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Seasonal variation in the incidence of preeclampsia based on the time of conception

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Abstract: 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. 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. 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. 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.

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1. 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 P140 mm Hg or diastolic blood pressure P90 mm Hg) (Wellington and Mulla, 2012. Harapan et al., 2012), 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 complication (Scott et al., 2003). It accounts for approximately 50,000 maternal deaths worldwide each year (Soroori **et al., 2007).**

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 (Wellington and Mulla, 2012. Cunningham et al 2010).

Infantile outcome of PE pregnancies depends chiefly on the age of gestation in delivery and on the severity of the disease (Scott et al., 2003).

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 (Wellington and Mulla, 2012).

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 (Cunningham, et al, 2010,. Phillips, et al 2004), 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 (Scott et al., 2003).

As many hypotheses have emerged to offer a causal framework for the disease, PE has been named the 'disease of theories' (Wellington and Mulla, 2012). 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(Scott et al., 2003).

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 Phillips, et al (2004). In case the relationship is strong, conception could be avoided specially in high risk women (Refsum et al 2004). 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 (Phillips, et al 2004).

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.

2. Material 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.

3. Results

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 women based on month and season of the conception was assessed. The frequency percent of PE began to increase from April to reach its peal 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 ($p=0.038$).

4. Discussions

This study assessed the relation between the incidence of PE and conception time. The ultimate result indicated significantly higher occurrence in warm season's 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. (Phillips, et al. 2004) 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 (Bernstein et al. 1998). 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 (Tam et al 2008). Abbasssalizadeh and 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 (Abbasssalizadeh et al. 2007). Neela and et al supported the speculated relationship between increasing humidity and a lower temperature range with the increased incidence of eclampsia (Neela et al.2007).

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 resuit suggest that climate and environmental exposure may have an important role in the pathophysiology of PE (Shental et al.2010). 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 (Elongi et al, 2011). 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). (Wellington and Mulla, 2012)

The findings have implications for future research related to the aetiology of pre-eclampsia as well as for clinical care (Immink et al.2008).

Khojasteh and et al. (2012) 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 (Khojasteh and et al. 2012).

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 (Chesly et al. 1984).

They explained that more weddings in this month and higher probability of primigravid pregnancies account for this fact (Khojasteh et al 2012), 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) (Refsum et al 2004. Van Beek et al, 1998. Silver et al 1998. Spaanderman et al, 2001. Aardenburg et al, 2003. Kristal-Boneh et al, 1997. Shapiro, 1981. Morimoto et al, 1974) variation in temperature and humidity are other mechanisms that have been suggested (Phillips et al, 2004. Tam et al 2008. Subramaniam, 2007) 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 (Levine et al, 1997. Taufield et al, 1987. Zemel et al, 1990). Some studies have proposed variation in nutritional habits such as quantity of antioxidant intake in different seasons of year (Salvig et al, 1996. Chappell et al, 1999. Rajkovic et al 1997).

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 (Tam et al,2008. Subramanian, 2007).

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 (Aali and Janghorbani, 1996). 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 (Phillips et al 2004). 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.

5. 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.

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