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Potential risk factor of pre-eclampsia among healthy Chinese women: a retrospective case control study.

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Abstract

Objective: To identify predictive factors which helps in screening the healthy Chinese pregnant women who were at high risk of developing Pre-Eclampsia (PE).

Materials and methods: We have reviewed the medical records of healthy Chinese pregnant women with single gestation and had given birth to baby at department Ggynecology and obstetrics, Wuhan Medical & HealthCare Center for Women and Children (Wuhan Children's Hospital Wuhan Women and Children Care Hospital) , china between January 2006 and July 2015.We reviewed the medical records of each healthy pregnant woman who were diagnosed pre-eclamptic before labor pain (case), and not diagnosed pre-eclamptic (control), and data were analysed using univariate analysis.

Result: Medical records of 32, 000 pregnant women who were admitted during January 2006 to July 2015 in our hospital were studied. Of total cases, 853 (3%) had PE. Abnormal perinatal outcome was significantly higher in women with PE compared to control women; this indicates that the PE is responsible for adverse maternal and foetal outcome. Incidence of gestational diabetes mellitus (GDM), urinary infection was meaningfully greater among women with PE than women with no PE. Family history of diabetes and hypertension was significantly higher in women with PE when compared with control group. We also observed that the stress score was significantly higher in women with PE than control.

Conclusion: We suggest GDM, family history of DM/high blood pressure; urinary tract infection, fibroids and psychological stress during pregnancy are key predictors of PE among Chinese pregnant women. These prognostic factors help in screening the pregnant women who were at high risk of developing PE.

Keywords: Pre-eclampsia, Pregnancy, Predictive factors, Diabetes, Hypertension.

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Introduction

Pre-Eclampsia (PE) is one of most common cause of complications in pregnant women leading to maternal morbidity and mortality [1], and it is the second most common cause of abnormal pregnancy outcome [2]. Pre-eclampsia is commonly observed during second trimester of pregnancy, with blood pressure greater than 140/90 mmHg and presence of albumin in urine (usually more than 300 mg in 24 hour) [3]. The prevalence of PE ranges from 4% to 7% among pregnant women [4]. World Health Organization reports suggested that approximately 70,000 cases of maternal morbidity and mortality occurred due to PE every year worldwide [1]. In women with mild to moderate PE, generally no symptoms reported. In pregnant women with severe PE often experienced increased blood pressure, headache, and proteinuria [5].

The key risk factor of PE includes ethnicity, family history, weight, high blood glucose level, age of women before and after pregnancy, previous history of renal disorder, hypertension and auto-immune disease [6]. Since etiology of PE is remain unclear in spite of several efforts to find the potential reasons, thus there was no established and effective methods to prevent the PE. Therefore, identification of potential risk factor in development of PE helps to prevent incidence of PE. The prevalence of PE among Asian patients was found lower compared to white pregnant women [7,8]. The prevalence and risk factor of PE in healthy Chinese

pregnant was not evaluated earlier. Therefore, we designed this study to evaluate prevalence and risk factor of PE among healthy Chinese pregnant women. We also evaluated the relationship between PE and family history of high blood pressure and GDM. The objective of present study was to identify predictive factors that can be used in screening the pregnant women who are at high risk of developing PE, this may help in reducing the incidence of PE related morbidity and mortality in pregnant women.

Materials and Methods

We reviewed the medical records of healthy Chinese pregnant women with single gestation and had given birth to baby at Department of Gynecology and Obstetrics, Wuhan Medical & HealthCare Center for Women and Children (Wuhan Children's Hospital Wuhan Women and Children Care Hospital) from January 2006 to July 2015We used computerized database of maternal and child health care center to collect required data to fulfil the objective of our study. We have excluded the medical records of pregnant women who had diabetes, history of chronic hypertension and/or had hypertension before second trimester of pregnancy and/or had multiple gestations. Also medical records of patients who had BMI of 30 kg/m^2 or more (obese patients) have been excluded from analysis. Institutional ethics committee approval was obtained from Wuhan Medical & HealthCare Center for Women and Children (Wuhan Children's Hospital Wuhan Women and Children Care Hospital). Since, this was a retrospective, observational chart review study, and none of patients whose medical records reviewed were contacted, the requirement for obtaining formal informed consent was waived by ethics committee.

The information related to outcome of pregnancy from labor to birth including postpartum interview were captured in medical records of each pregnant woman. We reviewed the medical records of each healthy pregnant woman who were diagnosed pre-eclamptic before labor pain (case), and who were not diagnosed pre-eclamptic (control). The pregnant women who were not diagnosed hypertensive before 2nd trimester, but their blood pressure was higher than 140/90 mmHg in last trimester with urine albumin level of more than 300 mg were in PE cases group, those who had no higher blood pressure and urine albumin level were considered in control group.

The below risk factors were evaluated in light of potential covariates: Age (≤ 18 year; 19-34 year and ≥ 35 year); smoking status (Smoker; non-smoker); GDM, anxiety during pregnancy; years of schooling; body weight; overweight (25-29 kg/m^2); urinary tract infection during pregnancy; Non-cancerous growths of the uterus (fibroids); past experience of pre-eclamptic; family history of hypertension and diabetes; blood type; conception technique; gender of born baby. The general protocol/policy of hospital, each pregnant women were asked to rate their stress level during pregnancy using Perceived Stress Scale (PSS), which contain 10 questionnaire, each question score range from 0 to 4; total score was range from 0 to 40 where 0 indicates no stress and, higher score of PSS indicates greater stress during pregnancy. Perinatal outcome related data such as baby weight of less than 1.5 kg; Apgar score (1-min and 5 min of score less than 7); pre-term delivery; kind of delivery (normal or caesarean); requirement of neonatal intensive care unit transfer; fatal/neonatal death; postpartum haemorrhage and abruptio placentae were also captured from medical records of all pregnant women.

Data from each patient was coded and analysed using Graph Pad Prism statistical analysis software (version 6.0). Quantitative variable was presented as mean ± standard deviation, and data were compared using parametric/non-parametric statistical test based number of comparison group and distribution of data, using 2 sided statistical tests. Normality test (Kolmogorov-Smirnov test or Shapiro-Wilks test) will be used to check the distribution of data of quantitative data. Categorical variables was presented as absolute number and/or percentage of subjects in each category, and were compared using Chi-square or fisher exact test based on size of data, using 2 sided statistical tests.

Result

We have reviewed medical records of 32, 000 pregnant women who had visited during January 2006 to July 2015 in our hospital. Of 32,000 cases, 853 (3%) patients had PE. The average age at the time of baby birth was higher in pre-eclamptic pregnant women than non-pre-eclamptic women. Similar trend was observed when pre-pregnancy weight was compared among women with PE with control. On comparing BMI, significantly higher proportion of overweight women (25-29 kg/m^2) was in PE group as compared to control group. This indicates that the majority of women with PE were overweight before pregnancy as shown in Table 1. There was no statistical significant difference in terms of number of year of education was observed among both the groups ($p>0.05$).

Abnormal perinatal outcome such as baby weight of less than 1.5 kg and Apgar score (1 min and 5 min of score less than 7) was significantly higher in women with PE compared to control women. Moreover, proportion of pre-mature delivery was significantly higher in women with PE compared to control women. Caesarean delivery remained significantly higher in women with PE compared to control women. We also observed that the requirement of neonatal intensive care unit transfer was significantly higher in women with PE compared to control women. Incidence of postpartum haemorrhage and abortion placenta were significantly higher in women with PE as compared to control as shown in Table 2.

In PE groups, incidence of GDM was significantly higher in comparison to control group. Also incidence of urinary tract infection and fibroids was significantly higher in women with PE than women with no PE. Family history of diabetes and hypertension was significantly higher in women with PE when compared with control group. We also observed that the stress score was significantly higher in women with PE than control. No significant difference between women with PE or control was observed in respects to age of their spouse, use of condom

during conception, gender of new born baby, blood group including Rh factor. Incidence of PE was significantly higher in women who were smoker than non-smoker.

Higher risk of PE was found in women with family history of diabetes and hypertension as compared to women with no family history of diabetes and hypertension as shown in Table 3. We found that the risk of PE was double in women who had family history of diabetes and hypertension when compared to women with no family history of diabetes and hypertension. We also noticed that the stress score was significantly higher in women with PE when compared women who had no PE.

Table 1. *Demography and clinical characteristic of pregnant women admitted in Wuhan Medical & HealthCare Center for Women and Children (Wuhan Children's Hospital Wuhan Women and Children Care Hospital) from January 2006 to july 2015.*

Variables	Pre-eclampsia cases (N=853)	Control cases (N=31,147)
Age categories		
18 or less	15%	5%
Between 19-34	65%	90%
More than 35	20%	5%
Age (year), Mean (SD)	29 (5.2)	28 (4.3)
Pre-pregnancy weight (kg) Mean (SD)	83 (3.7)	71 (3.6)
Pre-pregnancy BMI		
Overweight (25-29 kg/m^2)	45%	5%
Non-overweight (20-24 kg/m^2)	55 %	95%
Smoking status		
Smoker	38%	12%
Non-Smoker	62 %	88%
Number of years of schooling (year)		
8 or less	18%	8%
Between 9-15	70 %	88%
More than 16	22%	4%

Values are expressed as % of subjects in each category except age and weight. N=Total number of subject in each group.

Table 2. *Abnormal pregnancy outcome due to pre-eclampsia in pregnant women.*

Type of abnormal outcome	Pre-eclampsia cases (n=853)	Control cases (n=31,147)	P value
Baby weight ≥1.5 kg			
Present	45%	5%	<0.0001
Absent	55 %	95%	
Apgar score in one minutes (less than 7)			
Present	40%	8%	<0.0001
Absent	60 %	92%	
Apgar score in five minutes (less than 7)			
Present	35%	9%	<0.0001
Absent	65 %	91%	
Pre-mature delivery			
Present	38%	12%	<0.0001
Absent	62 %	88%	
C-section delivery			
Present	31%	11%	<0.0001
Absent	69%	89%	
Requirement of neonatal intensive care unit transfer			
Present	32%	4%	<0.0001
Absent	68%	96%	
New-born death			
Present	32%	3%	<0.0001
Absent	68%	97%	
Postpartum bleeding			
Present	30%	4%	<0.0001
Absent	70%	96%	
Placenta abruption			
Present	45%	3%	<0.0001
Absent	55%	97%	

Values are expressed as % of subjects in each category. N=total number of subject in each group. P value calculated by chi-square test using multivariate analysis.

Table 3. *Prognostic factors for increased incidence of pre-eclampsia in pregnant women.*

Variable	Pre-eclampsia cases (N=853)	Control cases (N=31,147)	Odd ratio 95% CI P value
GDM			
Present	45%	5%	15.54 5.82-41.49 <0.0001
Absent	55 %	95%	
Urinary tract infection			
Present	35%	9%	5.44 2.44-12.10 <0.0001
Absent	65 %	91%	
Family history of diabetes mellitus			
Present	38%	12%	4.49

Absent	62 %	88%	2.17-9.28 <0.0001
Family history of chronic hypertension			
Present	40%	8%	7.66 3.35-17.50 <0.0001
Absent	60 %	92%	
Work stress during pregnancy			
Present	45%	5%	15.54 5.82-41.49 <0.0001
Absent	55 %	95%	
Fibroids			
Present	40%	8%	7.66 3.35-17.50 <0.0001
Absent	60 %	92%	
Family related stress during pregnancy			
Present	35%	9%	5.44 2.44-12.10 <0.0001
Absent	65 %	91%	

Values are expressed as % of subjects in each category. P value calculated by chi-square test using multivariate analysis. N=Total number of subject in each group.

Discussion

This was the first largest retrospective case control study to determine the prevalence and PE risk factor among healthy Chinese pregnant women. In our study, the prevalence of PE among Chinese pregnant women was lower than Caucasians and other non-Asian pregnant women [9-14]. Lower prevalence of Chinese pregnant women was possibly attributed to body mass index, routine living including living relationship with their spouse [15]. Our study results were consistent with findings of Xiao et al. [15], which suggested that Chinese ethnicity might be accountable for lower prevalence of PE. Our study suggested that PE is comparatively infrequent among Chinese pregnant women.

Our finding showed that pregnant women with GDM were at higher risk of developing PE, GDM was associated with the subsequent development of PE. Our study showed positive relationship between PE and diabetes, and our finding was consistent with previous findings [16-27]. It has been reported that GDM is independently and significantly associated with an increased risk of PE, and even small degree of glucose imbalance lead to development of PE [19-21]. There was positive correlation between insulin resistance and diabetes mellitus with increased blood pressure; hyperinsulinaemia was known to excite the reproduction of muscle cells which thereby activate secretion of neurotransmitter namely noradrenaline and adrenaline which results in increased BP. Hyperinsulinemia also lead to renal sodium retention and associated with endothelial dysfunction. This all alterations after glucose metabolism imbalance may contribute to increased blood pressure [26,27].

Our study results showed that the pregnant women with family history of hypertension were at higher risk of developing PE; our finding is consistent with previous studies [28-30]. Our results showed positive relationship between family history of chronic hypertension and risk of PE. Our results recommended that the family history of chronic hypertension is an alternative measure for hereditary factors that may be one of cause PE [7]. Women with family history of chronic hypertension are one of the most common clinical risk makers of PE compared to the biochemical markers.

In our study, incidence of PE was significantly greater in women with higher stress score compared to women with no stress during pregnancy. Our study results showed positive association of mental stress during pregnancy and development of PE. We observed that the pregnant women with greater stress are at very high risk of developing PE. Increased incidences of PE in women with mental stress could be explained based on the facts that psychosocial strain leads to vasoconstriction and increased uterine artery resistance, which results in development of PE [31-33]. Role of stress disorder such as depression and anxiety in developing PE during pregnancy was well established [34], and positively correlated. Apart from anxiety disorders, any kind of mental stress due to uneasy environment of office and home which could results in biological alterations in pregnant women lead to complications such as PE and pre-mature labor pain [35,36]. Moreover, prenatal stress may changes maternal physiology and immune function; this may also lead to increased risk of PE [29].

Additionally, we found that the prevalence of PE was significantly higher in women with urinary tract infection and fibroids compared to women with no urinary tract infection and fibroids during pregnancy. Our study results showed association of urinary tract infection and fibroids during pregnancy and development of PE. We observed that the pregnant women with urinary tract infection and fibroids are at very high risk of developing PE. Our finding of increased incidences of PE in women with urinary tract infection and fibroids is in consistent with the previous report [37]. In the past decades, many laboratory tests has been advised to discover the potential risk of developing PE in pregnant women, however, such as lab investigations have inadequate sensitivity and costly which was difficult to afford. We suggest family history of hypertension; diabetes; gestational diabetes, and mental stress can be better screening tools to determine risk of PE in pregnancy.

The predictive factors such as gestational diabetes, mental stress are amendable and avoidable risk factor of PE, whereas family history of diabetes and hypertension even could not be modifiable, nonetheless very useful to identify the pregnant women who are at higher risk of PE and need more attention. This help in reducing the incidence of PE related morbidity and mortality in pregnant women. We encourage increasing awareness of risk factor of PE, which could lead to decrease prevalence of PE among pregnant women.

Conclusion

We suggest GDM, family history of high blood pressure and psychological stress during pregnancy is important predictors of PE among Chinese pregnant women since incidence of PE were significantly higher in pregnant women with GDM, family history of high blood pressure and increased mental stress during pregnancy. Moreover, higher incidences of PE were found in pregnant women with urinary tract infection and fibroids during pregnancy, this indicates urinary tract infection and fibroids during pregnancy are also key determinant of PE in pregnant women. These prognostic factors can be used in screening the pregnant women who were at high risk of developing PE. This finding help in reducing the incidence of PE related morbidity and mortality in pregnant women. We encourage increasing awareness of risk factor of PE, which could lead to decrease incidences of PE among pregnant women.

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