

Maternal Environmental Tobacco Smoke during Pregnancy and Risk of Congenital Heart

EMAN M. EL-SAYED, M.D.; MONA M. EL-GANZORY, M.D. and GHADA I. EL-MOKADEM, M.Sc.

The Department of Pediatrics, Faculty of Medicine, Ain Shams University

Abstract

Background: To examine the correlation between maternal environmental tobacco smoking during pregnancy as well as the risk of congenital heart defects (CHDs) incidence in offspring.

Aim of Study: To examine the correlation between maternal environmental tobacco smoking throughout pregnancy and the CHD incidence risk in offspring.

Patients and Methods: This is a case-control study that was conducted on two groups of patients presented to the Pediatric Cardiology Unit, Ain Shams University Hospitals, including group 1: 120 mother of live born infant diagnosed with congenital heart disease confirmed by echocardiography done by a specialized echocardiologist, And group 2: 120 mother of infant with normal heart, using questionnaire. Work start at May 2020 and end in May 2021.

Results: There was a statistically significant increase in the incidence of CHDs among children whose mothers have been exposed to smoking during pregnancy than those with no history of exposure (p -value=0.003). There was also a substantially elevated risk of CHD with respect to time of exposure during pregnancy (p -value=0.001). Additionally, There was a statistically significant increase in CHDs incidence among children whose mothers had a history of the first trimester and preconception smoking exposure. ETS (ENVIRONMENTAL TOBACCO SMOKE) >15 min per day (p -value=0.007 being more in group of mothers with children with CHDs).

Conclusions: Maternal exposure to smoking substantially impacts the increased incidence of CHDs in general. This study observed that maternal ETS >15 minutes per day (passive smoking) is associated with increased CHDs.

Key Words: Environmental tobacco smoking – CHD – Pregnancy.

Introduction

CONGENITAL heart diseases (CHDs) are prevalent congenital deformities and remain a significant mortality reason in infancy and childhood,

impacting approximately one percent of live infants born worldwide. CHDs account for one-tenth of all newborn mortality and account for one-third of all anomaly-related deaths. CHD infants occupy 25 to 30% of the beds in the pediatric ICU. Consequently, a substantial health care proportion is devoted to this illness [1].

Smoking throughout pregnancy may lead to alterations in fetal growth, as well as a poor deteriorated birth outcome. Most of the genetic as well as molecular factors causing poor health impacts in children, have recently been elucidated. In this respect, it has been discovered that getting exposed to passive smoking in infants is connected with alterations in microRNA, levels of genes, hormones, enzymes, and finally, the expression of protein expressions. Passive smoking exposure is a significant inducer of oxidative stress pathways. The health consequences of exposure might be exacerbated by genetic susceptibility. Epigenetic factors may impact illness risk as well as gene expression in utero [2].

Maternal smoking is a severe public health issue since it elevates the risk of congenital abnormalities, diminished birth weight, preterm delivery, fetal morbidity, and mortality, as well as preterm birth. The actual consequences of smoking e-cigarettes within pregnancy's first trimester—the era of organogenesis—remain largely unclear. In addition, increasing evidence suggests that even nicotine-free e-cigarette aerosols can impair the growing conceptus, indicating that liquid e-cigarette elements, especially flavorings, can be developmental toxins [3].

It is believed that passive smoking includes over 4000 hazardous chemicals and approximately 69 cancer-causing compounds, which may have the same influence on the body as well as health as

Correspondence to: Dr. Ghada I. El-Mokadem,
[E-Mail: hnttmr011@gmail.com](mailto:hnttmr011@gmail.com)

active smoking, triggering inflammations, and elevated risk of several forms of cancer, as well as coronary heart disease. When passive smoking exposure is regular and extended, the dangers increase correspondingly [4].

Along with its impact on the maternal circulation, nicotine rapidly passes through the placenta and has a significant impact on the placental vasculature as well as on the fetus [5].

Cardiac remodeling after chronic as well as acute exposure to smoking encompasses oxidative stress, metabolic impairment, inflammation, cell death, and direct effect on the myocardium inducing smoking cardiomyopathy [6].

Patients and Methods

The present case-control study was carried out on patients presented to (the Pediatric Cardiology Unit, Ain Shams University Hospitals, including the mothers of Live born infants diagnosed with

congenital heart disease confirmed by echocardiography done by a specialized echocardiologist, using questionnaire. This case-control study was conducted on 240 mothers of children (120 mothers of children with CHDs and 120 mothers of children with normal heart). All cases were recruited when their children were less than 1 year to minimize recall bias.

Results

There was a statistically significant increase incidence of CHDs among children whose mothers had been exposed to smoking during pregnancy than those with no history of exposure (p -value = 0.003). There was a statistically significant increase incidence of CHDs among children whose mothers had a history of the first trimester and preconception smoking exposure (p -value 0.001), also those who had ETS (ENVIRONMENTAL TOBACCO SMOKE) exposure > 15min per day (p -value = 0.007); as shown in Table (1).

Table (1): Comparing the studied groups as regards smoking exposure.

		Groups		Chi-Square	p -value	Sig.
		Normal heart	CHD			
<i>Exposure during pregnancy:</i>						
No:	N.	66	43	8.891	0.003	HS
	%	55.0%	35.8%			
Yes:	N.	54	77			
	%	45.0%	64.2%			
<i>Time of Exposure during pregnancy:</i>						
Other time of pregnancy:	N.	67	8	12.396	0.001	HS
	%	55.8%	42.5%			
First trimester and preconception:	N.	53	69			
	%	44.2%	57.5%			
<i>Active smoking:</i>						
No.:	N.	117	119	1.017	0.313	NS
	%	97.5%	99.2%			
Yes:	N.	3	1			
	%	2.5%	0.8%			
<i>ETS (Environmental Tobacco Smoke) >15 min:</i>						
No:	N.	66	45	7.392	0.007	HS
	%	55.0%	37.5%			
Yes:	N.	54	75			
	%	45.0%	62.5%			
<i>Father smoking:</i>						
No:	N.	66	47	6.037	0.014	S
	%	55.0%	39.2%			
Yes:	N.	54	73			
	%	45.0%	60.8%			
<i>N of cigarette/day:</i>						
No:	N.	66	45	7.625	0.050	S
	%	55.0%	37.5%			
1 - 9:	N.	4	4			
	%	3.3%	3.3%			
10 - 19:	N.	32	46			
	%	26.7%	38.3%			
>20:	N.	18	25			
	%	15.0%	20.8%			

From analysing the data logistic regression analyses of CHDs risk factors in children with mothers who had a history of smoking exposure during pregnancy demonstrated that history of paternal smoking, paternal drug abuse, resident

proximity to the main road, number of CHDs, and CHD was statistically significant with p -value <0.05 and only history of paternal smoking with (p -value = 0.000) was statistically significant. As shown in Table (2).

Table (2): Univariate and multivariate logistic regression analysis of CHD risk factors in children with mothers who had a history of smoking exposure during pregnancy.

	Uni-variety				Multi-variety			
	p -value	Odds ratio (OR)	95% C.I. for OR		p -value	Odds ratio (OR)	95% C.I. for OR	
			Lower	Upper			Lower	Upper
Age >1	0.046	1.996	1.014	3.930	0.380	3.418	0.220	53.057
Paternal (paternal) smoking	0.000	2721.599	313.128	23655.144	0.000	4703.661	339.009	65262.076
Paternal (paternal) drug abuse	0.014	12.923	1.671	99.939	0.682	0.442	0.009	22.013
Resident proximity to main road	0.000	4.672	2.214	9.858	0.062	6.183	0.913	41.866
No. of congenital heart Acyanotic	0.011	1.592	1.111	2.280	0.807	0.812	0.153	4.310
	0.023	1.842	1.086	3.126	0.309	4.209	0.265	66.960

Discussion

The etiology of congenital heart diseases is still largely unknown. Many cases of CHDs are multifactorial and result from a combination of genetic predisposition and environmental risk factors. Approximately 15% to 20% of infants with congenital heart diseases are related to known chromosomal abnormalities [1].

According to WHO, in 2020, 1.30 billion people were using tobacco globally; according to the Global Burden of Disease Study, Tobacco kills more than 8 million people worldwide each year. More than 7 million of those deaths are directly related to tobacco use, while approximately 1.2 million are caused by non-smokers being exposed to passive smoking [7].

The current study aims to investigate the association between maternal environmental tobacco smoking during pregnancy and the risk of incidence of congenital heart defects (CHDs) among offspring.

This case-control study was conducted on 240 mothers of children and was divided into group (1) 120 mothers of children with CHD and group (2) 120 mothers of children with normal heart. In this study, all cases were recruited when their children were less than one year old, without any extracardiac anomalies. Also, cases that had a family history of heart defects were excluded.

To investigate the effect of smoking exposure during pregnancy and the incidence of CHDs. Mothers included in the study were medical-free

during pregnancy, mothers who had no history of drug abuse or medication used during pregnancy. In addition, mothers who were exposed to radiological exposure and teratogenic exposure during pregnancy were excluded from our study.

Group 1: From the 120 mothers of children with CHDs, 77 cases (64.2%) had been exposed to smoking.

There were 47 cases had been exposed to 1-9 cigarettes per day, 25 cases had been exposed to 11-19 cigarettes per day, and only five cases had been exposed to more than 20 cigarettes per day.

Group 2: From 120 mothers of children with normal hearts, There were 54 mothers (45%) had been exposed to passive smoking, 32 cases had been exposed to 1-9 cigarettes per day, 17 cases had been exposed to 11-19 cigarettes per day, and five cases had been exposed to more than 20 cigarettes per day.

In this study, we found that a significant proportion of women (61.6%) were passively smoking.

This study revealed a statistically significant increased exposure to smoking during pregnancy among mothers of children with CHD (62.5%) than mothers of children with normal heart (47%) with (p -value=0.003), which is consistent with a study done by Li et al. [8], which was conducted on a total of 2,259 subjects, including 695 cases and 1 564 controls were included in this study. Passive smokers accounted for 26.76% in the case group while only 6.01% in the control group.

Also, this finding is similar to a meta-analysis study done by Zhang et al. [9] that supports the cardiovascular teratogenic effect of maternal smoking during pregnancy, and their offspring may suffer from approximately a 10% relative increase in the risk of CHDs on average.

This finding aligns with Li et al. [10] who conducted a case-control study on 229 mothers with children having CHD and 284 mothers with children having normal heart and found statistically significant increased exposure to smoking among children with CHD than the control group.

According to the findings of a meta-analysis conducted by Zhang et al. [9], eight studies out of 23 showed a significant association between maternal smoking and CHD with a pooled RR of 1.11 (95% CI: 1.04, 1.18). Also, another study by Meidan et al. [11] conducted in Montreal, Quebec, Canada on women who gave birth to infants with a history of maternal exposure to smoking in comparison to women with no history of exposure to smoking revealed a statistically significant higher exposure to smoking among women who gave birth to children with CHD with (p -value <0.05).

With regard to the current study, it revealed an association between maternal exposure to smoking dose (number of cigarettes) and risk of CHD with (a p -value=0.05), which is compatible with Karatza et al. [12], who compared 157 neonates with CHD and their mothers to 208 normal neonates and their mothers and found a statistically significant association between the dose-effect of cigarette smoking ≥ 11 cigarettes/day and the incidence of CHDs with (p -value=0.000).

The same finding was reported by Zhang et al. [9], who detected a statistically significant association between septal defects and the number of cigarettes (up to 15/days).

Furthermore, the current study's findings revealed that exposure to smoking during the first trimester increases the risk of congenital heart disease with (a p -value=0.001). Similarly, a study done by Sullivan et al. [13] on 14,128 women with babies who had CHD in addition to 60,938 controls revealed statistically significant increased CHD among children who had mothers with a history of smoking exposure during the first trimester with (a p -value <0.001).

Regarding paternal smoking, our study demonstrated increased CHDs with (p -value=0.014) being more in mothers of children with CHD.

This finding is consistent with Zhao et al. [14], who illustrated that maternal active smoking, maternal passive smoking, and paternal smoking increased the risk of CHDs in offspring. Preventing parental smoking during peri-pregnancy is a priority for CHDs prevention.

Also, this finding is consistent with the study done by Baardman et al. [15], which was conducted on 797 children with CHD in addition to 322 controls to investigate the interaction between maternal smoking and risk of CHD and revealed a statistically significant association between paternal smoking and risk of CHD among children. Our findings are consistent with a study done by Zhao et al. [14] who found that paternal active smoking was significantly associated with (CHD risk of 1.74 OR, 95% CI:1.48-2.06 with a p -value <0.01).

There was a statistically significant increase in the incidence of CHDs regards ETS (ENVIRONMENTAL TOBACCO SMOKE) >15min/day with (a p -value=0.007) which aligns with a matched case-control study of 9452 live born infants and stillborn foetuses which was conducted in china and revealed that mothers exposed to ETS during the first trimester of pregnancy were more likely to have infants with CHD than mothers who did not (OR=1.44, 95% CI 1.25-1.66) [16].

The results indicated that the most commonly detected CHDs among the included children, were VSD (23.3%), ASD (21.7%), TOF (2.9%), PS (2.5%), and others such as DORV(2.1%). Similar to what was reported in a study done by Giraldo-Grueso et al. [17] in 2020 who found that VSD (13.72%) was the most prevalent CHDs detected, followed by ASD (10.11%).

There was a statistically significant increase in the incidence of VSD among children regarding mother smoking history exposure during pregnancy with (a p -value=0.004) as most of the children with VSD had a history of mother exposure to smoking during pregnancy, especially in the first trimester and preconception. This finding goes in line with a study which was conducted on 9452 live born birth to evaluate high-risk populations for CHD and revealed statistically significant increased VSD occurrence among infants with mothers exposed to smoking with (a p -value <0.001) [16]. The same finding was reported by the Kovalenko et al. [18] study, which found an increased risk of VSDs was observed among infants born to mothers who smoked during pregnancy with (OR=1.35; 95% CI 1.02-1.80).

Conclusion:

Our study concluded that maternal exposure to smoking has a significant impact on increased incidence of CHDs in general. This study observed that maternal ETS >15 minutes/day (passive smoking) is associated with CHDs.

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تأثير دخان التبغ البيئي على الأم أثناء الحمل وخطر الإصابة بعيوب القلب الخلقية

الهدف من الدراسة: تهدف هذه الدراسة إلى بيان العلاقة بين تعرض الأمهات للتدخين البيئي السلبي أثناء الحمل وعلاقته بظهور عيوب خلقية في القلب لدى الأطفال.

المرضى والطرق: تم إجراء دراسة حالة وضبط على المرضى الذين قدموا إلى وحدة أمراض القلب للأطفال والمراهقين بمستشفيات جامعة عين شمس، وتم تقسيمهم إلى ١٢٠ أم لرضيع حتى مصاب بمرض قلبي خلقي تم تأكيده بواسطة تخطيط صدى القلب بواسطة أخصائي صدى القلب المتخصص. و ١٢٠ أم لرضيع حتى بقلب سليم مستخدمين استبيان

النتائج: كانت هناك زيادة ذات دلالة إحصائية في أمراض الشرايين التاجية بين الأطفال الذين تعرضت أمهاتهم للتدخين أثناء الحمل مقارنة بأولئك الذين ليس لديهم تاريخ من التعرض القيمة الاحتمالية = ٠.٠٠٣ تكون مرتفعة للأطفال المصابين بأمراض الشرايين التاجية). كان هناك أيضاً خطر مرتفع بشكل كبير للإصابة بأمراض القلب التاجية فيما يتعلق بوقت التعرض أثناء الحمل (القيمة الاحتمالية = ٠.٠٠٠١. بالإضافة إلى ذلك، كانت هناك زيادة ذات دلالة إحصائية في أمراض الشرايين التاجية بين الأطفال الذين كان لأمهاتهم تاريخ من التعرض للتدخين في الثلث الأول من الحمل وقبل الحمل، تدخين التبغ البيئي >١٥ دقيقة باليوم (القيمة الاحتمالية = ٠.٠٠٧).

الخلاصة (الاستنتاج): يؤثر تعرض الأمهات للتدخين بشكل كبير على زيادة حدوث أمراض الشرايين التاجية بشكل عام، ولوحظ أن تعرض الأم للتدخين البيئي لدى الأم >١٥ دقيقة باليوم (تدخين سلبي) مرتبط بأمراض القلب التاجية.