ORIGINAL RESEARCH

A Case-Control Study on Risk Factors of Pre-Eclampsia in Bankura Sammilani Medical College and Hospital, West Bengal

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Abstract

Background and Aim: Pre-eclampsia manifests typically as hypertension especially when target organ damage occurs in the absence of proteinuria. It occurs in around 5% fraction of pregnant women worldwide and associated with several underlying risk factors. Risk factors have been categorized in to various aspects depending on their origin. The ultimate goal of this study was to study the risk factors of pre-eclampsia among cases & control.

Materials and Methods: The study was performed in the post-natal ward of department of Obstetrics and Gynecology of the institute in 18 months. It was a Case-Control analysis type of study in which cases & controls were taken as 1:1. Study population was 75 diagnosed cases of pre-eclampsia and normal pregnant women admitted during the period of data collection. Informed written consent was taken from every patient before conducting the study. Data collection was done for 9 months byinterview using predesigned & pretested semi-structural questionnaire, clinical examination as well as reviewing the medical records & laboratory reports. Proportion of different risk factors among the cases & control was calculated then the odds ratio for each of the risk factor was ascertained.

Statistical Analysis and Results: The collected data was compiled and entered in to master spread sheet of MS Excel. Gantt Chart was used for inputs of various responses. Statistical analysis was performed with help of statistical software SPSS version 22.0. Test of proportion is used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. P value less than 0.05 was considered as significant. There was statistical significance in the two groups related to hemoglobin ($p=0.006 < 0.05$). Therefore high hemoglobin level is a risk factor for pre- eclampsia. Results also confirmed that 82.7% of pre-eclampsia cases has hemoglobin >10gm% while 62.7% of control hashemoglobin>10gm%.

Conclusion: Author concluded that the risk for the occurrence of pre-eclampsia were primarily gestational age, complaints, proteinuria, hemoglobin,past history of PIH, chronic hypertension and body mass index. Complaints like epigastric pain,eye symptoms edema, headache was present in significant number of cases. Other important studied factors like past history of pre-eclampsia, chronic hypertension are also associated with the increasesrisk of occurrence of pre-eclampsia.

Keywords: Pre-Eclampsia, Proteinuria, Hemoglobin, Headache, Case-Control Analysis, Risk Factors

Introduction

Pre-eclampsia is a multifactorial and multisystemic disease specific to gestation that is classically diagnosed by the presence of hypertension associated with proteinuria manifested in a previously normotensive pregnant woman after the 20th week of gestation.[1] The multisystemic nature of pre-eclampsia implies the possibility of evolution to more severe situations such as eclampsia, hemorrhagic stroke, hemolysis, elevated liver enzymes, and a low platelet count (HELLP) syndrome, renal failure, pulmonary edema, and death.[2] Eclampsia refers to the occurrence of generalized tonic-clonic seizures or coma in a pregnant woman with pre-eclampsia,and is one of the most serious complications of the disease.[3] The incidence of preeclampsia is 2-10% depending on the population studied and definition of preeclampsia.[4-6] It occurs in 4-7% of pregnant women worldwide. It is a major cause of maternal and neonatal morbidity and mortality, the definite etiology of which still remains unknown. The factors that have been postulated to influence the development of preeclampsia among mothers include diabetes mellitus, obesity, multiple pregnancy, primiparity, personal and family history of

preeclampsia and chronic hypertension. In developing countries, evidence of the association between these factors and preeclampsia is scarce.[3,5,12,17] In non-interventional, pre-eclamptic cases may progress further to the dreaded complications like; eclampsia, HELLP syndrome, pulmonary edema, abruption placentae, postpartum circulatory collapse, acute renal failure, hepatic rupture, cerebral hemorrhage and visual disturbances including death. The pathophysiology of pre-eclampsia is not precisely known but a two-step model that is widely accepted has been described. The physiological change during a normal pregnancy involves spiral artery remodeling.[7-11] Trophoblasts invade and replace the arteries' endothelial cells and induce arterial smooth muscle cell apoptosis, resulting in large non vasoactive vessels. Risk factors have been categorized in to various aspects depending on their origin. Maternal-specific risk factors include history of previous pre-eclampsia, maternal age, long interval between pregnancies, family history. Partner-related risk factors include nulliparity/primipaternity, limited sperm exposure, donor insemination. Presence of specific underlying disorders includes chronic hypertension and renal disease, obesity, insulin resistance, low maternal birth weight, gestational diabetes, type-1 diabetes mellitus, activated protein C resistance (factor V Leiden), protein S, deficiency, antiphospholipid antibodies. Pregnancy-associated risk factors include multiple pregnancy, fetus with chromosomal anomalies (trisomy 13), hydatidiform moles. Therefore keeping all these facts, the present study is undertaken to access the role of relevant risk factors in development of preeclampsia.

Aim

To study risk factors of pre-eclampsia among cases & control.

Objectives

To ascertain the risk factors of pre-eclampsia among the pregnant women attending Bankura Sammilani Medical College and Hospital, West Bengal. To find out the difference in risk factors, if any, among the study subjects having early and late onset of pre-eclampsia**.**

Materials and Methods

The study was planned, abstracted and conducted in the post-natal ward of department of Obstetrics and Gynecology of the Bankura Sammilani Medical College & Hospital, West Bengal within a time frame of about 18 months (Preparatory phase: 3 months, Phase of data collection: 9 months, Phase of analysis: 4 months, Writing up of report submission: 2 months, April 2019 to September 2020) from acceptance of synopsis. Authors have finalized study design as case-control type of analytical study. Case -Control study in which cases & controls were included @ 1:1. Those pregnant women diagnosed as having pre-eclampsia were taken as 'cases' and normal pregnant women as control. The study was conducted after obtaining permission from the West Bengal University of Health Sciences (WBUHS), approval of ethics community of Bankura Sammilani Medical College as well as informed consent of each participant. Study population was 75 diagnosed cases of pre-eclampsia and normal pregnant women admitted during the period of data collection. Informed written consent was taken from every patient before conducting the study. As per previous hospital records, on an average 40 cases of pre-eclampsia are managed per month that is more or less 8-10 cases per week. Data collection was done for 9 months that is 38 weeks (recorded twice/week). The days in each week was selected by simple random sampling technique using lottery method done at the beginning of week. Inclusion criteria were all pregnant women who will be willing to participate in study. Precise data for the proposed study was collected by interview using predesigned & pretested semi-structural questionnaire, clinical examination as well as reviewing the medical records & laboratory reports. From the data, the proportion of various risk factors among the cases & control was calculated then the odds ratio for each of the risk factor was ascertained. Laboratory Investigation pertaining to kidney functions, glucose homeostasis of the body was done as per recommended procedure. For renal function; serum urea, serum creatinine albumin in urine was tested. For Glucose homeostasis; fasting plasma glucose, post prandial plasma glucose was assessed. Data was analyzed from the above shortlisted cases pertaining to evaluate the relation of putative risk factors with pre-eclampsia.

Statistical plan of Data Analysis

The collected data was compiled in Microsoft Excel sheet after checking accuracy. Then the data was described by various parameters like mean, standard deviation (SD), median, range etc. for continuous variables and proportion, interquartile range (IQR) for categorical variables. Gantt Chart was used for inputs of various responses.

Methodology

Study was performed in line with Helsinki Declaration of Human Ethics (2008). Firstly, a certain number of pregnant mothers have been shortlist who admitted in Post Natal Ward, BSMCH. 1st Group (Cases) has diagnosed cases of Pre-eclampsia while 2nd Group (Control) has normal case of pregnancy. Then collection of data is performed under following parameters: Age, Duration of marriage, gestational age in weeks, parity, gravida, epigastric pain, eye symptom, edema, headache, age of menarche, age at 1st conception, number of previous living issue, interpregnancy period, previous abortion, sex of last child, body mass index, proteinuria, hemoglobin, past h\o pre-eclampsia, family h\o pre-eclampsia, chronic hypertension, renal disease, gestational diabetes. Then

analysis and comparison of data was done between the two studied groups.

Statistical Analysis and Results

Statistical Analysis was performed with help of statistical software SPSS. Descriptive statistical analysis is performed to calculate the means with corresponding standard deviations (SD). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. t-test was used to compare the means of the two groups. Fisher Exact test was used where Chi-square (χ^2) test was not applicable. Odds Ratio (OR) with 95% confidence interval (CI) had been calculated to find the risk factors. $p<0.05$ was taken to be statistically significant.

Table-1: Distribution of age group and the patients of the two groups

			Groups		Total
			case	control	
AGE (in year)	15-20yrs	Count	32	29	61
		% within AGE	52.5%	47.5%	100.0%
		% within case/ control	42.7%	38.7%	40.7%
	21-25yrs	Count	30	37	67
		% within AGE	44.8%	55.2%	100.0%
		% within case/ control	40.0%	49.3%	44.7%
	26-30yrs	Count	9	7	16
		% within AGE	56.3%	43.8%	100.0%
		% within case/ control	12.0%	9.3%	10.7%
	30-35yrs	Count	4	2	6
		% within AGE	66.7%	33.3%	100.0%
		% within case/ control	5.3%	2.7%	4.0%
Total		Count	75	75	150
		% within AGE	50.0%	50.0%	100.0%
		% within case/ control	100.0%	100.0%	100.0%
Mean ± SD (in years)			22.07±3.96	21.65±3.05	

Chi-Square Tests			
	Value	df	Asymptotic Significance(2-sided)
Pearson Chi-Square	1.796[a]	3	.616
Likelihood Ratio	1.811	3	.613
Linear-by-Linear Association	.095	1	.757
N of Valid Cases	150		
Chi-square=1.796; p=0.616NS- Not Significant, Chi-square test showed that there was no significant association between age group and patientsof the two groups (p=0.616 > 0.05).			

Table- 2: Distribution of Age 1st conception between the two groups

			case/ control		Total
			case	control	
AGE AT 1 CONCEPTION (in year)	<or=18yrs	Count	16	21	37
		% within AGE AT 1CONCEPTION	43.2%	56.8%	100.0%
		% within case/ control	21.3%	28.0%	24.7%
	>18yrs	Count	59	54	113
		% within AGE AT 1CONCEPTION	52.2%	47.8%	100.0%
		% within case/ control	78.7%	72.0%	75.3%
Total		Count	75	75	150
		% within AGE AT 1CONCEPTION	50.0%	50.0%	100.0%
		% within case/ control	100.0%	100.0%	100.0%
Mean ± SD (in years)			21.07±3.30	20.35±2.24	

Chi-Square Tests					
	Value	df	Asymptotic Significance (2-sided)	Exact Sig.	Exact Sig.
Pearson Chi-Square	.897[a]	1	.344		
Continuity Correction[b]	.574	1	.449		
Likelihood Ratio	.899	1	.343		

Fisher's Exact Test				.449	.224
Linear-by LinearAssociation	.891	1	.345		
N of Valid Cases	150				
Chi-square = 0.897; p = 0.344, NS- Not Significant, Chi-square test showed that there was no significant association between the age of 1st conception and patients of the two groups (p=0.344 > 0.05)					

Table- 3: Distribution of Interpregnancy period (in years) between the two groups

			case/ control		Total
			case	control	
INTERPREGNANCY PERIOD (in years)	<or=3yrs	Count	64	65	129
		% within INTERPREGNANCY PERIOD (in yrs)	49.6%	50.4%	100.0%
		% within case/ control	85.3%	86.7%	86.0%
	>3yrs	Count	11	10	21
		% within INTERPREGNANCY PERIOD (in yrs)	52.4%	47.6%	100.0%
		% within case/ control	14.7%	13.3%	14.0%
Total		Count	75	75	150
		% within INTERPREGNANCY PERIOD (in yrs)	50.0%	50.0%	100.0%
		% within case/ control	100.0%	100.0%	100.0%
Mean ± SD (in years)			0.96±2.03	1.00±1.67	

Chi-Square Tests

	Value	Df	Asymptotic Significance (2-sided)	xact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.055[a]	1	.814		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.055	1	.814		
Fisher's Exact Test				1.000	.500
Linear-by-LinearAssociation	.055	1	.815		
N of Valid Cases	150				

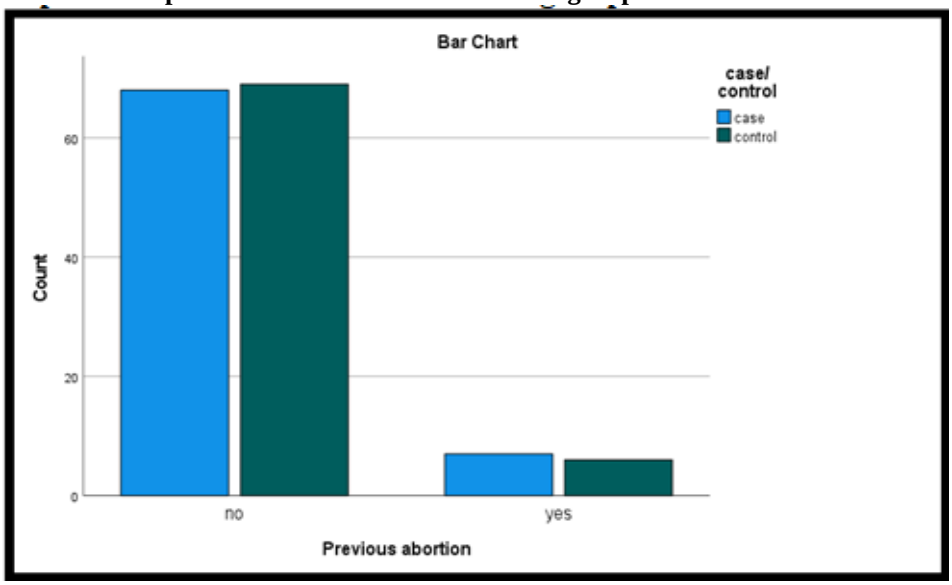
Table- 4: Distribution of previous Abortion between the two groups

			case/ control		Total
			case	control	
Previous abortion	No	Count	68	69	137
		% within Previous abortion	49.6%	50.4%	100.0%
		% within case/ control	90.7%	92.0%	91.3%
	yes	Count	7	6	13
		% within Previous abortion	53.8%	46.2%	100.0%
		% within case/ control	9.3%	8.0%	8.7%
Total		Count	75	75	150
		% within Previous abortion	50.0%	50.0%	100.0%
		% within case/ control	100.0%	100.0%	100.0%
Mean ± SD			0.09±0.29	0.08±0.27	

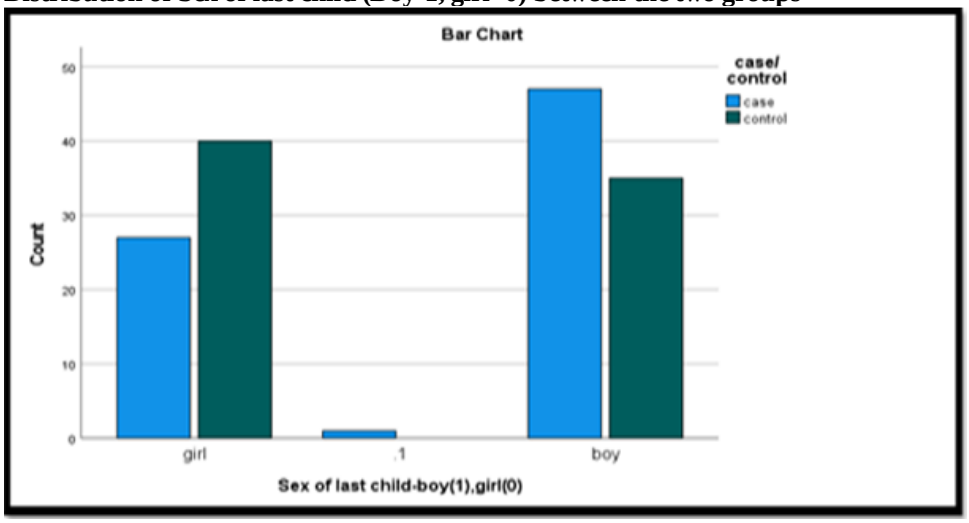
Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig.	Exact Sig.
Pearson Chi-Square	.084[a]	1	.772		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.084	1	.772		
Fisher's Exact Test				1.000	.500
Linear-by-Linear Association	.084	1	.772		
N of Valid Cases	150				

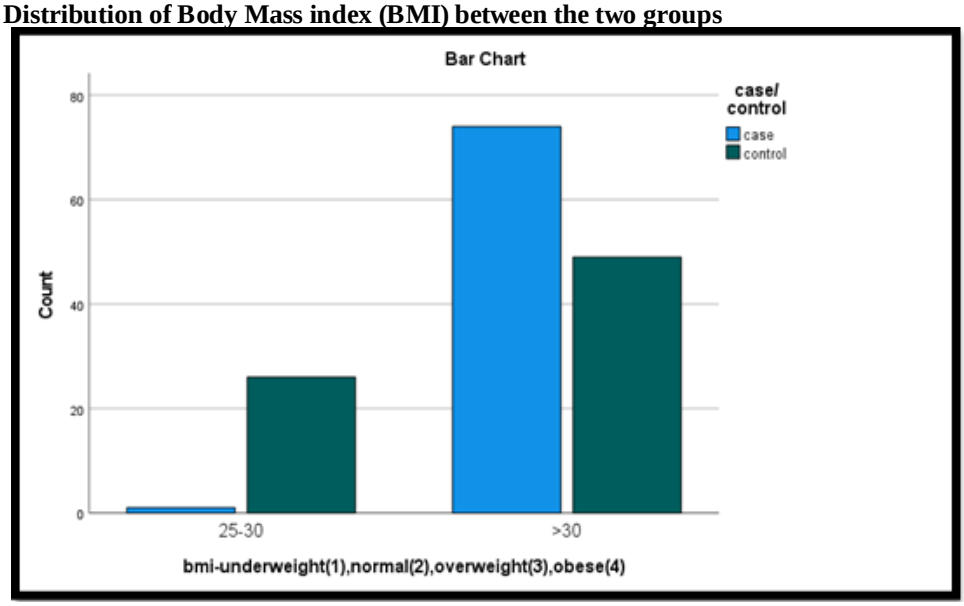
Graph- 1: Distribution of previous Abortion between the two groups



Graph- 2: Distribution of Sex of last child (Boy-1, girl- 0) between the two groups



Graph- 3: Distribution of Body Mass index (BMI) between the two groups



Discussion

The present study is conducted as a hospital-based case-control study. There were 75 cases of Pre-eclampsia diagnosed women and 75 cases of matched control without pre-eclampsia selected for study of comparison of risk factors contributing to pre-eclampsia among these twogroups. The present study showed that there was no significant association between age and patients of two groups (p=0.616 > 0.05). The mean age of mother in occurrence of pre-eclampsia was 22.07±3.96years with a range of 15 to 25years while the mean age of control was 21.65±3.05 years with in a range of 15 to 25 years. There was no association between age and pre-eclampsia and both the groups are matched for this risk factor. Pre-eclampsia is recognized to more commonly complicate a woman's first pregnancy. These findings were in accordance with several other studies in the literature.[12-15] A largepopulation-based study reported that primiparous women were at increased risk of pre- eclampsia compared with multiparous women (OR 3.6, 95% CI 2.6–5.0). A recent population- based cohort study reported that nulliparity significantly increased the risk of late-onset pre- eclampsia when compared with early-onset disease. Parity was not a risk factor in the present study because it was a small single centered study. The present study shows that there was significant association between gestational age and patients of the two group (p=0.006<0.05). CASES show preterm late onset pre-eclampsia.40.0% of pre-eclampsia mother had preterm delivery of gestational age ≤37 weeks and 22.7% of control had preterm delivery of gestational age of ≤37 weeks. Hence the present study showed preterm late-onset pre -eclampsia has happened. There was no significant association between epigastric pain and patients of the two groups(p=0.155> 0.05), as the patients reported with pre-eclampsia cases was less severe. There was significant association between eye symptoms and patients of the two groups (p=0.002 < 0.05). There was significant association between edema and patients of the two groups (p=0.000 < 0.05). There was significant association between headache and patients of the two groups (p=0.000 <0.05). This was due to pre-eclampsia is a vasospasm vascular disease leading to headache. Complaints like epigastric pain was present in 2.7%of pre-eclampsia cases and 0.0% in control,eye symptoms was present in 12.0% in pre-eclampsia cases and 0.0% in control, edema was present in 81.3% of pre-eclampsia cases and 17.3% in control ,headache was present in 73.3% of pre-eclampsia cases and 13.3% in control .Hence complaints significantly associated to pre- eclampsia. These inferences were in accordance with the resuts and outcomes of other pioneer researches in the litratryre.[16-20] Women experiencing menarche at ≤ 12 years were at an increased risk for preeclampsia than women experiencing menarche at later ages (OR = 6.81, 95% CI: 0.93, 50.03). Analysis of data obtained from the Norwegian Mother and Child Cohort Study suggested that there may be an increased risk of pre-eclampsia for women with recurrent miscarriages (adjusted OR 1.51, 95% CI 0.80–2.83), although this was not statistically significant. Similar findings were reported from a Canadian study where history of prior abortion had no effect on risk of pre-eclampsia. However, for women who had recurrent spontaneous abortions and infertility treatment, a three-fold increased risk of pre-eclampsia was seen compared with controls. The present study shows that there was no significant association between previous abortion and patients of the two groups (p=0.772 > 0.05) as there was limited previous abortionwhich may be the reason for non-association of previous abortion with pre-eclampsia. The risk of pre-eclampsia is generally lower in the second pregnancy if conceived with the same partner. After adjustment for the presence or absence of a change of partner and maternal age, the odds for pre-eclampsia for each 1-year increase in the birth interval were increased (OR 1.12, 95% CI 1.11–1.13). In a large cohort study, a birth interval of more than 4 years increased the risk of pre-eclampsia in women who had no prior history (OR 1.4, 95% CI 1.2– 1.6).The present study showed that there was no significant association between interpregnancy period and patients of the two groups (p=0.814 > 0.05).Hence it was not risk factor contributing to pre-eclampsia because both groups matched for it. A large population-based study reported that short stature of women (□164 cm/5'5") predisposed them to an increased risk of severe pre-eclampsia. Women who are overweight or obese are known to be at increased risk for pre-eclampsia. A recent meta-analysis concluded that overweight/obesity as well as maternal adiposity is associated with an increased risk of pre-eclampsia. Increased BMI is an important risk factor for pre-eclampsia and severe pre- eclampsia with an attributable risk of 64%.The present study showed that there was significant association between Body Mass Index and patients of the two groups (p=0.000 < 0.05). Proteinuria is routinely measured during pregnancy, especially in women with new-onset hypertension occurring after 20 weeks' gestation to establish the diagnosis of pre-eclampsia documentation of proteinuria early in pregnancy is associated with an increased risk of pre- eclampsia (see Pre-existing medical conditions, above). Recently, significant attention has been devoted to the role of albuminuria, and more specifically for lower levels of albuminuria (or 'microalbuminuria') for the prediction of pre-eclampsia. Prediction of pre-eclampsia in early pregnancy (17–20 weeks) by estimating the albumin: creatinine ratio was also performed using high-performance liquid chromatography (HPLC). Various quantities are commonly measured during the pregnancy and hemoglobin level is oneof them. The high levels of hemoglobin may increase the risk of preeclampsia. Several authors showed that high hemoglobin in the

first and third trimester is associated with preeclampsia (P < 0.01). The present study showed that there was statistical significance in the two groups related to hemoglobin (p=0.006 < 0.05).Hence high hemoglobin level is a risk factor for pre-eclampsia.82.7% of pre-eclampsia cases has hemoglobin >10gm% while 62.7% of control has hemoglobin >10gm%. Theese outcomes were highly comparables with other similar studies.[21-25] In a primigravida, a family history of pre-eclampsia is associated with a fourfold increased riskof severe pre-eclampsia. This clinical history identifies a group who warrant close clinical surveillance during pregnancy. Our study has no statistical significance in the two group related to family history of pre-eclampsia (p=1.000 > 0.05). Hence it was not risk factor contributing to pre-eclampsia because both groups matched for it. Our study has statistical significance between chronic hypertension and patients of the two group (p= 0.008 < 0.05).41.3% of pre-eclampsia cases shows chronic hypertension while 21.3% of control has not chronic hypertension. Hence chronic hypertension is significant risk factor for occurrence of pre-eclampsia.

Conclusion

Within the limitations of the study author concluded that the risk factors which present study has identified leading to occurrence of pre-eclampsia. They were mainly gestational age, complaints, proteinuria, hemoglobin,past history of PIH, chronic hypertension and body mass index. The present study has confirmed the event of preterm late-onset pre-eclampsia. Complaints like epigastric pain, eye symptoms edema, headache was present and noticed in considerable number of cases. Hence complaints significantly lead to pre-eclampsia. Similarly, obesity is significant risk factor for pre-eclampsia. Hemoconcentration due to reduced plasma volume has also been shown to accentuate the occurrences of pre-eclampsia. Other significant studied factors like past history of pre-eclampsia, chronic hypertension are also associated with the increases risk of occurrence of pre-eclampsia. Family history of pre-eclampsia, renal disease, gestational diabetes has not shown any significant difference between case and control. Both the groups matched for these risk factors. Further Multi-centric cohort study is necessary for coming to definitive conclusion regardingrisk factors. It is also advisable to consider clinical pre-conceptional risk factors, advice good nutrition, insist on correct BP measurement and look for proteinuria, usage of aspirin and iron and calcium supplements.

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