NEURAL TUBE DEFECTS AMONG INFANTS DELIVERED OF MOTHERS WITH TOBACCO SMOKE EXPOSURE

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ABSTRACT

Objective: to verify the occurrence of congenital neural tube anomalies among the newborns of pregnant women who had experienced exposure to tobacco smoke.

Design: A cross sectional study of pregnant women at delivery considering their newborns as a gestational cohort.

Methods: A systematic random sample of 2300 pregnant women who attended for labour at Maternity and Children hospital in Najaf city were interviewed for history of tobacco smoke exposure during the period 2002-2004. The sample was subdivided into exposed and unexposed women to tobacco smoke. The newborns were clinically examined by a pediatrician for presence of any congenital anomalies especially neural tube defects.

Results: The over all newly delivered newborns with congenital anomalies were 3.4% among smoker mothers, and 1.9% among nonsmokers (including small defects). The most frequent neural tube defects among smoker mothers were anencephaly (1.8%) and spina bifida (1.2%), versus 0.7% and 0.6% respectively among non smokers or unexposed women (P<0.05). There was some increase in the risk of such defects among exposed women to tobacco smoke who did not take folic acid in relation to unexposed in spite of no statistically significant difference. Also there was no significant difference in the distribution of neural tube defects between those women who live in urban or rural areas or between different age groups.

Conclusion: Smoking is a risk factor for neural tube defects.

INTRODUCTION

Congenital anomalies and genetic disorders have assumed an important role as a cause of morbidity and mortality during the first month of life. Not all malformations are detected at birth, 2% of newborns have serious malformations that have surgical or cosmetic importance[1]. There are multiple causes of birth defects or genetic disorders, including chromosomal abnormalities, single gene disorder, environmental agents, and many still classified as unknown[2]. Neural tube defects (meningomyeloceles) result from failure of neural tube closure during the third to fourth week of gestation. They include anencephaly, Spina bifida and Encephalocele. The incidence has been as high as 4-5 per 1000 births in some areas of UK. Generally the incidence is 1-3 per 1000 births in a first child, 2-3% in a second child with one previous affected sibling, and 5% in a third child with two previous affected siblings[3]. There is a thin membrane covering the defect and the leakage of spinal fluid is not uncommon predisposing the infant to infection. Immediate closure of the defect confers a 90% chance of survival. The most studied congenital defect in association with maternal smoking has been cleft lip and cleft palate. Gestational smoking has been associated with low-birth-weight infants and increased infant mortality[3]. It was found that cigarette smoking during pregnancy was associated with cleft defects, with odds ratios of 2.56 and 2.39 for cleft lip and cleft palate, respectively[4]. One paper in Missouri (1989) reported no association[5]. Maternal smoking during pregnancy was found to be a risk of congenital urinary tract anomalies[6]. Evans et al, in reviewing 67,609 singleton births, noted a small increase in neural tube defects associated with maternal smoking[7]. Because the evidence on this clinical question has been very inconsistent, this subject, particularly in population like those in Iraq, requires further investigation.

The aim of this study was to investigate the relation between smoking during pregnancy and neural tube defects in the main Maternity and Children hospital in Najaf Governorate.

PATIENTS AND METHODS

Patients and study design:

A systematic random sample was done of mothers who gave births to a single live infant at Maternity and Children Hospital in Najaf governorate during the period January 1st 2002 to December 31st, 2004. The mothers who were included in the sample delivered a single live infant and having available maternal demographic data in addition to data of congenital anomalies especially neural tube defects identified among the newly delivered infants. Although it was a cross-sectional sample of mothers at birth, but it resembled ***a gestational cohort*** for their newborns. The

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criteria for maternal exclusion included; a history of drug abuse *(narcotics, barbiturates, amphetamines, opiates, or mixed, and any drug contraindicated or risky for the pregnant women)*, epilepsy during pregnancy, history of psychotic illnesses *(manic-depressive illness, unipolar or bipolar disorders, and schizophrenia)*, a history of diethylstilbestrol exposure, rubella infection and exposure to accidental radiation.

Data collection

The data on maternal smoking was collected from mothers attending the hospital for delivery. They were categorized into; smokers *(who smoked about one pack of tobacco per day and excluded other pregnant who mentioned less than this level),* passive smokers *(exposed from their heavy smoker husbands)*, and nonsmokers. The other variables included; maternal age, gestational age, residence, folic acid administered, 1-minute Apgar, 5-minute Apgar, and history of diabetes. The women were asked whether they smoked during their pregnancy, and if they did, they were asked to quantify their smoking. All data on congenital birth defects were collected at the time of the infant's birth when the baby was examined and diagnosed by the pediatrician. Neural tube defects had been categorized into three main disorders; anencephaly, spina bifida and encephalocele. All the recorded congenital defects were of surgical and cosmetic importance in addition to cardiac defects.

Chi-squared and independent t-test was applied in statistical analysis of data at 0.05 level of significance. Moreover, calculation of relative risk (for newborns as a gestational cohort) to assess the strength of association had been used.

RESULTS

Interviewing of the mothers attending or referred to deliver at the main Maternity and Children hospital in Najaf verified that the prevalence of smoking among them was 7.6%, and 44.3% of mothers were passively exposed from their heavily smoking husbands (Table-1).

The smoker and non smoker women had no significant differences in the main characteristics other than mean gestational age and the birth weight of newborns (Table-2).

The incidence of neural tube defects among newborns of smoker and passive smoker mothers was higher than non smokers (3.4% versus 1.9%) as shown in (Table-3).

The smoker and passive smoker mothers had relative risk of 1.8 to develop neural tube defects than non smokers (Table-4).

It was found that the risk of neural tube defects was higher among newborns of mothers who did not take folic acid drug than those who took it even after conception. (Table-5).

There was no significant difference (P>0.05) in the mean age of the mothers who gave infants with neural tube defects between smokers and non smokers, nor in their urban and rural residence which might reflect the environmental effect.(Table 6,7)

Table 1. ***Prevalence of tobacco smoking among pregnant women attended for delivery in Najaf, 2002-2004***

Smoking exposure	Mothers	%
Smokers	174	7.6
Passive smoker	1020	44.3
Non smoker not exposed	1106	48.1
Total	2300	100

Table 2. ***Gestational cohort for maternal smoking and neural tube defects.***

Variables	Smokers (n=174)	Non smokers (n=1106)	P-value
Age, mean (years)	28.7	27.5	>0.05
Gestational age mean (weeks)	37.6	39.7	<0.05
Diabetes, No. (%)	6(3.5)	44(40)	>0.05
Birth weight (g)	2782	3135	<0.05
Apgar, 1 minute	8.8	9.0	>0.05
Apgar, 5 minute	9.4	9.6	>0.05

Passively exposed (n=1020) had been excluded from analysis.

Table 3. *Incidence of neural tube defects in newborns according to their mother exposure to tobacco smoke*

Mothers exposure to tobacco smoke	Newborns with neural tube defects							
	Anencephaly*		Spina bifida*		Encephalocele		Total	
	No.	%	No.	%	No.	%	No.	%
Exposed (n=1194)	16	1.3	14	1.2	11	0.9	41	3.4*
Not exposed (n=1106)	8	0.7	7	0.6	6	0.5	21	1.9*
Total (n=2300)	24	1.04	21	0.9	17	0.7	62	2.7

* **P<0.05**

Table 4. *Adjusted relative risks for maternal smoking and the risk of neural tube defects*

Mothers exposure to tobacco smoke	Newborns with neural tube defects											
	Anencephaly*			Spina bifida*			Encephalocele			Total		
	No.	%	RR*	No.	%	RR	No.	%	RR	No.	%	RR
Smoker (n=174)	3	1.8	2.3	2	1.2	2.0	1	0.7	1.4	6	3.4	1.8
Passive smoker (n=1020)	13	1.2	1.5	12	1.2	2.0	10	1.0	2.0	35	3.4	1.8
Non smoker (n=1106)	8	0.7	1.0	7	0.6	1.0	6	0.5	1.0	21	1.9	
Total	24	0.9	1.1	21	1.0	1.7	17	0.7	1.4	62	2.7	

Table 5. *Risk of neural tube defects in smoker mothers according to folic acid tablet ingestion*

Mothers	Newborns with neural tube defects											
	Anencephaly*			Spina bifida*			Encephalocele			Total		
	No.	%	RR*	No.	%	RR	No.	%	RR	No.	%	RR
Smoker (n=174)	0	0	0	4	2.3	1.5	2	1.2	3.0	6	3.4	1.8
Passive smoker (n=1020)	3	0.3	3.0	24	2.4	1.6	8	0.8	2.0	35	3.4	1.8
Non smoker (n=1106)	1	0.1		16	1.5		4	0.4		21	1.9	
Total (n=2300)	4	0.2		44	1.9		14	0.6		62	2.7	

***P>0.05**

Table 6. *Mean age (years) of smoker and non smoker mothers by neural tube defects*

Neural tube defects	Smokers (N=147)		Non smokers (N=1106)		P-value
	N	X±SE		X±SE	
Anencephaly	3	29.6±2.8	8	28.7±3.2	>0.05
Spina bifida	2	25.9±4.1	7	26.2±2.9	>0.05
Encephalocele	1	30.2±2.3	6	27.6±3.4	>0.05

***Passively exposed mothers (n=1020) had been excluded from analysis**

Table 7. *Distribution of neural tube defects by place of residence.*

Neural tube defects	Urban		Rural		Total		P-value
	No.	%	No.	%	No.	%	
Anencephaly	13	54.2	11	45.8	24	100	>0.05
Spina bifida	11	52.4	10	47.6	21	100	>0.05
Encephalocele	9	53	8	47	17	100	>0.05

P>0.05

DISCUSSION

Smoking during pregnancy is hazardous as it poses numerous risks to both the mother and the unborn child[8]. Neural tube defects are examples of disorders with multifactorial inheritance including environmental factors such as tobacco smoking which is considered as a teratogenic agent[9]. The current study verified that the prevalence of smoker mothers during pregnancy was so low (7.6%) while 44.3 % of nonsmokers were exposed to indoor tobacco smoke from their heavy smoker husbands. The important effect of tobacco on pregnant women was the low birth weight infants which make tobacco one of the most preventable causes of low birth weight[9]. The U.S Surgeon General report (1980) which revealed that 20-40% of all low birth weight infants could be attributed to smoking. The current study demonstrated a relative risk of neural tube defects about twice times among smokers and passive smokers of more than one pack of cigarettes a day than non smokers which may be related to the teratogenic effect of tobacco due to its effect on reduction of serum folic acid level[9]. Shiono, et al, (1986) reported that mothers who smoke have infants that are smaller and of shorter gestational age. The indoor exposure of tobacco smoke from the husbands played a role in the elevated frequency of congenital defects but such exposure or any exposure history from cigars, pipes, chewing tobacco, or even second-hand smoke was not ascertained[10]. The physiological mechanisms responsible for the adverse consequences of cigarette smoking during pregnancy center on carbon monoxide which reduces the oxygen-carrying capacity to the fetal tissue and nicotine which crosses the placenta and reduces the uterine blood flow and affects fetal oxygenation and acid-base balance[10,11]. Recent studies reported that cigarette smoking reduces serum level of folic acid[12] which is consistent with the result of this study by finding some increase in the risk of neural tube defects among newborns of smoker pregnant women who did not take folic acid drug.

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