



Journal of Medical Sciences

ISSN 1682-4474

science
alert

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JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

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Preconception Period of Seminal Fluid Exposure and Prevalence of Preeclampsia in Primigravida Women

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Preeclampsia is a major cause of morbidity and mortality in mothers, fetuses and neonates worldwide. We conducted a case-control study on 100 preeclamptic women (Case Group) and 100 normotensive pregnant women (Control Group) to investigate that if preconception period of seminal fluid exposure affects the prevalence of preeclampsia in primigravida women. The relation of use of barrier contraceptive method and preeclampsia in primigravida women was significant, so that primigravida women using the condom or withdrawal method, are in higher risk of being preeclamptic ($p = 0.007$). There was significant relation between weekly number of coitus before conception and preeclampsia, so that the women with more frequent coitus before conception are at lower risk of preeclampsia ($p = 0.000$). The average age of primigravida preeclamptic women was 24 ± 3.33 years in comparison with 22.92 ± 3.80 years in control group. Our data suggest that prevalence of preeclampsia in primigravida women is associated with weekly number of coitus before conception and the use of barrier contraceptive method.

Key words: Preeclampsia, coitus, primigravida, contraception, seminal fluid

INTRODUCTION

Preeclampsia is a pregnancy-specific syndrome; it is a major cause of morbidity and mortality in mothers, fetuses and neonates worldwide, with 5-10% of human births being affected. The cause is still uncertain and many controversies exist concerning its management. The etiology of preeclampsia remains unknown, but the primigravida adolescent as such as multigravida older women whom have conceived with a new sexual partner have a greater risk; this has been associated also with the use of barrier contraceptive methods that prevent exposure to sperm with the endometrial cavity (condoms, diaphragms, spermicides, withdrawal) (Gutman *et al.*, 2006; Hall *et al.*, 2001; Hernandez-Valencia *et al.*, 2000). Non-barrier contraceptive methods or the exposure of paternal spermatic antigens is protective against development of preeclampsia. Further immunological studies are necessary to determine the role of contraception methods and preeclampsia (Hernandez-Valencia *et al.*, 2000).

The etiology of preeclampsia is often considered to be purely maternal, i.e., maternal constitutional factors that impair maternal cardiovascular/endothelial mechanisms normally required to cope with the specific pregnancy demands, being primarily a generalized inflammatory response and a hyperdynamic circulation. Recent data strongly indicate an important role for the male partner in the causation of this common pregnancy disorder (Dekker, 2002). An inverse relationship has been suggested between the duration of sexual co-habitation and the incidence of Pregnancy-Induced Hypertension (PIH) with rates of PIH in excess of 30% for under 4 months sexual co-habitation and rates of below 10% for over 12 months (Hernandez-Valencia *et al.*, 2000; Darmochwal-Kolarz, 2005).

Normal pregnancy is thought to be associated with a state of tolerance to the foreign antigens of the fetus, whereas in preeclamptic women this immunological tolerance might be hampered. Koelman *et al.* (2000) showed that oral sex and swallowing sperm is correlated with a diminished occurrence of preeclampsia which fits in the existing idea that a paternal factor is involved in the occurrence of preeclampsia.

Also, exposure to semen provides protection against developing preeclampsia. A more or less prolonged period of sperm exposure provides a partial protection against pregnancy-induced hypertensive disorders (Dekker *et al.*, 1998).

Our purpose from this study was to investigate that if preconception period of seminal fluid exposure affects the prevalence of preeclampsia in primigravida women.

MATERIALS AND METHODS

The comparative case-control prospective study performed on 200 primigravida women presenting to Tabriz Al-Zahra and Taleghani Hospitals since Nov 2004 to Nov 2005. The data were collected by completing the questionnaire through interview with 100 preeclamptic women without any known risk factor (Case Group) and 100 normotensive pregnant women (Control Group).

The informed consent was signed by all women before inclusion in the study. Exclusion criteria were: 1) having a known risk factor for preeclampsia (such as diabetes mellitus, autoimmune disease, or hypertension), 2) multifetal pregnancy.

The collected data were as following: maternal age, duration of marriage before conception, weekly number of coitus before conception, contraceptive method, the time between contraceptive discontinuation and conception, BMI before conception, presence or absence of preeclampsia.

The collected data were analyzed by SPSS statistical software using t-test and Mann Whitney test for quantitative variables and the p-values of less than 0.05 was considered as statistically significant.

RESULTS

The baseline characteristics of the studied women and their difference in case and control groups have been showed in Table 1. The relation of use from barrier contraceptive method and preeclampsia in primigravida women was statistically significant, so that primigravida women using the condom or withdrawal method, are in higher risk of being preeclamptic (p = 0.007) (Table 2).

According to the Table 3, there is statistically significant relation between weekly number of coitus before conception and preeclampsia in primigravida women, so that the women with more frequent coitus before conception are at lower risk of preeclampsia (p = 0.000).

Table 1: Baseline characteristics of the studied women

Parameters	Case	Control	p-value
Average age	24.00±0.33	22.9±0.38	0.036
Average BMI	25.01±0.23	25.6±2.8	0.024
Average duration of pre-conception marriage	9.50±1.08	16.5±0.22	0.000
Coitus number in prior week	2.8±0.14	3.8±0.24	0.062

Table 2: Contraception methods in the studied women before pregnancy

Parameters	Case (%)	Control (%)
No contraception	55(55)	76(76)
Condom	13(13)	3(3)
OCP	9(9)	7(7)
withdrawal	23(23)	14(14)

Table 3: Comparison of weekly number of coitus before conception and BMI in case and control groups

Parameters		Case (%)	Control (%)
Weekly No. of coitus before conception	1 time	16(16)	18(18)
	2 times	33(33)	18(18)
	3 times	25(25)	19(19)
	4 times	8(8)	5(5)
	5 times	10(10)	9(9)
	6 times	3(3)	7(7)
	7 times	1(1)	23(23)
	8 times	1(1)	0(0)
	No response	1(1)	1(1)

The average duration from contraceptive-discontinuation to conception was 16.49±28.43 months in primigravida women without preeclampsia and 3.56±5.03 months in primigravida preeclamptic women with significant difference between two groups (p = 0.000).

DISCUSSION

Preeclampsia-eclampsia is due to the failure of extra-villous cytotrophoblast to invade the maternal uterine spiral arteries to a sufficient depth, inducing poor vascular exchanges between the mother and the placenta. This physiological endovascular trophoblast invasion represents a remarkable immunological placental-maternal interaction (Hernandez-Valencia *et al.*, 2000). An immunological factor has been suspected because fetal antigens could cause antigenic reaction with the maternal immunological apparatus, for first exposure at these antigens, since the fetus is considered like an allotransplantation. This is supported in some studies that report that the use of condoms, spermicides and withdrawal are associated with developing of preeclampsia in subsequent pregnancy and another hand indicate at cohabitation preceded for long period, practiced oral sex and use of contraceptive methods that permit exposure to sperm viable with uterus decreased the prevalence of preeclampsia (Hall *et al.*, 2001; Hernandez-Valencia *et al.*, 2000).

The immunological theories of hypertensive disease are also supported by the finding that oocyte donation may be associated with increased rates of the disease. A rate of 25.7% gestational hypertension in 35 recipients of oocyte donation versus 4.2% in a control group of 95 IVF patients has been reported in one series (Hall *et al.*, 2001). A group in the UK has studied a cohort of 33 women conceiving with donor spermatozoa, 27 with donor eggs and 12 women with embryo donation and compared them with a control group of matched patients conceiving spontaneously (Salha *et al.*, 1999). They found the incidence of both Pregnancy Induced Hypertension (PIH) and pre-eclampsia to be increased in the group with

donated gametes (12.5 and 18.1%, respectively). Another study of 1552 donor insemination pregnancies has reported an odds ratio of 1.4 for the development of pre-eclampsia when compared to normally conceived pregnancies, although the details of the classification of the data are not given clearly (Hall *et al.*, 2001; Hoy *et al.*, 1999). An inverse relationship between the self-reported duration of sexual co-habitation before conception and the incidence of PIH has been reported in a population of Caribbean women (Hall *et al.*, 2001; Robillard *et al.*, 1994). The incidence of PIH in pregnancies where the duration of co-habitation was under 4 months was 32% and the incidence when the duration of co-habitation was over 12 months was 3%. This would seem to support the theory that immunological exposure to semen protects against PIH (Hall *et al.*, 2001).

Robillard *et al.* (1994) studied the duration of sexual cohabitation with the father prior to conception and the incidence of pregnancy-induced hypertension. During a five-month period, 1011 consecutive women who delivered in an obstetric unit were interviewed about paternity and duration of sexual cohabitation before conception. The incidence of pregnancy-induced hypertension was 11.9% among primigravidae, 4.7% among same-paternity multigravidae and 24.0% among new-paternity multigravidae. For both primigravidae and multigravidae, length of sexual cohabitation before conception was inversely related to the incidence of pregnancy-induced hypertension. Similar results were observed after control for race, education, maternal age, marital status and number of pregnancies. They concluded that an extended duration of sexual cohabitation before conception may protect against pregnancy-induced hypertension.

Our study on 100 preeclamptic women and 100 normotensive pregnant women showed that the risk of preeclampsia is inversely related with duration of cohabitation before subsequent pregnancy.

The incidence of pre-eclampsia is associated with a change in paternity and the duration of cohabitation. However, case-control study did not showed a significant difference between women with pre-eclampsia and their controls in respect to the duration of cohabitation (Mahomed and Moodley, 2000). Darmochwal showed that the possible immunological etiology of pre-eclampsia has been suggested because of some clinical and epidemiological observations. It has been observed lately that there is a protective effect of sperm exposure and that the duration of sexual cohabitation before conception is inversely related to the risk of pre-eclampsia (Darmochwal-Kolarz, 2005).

In our study the primigravida women using barrier contraceptive methods were at higher risk of preeclampsia. The immune maladaptation theory suggests that tolerance to paternal antigens, resulting from prolonged exposure to sperm, protects against the development of preeclampsia. Ness *et al.* (2004) tested whether barrier contraception and shorter sexual experience with the father of the pregnancy would increase the risk of preeclampsia. However, their data did not support the immune maladaptation theory of preeclampsia.

Multivariate analysis supported the hypothesis: Condoms, diaphragms, spermicides and withdrawal increased the risk of preeclampsia 2.4 fold. Estimates of the total number of exposures to sperm and semen for the cases and controls suggested a dose-response relation, with greater exposure providing more protection (Klonoff-Cohen *et al.*, 1989; Dekker, 2002). Klonoff-Cohen *et al.* (1989) conducted a case-control study comparing the contraceptive and reproductive histories of 110 primiparous women with preeclampsia with 115 pregnant women without preeclampsia. Their results were supportive of the hypothesis that birth control methods that prevent sperm exposure may play a role in the etiology of preeclampsia.

Einarsson *et al.* (2003) in a case-control study over 113 cases (primigravida preeclamptic women) and 226 controls (primigravida women without preeclampsia) showed that length of sperm exposure has influence on the risk of preeclampsia. So that, fewer than 4 months of cohabitation among users of barrier methods for contraception was associated with a significantly increased risk for preeclampsia.

Gratacos *et al.* (1996) evaluated the duration of sexual cohabitation with the father and the use of contraceptive methods among 113 primigravida women with pregnancy-induced hypertension and 109 age- and parity-matched controls to estimate the impact of the exposure to spermatozoa on the risk of developing pregnancy-induced hypertension. They concluded that the duration of unprotected sexual cohabitation was approximately 50% shorter in women with pregnancy-induced hypertension ($p < 0.0001$), regardless of the contraceptive method previously used.

Our study showed that primigravida women with high preconception BMI are in increased risk of preeclampsia. Vatten *et al.* (2003) showed that maternal preeclampsia was associated with higher weight and BMI. The risk of preeclampsia rises with increasing prepregnancy BMI. Preeclampsia risk rises through most of the BMI distribution. The dramatic elevation in overweight prevalence in the United States may increase

preeclampsia incidence in the future (Bodnar *et al.*, 2005). Our study showed that primigravida women with more frequent coitus before conception are in lower risk of preeclampsia. However, Einarsson *et al.* (2003) in a case-control study over 113 cases (primigravida preeclamptic women) and 226 controls (primigravida women without preeclampsia) showed that the risk of preeclampsia is not associated with Weekly number of coitus before conception.

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