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Hypertensive Disorders in Pregnancy Increase the Risk of Future Cardiovascular Disease

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ABSTRACT

Objective: Our study was designed with aim to observe all pregnancy-related hypertensive disorders and investigate the association of HPD and cardiovascular disorders.

Methodology: This case-control study was conducted in Karachi Institute of Heart Diseases Karachi Pakistan from the June 2020 to the June 2021. Hypertension was defined after the 3 days of consistent observations of systolic pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg during a cardiologist visit. All forms of hypertension were included in our research. We used SPSS 23.0 for comparing gestational hypertension and pre-eclampsia among case and control groups. Four crude and logistic regression models were used to represent the association of pregnancy-related hypertensive disorders and cardiovascular disease.

Results: For this research total of 512 participants were recruited from which 339 (66.2%) were controlled and 173 (33.7%) were categorized into case groups. Control was younger compared to cases with fewer pregnancies (3 pregnancies) as compared to control (5 pregnancies). Gestational hypertension was highly observed in the case group (11.6%) whereas the control group reported high prevalence of preeclampsia (12.8%) than the case group (8.7%). The adjusted odds ratios represent no association of pregnancy-related hypertensive disorders with cardiovascular diseases. However, an inverse relationship was observed by adjusted odds ratios. On the other hand, the polytomous model manifested a positive association of gestational hypertension with CVD when compared with covariates.

Conclusion: We concluded that gestational hypertension is associated with the future risk of cardiovascular diseases. However, the logistic regression model failed to find any relationship of hypertensive pregnancy disorder with cardiovascular disorders.

Key words: Hypertensive pregnancy disorder, Cardiovascular disease, Gestational hypertension, Preeclampsia

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INTRODUCTION

Hypertensive disorders of pregnancy are one of the most challenging disorders in the world. All around the world, almost 5% to 10% of pregnancies are affected by hypertensive pregnancy disorder (HPD) [1]. These disorders are highly associated with the future risk of cardiovascular events compared to the other women [2]. Preeclampsia is the most serious type of HPD. Moreover, gestational hypertension is mostly associated with proteinuria [3]. Both forms of HPD; preeclampsia and gestational hypertension may contribute to chronic hypertension. The severity of preeclampsia is highly associated with future risk of cardiovascular events as compared to mild or moderate disease [2]. Preeclampsia and gestational hypertension are recognized factors of maternal morbidity and mortality. According to a world health organization survey, 2.7% of incidents of hypertensive pregnancy disorders were observed from the year 2004 to 2008 [4]. However, 2.2% incidents of

preeclampsia, 0.3% of gestational hypertension, and eclampsia were reported in the same report. The survey conducted in the African region reported 5.6% incidents of preeclampsia and 2.9% of eclampsia from the year 2002 to 2008 [5]. These disorders negatively influenced the postpartum health outcomes. The study of William [6] and Roberts [7] highlights that HPD is not directly associated with cardiovascular diseases they unfold the risks of CVD which may cause CVD events. Many other studies reported that HPD enhanced 1.5% to 2% risk of future cardiovascular disorders [8-10]. However, a very limited amount of studies were produced in past. Our study was designed with aim to observe all pregnancy-related hypertensive disorders and investigate the association of HPD and cardiovascular disorders.

METHODOLOGY

This case-control study was conducted in Karachi Institute of Heart Diseases Karachi Pakistan from the June 2020 to the June 2021. This is one of the biggest pediatric hospitals of Karachi equipped with instruments related to maternal and pediatric care. All the patients with complete administrative data including mother name birth date, age, phone number, etc. All the mothers aged 18 to 45 years, diagnosed with arteriosclerotic cardiovascular diseases were recruited in case group. In the control group, we recruited all the mothers with no exposure of cardiovascular disorders admitted to the gynecology department at the same time of diagnosed cases. We excluded all the patients with a history of diabetes mellitus, renal disease, pregnant women less than 6 months, and those who were already suffering from cardiovascular diseases. Patients with coronary artery disease, cerebrovascular disease, and hypertension were merged into the case group. In case of the absence of a diagnosis, we analyzed the drug prescriptions of patients and classified patients accordingly. Hypertension was defined after the 3 days of consistent observations of systolic pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg during a cardiologist visit. All forms of hypertension were included in our research. The history of hypertension disorders was taken from a phone interview. A standardized questionnaire was extracted from Diehl et al12 who studied the sensitivity and specificity of preeclampsia among women. This questionnaire had questions related to hypertension type, hypertension diagnosis, a prescribed drug for lowering blood pressure, and the presence of protein in the urine. For this research consent was taken from the ethical committee and research department of the hospital. We followed all the principles mentioned in Heliniski's laws. Patients were well informed by the objectives and consequences of the research. Volunteer participation was encouraged. Written consent was asked from patients before observing the research targets.

We used SPSS 23.0 for comparing gestational hypertension and pre-eclampsia among case and control groups. Four crude and logistic regression models were used to represent the association of pregnancy-related hypertensive disorders and cardiovascular disease. In the first model, we correlated each type of cardiovascular disorder with gestational hypertension and preeclampsia (A1). In the second model (A2) we compared the results of women with preeclampsia and women with no history of hypertensive disorders of pregnancy. The third model (A3) was used to represent the comparison of gestational hypertension vs no hypertension and the fourth was used to compare the results of treated hypertension with A1, A2, and A3 models. Smoking status, multiple gestations, number of pregnancies, family history of cardiovascular diseases, and age was used for adjusted analysis. The propensity score of each patient was calculated for comparing these covariates. The propensity score was categorized into six classes and used in models 1-3 whereas multiple logistic regression was used in the 4th model with these covariates13. 95% confidence interval was set for crude and adjusted models. E values were used to compare the exposure-outcome relationship.

RESULTS

For this research total of 512 participants were recruited from which 339 (66.2%) were controlled and 173 (33.7%) were categorized into case groups. Control was younger compared to cases with fewer pregnancies (3 pregnancies) as compared to control (5 pregnancies). Regarding educational attainment, we observed that controls were more educated than case groups. In the control group total of 37% population had higher education whereas the higher education ratio among cases was only 19.4%. The prevalence of only secondary education was slightly high in both groups. We observed that 17% case group was widows and 5.88% were divorced and single parents. Comparing the results with the control group we observed that controls had only a 1.49% ratio of widows and only 1% were divorced. The proportion of divorces was observed as (<1% and 6%) in the control versus case groups. We did not find any statistically significant difference in terms of family history of cardiovascular diseases, multiple pregnancies, and smoking (Table 1).

In Table 2 the prevalence of self-reported HPD was recorded. We observed quite similar results of hypertensive disorders of pregnancy in the case (20.3%) and control groups (21.8%).

However, gestational hypertension was highly observed in the case group (11.6%) whereas the control group reported high prevalence of preeclampsia (12.8%) than the case group (8.7%). Table 3 represents the crude and adjusted analysis. The adjusted odds ratios represent no association of pregnancy-related hypertensive disorders with cardiovascular diseases. However, an inverse relationship was observed by adjusted odds ratios. On the other hand, the polytomous model manifested a positive association of gestational hypertension with CVD when compared with covariates. Interestingly the comparison of covariates with a dichotomous model represented inverse association with preeclampsia and cardiovascular events.

Table 1: Demographic characteristics of case versus control [12].

Variables	Total (n=512)	Controls (n= 339)	Case (n= 173)	P-value
Diagnosis median age	34	29	49	<0.001
Missing observations	24	21	3	
Number of pregnancies (median)	3	3	5	<0.001
Missing observations	5	2	3	
Marital Status				
Missing observations	7	4	3	<0.001
Couple	357 (70.3%)	242 (72.2%)	115 (67.6%)	
Divorced	13 (2.57%)	3 (0.89%)	10 (5.88%)	
Widow	34 (6.73%)	5 (1.49%)	29 (17.1%)	
Education status				
Missing observations	12	9	3	<0.001
Higher education	155 (31%)	122 (37%)	33 (19.4%)	
Less than secondary	85 (17%)	36 (10.9%)	49 (28.8%)	
Secondary	260 (52%)	172 (52.1%)	88 (52.8%)	
Smoking status				
Missing observations	11	8	3	0.377
Never smoke	448 (89.4%)	298 (90%)	150 (88.2%)	
Former smokers	40 (7.98%)	23 (6.95%)	17 (10%)	
Multiple pregnancies				
Missing observations	5	4	1	0.212
No	420 (82.8%)	272 (81.2%)	148 (86%)	
Yes	87 (17.2%)	63 (18.8%)	24 (14%)	
Family history of CVD				
Missing observations	4	1	3	0.634
No	272 (53.5%)	184 (54.4%)	88 (51.8%)	
Yes	236 (46.5%)	154 (45.6%)	82 (48.2%)	

Table 2: Exposure distribution of case vs. control [12].

Variables	Total	Case	Controls	P-value
Hypertensive Disorders of pregnancies (dichotomous model)				0.8
Missing observations	23	1	22	
No	385 (78.7%)	137 (79.7%)	248 (78.2%)	
Yes	104 (21.3%)	35 (20.03%)	69 (21.8%)	
Hypertensive Disorders of pregnancies (polytomous model)				0.2
Missing observations	27	1	26	
No	385 (79.4%)	132 (79.7%)	248 (79.2%)	
Preeclampsia	45 (9.28%)	20 (11.6%)	25 (7.99%)	
Gestational hypertension	55 (11.3%)	15 (8.72%)	40 (12.82%)	

Table 3: Crude and adjusted analysis of case vs. control [12].

Exposure	Adjusted results	Unadjusted results	E- value
	Odd ratios (95% C.I)	Odd ratios (95% C.I)	
Propensity score with dichotomous exposure of logistic regression model			
HPD	n = 448	n= 489	1.7
	0.83 (0.51- 1.34)	0.92 (0.58 - 1.45)	
Preeclampsia	n =403	n= 403	3.87
	0.45 (0.22 - 0.89)	0.61 (0.32 - 1.18)	
Gestational hypertension	n =395	n = 395	2.3
	1.47 (0.77 - 2.79)	1.37 (0.73 to 2.57)	
Multiple regression analysis of Polytomous model exposure with covariates			
Hypertensive Disorders of pregnancy	n = 321	n= 385	
Preeclampsia	0.28 (0.10 - 0.72)	0.68 (0.36 - 1.27)	6.6
Gestational hypertension	2.33 (0.99 - 5.50)	1.45 (0.78 - 2.7)	4.09
No HPD history	1	1	

DISCUSSION

Our research observed a positive association of cardiovascular diseases with gestational hypertension. Whereas the inverse counterintuitive correlation was found between preeclampsia and cardiovascular diseases. These results are in contradiction with the previous studies of Bhattacharya et al. [8], McDonald et al. [2], Kestenbaum et al. [13], and Ray et al. [14]. All these mentioned studies found a positive association of preeclampsia with cardiovascular diseases. This happened due to the selective biases of our study. Our control group was relatively younger than the case group with recent pregnancies. Secondly, we assumed that pediatric selection bias is the major reason for observing the inverse association of cardiovascular disorders with preeclampsia. Preeclampsia was highly observed in the control group as compared to cases. Our results depict that women who suffer from gestational hypertension are at a greater risk of suffering from hypertension in the future compared to women with preeclampsia. These results are comparable with the results of Kestembaun et al. [13] study. In his study, he observed that women suffering from gestational hypertension had a 2.8% relative risk of cardiovascular disease in the future when compared with preeclampsia [13]. We observed a low E value (1.70) for the association of HPD and cardiovascular disease. This demonstrates that we failed to find an association between both variables. In polytomous model, our results depict a strong positive association of gestational hypertension with CVD however dichotomous model shows a weaker association. This could be happened due to the high estimated E power in the polytomous model. In past, the study of Valdiviezo et al. [15] and Klemmensen et al. [16] observed similar results in terms of low sensitivity even they had low power of E. Low sensitivity of E value demonstrate that we did not find any effect for gestational hypertension in the dichotomous model. However, the overall polytomous model show a strong positive association of gestational hypertension with CVD.

The study of Veerbeek et al. [17] revealed that the patients with gestational hypertension have a high potential risk of cardiovascular disorders and will suffer from high blood pressure for 2 to 5 years after their pregnancies. This risk is relatively low in group of preeclampsia hypertension. However, his study was done on a small number of women, yet a correct diagnosis about subtype hypertension was made which these females faced during their pregnancy. Impaired carbohydrates and lipid metabolism was highly observed in patients with HPD [18]. Some studies reported increased insulin resistance due to HPD [19]. Very low-density lipoprotein cholesterol and low-density lipoprotein were widely observed in HPD patients. These changes may contribute to endothelial dysfunction in the future [20,21]. The study of Robert and Hubel7 claimed that pregnancy-related hypertension has not been linked with cardiovascular disorders. More population-based studies are needed to evaluate the association of CVD and HPD for the future.

CONCLUSION

We concluded that gestational hypertension is associated with the future risk of cardiovascular diseases. However, the logistic regression model failed to find any relationship of hypertensive pregnancy disorder with cardiovascular disorders.

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