%) (Table-4). Non vegetarian had odds of Preeclampsia 1.6 times than that in vegetarians. Smoking and tobacco chewing was not found to be associated with preecmlampsia.

The variables that were found to be significant in bivariate analysis were then entered in the regression model for stepwise multiple regression analysis. Age >30 years, Preobese (BMI=25-29.9), obese (BMI≥30 Kg/m2), Primiparity, age of menarche at 12 years and rural residence were found to be independent risk factors associated with Preeclampsia (table-5).

On applying multiple logistic regression, patients with age >30 years were found to have 2.87 times risk of preeclamsia as compared to age <30 years. Primipara mothers had 4.5 times risk as compared to multipara mothers. As compared to normal and underweight, preobese and obese were having 3.23 times and 8.28 times more risk of PE respectively.

Risk of Preeclampsia was 2.59 times high in patients with age of menarche < 12 years as compared to those in which age >12 years. Similarly rural residents were having 1.67 times higher risk for preeclampsia as compared to urban residents.

DISCUSSION

Present study aimed to determine the socio-demographic and clinical factors that increase risk of Preeclampsia. Though, many socio-demographic factors were found to be associated with Preeclampsia in bivariate analysis, multiple logistic regression analysis selected out the independent risk factors for Preeclampsia.

Maternal age >30 years was found to increase the risk of Preeclampsia (OR=2.87; 1.03-7.99). Various studies.[8-25-26-28] have also reported advanced maternal age >30/35 years to be associated with Preeclampsia. Increased age of women is an important risk factor probably due to increased villous reaction leading to pre-eclampsia in a woman greater

Table 1: Distribution of Study Population according to Socio-demographic characteristics

Socio-demographic characteristics	No.	Case		Control		Total		Odds ratio (95% CL)	P value
		%	No.	%	No.	%			
Age Group (years)	≤20	45	25.0	19	10.6	64	17.8	1.547(0.977-2.45)	<0.001
	21-25	85	47.2	102	56.7	187	51.9	-	
	26-30	36	20.0	52	28.9	88	24.4	0.831(0.497-1.38)	
	>30	14	7.8	7	3.9	21	5.8	2.400(0.92-6.217)	
Religion	Hindu	137	76.1	138	76.7	275	76.4	0.970(0.59-1.577)	1.000
	Muslim	43	23.8	42	23.3	85	23.6	-	
Residence	Urban	56	31.1	80	44.4	136	37.8	-	0.033
	Rural	113	62.8	91	50.6	204	56.7	1.774(1.143-2.75)	
	Slum	11	6.1	9	5.0	20	5.6	1.746(0.679-4.49)	
Family Type	Nuclear	18	10.0	36	20.0	54	15.0	0.53(0.219-1.289)	0.025
	Joint	146	81.1	127	70.6	273	75.8	1.221(0.59-2.517)	
	3 generation	16	8.9	17	9.4	33	9.2	-	
Education	Illiterate	70	38.9	65	36.1	135	37.5	1.533(0.837-2.81)	0.358
	Primary	26	14.4	24	13.3	50	13.9	1.542(0.73-3.257)	
	Middle	21	11.7	15	8.3	36	10.0	1.992(0.868-4.57)	
	High	26	14.4	37	20.5	63	17.5	-	
	Post High school	14	7.78	22	12.2	36	10.0	0.906(0.39-2.091)	
	Graduation /PG	23	12.8	17	9.44	40	11.1	1.925(0.86-4.297)	
Occupation	House Wife	160	88.9	161	89.4	321	89.2	0.944(0.486-1.84)	1.000
	Working	20	11.1	19	10.6	39	10.8	-	
Education Head of family	Illiterate	53	29.4	57	31.7	110	30.6	1.051(0.536-2.06)	0.007
	Primary	45	25.0	24	13.3	69	19.2	2.120(1.003-4.480)	
	Middle	22	12.2	19	10.6	41	11.4	1.309(0.57-3.007)	
	High	23	12.8	26	14.4	49	13.6	-	
	Post H	15	8.33	36	20.0	51	14.2	0.471(0.207-1.07)	
	Graduate	20	11.1	18	10.	38	10.6	1.256(0.538-2.94)	
	Honors'	2	1.11	0	0.0	2	0.6	NA	
Socio-economic status	I	4	2.2	4	2.22	8	2.22	1.044(0.246- 4.43)	1.000
	II	85	47.2	76	42.2	161	44.7	1.168(0.70-1.951)	
	III	45	25	47	26.1	92	25.6	--	
	IV	46	25.6	53	29.4	99	27.5	0.906(0.513-1.60)	

than 30years, as has been found in other studies.[13-15] Age of menarche at 12 years was found to be a significant risk factor for Preeclampsia (OR=2.59; 1.53-4.40), similar to finding of Ramesh *et al*[4] (2014). Early menarche (≤12 y) has been associated with increased risk of CVD events in other studies potentially mediated by increased adiposity associated with early menarche.[25] Present study found Prim parity to be an independent risk factor for development of Preeclampsia (OR=4.51; 2.76-7.36) as has been found in many studies.[24,25-27-32-33] This is because prim parity is due to initial trophoblastic invasion and how the mother reacts to it. The failure of the normal invasion of trophoblastic cells leads to maladaptation of the spiral arterioles, which are related to the causation of pre-eclampsia.[34] In this study, Rural Residence was found to a significant risk factor for development of Preeclampsia. This correlated with the findings of a national cross sectional study (NFHS-05-06) by Sutapa Agrawal *et al.*[35] In present study, BMI 25-29.9 Kg/m^2 (Preobese; OR=3.23; 1.66-6.29), and BMI ≥30Kg/m^2 (obese; OR=8.28; 2.89-27.55) were found to be independent risk factors for Preeclampsia. Overweight and obesity have been reported as significant risk factor by many studies.[7-13-17,18-25,26-33]

Table 2: Distribution of Study population according to obstetric characteristics

Obstetric characteristics	No.	Case		Control		Total		Odds ratio (95% CL)	P value
		%	No.	%	No.	%			
Age at Menarche (years)	11	10	5.6	4	2.2	14	3.9	4.53(1.222-16.800)	<0.001
	12	73	40.6	38	21.1	111	30.8	3.482(1.686- 7.192)	
	13	79	43.9	98	54.4	177	49.2	1.461(0.741-2.88)	
	14	16	8.9	39	21.7	55	15.3	-	
	15	2	1.1	1	0.6	3	0.8	3.625(0.305-3.153)	
Parity	1	117	65.0	56	31.1	173	48.1	2.388(1.226-4.651)	<0.001
	2	30	16.7	81	45.0	111	30.8	0.423(0.206-0.870)	
	3	21	11.7	24	13.3	45	12.5	-	
	4	8	4.4	14	7.8	22	6.1	0.653(0.229-1.86)	
	5	4	2.2	5	2.8	9	2.5	0.914(0.217- 3.856)	
Age at 1ST Conception	≤20	103	57.2	118	65.6	221	61.4	--	0.034
	21-25	72	40.0	62	34.4	134	37.2	1.330(0.865- 2.046)	
	>25	5	2.8	0	0.0	5	1.4	NA	
previous Abortion	No	37	20.6	31	17.3	68	18.9	1.244(0.732-2.112)	0.501
	Yes	143	79.4	149	82.7	292	81.1	-	
Inter pregnancy period	<3 years	36	57.2	79	63.7	115	61.5	0.759(0.409-1.410)	0.476
	≥3 years	27	42.9	45	36.3	72	38.5	-	
Sex of Last Child	Male	28	44.4	55	44.5	83	28	1.004(0.545-1.848)	0.885
	Female	35	55.6	69	55.6	104	35	-	

Table 3: Distribution of Study population according to present pregnancy characteristics

ANC characteristics	No.	Case		Control		Total		Odds ratio (95% CL)	P value
		%	No.	%	No.	%			
Completion of ANC	No	81	45	83	46.1	164	45.6	0.956(0.63-1.448)	0.916
	Yes	99	55	97	53.9	196	54.4	-	
Trimester of 1st ANC visit	1	74	41.1	74	41.1	148	41.1	-	0.948
	2	88	48.9	94	52.2	182	50.6	0.936 (0.607-1.45)	
	3	10	5.6	11	6.1	21	5.8	0.909 (0.364-2.27)	
TT immunization	Incomplete	4	2.22	0	0.00	4	1.11	-	0.131
	Complete	176	97.8	180	100	356	98.9	-	
IFA tablets taken	Not taken	23	12.8	17	9.44	40	11.1	1.207 (0.55-2.640)	0.218
	<50	67	37.2	57	31.7	124	34.4	1.048 (0.58-1.886)	
	50-100	53	29.4	73	40.6	126	35.0	0.648(0.36 -1.165)	
	100	37	20.6	33	18.3	70	19.4	-	
Gestational Diabetes (N=135)	No	18	20.7	7	14.6	25	18.5	1.528(0.588-3.97)	0.520
	Yes	69	79.3	41	85.4	110	81.5	-	
Gestation	Single	172	95.6	169	93.9	341	94.7	-	0.637
	Twin	8	4.4	11	6.1	19	5.3	0.715(0.280-1.82)	
Hemoglobin level	Normal	35	19.4	18	10	53	14.7	-	0.034
	Mild Anaemia	19	10.6	30	16.7	49	13.6	0.326 (0.15- 0.73)	
	Moderate Anaemia	107	59.4	118	65.6	225	62.5	0.466(0.249- 0.87)	
	Severe Anaemia	19	10.6	14	7.8	33	9.2	0.698(0.285-1.71)	

Table 4: Distribution of Study population according to Clinical characteristics

		Case		Control		Total		Odds ratio (95% CL)	P value
		No.	%	No.	%	No.	%		
BMI	Under weight	17	9.4	20	11.1	37	10.3	1.133(0.565-2.27)	
	Normal	102	56.7	136	75.6	238	66.1	--	<0.001
	Preobese	41	22.8	20	11.1	61	16.9	2.733 (1.51-4.946)	
	Obese	20	11.1	4	2.2	24	6.7	6.667(2.211- 20.1)	
Blood Group	A	22	15.8	28	21.1	50	18.4	0.818 (0.41-1.618)	
	AB	20	14.4	23	17.3	43	15.8	0.905(0.44-1.852)	0.284
	B	49	35.3	51	38.4	100	36.8	-	
	O	48	34.5	31	23.3	79	29	1.612(0.886-2.93)	
Rh factor	Positive	131	94.2	114	85.7	245	90.1	2.729(1.15-6.471)	0.032
	Negative	8	5.8	19	14.3	27	9.9	-	
personal History of	Preeclampsia[1]	18	28.6	0	0.0	18	9.6	-	<0.001
	Hypertension	**0**		0		0		-	
	Diabetes Mellitus	**1**	0.6	**0**		**1**	0.3	-	1.000
	Renal Disease	**0**		0		0		-	
	CVD	0		0		0		-	
Family History	Preeclampsia	1	0.6	0		1	0.3	NA	<0.001
	Hypertension	**40**	22.2	**20**	11.1	**60**	16.7	2.28(1.27-4.09)	0.007
Diet	Non Vegetarian	67	37.2	48	26.7	115	31.9	1.631(1.042-2.551)	0.042
	Vegetarian	113	62.8	132	73.3	245	68.1	-	

[1]. In Multiparous women

Table 5: Multiple Logistic Regression analysis

Variable	Coefficient	Std. Error	Odds ratio	95% CI	P value
Age<30 years (Reference category)	-	-	-	-	-
Age>30 years	1.05429	0.52293	2.8699	1.0298-7.9984	0.0438
Normal and underweight (Reference category)	-	-	-	-	-
Preobese (BMI 25-29.9 kg/m^2)	1.17387	0.33953	3.2345	1.6626-6.2925	0.0005
Obese (BMI≥30 Kg/m^2)	2.11400	0.61334	8.2813	2.4889-27.5537	0.0006
Multiparity (Reference category)	-	-	-	-	-
Primiparity	1.50664	0.24977	4.5116	2.7652-7.3609	<0.0001
Age of menarche > 12 years (Reference category)	-	-	-	-	-
Age of menarche < 12 years	0.95307	0.26933	2.5937	1.5299-4.3971	0.0004
Urban residence (Reference category)	-	-	-	-	-
Rural residence	0.51211	0.25004	1.6688	1.0223-2.7242	0.0405
Constant	-1.6805				

CONCLUSION

Age>30 years, Preobese, Obese, Primiparity, early age of menarche (12 years) and Rural residence as significant predictor for development of Preeclampsia. Most of these factors are non-modifiable, but can be used to screen women dursing antenatal visits to identify those at higher risk of Preeclampsia.

CONFLICT OF INTEREST

None declared

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