ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2020; 6(2): 158-162
www.allresearchjournal.com
Received: 13-12-2019
Accepted: 17-01-2020

Dr. I Indira
Associate Professor, Government Maternity Hospital, Tirupati, Andhra Pradesh, India

Dr. Ch Roja
Post Graduate, Government Maternity Hospital, Tirupati, Andhra Pradesh, India

Correspondence Author:
Dr. I Indira
Associate Professor, Government Maternity Hospital, Tirupati, Andhra Pradesh, India

Study of Risk Factors of Pre-eclampsia/gestational hypertension in other than first viable Pregnancy

Dr. I Indira and Dr. Ch Roja

Abstract
Background: Knowledge about the risk factors and identification of risk factors for pre-eclampsia/gestational hypertension is essential to identify the women who are at risk. So this study was conducted to determine the risk factors that will reduce the incidence of pre-eclampsia/gestational hypertensionin in women in other than their first viable pregnancy.
Methodology: The present study was a Hospital-based Case-control study which was undertaken in Government maternity hospital, Tirupati, and it included 100 women who developed preeclampsia or gestational hypertension denovo in other than first viable pregnancy as study group and 100 age and gravidity matched women without hypertension as the control group.
Results: preeclampsia /gestational hypertension was significantly associated with, risk factor like family history of hypertension [odds ratio 4.19,95% CI 2.021 – 8.687,], history of spontaneous preterm births [odds ratio 1.41,95% CI 0.679 – 2.957], history of spontaneous abortions [odds ratio. 43, 95% CI 0.794 – 2.575] interpregnancy interval of more than 2years [odds ratio 0.156,95% CI 0.083 – 0.297,] is found to be aa protective factor for pre-eclampsia /gestational hypertension. Results are inconsistent in the case of PCOS [P>0.05] and anemia [P>0.05] whereas overweight (BMI=25-29.9) and obesity (BMI≥30 Kg/ m2) were found to be independent risk factors associated with Preeclampsia/gestational hypertension.
Conclusion: Modifiable risk factors like overweight, Obesity, anemia, PCOS were found as a significant predictor for the development of Preeclampsia/ gestational hypertension. Other nonmodifiable risk factors like a family history of hypertension, history of preterm births and spontaneous abortions can be used to screen women during antenatal visits to identify those at higher risk of Preeclampsia/gestational hypertension.

Keywords: Preeclampsia, gestational hypertension, Risk Factor, Pregnancy

1. Introduction
Approximately 5-10% of women develop hypertension during the course of their pregnancies [1]. The incidence of preeclampsia in nulliparous women ranges from 3 to 10 percent. The incidence of preeclampsia in multiparous also varies and ranges from 1.4 to 4%. Preeclampsia and gestational hypertension are the most prevalent forms of hypertensive disorders in pregnancy and considered to be a disease of nulliparity, whereas older women are at higher risk for chronic hypertension with superimposed preeclampsia [1]. The lower risk of pre-eclampsia /gestational hypertension among multiparous women is due to desensitization after exposure to paternal antigens in the placenta during the previous pregnancies [2]. This lower risk in multipara has also been attributed to smoother trophoblastic invasion after modification of maternal spiral arteries during the first pregnancy [3]. So the incidence of preeclampsia/gestational hypertension in the second pregnancy is less than in the first pregnancy. But this may be altered by the onset of risk factors that arisedenovo after the first pregnancy. There is a need to identify the risk factors for hypertension complicating pregnancy in multigravida as literature is scanty in this regard.

Aim
It is to determine the risk factors among women who did not have hypertensive disorders in the first viable pregnancy but having preeclampsia/gestational hypertension in subsequent pregnancies.

Study Design: A case control study.
Study Setting: Government maternity Hospital, Tirupati.

Study Population
Cases: Women without any hypertensive disorders in first viable pregnancy but having preeclampsia/gestational hypertension in present pregnancy admitted in Government Maternity Hospital, Tirupati.

Controls: Age and gravidity matched pregnant Women without hypertension in previous and in the current pregnancy.

Inclusion Criteria: Women without any hypertensive disorders in the first viable pregnancy, but having preeclampsia /gestational hypertension in present pregnancy were included as cases. Women without hypertension, even in previous and present pregnancy, were included as controls. Both cases and controls include women who had given consent.

Exclusion Criteria: Women with hypertensive disorders in the first viable pregnancy.

Methods and Methodology
Information was collected from their previous and present medical records and by taking a history from the patient through a proforma.

Methodology
Hypertension during pregnancy was diagnosed when the systolic pressure is 140mm of Hg or more and a diastolic pressure of 90mm of Hg or more on two occasions at least 4- 6hrs apart within seven days (28). A single reading of diastolic pressure above 110mm of Hg in pregnant women is considered as hypertension for the purpose of evaluation and management.

Gestational Hypertension
New-onset hypertension developing after 20 weeks of gestation, during labor, or in the first 24 hours postpartum, without proteinuria, or any other systemic features of preeclampsia, in a previously normotensive, non-proteinuric woman and the blood pressure resolves within 12 weeks postpartum.

Preeclampsia
Hypertension associated with proteinuria greater than 0.3g/L in a 24-hour urine collection or 1+ by a qualitative urine examination after 20 weeks of gestation. Preeclampsia is a pregnancy-specific syndrome with onset after 20 weeks of gestation, similar to Gestational Hypertension, which resolves with the termination of pregnancy. It is a multisystem disorder not limited to Hypertension and Proteinuria, and proteinuria being an essential diagnostic criterion.
A detailed history elicited regarding Socio-demographic factors like age, education, occupation, socioeconomic status, residence and living conditions, personal history like diet, smoking, alcohol intake, marital life, interpregnancy interval, history of abortions, previous spontaneous preterm births. A detailed obstetric history and family history was elicited.

Statistical Analysis
All the information collected and recorded in the pre-designed proforma. The data will be entered in MS excel 2007 Microsoft corporation publication and analyzed using Epi Info CDC Version 7.2.0.1 Statistical significance for continuous variables will be tested using student t-test and discrete variables using CHI-SQUARE test. Frequencies will be described using percentages

Results

Table 1: Demographics Study and Control Groups

Sl No	Characteristics	Study Group (n=100)	Control Group (n=100)
1.	**Age (Years)**	27.06±4.479	25.81 ± 4.180
	25 Years and below	45 (45.0)	45 (45.0)
	26-30Years	31 (31.0)	31 (31.0)
	30 Years above	24 (24.0)	24 (24.0)
2.	**Education**		
	Uneducated	16(16.0)	6 (6.00)
	Primary	27(27.0)	36 (36.0)
	Secondary	47 (47.0)	46 (46.0)
	Degree	10(10.0)	12 (12.0)
3.	**Occupation**		
	House Wife	95 (95.0)	91 (91.0)
	Worker	5 (5.0)	9 (9.0)
4.	**Socio-Economic Status**		
	Upper Class	12	11
	Middle Class	56	72
	Lower Class	32	17
5.	**Residence**		
	Rural	73	66
	Urban	27	34
6.	**Religion**		
	Religion	85 (85.0)	92 (92.0)
	Hindu	11 (11.0)	5 (5.0)
	Muslim	4 (4.0)	3 (3.0)

In the above table, in both the study and control group, most of the women are 25years and below and came from rural areas so they, completed up to their secondary school and belongs to the middle class, housewives and Hindus.

Table 2: Parity of Study Group and Control Group

Parity	Group			
	Study		Control	
	No. of Patients	%	No. of Patients	%
Primipara	44	44.0	44	44.0
Parity 2	29	29.0	29	29.0
Parity 3 And Above	27	27.0	27	27.0

Most of the women in the study group and the control group are primipara. Almost an equal number of women are parity two and parity three and above.

Risk Factors

Table 3: Pre-Pregnancy Bmi

Sl No	Pre Pregnancy Bmi	Study Group	Control Group	Odds Ratio	χ2 (p-value)	Remarks
1.	18.5-24.9[normal]	56	79	1.48	12.51** (0.001)	P<0.001
2.	25- 29.9[over weight]	32	17	1.54		
3.	>=30[obese]	12	4	2.75		

From the above table, it was found that women with pre-eclampsia are more likely to be overweight and obese and a significant association was present between prepregnancy BMI and the risk of pre-eclampsia /gestational hypertension.

Table 4: Other Risk Factors

Sl No	Risk Factors		Study group	Control group	Odds Ratio	95% CI	P-value
1.	Inter Pregnancy Interval >2yrs	Yes	40	81	0.156	0.083 – 0.297	**P<0.001
		No	60	19			
		No	41	56			
2.	Pre Term Births	Yes	20	15	1.417	0.679 – 2.957	NSP>0.05
		No	80	85			
3.	Family H/O Htn	Yes	36	12	4.191	2.021 – 8.687	**P<0.001
		No	63	88			
4.	Pcod	Yes	14	9	1.646	0.677 - 3.999	NSP>0.05
		No	86	91			
5.	H/O Abortions	Yes	38	30	1.430	0.794 – 2.575	NSP>0.05
		No	62	70			
6.	Anemia	Yes	41	35	1.291	0.728 – 2.288	NSP>0.05
		No	59	65			

From the above table, it was observed that the interpregnancy interval of more than 2years is aprotective factor and family history of hypertension, history of spontaneous preterm births, history of spontaneous abortions are risk factors for pre-eclampsia /gestational hypertension. Results are inconsistent in the case of PCOS and anemia.

Discussion

The present study was undertaken in Government maternity hospital, Tirupati, and it included 100 women who developed preeclampsia or gestational hypertension denovo in other than first pregnancy and 100 age and gravidity matched women without hypertension as controls.

Age

The mean age of the study group in the present study is 27.06 ± 4.479years and of the control group is 25.81 ± 4.180years. there is no statistically significant difference in age between the study group and control group, thereby eliminating age as a confounding variable. Another Indian study conducted on the relationship between maternal age and preeclampsia at BGH Jharkhand had taken the mean Age of 26.75 ± 6.71 which was almost similar to the present study [4]. This may be because of the similarity of the obstetric population in the two studies, rural, less educated and marriage at a younger age.

In the present study, 45% of the study population was 25years and below, and 37% of the study population was between the age group of 26-30years, and 14% of the study population was above 30years.In the present study, most of the women came from rural areas so early age of marriage and less spacing may be the cause for more number of cases below 25years. Age has a significant influence on the incidence of hypertensive disorders of pregnancy. Advanced maternal age, irrespective of parity of a woman, is a considerable risk factor for the development of hypertensive disorders of pregnancy. A prospective study conducted at BGH Jharkhand concluded that the teenage age group and after thirty years of age are more prone for development of pre eclampsia [4]. In the present study, too women above 30years accounted for 14% of all cases of pre-eclampsia/gestational hypertension.

Parity

In the present study, 44% of women are primipara, 29% of women are parity 2and 27% of women parity -3 and above. We have matched the study and control group with respect to parity so that confounding bias is ruled out.

Demographics

Educational Status

The majority of the women in the study group and control groups studied up to secondary school, followed by primary education and graduation. Both study and control groups are similar in educational qualifications.

Occupation

Most of the women in the study group and the control group are housewives.

Socio-Economic Status

The majority of women in both groups belonged to the middle class.

Residence and Ethnicity

The majority of women in both groups came from rural areas and Hindus.

Risk Factors

Pre-Pregnancy Body Mass Index

In the present study, 56% of the study group and 72% of the control group had pre-pregnancy BMI in the normal range. Women with pre-eclampsia are 1.58times more likely to be overweight and 2.75 times more likely to be obese than controls. A case-control study done in SMS medical college

[2017] Rajasthan also found that overweight and obesity were independent risk factors for pre-eclampsia [5]. A registry-based Tanzanian survey also found a positive association between pre-pregnancy BMI and risk of preeclampsia [6].

Swedish birth registry-based study also found that there is an association between increasing BMI and the risk of pre-eclampsia, and it was strongly associated with term pregnancies than preterm pregnancies [7]. It was explained by the fact that early and severe preeclampsia more often originates in the placenta, whereas mild preeclampsia of late origin is more related to metabolic disease and hence more commonly associated with high BMI [8].

Family History of Hypertension

In women with a family history of hypertension, endothelial changes also appear to involve a relative deficiency in the production of nitric oxide, a vasodilator, and inhibitor of platelet aggregation, along with increased production of endothelin-I, which is an extremely potent vasoconstrictor and activator of platelets. The net effect would be arteriolar constriction leading to hypoxic/ischemic damage in different vascular beds, systemic hypertension, and worsening placental ischemia. In the present study, the study group had a more likelihood of a family history of hypertension compared to the control group [odds ratio 2.1,95% CI 2.021 – 8.687 P<0.001]. A case-control study conducted in public health facilities of Bihar shows that a Family history of hypertension was the most dominant risk factor for preeclampsia in pregnant women [9].

Inter Pregnancy Interval

The risk of hypertensive disorders in multiparous women are less compared to primipara. But the biologic mechanisms behind this phenomenon remain unclear [11]. In the present study interpregnancy of >2yrs [odds ratio 0.155, 95% CI 0.083 – 0.297, P<0.001] was negatively associated with pre-eclampsia/gestational hypertension.

An explanation for this is based on mean arterial pressure. MAP was lower in the second pregnancy (by approximately two mmHg) for very short interpregnancy intervals. However, this difference diminished when the interval increased, and it totally disappeared for intervals longer than two years.

Bernstein *et al.* [10] hypothesized that cardiovascular adaptation achieved during one pregnancy may facilitate vascular compliance in the next pregnancy, reducing the risk of hypertensive disorders in subsequent pregnancies. A study conducted by Mikolajczyk *et al.* concluded that the protective effect of parity on blood pressure is short-lived, and it lasts for <2–3 years [11]. Two recent epidemiologic studies showed that the risk of preeclampsia in multiparous women returned to the level of primiparous women after an interpregnancy interval of 6–10years [12, 13]. But the exact cut off in terms of the interpregnancy interval as a risk factor for preeclampsia was not defined in any of these studies.

History of Abortions

Normal pregnancies interrupted in early pregnancy may induce immunological changes that reduce the risk of pre-eclampsia in a subsequent pregnancy. The present study found a linear correlation between previous spontaneous abortion and pre eclampsia [ODDS RATIO 1.43 95% CI 0.794 – 2.575, ^{NS}P>0.05]. Other studies found that induced abortions conferred a protective effect against the development of pre-eclampsia in the subsequent pregnancy. They attributed this to be due to protection from immunological changes [14]. But the present study results found that the history of abortions was one of the risk factors for pre-eclampsia. It maybe because most of the abortions in the present study were spontaneous abortions.

History of Spontaneous Preterm Births

chorioamnionitis and Recurrent placental dysfunction may predispose to preterm birth, with or without PROM, in the first pregnancy followed by preeclampsia in subsequent pregnancy [15]. In the present study history of preterm births [odds ratio 1.25,95%CI 0.679 – 2.957] was positively associated with pre-eclampsia /gestational hypertension.A population-based cohort study conducted, based on Medical Birth Registry of Norway found that after preterm birth without preeclampsia in the first pregnancy, the risk of preeclampsia in the second pregnancy was 4–7 fold more than after term birth [15, 16] Improper remodeling of the uterine spiral arteries in early pregnancy may lead to preterm birth. These decidua changes may lead to reduced placental perfusion, cause preterm birth as well as subsequent dysfunction of the maternal vascular endothelium leading to pre-eclampsia in subsequent pregnancies. Another pathologythat causes preeclampsia and preterm labor in addition to endothelial dysfunction is generalized systemic inflammation with chorioamnionitis (non-microbiological or microbiological) [17].

History of Anemia

The higher incidence of pre-eclampsia in women with anemia is explained by the deficiency of micronutrients and antioxidants. Reduced serum levels of calcium, magnesium and zinc during pregnancy might be possible contributors to the development of preeclampsia [18]. In the present study also anemia was positively associated with pre-eclampsia [odds ratio 1.06,95% CI0.728 – 2.288,P>0.05]. A case-control study conducted at Kassala hospital, eastern Sudan [2011] found that greater the severity of the anemia during pregnancy, the higher the risk of preeclampsia [19]. A prospective case-control study conducted in Sultania Zanana Hospital, Bhopal [2018], found a higher incidence of maternal complications in women with preeclampsia with anemia [20]. It might be difficult to determine that anemia was the cause or effect of preeclampsia/ eclampsia in this study as most of the people came from rural areas and the prevalence of anemia is more in our hospital and we have not considered the severity of anemia.

Pcos

In the present study history of PCOS is similar in both the study group and control group; hence no correlation is found [^{NS}P>0.05]. A case-control study done in BOSTON also found no consistent association between PCOS and preeclampsia [21]. This may be due to heterogeneity within the PCOS population. Recent data suggest that the risk of adverse pregnancy outcomes varies with the PCOS phenotype, and the hyperandrogenic features of PCOS may drive the association between PCOS and preeclampsia. Further investigation is necessary to determine if there are particular subgroups of PCOS patients who are at increased risk for preeclampsia or if the association is due to infertility.

Strengths and Limitations

Multiple risk factors were taken and studied in the present study. It might help to predict the risk of pre-eclampsia/gestational hypertension in future pregnancies for individual women, as well as to understand the etiology and find better approaches for prevention and treatment.

A large sample is needed to study the risk factors and to get more reliable results.

Conclusion

Identification and targeting the modifiable risk factors in pre-pregnancy and initial stages of pregnancy may help in reducing the incidence of preeclampsia / gestational hypertension in the subsequent pregnancy.

References

1. Gary Cunningham F, Kenneth J Leveno, Steven L Bloom, Catherine Y Spong, Jodi S Dashe, Barbara L Hoffman *et al*. Hypertensive Disorders In: Cunningham Leveno, Bloom S, editor. Williams Obstetrics 24th ed. USA, 2014, 728-69.
2. Odegard RA, Vatten LJ, Nilsen ST, Salvesen KA, Austgullen R. Risk factors and clinical manifestations of pre-eclampsia Br J Obstet Gynaecol. 2000; 107:1410-6.
3. Moore M, Redman CWG. Case-control study of severe pre-eclampsia of early-onset. BMJ. 1983; 287:580-3.
4. Neha Kumari, Kusum Dash, Roopam Singh. Relationship between Maternal Age and Preeclampsia. 2016; 15:55-57
5. Verma MK, Kapoor P, Yadav R, Manohar RK. Risk Factor Assessment for Preeclampsia: A Case-Control Study, Int J Med Public Health. 2017; 7(3):172-7.
6. Dorah Mrema, Rolv Terje Lie, Truls Østbye, Michael Johnson Mahande, Anne Kjersti Daltveit. The association between pre-pregnancy body mass index and risk of preeclampsia: a registry-based study from Tanzania BMC Pregnancy Childbirth 2018; 18:56. https://doi.org/10.1186/s12884-018-1687-3
7. Sohlberg S, Stephansson O, Cnattingius S, Wikstrom AK. Maternal body mass index, height, and risks of preeclampsia, Am J Hypertens. 2012; 25:120-5.
8. Valensise H, Vasapollo B, Gagliardi G, Novelli GP. Early and late preeclampsia: two different maternalhemodynamic states in the latent phase of the disease Hypertension 2008; 52:873-80.
9. Endeshaw, Mulualem, Abebe, Fantu, Bedimo, Melkamu *et al*. Family history of hypertension increases the risk of preeclampsia in pregnant women: A case-control study Universal Medicine 2016; 35:181-191.
10. Ira M Bernstein, Marjorie C Meyer, George Osol, Ken Ward. Intolerance to volume expansion: a theorized mechanism for the development of preeclampsia, Obstetrics & Gynecology, 1998; 92(2):306-30
11. Mikolajczyk RT, Zhang J, Ford J, Grewal J. Effects of interpregnancy interval on blood pressure in consecutive pregnancies, Am J Epidemiol. 2008; 168(4):422-426.
12. Basso O, Christensen K, Olsen J. Higher risk of pre-eclampsia after a change of partner. An effect of longer interpregnancy intervals? Epidemiology, 2001; 12:624-9.
13. Conde-Agudelo A, Belizan JM. Maternal morbidity and mortality associated with interpregnancy interval: A cross-sectional study BMJ. 2000; 321:1255-9
14. Trogstad L, Magnus P, Skjaerven R, Stoltenberg C. Previous abortions and risk of pre-eclampsia, Int J Epidemiol. 2008; 37(6):1333–1340.
15. Rasmussen S, Ebbing C, Irgens LM. Predicting preeclampsia from a history of preterm birth *PLoS One*. 2017; 12(7):e0181016. Published 2017 Jul 24.
16. Ghidini A, Salafia CM. Histologic placental lesions in women with recurrent preterm delivery, Acta Obstet Gynecol Scand. 2005; 84:547-50.
17. Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J, Versalovic J. The Placenta Harbors, a Unique Microbiome Sci Transl Med. 2014; 6:1-10.
18. Jain S, Sharma P, Kulshreshtha S, Mohan G, Singh S. The role of calcium, magnesium, and zinc in pre-eclampsia, Biol Trace Elem Res 2010; 133(2):162-70.
19. Ali AA, Rayis DA, Abdallah TM, Elbashir MI, Adam I. Severe anemia is associated with a higher risk for preeclampsia and poor perinatal outcomes in Kassala hospital, eastern Sudan, BMC Res Notes. 2011; 4:311.
20. Gupta G. A case-control study to evaluate correlation of anemia with severe preeclampsia, Int J Reprod Contracept Obstet Gynecol. 2018; 7:2773-7.
21. Aluko A, Joshi A, Styer AK, Young BC, Johnson KM, Hacker MR *et al*. Polycystic ovary syndrome and the risk of preeclampsia, Fertility and Sterility. 2019; 111:4.