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TOBACCO ABUSE EXPOSURE IN WOMEN AND ITS OUTCOMES TO PERINATAL AND CONGENITAL ANOMALIES IN NEWBORNS : A SYSTEMATIC REVIEW

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ABSTRACT

Background: *Pregnant women are at danger for tobacco smoke both actively and passively. Pregnant women are typically exposed to environmental tobacco smoke (ETS) in a variety of settings for varying durations of time. Cigarette smoke has a devastating effect on both pregnant women and the fetus.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 286 articles, whereas the results of our search on SagePub brought up 98 articles. The results of the search conducted for the last year of 2014 yielded a total 123 articles for PubMed and 6 articles for SagePub. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.*

Conclusion: *In summary, tobacco smoking has an influence on pregnant women's immune, hormonal, and metabolic systems. The chemical contained in tobacco smoke has been linked to various pregnancy complications that result in poor pregnancy outcomes, including preterm birth, spontaneous abortion, and harmful effects on newborns. Infants may suffer from respiratory, behavioral, and neurological disorders, SIDS, and other congenital anomalies.The effect of tobacco smoke, actively or passively, is related with poor outcomes for pregnant mothers and their offspring.*

Keyword: *Tobacco exposure, Congenital anomaly, Pregnancy*

INTRODUCTION

Passive smoking is a big public health concern worldwide. This could be especially true during susceptible periods, such as pregnancy. As a result, it is critical to enhance awareness of the relationship between mother and child health outcomes and maternal smoking exposure across different social groups.[1,2]

Pregnant women who smoke are more likely to have an ectopic pregnancy, spontaneous abortion, and other issues that affect both the pregnancy and the placenta. The fetus is also at risk of being exposed to tobacco smoke, which contains over thousands of toxic chemicals, particularly nicotine, tar, and carbon monoxide, which can affect the baby and produce undesirable diseases or deformities.[3]

Exposure of nonsmoking pregnant women to ambient tobacco smoke (ETS) is linked to a variety of negative perinatal outcomes, including lower birthweight, smaller head circumference, and stillbirth. There is an overall consistency in the literature about the negative effects of fetal and postnatal exposure to parental tobacco smoking on several outcomes: preterm birth, fetal growth restriction, low birth weight, sudden infant death syndrome, neurodevelopmental and behavioral problems, obesity, hypertension, type 2 diabetes, impaired lung function, asthma and wheezing.[4]

It has been suggested that pediatric asthma prevention programs should incorporate smoking cessation tactics aimed towards smokers who live in the homes of smoking and nonsmoking pregnant women. ETS acts as a cofactor with other stressors, such as recurrent infections, to produce wheezing, rather than as a factor that induces asthma, although in utero exposure raises physician-diagnosed asthma in the child.[5]

Congenital anomalies, often known as congenital malformations or birth defects, are structural or functional abnormalities that can be identified before or after birth. Every year, roughly 8 million infants worldwide (6% of total births) are born with a significant congenital abnormality.[6]

The relationship between mother cigarette smoking during pregnancy and congenital abnormalities is less apparent. Several studies have found that maternal cigarette smoking is significantly connected with an elevated risk of various types of congenital defects, including mouth clefts and congenital cardiovascular malformations. In contrast, some research found no link between maternal cigarette smoking and any form of congenital anomaly. Furthermore, a few studies also indicated a decreased risk of certain particular malformations among women who smoked during pregnancy, such as anomalies of the musculoskeletal system.[7]

The effects of tobacco smoke on infant congenital abnormalities have been studied. Tobacco smoking has been linked to embryonic heart malformations such as atrial septal defects, atrioventricular septal defects, transposition of major arteries, craniosynostotic cleft palate, and gastroschisis.[3]

The goal of this study was to investigate the relationship between self-reported passive smoking exposure during pregnancy and pregnancy problems and outcomes.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we review published literature about the tobacco abuse exposure in women and its outcomes to perinatal and congenital anomalies in newborns. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "tobacco" “anomalies” and “women” as keywords.The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *(("tobacco products"[MeSH Terms]*

OR ("tobacco"[All Fields] AND "products"[All Fields]) OR "tobacco products"[All Fields] OR "tobacco"[All Fields] OR "nicotiana"[MeSH Terms] OR "nicotiana"[All Fields] OR "tobacco s"[All Fields] OR "tobaccos"[All Fields]) AND ("abnormalities"[MeSH Subheading] OR "abnormalities"[All Fields] OR "anomalies"[All Fields] OR "anomalie"[All Fields] OR "anomaly"[All Fields]) AND ("womans"[All Fields] OR "women"[MeSH Terms] OR "women"[All Fields] OR "woman"[All Fields] OR "women s"[All Fields] OR "womens"[All Fields])) AND (2014:2024[pdat]) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

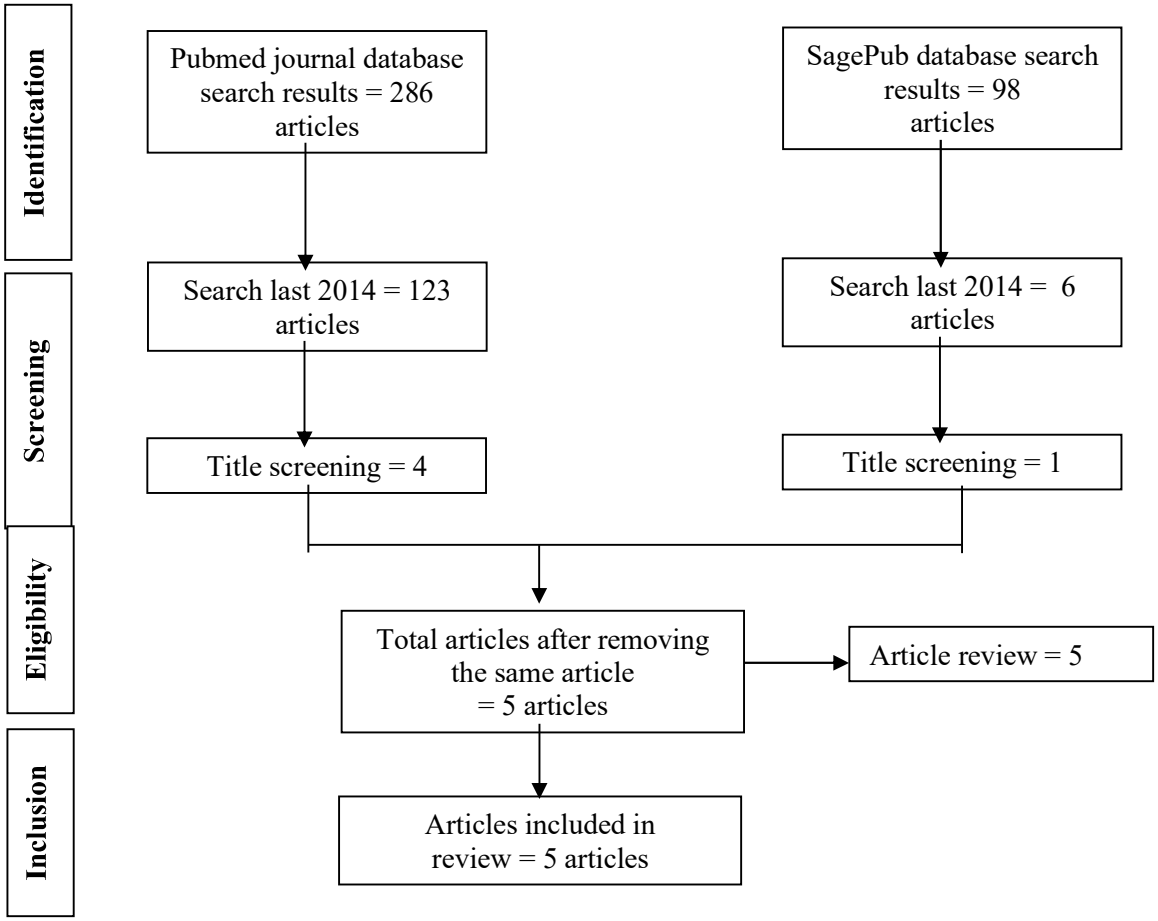

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 286 articles, whereas the results of our search on SagePub brought up 98 articles. The results of the search conducted for the last year of 2014 yielded a total 123 articles for PubMed and 6 articles for SagePub. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.

Borsari, et al[8] (2018) showed that there is evidence that maternal tobacco smoking interacts with pregestational diabetes to increase the risk of preterm birth and congenital abnormalities. Given the continued high frequency of smokers among pregnant women, including those with PGD, and the interplay with PGD, additional efforts to dissuade smoking during pregnancy among women with diabetes would have a significant public-health benefit. Further research, including bigger samples of pregnant women, would help to clarify the degree of this advantage and to deeply explore the relationship between smoking and diabetes on unfavorable pregnancy outcomes..

Chang, et al[9] (2019) showed that prenatal methamphetamine/tobacco exposure may cause delays in motor development, with fewer coherent fibers and poorer myelination in SCR and PCR only in male infants, however these anomalies may resolve by 3 to 4 months following stimulant discontinuation. In contrast, girls exposed to methamphetamine/tobacco had chronically less coherent ACR fibers, possibly because to increased dendritic branching or spine density caused by epigenetic factors. Persistently decreased diffusivity in the thalamus and internal capsule of all tobacco-exposed newborns indicates abnormal axonal growth. Prenatal methamphetamine and/or tobacco exposure may cause delayed motor development and white matter maturation in a sex and region-specific way.

Kumar, et al[10] (2021) showed that maternal SLT exposure during pregnancy may be related with villus hypoxia, which can lead to oxidative DNA damage. It is assumed that the negative effects of SLT exposure on the placenta could weaken the placental barrier, restrict nutrition and oxygen flow from mother to fetus, and hence be a cause of fetal growth restriction.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Borsari et al, 2018[8]	Italy	Cohort study	992 patients	The study included 992 women with PGD (10.5% smokers) and 4788 comparison women (11.9% smokers). The effects of PGD and maternal tobacco smoking were greater than additive for both preterm birth (excess prevalence due to interaction = 11.7%, excess ratio due to interaction = 1.5, RERI = 2.39, AP = 0.51, S = 2.82) and congenital anomalies (excess prevalence due to interaction = 2.2%, excess ratio due to interaction = 1.3, RERI = 1.33, AP = 0.49, S = 5.03). Joint effect on both endpoints was confirmed in the subgroup whose PGD status was validated.
Chang et al, 2019[9]	USA	Prospective longitudinal study	139 patients	Of the 139 infants evaluated, 72 were female (51.8%); the mean (SE) postmenstrual age at baseline was 41.5 (0.27) weeks. Methamphetamine/tobacco-exposed infants showed delayed developmental trajectories on active muscle tone (group × age, $P < .001$) and total neurologic scores (group × age, $P = .01$) that normalized by ages 3 to 4

				months. Only methamphetamine/tobacco-exposed boys had lower FA (group × age, $P = .02$) and higher diffusivities in superior (SCR) and posterior corona radiatae (PCR) (group × age × sex, $P = .002$; group × age × sex, $P = .01$) at baseline that normalized by age 3 months. Only methamphetamine/tobacco- and tobacco-exposed girls showed persistently lower FA in anterior corona radiata (ACR) (group, $P = .04$; group × age × sex, $P = .01$). Tobacco-exposed infants showed persistently lower axial diffusion in the thalamus and internal capsule across groups ($P = .02$).
Kumar et al, 2021[10]	India	Prospective longitudinal study	51 patients	Altered ultrastructural characteristics were observed in the tertiary villi of LBW group among SLT users which included endothelial cells protrusion into capillary lumen, degenerated nuclei, significant thickening of trophoblast basement membrane and vasculo-syncytial membrane, abnormalities of the microvilli, swollen or damaged mitochondria, and dilatation in endoplasmic reticulum cisternae. Furthermore, significant reduction in the perimeter, area, and number of the stromal capillary of the tertiary villi of placenta were found in LBW group as compared with NBW group from the SLT users. Enhanced expression for HIF-1α and oxidative DNA damage (8-OHdG) biomarker was observed in SLT users as compared with nonusers.
Shiohama et al, 2021[11]	Japan	Prospective cohort study	84.856 patients	Maternal perinatal clinical and social information by self-administered questionnaires, offspring's body size, and placental information were collected. Data were analyzed with binominal logistic regression analysis and path analysis. Logistic regression showed significantly elevated adjusted odds ratio (aOR) (1.653, 95% CI 1.387–1.969)

				for the impact of maternal smoking during pregnancy on their offspring's smaller HC at birth. Maternal exposure to environmental tobacco smoke in the non-smoking group did not increase aOR for the smaller HC. Path analysis showed that maternal smoking during pregnancy decreased the offspring's HC directly, but not indirectly via PWR or placental abnormalities. The quitting smoking during pregnancy group did not increase aOR for the smaller HC than the non-smoking group, suggesting that quitting smoking may reduce their offspring's neurological impairment even after pregnancy.
Duko et al, 2023[12]	Australia	Retrospective study	64.558 patients	Complete data were available for 64,558 mothers-children's pairs. Approximately 16% of children were exposed to maternal prenatal tobacco smoking. Children exposed to maternal prenatal tobacco smoking were more likely to be classified as developmentally vulnerable/at-risk on the physical health and wellbeing (RR = 1.40, 95%CI:1.36-1.45), social competence (RR = 1.42, 95%CI: 1.38-1.47), emotional maturity (RR = 1.34, 95%CI:1.30-1.39), language and cognitive skills (RR = 1.50, 95%CI:1.45-1.54), and communication skills and general knowledge (RR = 1.37, 95%CI:1.33-1.42) domains.

Shiohama, et al[11] (2021) showed that maternal smoking during pregnancy decreased offspring's HC independent of placental weight changes or placental abnormalities.

Duko, et al[12] (2023) showed that tobacco use during pregnancy may have an impact on early childhood development vulnerability. Early intervention to quit smoking before getting pregnant may lessen later childhood developmental susceptibility across various areas.

DISCUSSION

This systematic review involved a total of 150.596 data of patients or the prenatal and congenital anomalies with the mother had tobacco exposure in 5 observational studies. Environmental tobacco smoke (ETS) is a complicated mixture of smoke released by smokers, cigarette smoke, and ambient air2. Pregnant women who are exposed to ETS had higher amounts of carbon monoxide (CO), nicotine, and cotinin in their serum or urine, as well as in the fetal and amniotic fluid. ETS can affect pregnant women from the first to third semester. Pregnant women are frequently exposed to ETS in different locations and for varying durations. ETS exposure may occur at home, work, or outdoors.

One effect of the cigarette smoke exposure on pregnant women is its effect on the mother's immune system. In pregnancy changes occur in the mother's immune system to prevent rejection of the fetus. Exposure to ETS can cause changes in the

immune system of pregnant women. Changes include an increase in activated leukocytes and a decrease in the percentage of regulator T lymphocyte cells (Treg cells).[13]

Smoking during pregnancy disrupts the equilibrium between Th1 and Th2 cells, leading to increased production of cytokines, proinflammatory chemokines, and Th1 growth factors. Additionally, smokers have a larger percentage of macrophage and NK cell residues throughout the first semester.[13]

Nicotine exposure in pregnant women can cause vascular placental vasoconstriction, decrease placental blood flow, and impair trophoblast invasion, which inhibits proper placental circularization and produces placental hypoxia, disrupting placental invasion. Placenta previa is a type of placental invasion disorder4. Nicotine has been shown to significantly reduce the mitotic capacity of cytotrophoblast tissue in vitro. This impact is also observed in smoking women. This impact may explain the process of poor placental development during early pregnancy due to placental ischemia, which can result in fetal death. Low placental weight is significantly connected to LBW.[3]

In addition to nicotine and cotinin, smokers have the greatest amounts of CO. The presence of CO in the body reduces oxygen binding to hemoglobin due to hemoglobin's increased affinity for CO. CO Exposure to the fetus hinders the release of oxygen, which is then transformed into carboxyhemoglobin. The result is a decrease in tissue oxygenation due to competitive inhibition with oxyhemoglobin. Prolonged CO exposure in pregnant women can cause considerable lasting damage to a fetus' brain, which is sensitive to hypoxia. Nicotine is also thought to have a negative impact due to the activation of nicotine cholinergic receptors and their neuroteratogenic properties. Nicotine also disrupts microRNA, which is necessary for the maturation of fetal stem cells.[13]

Active smoker moms are regarded as a risk factor for preterm birth, accounting for around 14% of all preterm deliveries. The CYP1A1 genotype and GST (glutathione S-transferase) are one mechanism linking cigarette exposure to premature birth. Abnormalities in these genes make moms more susceptible to dangerous chemicals like cigarette smoke. Cotinin levels, as a biomarker of cigarette exposure, are also substantially associated with premature birth.4 Munmun et al.'s research also highlights the dangers of nonsmoking tobacco. This demonstrates that nonsmoking tobacco (chewed and swallowed) increases the risk of premature delivery.[3]

Prostagladin has been shown to induce labor. In smokers, the amniotic membrane and amniotic fluid include prostaglandin levels such as F2-isoprostane, which is a marker of oxidative stress. F2-isoprostane levels increased thrice compared to nonsmokers. Increased F2-isoprostane levels are thought to be a mechanism that links smoking to premature delivery. Smoking is also thought to boost the uterus' sensitivity to contractile hormones.[3]

The effects of tobacco smoke on infant congenital abnormalities have been studied. Tobacco smoking has been linked to embryonic heart malformations such as atrial septal defects, atrioventricular septal defects, transposition of major arteries, craniosynostotic cleft palate, and gastroschisis.[3]

CONCLUSION

In summary, tobacco smoking has an influence on pregnant women's immune, hormonal, and metabolic systems. The chemical contained in tobacco smoke has been linked to various pregnancy complications that result in poor pregnancy outcomes, including preterm birth, spontaneous abortion, and harmful effects on newborns. Infants may suffer from respiratory, behavioral, and neurological disorders, SIDS, and other congenital anomalies.The effect of tobacco smoke, actively or passively, is related with poor outcomes for pregnant mothers and their offspring.

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