

Seasonal Variation in the Incidence of Preeclampsia Based on the time of conception

H. Mohaddesi and F. Nanbakhsh

Nursing and Midwifery Faculty, Urmia University of Medical Sciences, Urmia, Iran

Abstract: *Introduction:* Approximately 3-8% of pregnancies are complicated by preeclampsia (PE) and complications of pregnancy-related hypertensive disorders that are the third leading cause of maternal deaths. This study was conducted to assess the incidence of preeclampsia in women based on month and season of the conception in northwestern Iran. *Material and Methods:* The present investigation is a descriptive analytic cross-sectional study including all pregnant women with singleton pregnancies admitted to the Urmia Medical Science University due to preeclampsia, 2007-2008. From 2824 women with singleton pregnancy, 166 of them had preeclampsia and 2658 did not. In all cases, the onset of pregnancy was determined and the *relationship* between month (season) of pregnancy and occurrence of preeclampsia was studied. The general information, primary characteristics and the history of the two groups were collected and compared. *Results:* The age, gravidity and parity in the affected group were lower and difference was statically significant. Being nulligravid and having previous abortion was higher in the case group; and the difference was not statically significant. *Conclusion:* Preeclampsia incidence increased in cases of conception in warm and hot season's esp. in summer. The average temperature of conception is higher in women with preeclampsia but the difference is not statically significant. Therefore, it is suggested to hold training classes for young couples in order to avoid such disorders.

Key words: Seasonal variation • Incidence of preeclampsia • Timing of conception • Northwestern Iran

INTRODUCTION

Preeclampsia (PE) is a multisystem disorder of pregnancy characterized by the presence of clinical signs including proteinuria (300 mg or greater in a 24-h urine specimen and/ or protein to creatinine ratio of >0.30) and hypertension (defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg) [1,2], that develops after 20 weeks of gestation. It has been estimated that PE affects 3–5% of pregnancies worldwide recently, it has been reported that PE complicates 3-8% of pregnancies PE increases the maternal and fetal complications [3]. It accounts for approximately 50,000 maternal deaths worldwide each year [4].

In the USA, approximately 5-7% of pregnancies are complicated by PE and complications of pregnancy-related hypertensive disease, which are the third leading cause of maternal deaths [1,5].

Infantile outcome of PE pregnancies depends chiefly on the age of gestation in delivery and on the severity of the disease[3].

Early diagnosis and close observation of women with PE is vital since the risk of placental abruption, acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation and even maternal death increases[1].

Some well established risk factors for PE include nulliparity diabetes mellitus, nephropathy, collagen vascular disease, antiphospholipid antibody syndrome, molar pregnancy, fetal hydrops, multiple-pregnancy, positive history of chronic hypertension, obesity, maternal infection, positive family history of PE and fatal aneuploidy [5,7]. However the main etiology of PE is not clear, smoking has been found to decrease the risk of PE among underweight and normal-weight women but not in overweight women [3].

As many hypotheses have emerged to offer a causal framework for the disease, PE has been named the 'disease of theories' [1]. Although there is no definitive answer for the cause or causes of PE, some basic causes may be genetic predisposition, thrombophilia, functional radiation in prostaglandin, endothelial injury, change in

amount of nitric oxide (NO), increasing free radicals, abnormal invasion of erythroblasts, abnormal metabolism of calcium, or nutrition deficiencies [3].

Because the main etiology is unclear and the theories about mechanisms and preventive factors in high risk patients are not completely proven and their application is not desirably effective, so seeking unknown factors, like the season of conception, which affect the occurrence of PE is of importance.

Phillips, *et al* studied the relation between seasonal variations in PE based on timing of conception. The goal of this study was to assess the occurrence of PE and its relationships with month and season occurrence of the conception. In this study 142 women affected by PE were studied. The results showed that the conception in summer significantly increases the risk of PE [7]. In case the relationship is strong, conception could be avoided specially in high risk women. [8]. They found the highest risk of PE in conceptions occurring in the summer, whereas there was no significant variation in the incidence of PE based on the timing of delivery.

In Ghana, more cases of eclampsia have been noted in the rainy season. However; there are some studies that show no significant correlation between seasonal change and PE [7].

If there is a relationship between PE and the season of the conception, it is possible to avoid the pregnancy of women in the risk. This study was conducted to find the seasonal variation on the incidence of PE.

MATERIALS AND METHODS

The present investigation is a cross-sectional descriptive and analytic study including all pregnant women with singleton pregnancies admitted to the Urmia Medical Science University, I.R.IRAN (Motahhari

hospital) due to PE in a one year period, March 21, 2007 to March 21, 2008. Their pregnancies were term (equal to or more than 37 weeks, =37weeks) as defined by the American college of obstetricians and Gynaecologists (ACOG). Women with multiple pregnancies, positive history of coagulative disease and anti phospholipids syndrome, history of chronic hyper tension, or chronic renal disease and patients with incomplete records were excluded. The records of the study cases were assessed for the parameters of inclusion criteria and exclusion criteria then month and season of conception based and the age of pregnancy was calculated by LMP. This time was entered to the questioner and was studied. The registered information was parity, maternal age, date of birth, occurrence of hypertension (BP-140.90), PE (BP-140.90 and 1+ proteinuria dipstick or more than 300 mg protein in a 24-hour urine analysis) and eclampsia (PE and convulsion). In this study 2824 women with singleton pregnancy were enrolled due to the criteria which 166 of the contracted PE and 2658 did not. T-test, fisher, chi square test were used. The collected data were analyzed by SPSS 16. P value under 0.05 ($p < 0.05$) was considered statistically significant.

RESULT

This study enrolled 2824 women with singleton pregnancies, 166 of them were affected by PE and 2658 were devoid of it. The general information, primary characteristics and history of the two groups are indicated in the tables 1 and 2. The items of the two groups were compared. The age, gravidity and parity in the affected group were lower and difference was statically significant. Being nulligravid and having previous abortion was higher in the case group; and the difference was not statically significant. In this study the incidence of PE in

Table 1: The comparison of quantitative variables between both studied groups.

Group	Variable	Age (year)	Gravidity	Parity	Abortion	Body Temp. at pregnancy Initiation (C°)
Cases without PE	Mean	31.6	2.8	1.7	.10	12.1
	Standard Deviation	6.0	2.5	2.3	6.0	9.6
	Min.	18.0	.00	.00	.00	-2.0
	Max.	48.0	9.0	7.0	5.0	25.5
Cases with PE	Average	27.7	1.5	8.0	.20	13.4
	Standard Deviation	6.7	2.3	1.7	.60	10.2
	Min.	18.0	0.0	.00	.00	-2.0
	Max.	45.0	11.0	9.0	4.0	25.5
P-value		001.0>*	001.0>*	001.0*	128.0	068.0*

Table 2: The comparison of qualitative variables between both studied groups.

Variable	Cases with PE (n=166	Cases without PE (n=2658)	OR	CI	p
nulligravity	(% 8.57)96	(% 2.34)910	6.2	9.1-6.3	001.0>
previous PE	(% 8.1)3	(% 7.0)19	6.2	7.0-7.8	136.0
previous abortion	(% 5.14)24	(% 3.9)246	7.1	1.1- 6.2	027.0

Table 3: The incidence of PE in the studied groups, based on the month of initiation of the pregnancy.

the month of pregnancy initiation	PE		total
	yes	NO	
	NO (%)	NO (%)	NO (%)
April	12 (5?)	228 (95?)	240 (100?)
May	19 (2.5?)	345 (8.94?)	364 (100?)
June	18 (2.7?)	231 (8.92?)	249 (100?)
July	13 (2.7?)	168 (8.92?)	181 (100?)
August	16 (5.8?)	172 (5.91?)	188 (100?)
September	20 (9.8?)	205 (1.91?)	225 (100?)
October	7 (5.3?)	192 (5.96?)	199 (100?)
November	10 (4?)	238 (96?)	248 (100?)
December	19 (7?)	254 (93?)	273 (100?)
January	11 (2.5?)	200 (8.94?)	211 (100?)
February	13 3.5))	230 7.94))	243 100))
March	8 9.3))	195 1(.96)	203 100))
total	166 9.5))	2658 1.94))	2824 100))

(Pearson Chi- Square: P= 0.243)

Table 4: The incidence of PE in the studied groups, based on the season of initiation of the pregnancy.

	PE					
	-----				Total	
	Yes		NO			-----
Season	NO(%)		NO(%)		NO(%)	
Spring	49	7.5%	804	3.94%	853	100%
Summer	49	2.8%	545	8.91%	594	100%
Full	36	5%	684	95%	720	100%
Winter	32	9.4%	625	1.95%	657	100%
Total	166	9.5%	2658	1.94%	2824	100%

Pearson Chi square: (P= 0.04)

women based on month and season of the conception was assessed. The frequency percent of PE began to increase from April to reach its peak in August. Then it decreased until March. However the difference was not statically significant (p=0.243) (Table 3 and Figure 1).

The frequency percent of conception in the summer of the case group and conception in the autumn and winter of the control group was higher and

the difference was statically significant (p<0.04). The conception in spring lacked significant difference (Table 4 and Figure 2) also the frequency percent of conceptions in warm seasons (spring and summer) for the case group and conception in cold seasons (Autumn and winter) for the control group was higher and the difference was statically significant (p=0.038).

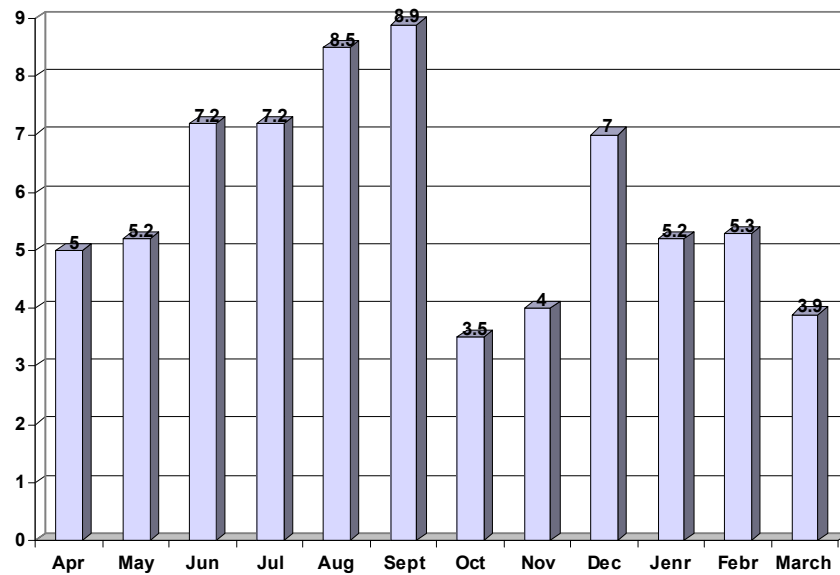


Fig. 1: The incidence of PE in the studied groups, based on the month of initiation of the pregnancy.

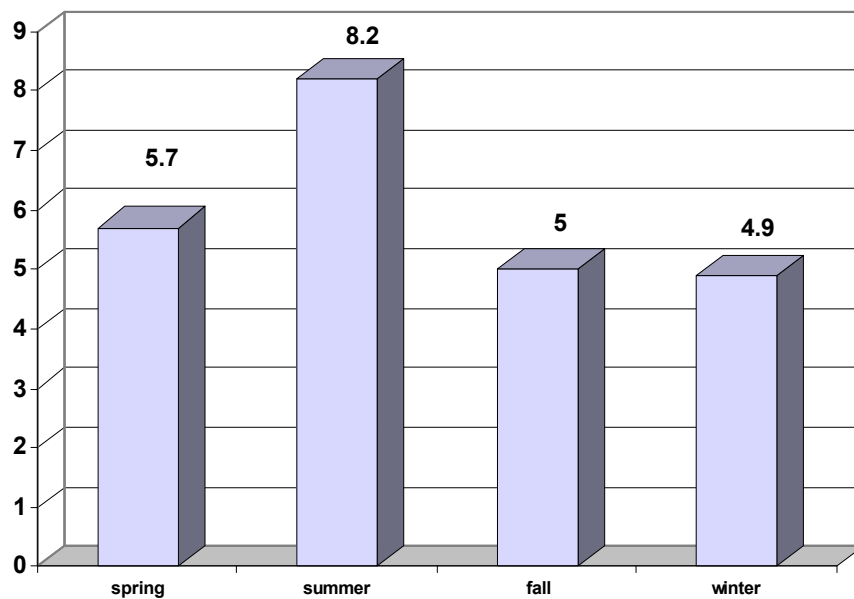


Fig. 2: The incidence of PE in the studied groups, based on the season of initiation of the pregnancy.

DISCUSSION

This study assessed the relation between the incidence of PE and conception time. The ultimate result indicated significantly higher occurrence in warm seasons esp. in the summer. In particular, few studies have assessed this relation: Phillips and *et al.* (2004) conducted a study in USA enrolling 142 primipar women with singleton pregnancy which were afflicted with PE

and compared their conception time with 7762 primipara women with singleton pregnancies lacking the condition. This study showed the conceptions in summer and in June, August has the highest risk and in March has the lowest risk of PE. This relation was not dependant to other risk factors such as low age of mother [7] in another study conducted is USA by Rudra and *et al.* (2005) 6680 cases of PE were included and their conception time was compared with unaffected cases. The study showed that

conceptions in warm seasons (spring and summer) results in the highest risk and conceptions in cold was independent of other risk factors of PE [9]. In another study by Tam and *et al* (2008) conducted in Hong Kong, 245 women affected by PE were assessed. In this study once more conception in summer (especially in June) accompanied the highest risk of PE. The occurrence of PE in cold seasons was the least [10]. Abbasssalizadeh *et al.* (2007) assessed 99 women suffering from PE in comparison with 1917 control in Tabriz, Iran. The study concluded that the conception time in July and October is directly and significantly related to the incident of PE [11]. Neela and *et al* supported the speculated relationship between increasing humidity and a lower temperature range with the increased incidence of eclampsia [12].

PE is significantly more common in the Jewish population. However, both populations demonstrate the same seasonal pattern, with higher incidence of PE in the winter months.

In result suggest that climate and environmental exposure may have an important role in the pathophysiology of PE [13]. The seasonal distribution reveals that the incidence of PE is significantly higher during the dry season than during the rainy season, but probably is not directly related to meteorological factors but rather on the nutritional deficiencies caused by the low rate of precipitations. [14]. Seasonal variation was minimal with the lowest prevalence detected in the fall (3.89%) and a peak of 4.1% in the winter. The highest monthly prevalence was found in January (4.4%). After adjusting for maternal age, race and other potential confounders, women who were admitted in the fall for delivery were 6% less likely than women who were admitted in the winter to have PE: adjusted OR = 0.94, 95% CI: 0.89-0.99, P = 0.02). [1].

The findings have implications for future research related to the aetiology of pre-eclampsia as well as for clinical care. [15]

Khojasteh and *et al.* (2011) found a relationship between the number of PE incidence and season. Therefore, precautions should be considered in those seasons in which the PE is increased. Attention to this prenatal care centers may help to decrease such serious side effects that endanger the health of both mother and fetus [16].

As it is evident our results are in agreement with the results of other studies. Discovering seasonal variation of PE occurrence seems an ancient subject. Antique books indicate that Hippocrates was attentive to this relation at the first place. After 1756 Smalliean *et al.* assessed and

presented the variation of PE occurrence due to season, temperature and rainfall amount, also, Chesly and *et al.* (1984) showed that conceptions in June is more probable to result in pregnancy complicated by PE[17].

They explained that more weddings in this month and higher probability of primigravid pregnancies account for this fact [17] however, the main aetiology of the seasonal variation PE occurrence is not known properly. Some studies justification of the higher occurrence of PE in warm seasons (decreased plasma volume in early times of pregnancy) [8,18-24] variation in temperature and humidity are other mechanisms that have been suggested [7, 10, 25] circadian cycle change is another probable cause for this relation. The change has been introduced as reduced sunshine and sub sequent decrease in vitamin D synthesis which result in altered calcium metabolism [26-28]. Some studies have proposed variation in nutritional habits such as quantity of antioxidant intake in different seasons of year [29-31].

The relation between delivery time and PE incidence were assessed in different studies and controversial results have been reported: some studies showed delivery in warm seasons increased the risk of PE [10, 25].

Some other studies showed the same relation for cold seasons. This class of studies possess an outstanding percentage [6,7]. In other studies (two studies in Kerman, Iran and Tehran, Iran) no such relation was found [32, 33]. Considering the result of studies which indicate higher incidence of PE, it could be estimated that conceptions in warm seasons would increase the incidence of PE. Even though many of these patients deliver in preterm and estimating their conception date would be inaccurate [7]. However, it can be proposed that PE occurrence is a multifactor event and seasonal variation could have a role in it. Ultimately, the interaction of different involved factors would be determining. Our study shows the obvious (apparent) trend which is independent of other influencing parameters.

The trend indicates higher PE occurrence in conceptions of warm seasons and gradually decreases afterwards.

CONCLUSION

PE incidence increases in cases of conception in warm seasons and summer in particular. The average temperature of conception is higher in PE cases but the difference is not statically significant. Therefore, it is suggested to hold training classes for young couples in order to avoid such disorders.

ACKNOWLEDGEMENTS

The authors wish to thank the colleagues and patients that were kindly engaged and collaborated with us throughout this study.

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