

Frequency and factors leading to recurrent pre-eclampsia

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Abstract

Objective: To determine the frequency and factors leading to recurrent preeclampsia.

Methods: The cross-sectional study was conducted at the Jinnah Post Graduate Medical Centre, Karachi, from January 2011 to February 2012, and comprised parous subjects <40 years of age with history of preeclampsia in previous pregnancy/pregnancies with singleton pregnancy and gestational age of >20 weeks. Gestational age was determined by early scan with preeclampsia in index pregnancy. Data was collected through a specialised questionnaire and analysed using SPSS 16.

Results: Of the 479 patients seen with preeclampsia, 121(25.26%) were of recurrent preeclampsia. The mean age of such patients was 29.7±4.9 years (range: 20-39 years). Further, 84(69.42%) patients were multipara and 40(33.05%) were grand multipara. Mean body mass index was 29.97±6.2 (range: 18-54).

Besides, 28(23.14%) patients had gestational diabetes; 7(5.78%) were known diabetics; 24(19.83%) had chronic hypertension; 2(1.7%) patients had chronic renal disease; and 1(0.8%) had connective tissue disorder.

Conclusion: Being over-weight, having gestational diabetes and chronic hypertension were main risk factors leading to recurrent preeclampsia.

Keywords: Recurrent preeclampsia, BMI, Gestational diabetes, Chronic hypertension. (JPMA 65: 1173; 2015)

Introduction

Preeclampsia is a multisystem disorder and is a serious pregnancy complication which mainly occurs after 20 weeks of pregnancy. Worldwide prevalence of preeclampsia ranges from 3-8% of pregnancies, and 8.5 million cases are reported yearly.¹ In the United Kingdom, it complicates approximately 4-6% of pregnancies.² Preeclampsia is the third leading cause of maternal mortality and morbidity worldwide.³ It has been estimated by World Health Organisation (WHO) that worldwide approximately 60,000 women die each year from preeclampsia⁴ and it causes 11% deaths in UK and 24% of all maternal deaths in India.⁵

The risk of preeclampsia in first pregnancy is 4.1% and which itself is the strongest risk factor for preeclampsia in subsequent pregnancies.⁶ Published recurrence rates of preeclampsia varies widely from 0-5%⁷ and even up to 65%.⁸

Women with one or more of the following factors are at increased risk of developing recurrent preeclampsia. Chronic hypertension (4%),⁷ diabetes mellitus (DM) (4%),⁷ gestational DM (GDM) (Adjusted odds ratio [OR] 2.20; 95 confidence interval [CI] 1.5-3.13),⁸ renal disease (0.08%),⁷

connective tissue disorders (OR 2.5; 95% CI 1.2-5.1)⁹ have been cited as risk factors. Besides, the risk with same partner as that in the first pregnancy was 1.3% while it increased to 1.5% (OR 1.14; 95% CI 1.04-1.26) with a new partner.¹⁰ Increased inter-pregnancy interval (>5 years; adjusted OR 2.37; 95% CI 1.88-2.99),⁸ inter-birth interval (OR 1.13 per year; 95% CI 1.12-1.14),¹⁰ obesity,⁷ previous gestational age at which preeclampsia occurred (65% if in 2nd trimester)¹¹ and previous history of preeclampsia have also been noted as relevant factors. Preeclampsia is associated with maternal and perinatal morbidity and mortality when it occurs in subsequent pregnancies which includes hypertension, eclampsia, cerebrovascular accidents, placental abruption, pulmonary oedema, renal failure, hepatic dysfunction or rupture, foetal risk including growth restriction in approximately 25% cases, premature delivery, and death in utero or as a result of prematurity (in about 20 per 1000 cases).⁸ Foetal loss is higher in women with recurrent preeclampsia (19%) than in women with preeclampsia who had a normotensive pregnancy history (4.7%).¹¹

Women who have had a pregnancy complicated by preeclampsia, especially those who suffered from significant maternal or perinatal morbidity, need specific counselling regarding recurrence of preeclampsia in order to make decision about further reproduction. The main aim in the management of these patients is to optimise maternal health before she embarks on pregnancy. Preconception counselling and evaluation of these

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patients have got a very important role in optimisation of maternal health, which included lifestyle modification and control of medical disorders by multidisciplinary approach. The patients should be counselled for early booking, frequent antenatal visit, maternal and foetal monitoring is necessary to detect development of any complications and timely intervention and delivery is required to reduce the maternal and foetal morbidity and mortality.

A thorough literature search but no study could be found on the subject from Pakistan. The current study was planned to assess the frequency and factors leading to recurrent preeclampsia in our local setup so that strategies could be developed to minimise maternal and foetal morbidity and mortality associated with recurrent preeclampsia in pregnancy.

Patients and Methods

The cross-sectional study was conducted in Unit 2 of the Department of Obstetrics and Gynaecology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from January 2011 to February 2012. The sample size was calculated by taking prevalence rate of 13% of recurrent preeclampsia,¹¹ taking 95% CI and the margin of error being 0.06%.

Purposive sampling technique was employed to collect subjects aged <40 years, parous with history of preeclampsia in previous pregnancy/pregnancies with singleton pregnancy, and with gestational age of >20 weeks which was determined by early scan with preeclampsia in index pregnancy. Preeclampsia was defined as an increase in blood pressure to at least 140/90mmHg after the 20th week of gestation, an increase in diastolic blood pressure (DBP) of at least 15mmHg from the level measured before the 20th week, an increase in systolic blood pressure (SBP) of at least 30mmHg from the level measured before the 20th week, combined with proteinuria (at least 0.3g per 24 hours). Subjects with age >40 years, primigravida, with multiple pregnancies, pregnancy-induced hypertension and thyroid disorders were excluded. Patients admitted with past history of preeclampsia and now presenting with preeclampsia who fulfilled the inclusion criteria were enrolled after taking informed, written and verbal consent. Specialised questionnaire was used to collect data. These patients were admitted through outpatient department (OPD) or emergency department (ED) for either blood pressure monitoring or induction of labour and delivery. Urinary protein estimation was done by 24-hour urinary protein collection. History of previous preeclampsia was confirmed by past medical records

available with the patients. According to Quetelets index,¹² body mass index (BMI) was categorised into underweight <20, normal 20-24, overweight 25-30, obese 30-35, and morbidly obese >35.

Inter-pregnancy interval (IPI) was calculated in months and was defined as the number of months between index pregnancy and preceding birth or miscarriage/termination of pregnancy, and inter-birth interval (IBI) was calculated as number of months between two subsequent births.

Current gestational age with which the patients presented to us with preeclampsia were calculated by last menstrual period or earliest dating scan in case a patient was not sure of dates.

For the confirmation of proteinuric hypertension, 24-hour urinary protein was used. Risk factors such as chronic hypertension, DM, GDM, renal disease and connective tissue disorders were identified.

Data was analysed using SPSS 16. Descriptive statistics were applied. Mean and standard deviation (SD) was calculated for age, parity, BMI, IPI, IBI and development of preeclampsia at present gestational age and that in previous pregnancy. Frequencies and percentages were calculated in chronic hypertension, DM, renal disease, connective tissue disorder, and change in paternity.

Results

Of the 479 patients with preeclampsia in the study, 121(25.26%) were of recurrent preeclampsia. The mean age of such patients was 29.7±4.9 years (range: 20-39 years). Patients between the age of 26 and 30 years were in majority with 45(37.19%) (Figure-1).

Besides, 84(69.42%) patients were multipara, and 40(33.05%) were grand multipara. Mean BMI was

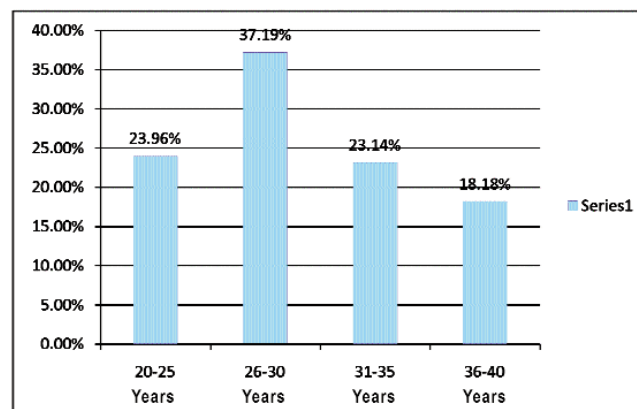


Figure-1: Age groups.

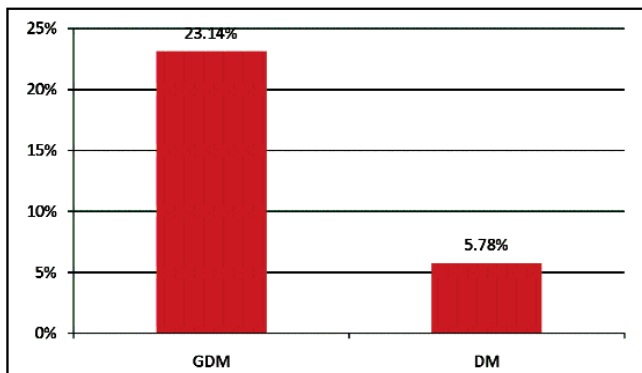


Figure-2: Prevalence of Diabetes mellitus (DM) and Gestational DM (GDM).

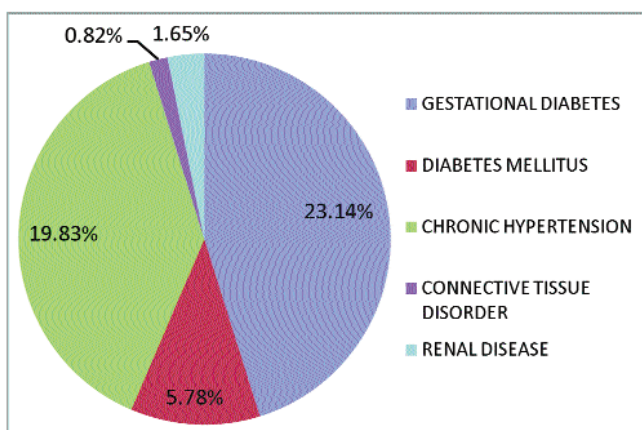


Figure-3: Medical disorders leading to recurrent preeclampsia.

29.97%±6.2 (range: 18-54), and 59(48.76%) patients were overweight, while 41(33.84%) were obese. Mean IPI was 37±25 months (range: 5-132 months). Of the total, 46(38.01%) patients had an IPI of 12-24 months.

Mean IBI 35±25 months (range: 10-132 months), and 48(40%) patients had IBI of 12-24 months.

GDM was found in 28(23.14%) patients, while 7(5.78%) were known diabetics (Figure-2).

Among other medical disorders, 24(19.83%) patients had chronic hypertension; 2(1.7%) had chronic renal disease; and 1(0.8%) had connective tissue disorder (Figure-3).

There was only 1(0.8%) patient with a change of partner.

The mean gestational age at which the patient presented with preeclampsia both in current and previous pregnancies were the same 35±3.3 weeks.

Discussion

A total of 479 patients with preeclampsia were seen

ANNEX-A: PERFORMA

BIODATA

Hospital#: _____
 Name: _____ Date of Admission: _____
 Age: _____
 Inpatient: _____ Outpatient: _____
 Address: _____
 Height: _____ Weight: _____ BMI: _____
 Marriage: _____ First: _____ Second: _____
 Last menstrual period: _____ Expected date of delivery: _____
 Blood pressure: _____ Proteinuria: _____

HISTORY OF PRESENT PREGNANCY

Gestational age: _____

PAST OBSTETRICAL HISTORY

Gravida: _____ Para: _____
 History of preeclampsia in previous pregnancy? _____
 Interpregnancy interval _____
PAST MEDICAL HISTORY
 Chronic hypertension _____
 Diabetes mellitus _____
 Renal disease _____
 Connective tissue disorder. _____

during the study period and 121 cases were of recurrent preeclampsia; an incidence of 25.26%. Published recurrent rate of preeclampsia may vary from 5% to 65%, and one study reported recurrence rate of 6.8%.⁸

In our study the risk of recurrent preeclampsia was high in age group between 26-30 years i.e. 37.19%. Risk of preeclampsia is known to increase with maternal age. A positive relationship between advanced maternal age and incidence of preeclampsia probably reflects a combined effect of ageing endothelium and higher incidence of other adverse factors, in particular increased booking blood pressure and BMI (high risk). A population-based retrospective cohort study found that the risk of recurrence of severe de novo preeclampsia was increased in women with age>35 years (adjusted OR: 3.79; 95% CI: 2.04-7.04; Reference 20-25 years.)⁸ But we found risk of recurrence in the younger age group between 26-30 years .Mean IPI was 37±25 months, while mean IBI was 35±25 months. When birth interval increases, it also increases the risk of recurrence, which is also seen in other studies.^{13,14} Conversely, in our study the risk of recurrence was found at lower interval between index pregnancy and previous pregnancies. Recurrent preeclampsia was common in IPI of 12-24 months i.e. 38%.

A study found that when the IBI was 10 years or more, the risk of preeclampsia was equal to that of nulliparous women and the OR for preeclampsia for each 1 year increase in IBI was about 1.12 (95% CI: 1.11-1.13).¹⁰

Obesity is major epidemic in developed countries that is now extending to developing countries. Obesity has important implications for pregnancy outcome and is associated with increased risk of preeclampsia of about 3 folds.¹⁵ The risk of preeclampsia typically doubles with each 5-7kg/m² increase in pre pregnancy BMI.^{16,17} High BMI is associated with preeclampsia.⁹ In addition to increased cytokine-mediated inflammation and oxidative stress,¹⁸ possible explanations¹⁹ include increased shear stress, dyslipidaemia,¹⁸ and increased sympathetic activity.²⁰ In our study, mean BMI was 29.9+6.2 (range: 18-54). And, 47.7% of the patients in our study with recurrent preeclampsia were obese.

Obesity is associated with insulin resistance. Hyperinsulinaemia, a marker of insulin resistance, has been shown to increase the risk of mild preeclampsia. The connection between obesity, insulin resistance and preeclampsia is complex and not fully understood.²¹ A study found that obese and overweight women had higher risk of recurrent preeclampsia (19.3% vs 14.2%) compared to those with normal BMI (11.2%).⁷

A 2010 population-based cohort study divided patients in 3 groups according to their BMI to see the recurrence of preeclampsia and found that recurrent preeclampsia in women who decreased their BMI between pregnancies was 12.8% (relative risk [RR]: 0.70; CI: 0.6-0.8) compared to 14.8% if BMI was maintained and 18.5% in those who increased BMI (RR: 1.29; CI: 1.2-1.38).²² Whether weight reduction prior to pregnancy or restricting weight gain during pregnancy will reduce the risk of preeclampsia is not established. However, the general health benefits of weight loss in obese individuals justify weight loss before pregnancy.²³

Inter-pregnancy weight reduction decreases the risk of recurrent preeclampsia so it should be encouraged in those who had preeclampsia previously.

Our study found 22% cases of recurrent preeclampsia with gestational diabetes and this was the main predictive factor of recurrent preeclampsia, while 7% cases were known diabetics. In one study, GDM (Adjusted OR: 2.20; 95CI: 1.5-3.13) and DM (Adjusted OR: 2.87; 95CI: 1.01-8.14) were not found to be predictive of recurrent preeclampsia perhaps because of low incidence of these condition and relatively small member of recurrent preeclampsia.⁸

Increased booking blood pressure is a major risk factor for pre-eclampsia.^{24,25} Chronic hypertension was the third main factor for recurrent preeclampsia in our study, as 19.83% cases of recurrent preeclampsia were chronic

hypertensive. A study found that patient with chronic hypertension who required antihypertensive treatment at booking, which may reflect severe hypertension, were at increased risk of having recurrent preeclampsia.² It also found that women with chronic hypertension comprised 1/3rd of women with previous preeclampsia and was a significant risk factor for recurrent preeclampsia.²

Women with chronic renal disease have increased risk of developing preeclampsia and severe complication.²⁶ We saw only 2 cases of recurrent preeclampsia with history of chronic renal disease which shows that it was not among the main predictive factors in our study which is in contrast with findings of an earlier study which had found that chronic renal disease was a main predictor of recurrent preeclampsia (Adjusted OR: 17.99; CI: 3.50-92).⁸

Several studies showed a clear association between maternal thrombophilias and early onset of preeclampsia.²⁷ Systemic reviews^{28,29} have confirmed an overall higher rate of acquired (primarily antiphospholipids) and genetic thrombophilia in women with severe early onset preeclampsia compared with controls. In our study only 1 case of antiphospholipid syndrome with recurrent preeclampsia was seen, which was 0.82%.

Conclusion

There was 25.26% recurrence of preeclampsia, and being overweight, or having GDM and chronic hypertension were the main factors leading to recurrent preeclampsia.

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