Maternal tobacco consumption during pregnancy and risk of congenital heart diseases in offspring

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ABSTRACT

Background: Maternal tobacco consumption (both active and passive) during pregnancy as a risk factor for congenital heart diseases in offsprings has been studied by some workers with a small number of subjects hence requires to be evaluated through a study with a significant size of cohort. The objective of the study was to find out the association between maternal tobacco consumption and the risk of CHDs among their off-springs.

Methods: This is a hospital based, comparative, cross sectional, observational study. 518 children with CHDs, confirmed by echocardiography were included as cases and 240 children without any obvious congenital anomaly matched for age and sex were taken as controls. The following clinical observations were collected through questionnaires in a predesigned Performa: maternal and paternal tobacco consumption during pregnancy; maternal medical, gestational and obstetric history; and other birth defects.

Results: Children from case and control groups were comparable with respect to age and sex at the inclusion in the study. Out of the total 758 study participants, 73 children (14.01%) with CHDs had history of maternal tobacco consumption (active consumption) during pregnancy and 86 children (16.6%) with CHDs had history of paternal smoking habit (P value was highly significant).

Conclusions: Tobacco consumption during pregnancy (both active and passive) confer an increased risk of CHDs in their off-springs (p value <0.001).

Keywords: Congenital heart disease, Echocardiography, Tobacco consumption

INTRODUCTION

CHDs are the leading cause of infant deaths due to birth defects. It affects 6-8 babies in every 1000 live births.1, 2 While the prevalence of acquired heart disease has decreased over the past decade, CHD incidence has remained unchanged and CHD prevalence has increased likely due to increased exposure to adverse paragenetic factors, better detection and improved survival.

It is generally accepted that the group of CHD lesions follows a multifactorial inheritance model, which implicates both genetic and environmental factors in disease development.3 Maternal tobacco consumption during pregnancy, both active and passive, tends to increase the risk of CHDs. In India tobacco consumption in the form of smoking is less common in females. Because smoking is considered a social stigma in females in Indian scenario, so they prefer to chew tobacco, as this is non-revealing. Habit of tobacco chewing cannot be underestimated against smoking.

Possible mechanisms by which maternal tobacco consumption might result in CHDs remain to be defined.
However, given the complexity of the development of the cardiovascular system, such mechanisms are likely to involve a number of gene-gene, gene-environment, or environment-environment interactions, or a combination thereof. Results of studies in which the interaction of maternal smoking with polymorphisms in biotransformational enzymes and the risk of CHDs among offspring were investigated have suggested that various types of interactions might be involved. Hobbs et al. suggested a link between CHDs, smoking, and the 677 C→T polymorphism related to folate metabolism, and McDonald et al reported an interaction between methylenetetrahydrofolate reductase gene activity and tobacco exposure on serum folate levels, which suggests an antagonistic effect of smoking on serum folate levels.5

There is a need for further work to elucidate the extent to which these or other mechanisms involving the complex mixture of chemicals in tobacco consumption could be involved in the development of CHDs in children. So, we planned to find out correlation between maternal tobacco consumption during pregnancy and risk of CHDs in a representative sample of pediatric population.

METHODS

It is a hospital based, comparative, cross sectional, observational study and has been conducted in Sir Padampat Mother and Child Health Institute, Department of Paediatric Medicine, Tertiary Health Care, Medical College. Prior permission from the institutional ethical committee was obtained. Children attending outdoor, indoor and cardiac clinics whose ages were below 5 years and who were suspected for CHDs on the basis of sign and symptoms were subjected to various investigations e.g. chest X-ray, ECG, and 2D Echocardiography. After applying inclusion and exclusion criteria, the confirmed cases of CHDs were enrolled for study.

Written consent was obtained by parent(s) of all enrolled children. A predesigned performa was used to collect following informations: age and sex of children, tobacco consumption by mother and father (passive consumption) during first trimester of pregnancy.

Inclusion criteria

Children aged between 0-5 years, confirmed cases of CHDs diagnosed by clinical examination plus echocardiography with or without cardiac catheterization (study group), and children without any CHDs matched for age but not for gender, ethnicity or social class (control group).

Exclusion criteria

Unwilling guardians and; patients whose data regarding maternal tobacco consumption during pregnancy are not available.

Statistical analysis

Data was entered on excel sheet and analyzed statistically using XL-stat software. Quantitative data was summarized in form of Mean±SD. Qualitative data was summarized in the form of percentage and proportion and difference were analyzed using Chi-Square test. The Confidence interval for all the analysis was kept 95% and α-error of 5%.

RESULTS

Out of total 780 patients who were enrolled in the study, 22 subjects were excluded (of which 12 patients did not fulfill the inclusion criteria, in 8 patients parents refused to participate in the study and in 2 patients history was either doubtful or incomplete). 758 patients were finally included in the study. Total included subjects were further divided into study group which included 518 patients with CHDs and control group comprised of 240 patients without CHDs.

<table>
<thead>
<tr>
<th>Tobacco consumption</th>
<th>Subjects with CHDs (Study group) No. (%)</th>
<th>Subjects without CHDs (Control group) No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>73 (14.01)</td>
<td>5 (2.08)</td>
<td>78 (10.29)</td>
</tr>
<tr>
<td>Absent</td>
<td>445 (85.91)</td>
<td>235 (97.92)</td>
<td>680 (89.71)</td>
</tr>
<tr>
<td>Total</td>
<td>518 (100.00)</td>
<td>240 (100.00)</td>
<td>758 (100.00)</td>
</tr>
</tbody>
</table>

χ² = 25.620; df = 1; Odd ratio = 7.710; 95% CI = 3.0734-19.3419; P <0.001, HS

In the present study nearly 14.01% children with CHDs had history of maternal tobacco consumption (active consumption) during pregnancy (Table 1). Amongst these 4.11% had history of smoking and 95.89% had history of tobacco chewing. Both the routes of tobacco consumption expose the foetus to hazards of tobacco, one by inhalation route and the other by oral route.

<table>
<thead>
<tr>
<th>Paternal (passive) smoking</th>
<th>Study group A No. (%)</th>
<th>Study group B No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>86 (16.60)</td>
<td>8 (3.33)</td>
<td>94 (12.40)</td>
</tr>
<tr>
<td>Absent</td>
<td>432 (83.40)</td>
<td>232 (96.67)</td>
<td>664 (87.60)</td>
</tr>
<tr>
<td>Total</td>
<td>518 (100.00)</td>
<td>240 (100.00)</td>
<td>758 (100.00)</td>
</tr>
</tbody>
</table>

χ² = 26.580; df = 1; Odd ratio = 0.173; 95% CI = 0.082-0.364; P <0.001, HS
CHDs were found in significantly higher percentage of children born to mother with tobacco consumption during pregnancy (14.01%) than the control group (2.08%).

Out of total 518 children with CHD, paternal smoking habit during pregnancy was found in 86 patients (16.6%) while in control group only 8 patients (3.33%) had history of paternal smoking habit (Table 2). On analysing our data presence of CHDs in children were found to be associated with paternal smoking habit during pregnancy (p value < 0.001).

CHDs were found in significantly higher percentage in children of families in which paternal or passive smoking was present during pregnancy (16.60%) than the control group (3.33%).

**DISCUSSION**

In present study CHDs were found significantly higher in children born to mother with tobacco consumption (both active and passive consumption) during pregnancy than in those without tobacco consumption (p <0.001).

A relatively higher incidence of CHDs was observed in children born to mother with tobacco consumption during pregnancy by various workers.

Malik S et al in their case control study found that women who smoked anytime during the month before pregnancy to the end of the first trimester were more likely to have infants with septal heart defects than women who did not smoke during this time period (p value < 0.001).  

Kucienie R et al in their case control study concluded that maternal smoking during pregnancy tended to increase the risk of congenital heart defects by 48% (OR = 1.48; 95% CI: 0.82-2.67).  

Clinton J et al found statistically significant positive associations between first-trimester maternal cigarette consumption and the risk of secundum-type atrial septal defects [OR: 1.36 (95% confidence interval [CI]: 1.04-1.78)], right ventricular outflow tract defects [OR: 1.32 (95% CI: 1.06-1.65)], pulmonary valve stenosis [OR:1.35 (95% CI: 1.05-1.74)], truncus arteriosus [OR: 1.90 (95% CI: 1.04-3.45)], and levo-transposition of the great arteries [OR: 1.79 (95% CI:1.04-3.10)].

Ageliki A et al observed that in neonates with CHD 64 of 157 mothers (40.8%) reported smoking in pregnancy, whereas in the control group 41 of 208 mothers (19.7%) were smokers (p = 0.000). Logistic regression analysis with pregestational diabetes, history of influenza-like illness in the first trimester, therapeutic drug exposure in pregnancy, maternal age, parity, family history of CHD, infant gender, prematurity and paternal smoking, as potential confounding factors showed that periconceptional tobacco smoking was associated with increased risk of CHD in the offspring (OR = 2.750, 95% CI = 1.659-4.476, p = 0.00001).

Karatzas et al found that periconceptional tobacco smoking was associated with increased risk of CHD in the offspring (OR = 2.7).  

Lee LJ et al found that there is a positive association between maternal smoking during pregnancy and the risk of CHDs in children (RR: 1.11; 95% confidence interval [CI], 1.02-1.21; number of cases [n] = 18,282).

On analysing our data presence of CHDs in children were found to be associated with paternal smoking habit (passive smoking by mother during pregnancy) (p value <0.001).

Cresci M et al in their case control study found that Paternal smoking (≥15 cigarettes/day) was significantly associated with CHD risk (odds ratio [OR] 2.1, 95% confidence interval [CI] 1.3 to 3.5, p = 0.002).

Kuciene R et al found a statistically significant relationship between parental smoking and congenital heart defects. Parental, maternal, and paternal smoking was significantly associated with a 2.27-fold (adjusted OR = 2.27; 95% CI, 1.49-3.46), 2.2-fold (adjusted OR = 2.20; 95% CI, 1.01-4.79), and 1.45-fold (adjusted OR = 1.45; 95% CI, 1.03-2.03) increased risk of defects if compared with non-smoking parents.

The majority of studies are in support of a significant association between maternal tobacco consumption (both active and passive exposure) during pregnancy and presence of CHDs in their children. From our study results it can be concluded that active tobacco consumption as well as passive exposure of tobacco by mother during pregnancy are independent antenatal risk factors for causation of CHDs in children.

**CONCLUSION**

During last decades an increase in the incidence of CHDs has been reported by different workers. One explanation for the rising incidence of CHDs could be increased exposure to paragenetic (antenatal) risk factors to which foetus is exposed. Maternal tobacco consumption (both active and passive exposure) during pregnancy are independent antenatal risk factors for causation of CHDs in children (p <0.001). Tobacco exposure in the form of chewing and smoking by mother, and passive smoking by family members must be condemned by society as well as by governments.

However, we recommend more studies with larger number of study subjects to clear this issue further, regarding the degree of severity of exposure of tobacco and the duration of exposure and timing of exposure to tobacco during the entire pregnancy period. Further studies will also be required to find out whether there is
any difference in the mode of consumption of tobacco by mother during pregnancy i.e. chewing and smoking in the causation of CHDs in children.

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**Conflict of interest:** None declared  
**Ethical approval:** The study was approved by the Institutional Ethics Committee

**REFERENCES**
