

RISK OF PREECLAMPSIA IN PATERNAL SMOKING IN THREE MONTHS BEFORE UNTIL TIME OF CONCEPTION: A COHORT STUDY

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Abstract- Preeclampsia which happens in 5-10% of pregnancies is associated with maternal and prenatal morbidity and mortality in all over the world. Preeclampsia leads to high rates of preterm birth, small for gestational age infant. The objective of the present study was to evaluate the effects of paternal cigarette smoking before and in conception on risk of preeclampsia in non smoker women without exposure to second-hand tobacco smoke.

In this cohort study, 302 healthy pregnant nonsmoker women were entered. They were divided in two groups with non smoker husband (n=158) and smoker husband (n=144) in conception time. All of women reported no exposure of cigarette smoking before and in pregnancy. Rate of preeclampsia compared in two groups. Rate of preeclampsia is significantly higher in pregnant nonsmoker women that their husbands were smoker. (P=0.030) , OR= 2.808 [CI 95% 1.364 5.781]. Paternal smoking in three months before until time of conception is a risk factor for preeclampsia.

Key words: Paternal smoking, preeclampsia, pregnancy outcome

I. INTRODUCTION

Preeclampsia is a complication of human pregnancy with a great impact on maternal and prenatal morbidity and mortality in all of the world and especially in developing countries [1].

The exact etiology of preeclampsia is still unknown, however, many studies have demonstrated that preeclampsia is associated with failure of trophoblastic invasion of the maternal spiral arteries, leading to increased vascular resistance of the uterine arteries and decreased uteroplacental blood flow [2]. Not much is known about its epidemiology; previous studies have identified nulliparity and nulligravidity as risk factors, together with increasing maternal age, diabetes, urinary tract infection, autoimmune disease and obesity. Fetal risk factors include multiple gestations, hemolytic disease, trophoblastic disease and major malformations [3]. Recent studies have shown some paternal role for preeclampsia and both maternal and paternal transmission is a risk factor [4, 5]. Some studies showed that elderly father is a risk factor for preeclampsia [3]. In men, reproductive stem cells continuously are divided and they are sensitive in mutations [6]. There are

many different mechanisms for DNA repair during male meiosis [7], but chemical mutagens, heat oxidative stress are some conditions that can disturb mechanism of DNA repairing [8]. Cigarette smoke contains known mutagenic and carcinogenic substances, and is believed to have a significant negative effect on male fertility [9]. Definitely, cigarette smoking is linked to increased levels of reactive oxygen species (ROS) production, including hydrogen peroxide (H₂O₂), superoxide anion (O₂⁻), and/or hydroxyl radical (·OH) in seminal plasma [10, 11]. Several studies have shown the adverse effect of smoking on sperm parameters [12]. The presence of nicotine and its metabolite cotinine, and cadmium in the seminal plasma may induce degradation of sperm and its nuclear quality. Oxidative stress-induced DNA damage is one of the important causes of sperm parameters variation [13]. previous studies demonstrated that maternal smoking is protective for preeclampsia [14] but the effect of paternal smoking without maternal exposure on preeclampsia is not clear. Despite cigarette smoking is a known hazardous habit but more people seem to consume it. The highest prevalence of smoking is observed in young men during their reproductive age [15]. In Iran, 24.1% of men and 4.3% of women over the age of 15 are active smokers and this rate is increasing [13]. Although a lot of studies have been done on the effects of smoking on male reproductive function [10, 15, 16] but the role of paternal cigarette smoking before and in conception on preeclampsia seem to be limited in the literature. Therefore, the objective of the present study was to evaluate the effects of paternal cigarette smoking (before and in conception) on risk of preeclampsia in non smoker women without exposure to second-hand tobacco smoke.

II. MAIN TEXT

In this cohort study, 341 healthy pregnant nonsmoker women with singleton pregnancy based on excluded and included criteria enrolled. They were divided in two groups with non smoker husbands and with smoker husbands (among 3 months before until time of conception). Patients with a history of smoking were considered smokers and

those with no history of smoking were considered nonsmokers. Smokers should smoke at least one cigarette per day and if somebody quit smoking for at least one year consider nonsmoker. All of women have self reported of non exposure of smokes during pregnancy and they reported that their husband always smoke far from of them. The sample size calculation was based on risk factors of preeclampsia [17] and the pilot study. Included criteria were all of healthy nonsmoker women with one gradiva and nulliparous without previous abortion with gestational age ≤ 10 weeks. Excluded criteria were Addict person, drug consumer, Chronic disease, age under 20 and upper 35, had tried unsuccessfully to get pregnant for 1 year or longer at any time in the past, self reported to second hand smoking exposure, multiple pregnancy, Rh isoimmunization and in their husbands age upper 45 , history of cryptorchidism, orchitis,varicocele, inguinal hernia, testicular trauma, vasectomy, systemic or urogenital diseases, exposure to a specific substance or drug consumption and addict person. preeclampsia was defined by the onset, after 24 weeks' gestation, of a combination of hypertension, proteinuria and edema of the face or arms. Hypertension was defined as a rise in systolic blood pressure of 30+ mmHg, a rise in diastolic pressure of 15+ mmHg, or two consecutive measurements more than 6 hours apart of 140+ mmHg (systolic) or 90+ mmHg (diastolic). [3] All of women had perinatal care visit in Imam Khomeini hospital center until delivery. [gestational age ≤ 14 weeks (Every month), 14 weeks $<$ gestational age ≤ 28 weeks(every 2 weeks), 28 weeks $<$ gestational age until delivery (every week)]. Descriptive analyses were performed using the SPSS software. T test and χ^2 tests with a significance level of $\alpha=0.05$ and Odds Ratio were used for statistical analysis. The present study was approved by the Research Ethics Committee of the Faculty of Medicine in Islamic Azad University, Sari Branch.

341 individuals presenting to the Imam Khomeini hospital participated in this study. 5 women in smoker group and 2 women in non smoker group had abortion and finished their pregnancy before 20 weeks. 32 women did not do their prenatal care in this center and finally 302 women enrolled. (Figure 1) As shown in table 1, women in the two groups were similar in age, body mass index, hemoglobin. All of women had the same race and religion.

As shown in table 2 and 3, women with smoker husband had higher rate of preeclampsia and their neonates had lower Apgar score.

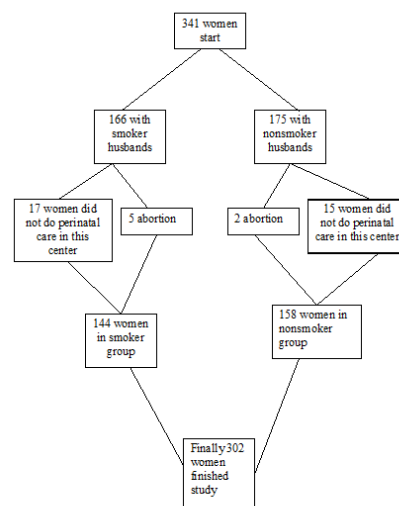


Table 1. Background of the women

With smoker husbands with nonsmoker husbands
P- value
N=144
N=158
BMI
26.63 ± 4.42
27.43±4.74
0.074
Age
26.81±4.32
26.33±3.91
0.217
Hemoglobin
12.00±1.17
12.12±1.02
0.199

Table 2. pregnancy outcome in two group women

Pregnancy outcome	smoker husbands N=144	nonsmoker husbands N=158	P- value	Odds-Ratio
Preeclampsia (n%)	27(12.05%)	12(20.16%)	0.003	2.808 (CI95% 1.364 5.781)
Gestational diabetes (n%)	13(9.02%)	14(8.86%)	0.559	1.024 (CI95% 0.463 2.252)
Still birth (n%)	3(2.08%)	2(1.26%)	0.456	1.660 (CI95% 0.273 10.076)
Placenta abruption (n%)	3(2.08%)	1(0.63%)	0.277	3.340 (CI95% 0.344 32.481)
Preterm labor (n%)	24 (16.6%)	17(10.75%)	0.08	1.673 (CI95% 0.858 3.261)

Table 3. Neonatal condition in birth time

Pregnancy outcome	smoker husbands N=144	nonsmoker husbands N=158	P- value
Gestational age(week)	37.53±3.09	38.11±2.63	0.328
Neonatal birth weight (cm)	3077.98±619.07	3226.47±575.25	0.479
Neonatal head circumference (cm)	33.28±2.11	33.31±1.65	0.219
Neonatal birth hight (cm)	48.66±2.85	48.65±2.61	0.584
Apgar in 1 minute	8.72±0.73	8.82±0.62	0.035

Figure1.

III. CONCLUSION

The research findings showed that 12.05 % of nonsmoking husband women had preeclampsia, while this number was estimated as 20.16% in the women with smoker husbands. χ^2 test showed that there would be a significant relation between husband smoking in conception and preeclampsia ($P=0.030$) and OR showed that paternal smoking increased the risk of preeclampsia in nonsmoker women for 2.808 fold.

Preeclampsia is often considered as simply a maternal disease with variable degrees of fetal involvement. More and more the unique immunogenetic maternal-paternal relationship is appreciated, and also the specific 'genetic conflict' that is characteristic of haemochorial placenta. the existence of the so-called 'dangerous' father [18]. There are several known antioxidants in cigarette smoke [19].

Oxidative stress is an important cause in pathophysiology of sperm in human [20]. Sepaniak et al demonstrated that smokers' spermatozoa have a significantly higher DNA fragmentation than non-smokers. These findings suggest that cigarette smoking may have deleterious effects on sperm nuclear quality [21]. Parazzini et al' study show that no relationship emerged between partner's smoking and risk of preeclampsia [22]. Previous studies demonstrated that maternal smoking is protective for preeclampsia [23].

In Parazzini et al' study maternal exposure didn't consider and this study confirms smokers women are at decreased risk of preeclampsia [22], but in our study non smoker women did not exposure smoke in pregnancy so they didn't benefit of protective effect of smoking for preeclampsia.

In our result, we showed that Apgar score in 1 and 5 minutes were lower in smoker group than nonsmoker group and this difference is statistically significant(in 1 min $p= 0.035$, in 5 min $p=0.007$)

Rate of preterm labor is higher in smoker group but this difference is not significant. Though gestational age and neonatal birth weight are lower in smoker group and this difference is not significant. It seems difference in gestational age and birth weight impact on Apgar score.

Paternal smoking increases the risk of preeclampsia. Therefore, smoking quitting programs for men are recommended at least for the high risk women for preeclampsia. Other study with large sample is needed.

IV. Conclusion:

Paternal smoking in three months before until time of conception is a risk factor for preeclampsia and low Apgar score and can increase mortality and morbidity of both mother and neonate.

ACKNOWLEDGMENT

Here it is necessary to appreciate friendly collaboration of Imam Khomeini hospital personnel in Sari who help us in this research.

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