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The Effects Of Electronic Cigarette Components On Female Fertility And Associated Prenatal Period

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Abstract – Over the past decade, there has been an alarming rate of increase in the usage of electronic cigarettes also known as vaping. The misapprehension that such alternative nicotine products are less harmful than conventional cigarettes has attracted vulnerable population groups which include middle and high-school students ,young adults, women with the desire to conceive and childbearing mothers who look for combustible cigarette replacements during gestational period. Vaping devices deliver nicotine-containing aerosols by heating e-fluids that have proven to be cytotoxic and teratogenic, justifying maternal vaping as a frequent cause of morbidity in the fetus. As a part of this study, we aim to develop a greater understanding of the consequences of e-cigarettes consumption in women of reproductive age and exposed fetuses.

Keywords – Electronic Cigarettes, Teratogenic, Maternal Vaping, Fetuses.

I. Introduction

Electronic nicotine delivery systems (ENDS) are battery powered devices consisting of a reservoir that holds the e-liquid and an atomizer which generates heat thereby aerosolizing the e-liquid, in doing so inspirable aerosols are produced.[1] On a broader spectrum there are sufficient studies justifying the respiratory, cardiovascular and CNS linked health hazards with vaping, however narrowly established are its effects on reproductive health.[2,3] With respect to pregnancy women perceive e-cigarettes usage as a route to abstain from consumption of tobacco-related carcinogens. Certainly e-cigarettes lack many chemicals which are found in commercial cigarettes, nonetheless there are a few common toxicants such as volatile organic compounds (VOC's), heavy metals, tobacco-specific nitrosamines (TSNAs), PAHs, and tobacco alkaloids which are established mutagenic and embryotoxic substances.Studies reveal that consumption of e-cigarettes in the late adolescent years lessens the likelihood of becoming pregnant by fifty percent in each fertile window.[1,4,5,6]

II. Methodologies

Despite the inherent limitations, this study involved a comprehensive search through databases such as Google Scholar and PubMed using keywords such as "e-cigarettes", "maternal e-smoking", " pregnancy" and "fetus".

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III. Result

In the existing literature, animal models used to study the effects of e-cigarettes hazards are 1) Xenopus laevis model for vanillin flavoring-induced craniofacial abnormalities in the embryo by dysregulation of retinoic acid signaling,[7] 2) Pregnant female Sprague- Dawley rats for cardiovascular risks,[8] 3) Rhesus monkey for abnormalities in fetal lung development via an increase in nicotinic acetylcholine receptors,[9] 4) Murine models for neurological and nephrological disorders.[9,10]

According to the implemented research, sufficient evidence suggests the negative effects of vaping on maternal-offspring health which are well-reasoned in this study.

IV. Discussion

A. Main components of e-cigarettes.

The two key e-liquid humectants are propylene glycol (PG) and vegetable glycerin (VG) which are heated to generate aerosols without combustion. The ratio of PG and VG in e-liquids vary based upon the preference for flavor (PG>VG) or cloud-chasing (VG>PG).The duo are popularized food additives and practically “non-toxic” when consumed orally. However they emit known neurological,immunological and reproductive toxicants called “BTEX” compounds which include acetaldehyde, acrolein, benzaldehyde, benzene, toluene, ethylbenzene, and xylene as a consequence of oxidation and thermal decomposition due to heating.[1,11,12]

The plethora of flavorings available is considered as the root cause of attraction towards vaping.Flavors such as “cherry-crush”, ”bubblegum”, ”methanol/minty”, ”citrus”, dessert like “vanilla cannoli", fruity “green apple “and “grapes” etc. are harmless for oral consumption but in terms of inhalation, these chemicals are proven carcinogens and teratogens as they directly enter the bloodstream in concentrations thousand folds comparable to ingestion.With respect to quantities of nicotine, vaping devices differ significantly as few deliver scant doses of nicotine labeled as ‘nicotine-free”, whilst others contain “nicotine salts” that are absorbed quickly in the bloodstream and deliver smooth throat hits at higher doses, unalike freebase nicotine which is frequently used in e-liquids compared to nicotine salts, it has a slower absorption rate in the bloodstream and provides a more advanced vaping experience followed by harsh throat hit at higher doses. Furthermore liquid nicotine can reach concentrations surpassing that of tobacco cigarettes.[1,11,13,14]

Nonetheless, even minimal exposure of nicotine is associated with negative fetal growth because of its potential to cross the fetal-placental barrier thus, increasing the amniotic fluid, fetal circulatory system and breast-milk levels of nicotine. [15] Altogether usage of e-cigarettes during pre-conception and early pregnancy period gives rise to unfavorable effects in the functioning of female reproductive organs and disrupts the fetus development due to hormonal and metabolic imbalances.

B. Motivation of use.

Regrettably maternal e-smoking has exponentially increased because of the unawareness and false presumption that e-cigarettes do not contain harmful substances in comparison to commercial cigarettes and that “nicotine-free” vaping devices could be used as safer alternatives during pregnancy.

Most women idealize that e-cigarettes may potentially help them quit smoking, while several women abide by EC’s as a cheaper alternative for regular tobacco. Some claim that smoke odors on their clothes and indoors is diminished comparatively. In continuation, the stigma associated with traditional smoking during pregnancy has convinced many that vaping in public places to a greater extent is socially acceptable and doesn’t showcase them as bad mothers.Lastly, studies prove that a key reason towards willingness to pay for e-cigarettes amongst pregnant smokers is the craving for sweet food like flavorings in e-juices.[16,17]

C. *Association between Vaping And Foetal Growth [Table 1]*

Four out of many experiments have been mentioned below which were conducted using animal models to evaluate the hazards evoked by maternal e-smoking on fetal growth.

1.Craniofacial Abnormality

For its effectiveness in predicting the possibility of a substance to be teratogenic or not, studies were conducted on aquatic developmental model, Xenopus laevis.It revealed that exposure of "vanillin" flavoring caused craniofacial defects in the developing embryo via dysregulation in the retinoic acid signaling pathway.[7]

Methodology involved transcriptomic analysis of embryonic facial tissue when exposed to e-liquid vapors of flavoring "vanillin", followed by gene analysis. RNA extracted from the facial tissues showed 50% gene alteration including decreased expression of five core retinoic acid pathway genes two of which are crabp1 and crabp2 i.e cytoplasmic retinoid binding proteins (CRABPs) which act as transporters and have protective function for RA and prevent its degradation.[7]

Since crabp1 and crabp2 genes are expressed in the developing craniofacial region of X. laevis, reduction in their concentration due to e-liquid exposure is proportional to reduced RA signaling resulting in craniofacial defects. Experiments conducted with e-juice that contained only nicotine, PG and VG proved to cause negligible craniofacial abnormalities justifying the presence of flavoring as the primary source of craniofacial abnormalities such as 1. Median cleft extending from primary palate to the root of oral cavity, 2. little to no presence of ethmoid plate, 3. Reduced size of forebrain, 4. Shortened olfactory nerve and 5.Narrower midface.[7]

2.Cardiovascular Abnormality

To evaluate the cardiovascular risks associated with e-cigarettes and experiment was conducted on "pregnant female Sprague-Dawley rats " using nicotine-free or nicotine-containing e-Cigarette aerosol for 1 hr/day, 5 days/wk, starting on gestational day 2 until weaning.[8]

It concluded that perinatal maternal vaping induced alteration in the arterial structure and function by impairing the aortic relaxation in exposed offsprings, which persisted into adulthood as well. It is worth mentioning that dysfunctions were seen with or without nicotine exposure. Establishing that even in "nicotine-free vapes", toxicants produced solely by heating of PG and VG are sufficient to cause vascular endothelial cell damage in the fetus.[8]

3.Pulmonary Abnormality

It has been proven that prenatal exposure of e-cigarettes aerosols on mouse 2 mg/kg/day and rhesus monkey 1.5 mg/kg/day is associated with growth abnormalities throughout the lungs via increase in nicotinic acetylcholine receptors (nAChRs) located on macrophages, epithelial lining cells, and fibroblasts. Microscopic anatomy and histochemistry of rhesus monkey fetal lung tissue revealed increase in collagen, wall thickness, and alveolar volume along with decrease in lung size and volume.[9]

4.Neurological and Nephrological Abnormality

In-utero electronic cigarette exposure is associated with neurological disorders like chronic neuropathology, dysregulation of neuronal metabolic regulation and ADHD(Attention Deficit Hyperactivity Disorder) in offspring. A conceivable reason for the above findings is alteration in the transcriptome of the frontal cortex and increase in global DNA methylation of the brain. It was observed that exposure of nicotine-free aerosols in murine models was associated with renal fibrosis, elevated kidney markers of oxidative stress and nephritis.[9,10]

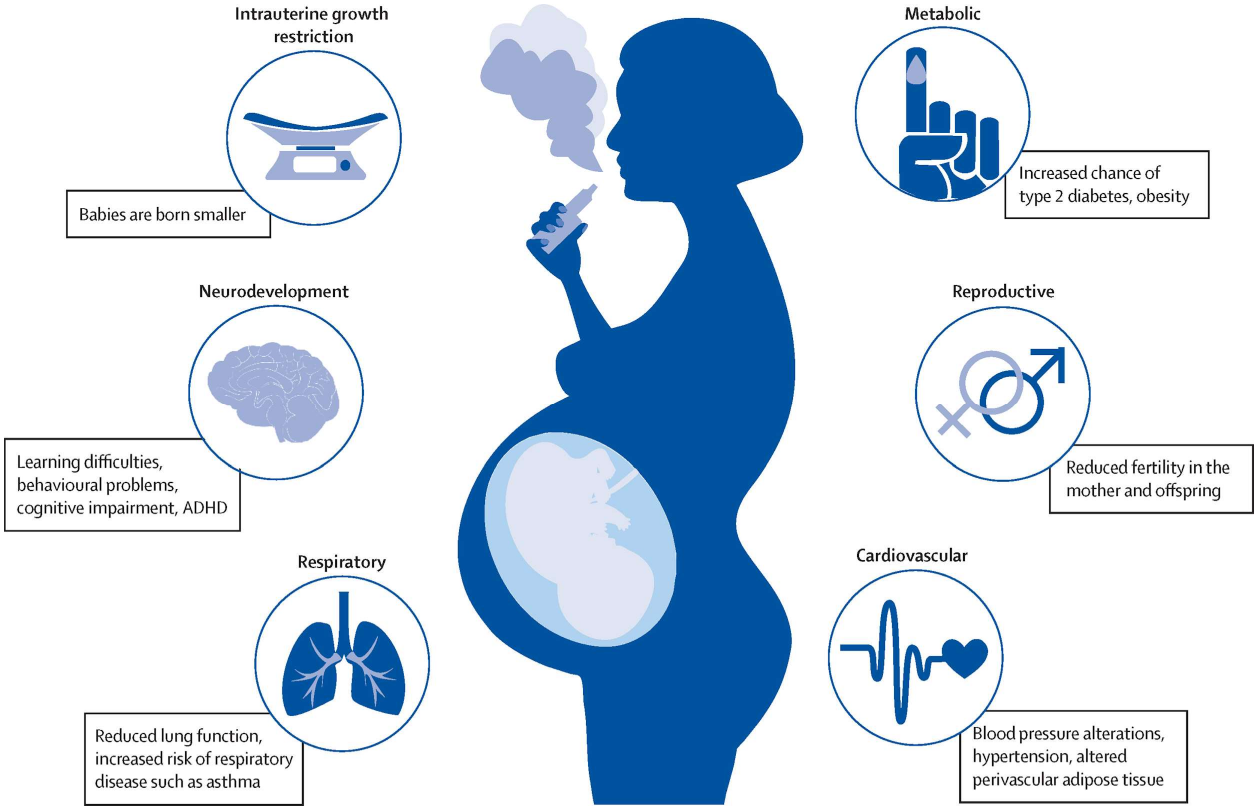
Table 1. Summary of animal models used to evaluate the hazards evoked by maternal e-smoking on fetal growth. [7,8,9,10]

1. Aquatic developmental model, Xenopus laevis.	Craniofacial Abnormality	Exposure of "vanillin" flavouring causes the following craniofacial defects in the developing embryo of Xenopus laevis via dysregulation in the retinoic acid signalling pathway. 1. Median cleft extending from primary palate to the root of oral cavity. 2. Little to no presence of ethmoid plate. 3. Reduced size of forebrain. 4. Shortened olfactory nerve. 5. Narrower midface.
2. Pregnant female Sprague-Dawley rats.	Cardiovascular Abnormality	1. Modified blood flow through umbilical artery and maternal uterine artery. 2. Vascular endothelial cells impairment.
3. Rhesus monkey	Pulmonary Abnormality	1. Impaired growth throughout the lungs via increase in nicotinic acetylcholine receptors (nAChRs). 2. Increased collagen, wall thickness, and alveolar volume along with decrease in lung size and volume.
4. Murine models	Neurological Abnormality	1. Chronic neuropathology. 2. Dysregulation of neuronal metabolic regulation. 3. ADHD(Attention Deficit Hyperactivity Disorder). 4. Inflammation in the hippocampus.
5. Murine models	Nephrological Abnormality	1. Renal fibrosis. 2. Elevated kidney markers of oxidative stress. 3. Nephritis.

D. Association Between Vaping And Female Fertility [Figure 1]

Effects of Vaping on Preconception Health and during Pregnancy.

Smoking e-cigarettes negatively influences female fertility in a number of ways including anovulation(wherein ovaries do not release an egg during your monthly cycle), diminished ovarian reserves, hormonal imbalances which in return causes metrorrhagia, oligomenorrhea and early menopause.Concomitant use of hormonal birth control pills and e-cigarettes significantly increases cardiovascular health risks such as strokes and blood clot formation caused by nicotine induced rise in blood pressure accompanied with estrogen provoked stress in blood vessels. Though existing literature is insubstantial it does suggest the high incidence rates of cervical, thyroid and skin cancer in female electronic cigarette users.Electronic cigarette consumption is associated with high risk pregnancy outcomes.E-smoking impairs the physiological cardiovascular adaptations that develop during pregnancy to counterbalance the rise in cardiac output demands,primarily impairing the uterine artery thereby reducing blood flow by 40% to the fetoplacental unit.Additionally electronic smoking devices emit nicotine aerosols that pose a significant risk for chorioamnionitis,ventricular arrhythmias, diminished endometrial receptivity, delayed embryo implantation, preterm-birth and neonatal death.[5,9,18,19,20]



[Figure 1] : Association between vaping and female fertility.

V. Limitations

Undoubtedly animal models cannot accurately mimic human reproductive system ,metabolic pathways and cellular internalization,yet they are the closest equivalents to derive a better understanding.Moreover at present there is a limited scope of information and resource availability wherein studies are conducted on human subjects to understand the possible effects of e-cigarettes.Additionally due time restrictions the aftermath of passive vaping and third-hand exposure of e-cigarettes have not been reported in this study.With that being said the outcome of vaping in women of fertile age, pregnant women and offspring exposed in utero are cautioning ,justifying further investigation and analysis involving human test subjects for such next-generation tobacco products linked carcinogens and teratogens as an absolute necessity.

VI. Conclusion

Considering all of the above,our study asserts that e-cigarettes cannot be viewed as an harmless substitute for combustible cigarettes at least during pregnancy as they emit nicotine,volatile organic compounds (VOC's) and other cytotoxic substances that are proven to be teratogenic. This is why awareness is critical for preventing the boom in e-cigarettes consumption in young adults including women of reproductive age, this could be achieved at governmental level by promoting "graphic warning labels " on vaping devices and at the healthcare level by following the 5 A's technique composed of ask,advise,assess,assist and arrange for the vulnerable population.[21]Ultimately,further studies to determine the negative implications of e-cigarette exposure in reproductive wellbeing and developing fetus are compelling necessity.

Conflicts of interest

There are no conflicts of interest.

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Ethical approval

Ethical approval was not required for this study.

Declaration of patient consent

Patients consent is not required as there are no patients in this study.

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References -

[1]. 1.Szumilas K, Szumilas P, Grzywacz A, Wilk A. The Effects of E-Cigarette Vapor Components on the Morphology and Function of the Male and Female Reproductive Systems: A Systematic Review. Int J Environ Res Public Health. 2020 Aug 24;17(17):6152. doi: 10.3390/ijerph17176152. PMID: 32847119; PMCID: PMC7504689.

[2]. 2.Burrage EN, Aboaziza E, Hare L, Reppert S, Moore J, Goldsmith WT, Kelley EE, Mills A, Dakhlallah D, Chantler PD, Olfert IM. Long-term cerebrovascular dysfunction in the offspring from maternal electronic cigarette use during pregnancy. Am J Physiol Heart Circ Physiol. 2021 Aug 1;321(2):H339-H352. doi: 10.1152/ajpheart.00206.2021. Epub 2021 Jun 25. PMID: 34170194; PMCID: PMC8410118.

[3]. 3.Oriakhi M. Vaping: An Emerging Health Hazard. Cureus. 2020 Mar 26;12(3):e7421. doi: 10.7759/cureus.7421. PMID: 32351806; PMCID: PMC7186084.

[4]. 4.Baeza-Loya S, Viswanath H, Carter A, Molfese DL, Velasquez KM, Baldwin PR, Thompson-Lake DG, Sharp C, Fowler JC, De La Garza R 2nd, Salas R. Perceptions about e-cigarette safety may lead to e-smoking during pregnancy. Bull Menninger Clin. 2014 Summer;78(3):243-52. doi: 10.1521/bumc.2014.78.3.243. PMID: 25247743; PMCID: PMC4458373.

[5]. 5.DeVito EE, Krishnan-Sarin S. E-cigarettes: Impact of E-Liquid Components and Device Characteristics on Nicotine Exposure. Curr Neuropharmacol. 2018;16(4):438-459. doi: 10.2174/1570159X15666171016164430. PMID: 29046158; PMCID: PMC6018193.

[6]. 6.Montjean D, Godin Pagé MH, Bélanger MC, Benkhalifa M, Miron P. An Overview of E-Cigarette Impact on Reproductive Health. Life (Basel). 2023 Mar 18;13(3):827. doi: 10.3390/life13030827. PMID: 36983982; PMCID: PMC10053939.

[7]. 7.Dickinson AJG, Turner SD, Wahl S, Kennedy AE, Wyatt BH, Howton DA. E-liquids and vanillin flavoring disrupts retinoic acid signaling and causes craniofacial defects in Xenopus embryos. Dev Biol. 2022 Jan;481:14-29. doi: 10.1016/j.ydbio.2021.09.004. Epub 2021 Sep 17. PMID: 34543654; PMCID: PMC8665092.

[8]. 8.Aboaziza E, Feaster K, Hare L, Chantler PD, Olfert IM. Maternal electronic cigarette use during pregnancy affects long-term arterial function in offspring. J Appl Physiol (1985). 2023 Jan 1;134(1):59-71. doi: 10.1152/japplphysiol.00582.2022. Epub 2022 Nov 23. PMID: 36417201; PMCID: PMC9762967.

[9]. 9.Orzabal M, Ramadoss J. Impact of Electronic Cigarette Aerosols on Pregnancy and Early Development. Curr Opin Toxicol. 2019 Apr;14:14-20. doi: 10.1016/j.cotox.2019.05.001. Epub 2019 May 22. PMID: 31214660; PMCID: PMC6581464.

[10]. 10.Mescolo F, Ferrante G and La Grutta S (2021) Effects of E-Cigarette Exposure on Prenatal Life and Childhood Respiratory Health: A Review of Current Evidence. Front. Pediatr. 9:711573. doi: 10.3389/fped.2021.711573

[11]. 11.Breland A, McCubbin A, Ashford K. Electronic nicotine delivery systems and pregnancy: Recent research on perceptions, cessation, and toxicant delivery. Birth Defects Res. 2019 Oct 15;111(17):1284-1293. doi: 10.1002/bdr2.1561. Epub 2019 Jul 31. PMID: 31364280; PMCID: PMC7121906.

[12]. 12.Montjean D, Godin Pagé MH, Bélanger MC, Benkhalifa M, Miron P. An Overview of E-Cigarette Impact on Reproductive Health. Life (Basel). 2023 Mar 18;13(3):827. doi: 10.3390/life13030827. PMID: 36983982; PMCID: PMC10053939.

[13]. 13.Ooi BG, Dutta D, Kazipeta K, Chong NS. Influence of the E-Cigarette Emission Profile by the Ratio of Glycerol to Propylene Glycol in E-Liquid Composition. ACS Omega. 2019 Aug 5;4(8):13338-13348. doi: 10.1021/acsomega.9b01504. PMID: 31460462; PMCID: PMC6705204.

[14]. 14.Sung B. Gender Difference in the Association Between E-Cigarette Use and Depression among US Adults. Osong Public Health Res Perspect. 2021 Feb;12(1):13-19. doi: 10.24171/j.phrp.2021.12.1.03. PMID: 33659150; PMCID: PMC7899230.

[15]. 15.Archie SR, Sifat AE, Zhang Y, Villalba H, Sharma S, Nozohouri S, Abbruscato TJ. Maternal e-cigarette use can disrupt postnatal blood-brain barrier (BBB) integrity and deteriorates motor, learning and memory function: influence of sex and age. Fluids Barriers CNS. 2023 Mar 10;20(1):17. doi: 10.1186/s12987-023-00416-5. PMID: 36899432; PMCID: PMC9999561.

[16]. 16.Bowker K, Orton S, Cooper S, Naughton F, Whitemore R, Lewis S, Bauld L, Sinclair L, Coleman T, Dickinson A, Ussher M. Views on and experiences of electronic cigarettes: a qualitative study of women who are pregnant or have recently given birth. BMC Pregnancy Childbirth. 2018 Jun 15;18(1):233. doi: 10.1186/s12884-018-1856-4. PMID: 29902987; PMCID: PMC6003107.

[17]. 17.Ashford K, Wiggins A, Butler K, Ickes M, Rayens MK, Hahn E. e-Cigarette Use and Perceived Harm Among Women of Childbearing Age Who Reported Tobacco Use During the Past Year. Nurs Res. 2016 Sep-Oct;65(5):408-14. doi: 10.1097/NNR.0000000000000176. PMID: 27579508; PMCID: PMC6698448.

[18]. 18.Vilcassim MJR, Stowe S, Majumder R, Subramaniam A, Sinkey RG. Electronic Cigarette Use during Pregnancy: Is It Harmful? Toxics. 2023 Mar 18;11(3):278. doi: 10.3390/toxics11030278. PMID: 36977043; PMCID: PMC10058591.

[19]. 19.Jandíková H, Dušková M, Stárka L. The influence of smoking and cessation on the human reproductive hormonal balance. Physiol Res. 2017 Sep 26;66(Suppl 3):S323-S331. doi: 10.33549/physiolres.933724. PMID: 28948816.

[20]. 20.Adamcová K, Kolátorová L, Chlupáčová T, Šimková M, Jandíková H, Pařízek A, Stárka L, Dušková M. Changes to fetal steroidogenesis caused by maternal smoking. Physiol Res. 2017 Sep 26;66(Suppl 3):S375-S386. doi: 10.33549/physiolres.933728. PMID: 28948822.

[21]. 21.Satterfield JM, Gregorich SE, Kalkhoran S, Lum PJ, Bloome J, Alvarado N, Muñoz RF, Vijayaraghavan M. Computer-Facilitated 5A's for Smoking Cessation: A Randomized Trial of Technology to Promote Provider Adherence. Am J Prev Med. 2018 Jul;55(1):35-43. doi: 10.1016/j.amepre.2018.04.009. Epub 2018 Jun 18. PMID: 29929682; PMCID: PMC6020838.