International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.
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https://ijpsat.org/
Vol. 48 No. 1 December 2024, pp. 611-622

Vaping's Silent Epidemic: Reproductive Harm And Misleading Safety Claims

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Abstract – Vaping, which has received considerable encouragement as a better choice than smoking, has gained popularity amongst the younger demographic as well as those individuals who wish to quit smoking. In this paper, we reviewed the literature available on the composition of e-liquids which revealed propylene glycol, glycerin, nicotine, formaldehyde, cadmium, volatile organic compounds, polycyclic aromatic hydrocarbons, and a number of other hazardous substances as the primary components. These substances, when inhaled through vaping have proven to negatively impact the reproductive systems of both men and women. While vaping lowers sperm quality and may affect erectile function in men, it has shown to disturb ovarian function, hormone balance, and fertility in women. It has even more disastrous effects on pregnant individuals causing complications like placental malfunction, premature births, and problems with fetal growth. Furthermore, adolescents who metabolize nicotine more rapidly than adults are more susceptible to addiction and may, in the near future, experience disastrous long-term effects. This study solicits the need for more research to eliminate misunderstandings about vaping's safety and emphasizes the need for increased awareness of its detrimental impacts, particularly in relation to reproductive health.

Keywords – Vaping, Reproductive Health, Reproductive Systems, Toxicology, Pregnancy, Spermatogenesis, Oogenesis.

1. INTRODUCTION

Vaping is the process of inhaling and exhaling an aerosol produced by an e-cigarette or a vape pen. An electronic cigarette (e-cigarette) more commonly known as a 'vape' is a vaporizer device that simulates tobacco smoking. It consists of an atomizer, a power source (battery), and a cartridge or tank-like container. The main difference between 'classic' cigarette smoking and vaping is that the user inhales vapors instead of smoke. The atomizer is a heating element that vaporizes a liquid solution called the e-liquid, which quickly cools into an aerosol of tiny droplets, vapor and air. (Fig. 1)

To understand the effects of Vaping on the human body and specifically the reproductive system, it is vital to understand the composition of the e-liquid being inhaled. E-liquid formulations can vary widely but a standard composition consists of propylene glycol and glycerin (95%) and a combination of flavorings, nicotine, and other additives (5%). The flavorings may be natural, artificial, or organic. Other than this, over 80 harmful chemicals such as formaldehyde and metallic nanoparticles have been found in e-liquids in trace quantities making it harmful to respiratory health (directly) and reproductive health (indirectly) along with effects on other organ systems.

There is a sudden increase in the rates of vape users in recent years and this could be due to a multitude of reasons. Most users revert to vaping as a method to try and quit smoking, whereas a large proportion of people use it as recreational or as an attempt to get around smoke-free laws. The wide choice of flavors and a lower price are also important factors as to why people prefer vapes over cigarettes. Vapes have been widely marketed as less harmful than traditional Tobacco cigarettes due to the formation of fewer carcinogenic byproducts of combustion. However, it is important to remember that the consequences are just as dire and maybe even more harmful when we specifically take reproductive health into perspective.

A PubMed database search shows a drastic increase in the number of publications containing the word 'vaping' or 'e-cigarette' over the past decade. This increase in relevant research is consistent with the increased use of Vapes over the past decade and should become a rising public concern with respect to its potential health impacts.

Statistics show that out of the general population, Vaping was more common in younger age groups (aged 18-24) as compared to the latter. (Fig. 2) Vaping may not cause immediate severe damage to any organ system, but it will progressively have degenerative effects. Especially in younger groups, who may, in the near future, face problems with fertility and development. The reasons for this may be vast, but vaping may be a contributing factor.

While several extremely informative articles have been published on the effect of Vaping on Respiratory health, this review article shifts its focus towards the Impact of Vaping and the toxicity of e-liquids on Reproductive health during adolescence and later on as well as the effects on fertility and pregnancy.

2. OBJECTIVE

This study examines the physiological effects of e-liquid composition in order to assess the detrimental effects of vaping on reproductive health. It focuses on the adverse effects on the reproductive systems of both men and women, including fertility, ovarian function, sperm quality, and hormonal balance. The study also looks at potential risks to adolescents and pregnant women, emphasizing the long-term effects of vaping. The ultimate goal is to increase awareness, clarify misconceptions regarding the safety of vaping, and promote further research to address the negative impacts it has on public health.

3. MATERIALS AND METHODS

25 articles have been analyzed for the literature review. Keywords such as (Vaping, Reproductive health, reproductive systems, toxicology, pregnancy, spermatogenesis, and oogenesis) were used for the literature searches in databases such as Google Scholar and PubMed.

4. RESULTS

According to the reviewed literature, we have established evidence of how vaping adversely impacts reproductive health: Vaping was shown to impair ovarian function and fertility in females and lower sperm quality in males, with high risk for placental dysfunction and adverse fetal outcomes in pregnant individuals. Adolescents are particularly susceptible to addiction and long-term reproductive health problems owing to their accelerated metabolism of nicotine. These reproductive issues are exacerbated by the dangerous compounds found in e-liquids, such as formaldehyde and cadmium. These results demonstrate the critical need for further understanding and research into the reproductive dangers of vaping.

5. DISCUSSION

6.1 Effect on the development of the reproductive system

The chemical composition of vapes have shown to cause specific effects according to their individual absorption and toxicology on the human body specifically during adolescence, some of them include:

- **Nicotine and its effects on the body :**

  Nicotine is a toxic compound that stimulates the release of adrenaline, which in turn elevates blood pressure and increases heart rate. This can lead to the heightening of the body's stress response and lead to significant risks over time in developing individuals. Studies have indicated that nicotine or tobacco exposure during adolescence increases the risk of developing psychiatric disorders, cognitive impairments, and attention deficits

  Absorption of nicotine in adolescents differs significantly compared to that of adults, due to developmental and physiological differences, these include:

  - **Brain Development:**
    - Nicotine can particularly alter the prefrontal cortex which is still developing during adolescence.
    - Nicotine exposure disrupts the signaling of acetylcholine and glutamate receptors in the prefrontal cortex, the region of the brain that is crucial for decision-making, impulse control, and planning making them more vulnerable to its effects.
    - Dopamine neurons of the ventral tegmental area are more sensitive to nicotine-induced long-term potentiation in adolescents compared to adults.
    - Adolescents experience broader effects on the ascending serotonin system with nicotine exposure as there is a wider range of targeted brain regions and different dose responses than adults.
    - Nicotine boosts physical activity in adolescent rodents whereas in adults it reduces locomotor activity.

  - **Metabolism of nicotine:**
    - Nicotine is metabolized faster in adolescents than in adults due to the increased activity of the nicotine metabolizing enzymes, This leads to more frequent nicotine consumption to maintain desired effects.
    - Adolescents generally consist of more active liver enzymes particularly CYP2A6, which helps to break down nicotine to cotinine, leading to faster metabolism in adolescents than adults.
    - Adolescents metabolize nicotine more rapidly than adults and are more vulnerable to its neurochemical effects and can develop dependence at lower levels of exposure compared to adults.

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- **Impact of vaping on adolescent reproductive health:**
    - **Sperm quality in adolescents**

      A range of studies have been conducted to find the effect of vaping on sperm quality in males, where critical factors such as sperm count, motility, and overall reproductive health were examined. Research indicates that exposure to nicotine leads to alteration of these parameters, Resulting in reduced sperm quality.

      Studies have also highlighted that adolescents who vape may experience the same negative impact on sperm parameters as those observed among traditional smokers

    - **Egg Health and Ovulation**

      A range of studies conducted on nicotine exposure have shown us the significant effects vaping has on female reproductive health, especially ovarian health and ovulation patterns. Studies have shown us that nicotine can disrupt ovarian function and alter hormonal balance which will ultimately lead to irregular ovulation.

6.2 Effect on female fertility

Vaping is not a safer option for young women who are already pregnant or want to conceive. Information regarding the risks of vaping and infertility should be provided. Researchers looked at how vaping affects female mice's fertility using a mouse model. During pregnancy, vaping may have second-generation consequences on the developing fetus. Following exposure, it was found that vaping before conception can postpone the implantation of a fertilized embryo in the uterus. Additionally, female offspring exposed to vaping were unable to gain the same amount of weight as control mice by the time they were 8.5 months old.

Risk of Vaping during Pregnancy

1. Delays embryo implantation.
2. Increases risk of miscarriages.
3. Leads to poor fetal development.
4. High risk of preterm births.
5. Lower birth weight (less than 2500 grams).

Comprehensive analyses have shown many of the substances present in vape can have a negative impact on reproductive health. These include:

- **Nicotine**
    - Raised risk of preterm births.
    - Induces spontaneous abortions in the first trimester of pregnancy.
    - Can impact the fetus's gestational and development rate ultimately impacting the birth weight negatively.
    - Lowers uterine flow and raises the mother's blood pressure and heart rate.
    - Increases catecholamine release, which can cause cardiomegaly in the fetus.

- **Nicotine exposure in Fetal development**
    - Fetal nicotine concentrations can be 15% greater than maternal levels after crossing the placenta.
    - Cotinine, the primary metabolite of nicotine, has a half-life of 15 to 20 days and a blood concentration that is ten times greater than that of nicotine.
    - It concentrates in amniotic fluid, breast milk, and fetal blood, which can cause a cascade of negative effects.

- **Cadmium**
    - Cadmium has been shown to negatively impact the maturation, fertilization, early cleavage, and blastocyst development rates of human, bovine, and murine oocytes at high concentrations.

- **Copper and nickel**
    - Copper has a dose-dependent effect on embryonic development.
    - Although the exact mechanism is yet unknown, women exposed to copper and nickel showed disruptions in ovarian steroidogenesis, including levels of oestradiol, FSHR, StAR, CYP11A1, CYP19A1, HSD3β1, and SF-1.
    - Increases inflammatory and apoptotic cell counts in ovaries.

- **Formaldehyde**
    - Elevated oxidative stress, which negatively affected rat ovarian histology by decreasing the number and size of mature follicles, according to research on the chemical's reprotoxicity in animal models.
    - Although there hasn't been much research on humans, formaldehyde is known to be reprotoxic.

- **VOCs and PAHs**
    - Affects embryo development and changes endocrine function.
    - Reduces the implantation rate and the chance of IVF success.
    - Additionally, passive smoking can affect one's chances of getting pregnant.

6.3 The impact on male fertility

Research conducted on laboratory rats has shown that e-liquids, either containing or not containing nicotine, induce oxidative stress and result in the significant enhancement in activity of antioxidant enzymes-superoxide dismutase, catalase, and glutathione S-transferase in rat testicular tissues.

At the British Fertility Society Conference in 2017, researcher Helen O'Neill emphasized the potential dangers electronic cigarettes pose to male fertility due to the added toxic chemicals in their flavorings. In her experiment, spermatozoa were exposed to cinnamon and bubble gum flavors at concentrations similar to average e-cigarette usage. The findings indicated that cinnamon-flavored vape

significantly impaired sperm motility, causing a substantial slowdown in movement. O'Neill and her team investigated the effects of cinnamon and bubble gum flavors on the seminiferous epithelium by exposing male mice to these substances.

The study concluded that the cinnamon flavor adversely affected the motility of sperm while the bubble gum flavor caused disruptions in the cells necessary for sperm production. Thus, the results of this study highlight the possible reproductive risks involved in components of e-cigarette flavorings.

In addition, the present study, along with findings from animal models, provides evidence that vaping could exert pathogenic effects on male reproductive health. This therefore urges caution on the part of vapers regarding reproductive health considerations.

Wawryk-Gawda and associates demonstrated, for the first time, apoptosis induction in spermatogonia and spermatocytes of male rats after exposure to e-cigarette vapor, as well as alterations of seminiferous epithelium morphology and malformations in the tunica albuginea.

Further studies have linked e-cigarette consumption with derangements in steroidogenesis and general testicular disorganization; in other instances, this would be coupled with "significant desquamation" of germ cells.

Besides, intraperitoneally injected e-cigarette liquid showed testicular toxicity and inflammation to male rats leading to:

- Sperm quantity and quality impairment.
- Loss of sperm density.
- Reduced number of sperm in epididymal counts.
- Lowering of the viability of sperm.

Furthermore, four weeks of inhalation of flavored e-cigarettes by male rats had significant augmentation in apoptosis in testes as well as increased incidence of teratozoospermia (looped tail, flagellar angulation, absence of flagellum). The studies further proved that e-cigarette exposure also affected sperm chromatin integrity, resulting in significant DNA damage at the testicular and sperm levels.

All these pose important issues about the possibilities by which e-cigarettes might affect the sperm cell as well as sperm viability and mortality.

Other research findings indicated that there may still be reproductive health risks associated with vaping even if no nicotine is present.

- Effect on male offspring:
    - Fetal development in male offspring exposed to e-cigarette vapors during in utero increased their likelihood of impaired fetal development.
    - Emerging studies have already shown that e-cigarettes are associated with oxidative stress affecting the endothelium-a potential pathway to erectile dysfunction (ED).

Thus, the main impact of Vaping on male fertility is:

- Impaired erectile function.
- Dose-dependent alteration of sperm parameters.

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6.4 Effects on Pregnancy

This misconception needs to be cleaved off the minds of common people and healthcare workers, which states that Vaping is an alternative to smoking cigarettes, especially for chronic users of cigarettes as a substitute smoking method during pregnancy. The greater effects of vaping during pregnancy are dangerous risks for maternal health, placental functions, and fetal development. Specific effects covered below are as follows:

1. **Placental Compromise**
    - **Nicotine :**
        - Nicotine, a primary component in many e-cigarette aerosols, crosses the placental barrier, leading to high concentrations in fetal serum and amniotic fluid.
        - This exposure has been linked to:
            - Reduced trophoblast function.
            - Impaired angiogenesis, essential for placental circulation.
    - **Nicotine-Free Aerosols:**
        - Even in the absence of nicotine, exposure to e-cigarette aerosols can damage placental cells.
        - Studies using human placental cells (HTR8/SVneo) demonstrated:
            - Significant reduction in placental cell function.
            - Impairment in vital processes such as angiogenesis.
    - **Alteration of Biomarkers:**
        - Exposure to e-cigarette components, including propylene glycol (PG) and vegetable glycerin (VG), reduces levels of critical placental biomarkers:
            - Decreased levels of IL-6, E2 (β-estradiol), and HO-1, critical for placental health.
2. **Fetal Developmental Risks**
    - Neurodevelopmental Impairment:
        - Animal studies show prenatal exposure to e-cigarette aerosols leads to:
            - Short-term memory deficits and learning disabilities in offspring.
            - Behavioral changes, including increased anxiety, hyperactivity, and risky exploratory behaviors.
        - Evidence of disrupted learning and memory performance was observed in mice exposed to propylene glycol and vegetable glycerin (base ingredients in most e-liquids) throughout gestation.

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- **Respiratory Development:**
  - E-cigarette aerosol exposure during pregnancy adversely affects fetal lung development:
    - Dysregulation of gene expression linked to lung diseases such as COPD and asthma.
    - Structural abnormalities in neonatal lungs, including enlarged distal airspaces and reduced alveolar growth, mimicking emphysematous changes.

- **Inflammation and Oxidative Stress:**
  - Exposure to vaping chemicals induces oxidative stress and inflammation, which can disrupt fetal organ development.
  - Compounds used for flavoring may break down into toxic substances, adding to the burden of inflammation.

- **Multi-System Effects:**
  - Prenatal exposure affects various systems:
    - Renal: Evidence of oxidative stress, inflammation, and fibrosis in offspring kidneys.
    - Immune: Altered immune responses due to vaping-related toxins.

3. Human Studies and Observations

- Adverse Birth Outcomes:
  - Pregnant women using e-cigarettes are at a higher risk of:
    - Delivering small-for-gestational-age (SGA) infants.
    - Preterm births and low birth weights.

- Comparison with Traditional Cigarettes:
  - E-cigarettes are not safer alternatives during pregnancy:
    - Studies show comparable risks of SGA, low birth weight, and preterm birth between e-cigarette users and traditional smokers.

4. Recommendations and Implications

- **Public Health Concerns:**
  - The widespread perception of e-cigarettes as safer alternatives is misleading, particularly for vulnerable groups like pregnant women.
  - Evidence strongly indicates that vaping during pregnancy contributes to long-term health risks for both the mother and the child.

- **Need for Further Research:**
  - Human studies remain limited, and larger cohorts are needed to understand the long-term consequences fully.
  - Further research should aim to:
    - Define the effects of specific vaping chemicals during pregnancy.
    - Investigate molecular mechanisms of developmental disruption.

6. CONCLUSION

The widespread perception of e-cigarettes as safer alternatives to cigarettes is misleading, particularly for vulnerable groups like pregnant women and adolescents. A standard composition of E-liquid generally consists of propylene glycol and glycerin (95%) and a combination of flavorings, nicotine, cadmium, copper, nickel, formaldehyde, VOCs, PAHs, and other additives (5%). Through this paper, after reviewing abundant literature we were led to the findings that vaping had many negative side effects on male and female reproductive systems. In women, it interrupts the ovarian function and disturbs hormonal balance which may cause irregular ovulation and potentially lead to long-term fertility issues. While men are more likely to suffer from erectile function impairment and reduction of sperm quality. In pregnant individuals, the risks are many and more severe including impairment in placental cell function and angiogenesis, fetal developmental risks, preterm births, and low birth weights. Adolescents metabolize nicotine more rapidly than adults and are more vulnerable to its neurochemical effects and can develop dependence at lower levels of exposure compared to adults. Ultimately, this research paper aims to educate and ensure a healthier future for individuals and their offspring. Thus, further research is needed to understand the long-term consequences fully and clear the myths around vaping.

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ISSN: 2509-0119.
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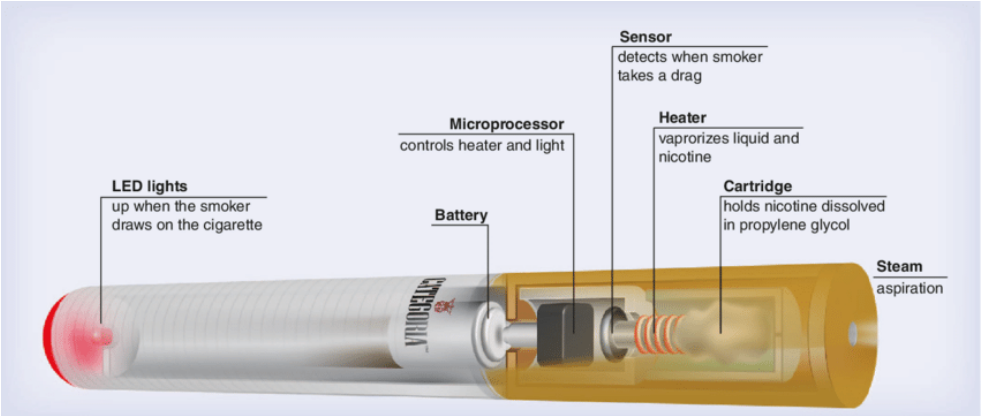
https://ijpsat.org/
Vol. 48 No. 1 December 2024, pp. 611-622

9. APPENDIX

9.1 Appendix A : Structured picture showing the internal components of a Vape (E-cigarette).

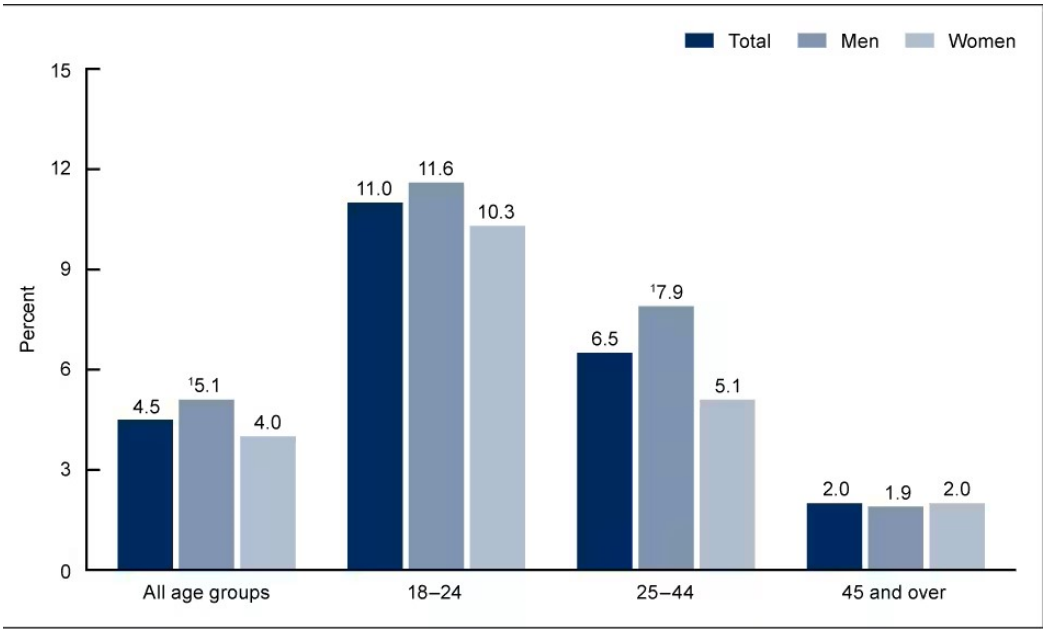
Diagram 1: Components of a Vape (E-cigarette)



Description: The above picture shows a detailed, labeled diagram of the components and functions of a Vape (E-cigarette).

9.2 Appendix B: Percentage of vape users across different age groups.

Diagram 1: Graph showing the age demographic of vape users in recent years.



Description: The above image shows a bar graph highlighting the percentage of vape users in different age groups.

10. DISCLOSURE

Acknowledgment

We thank the authors for their contribution to this project.

Ethical approval

Ethical approval was not required for this study

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.