ACUTE EFFECTS OF SMOKING CIGARETTES ON GRAVID UTERUS AND FETAL VIABILITY

By

Dalia Mahmoud Fahmy Ghanimah
Diploma of Gynecology and Obstetric
Ain Shams University 2002

A thesis

Submitted in Partial Fulfillment of the Requirements
for the Master Degree in Environmental Science
Department of Medical Science

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List of Abbreviations

11-β-HSD2	*11-β-hydroxysteroid dehydrogenase type 2*
AA	*Amino acid*
ACh	*Acetylcholine*
ADHD	*Attention deficit hyperactivity disorder*
ART	*Assisted reproductive technology*
BMI	*Body mass index*
BPD	*Biparietal diameter*
CCCT	*Clomiphene citrate challenge test*
CDC	*Center for disease control*
CI	*Confidence interval*
CTB	*Cytotrophoblast*
eNOS	*Endothelial nitric oxide synthase*
FasL	*Fas and Fas ligand*
FDA	*Food and drug administration*
FMO3	*Flavin-containing monooxygenase 3*
FSH	*Follicular stimulating hormone*
GSTM	*Glutathione S-transferase*
hCG	*Human chorionic gonadotropin*
HIFs	*Hypoxia-inducible transcription factors*
IGF	*Insulin-like growth factor*
IVF	*In vitro fertilization*
L-NNA	*NG-nitro-L-arginine*
MAOIs	*Monoamine oxidase inhibitors*
MT	*Metallothionein*
mtDNA	*Mitochondrial DNA*
nAChR	*Nicotinic acetylcholine receptors*
NAT	*Acetyl N-transferases*
NRT	*Nicotine replacement therapy*

PID	*Pelvic inflammatory disease*
PPROM	*Preterm premature rupture of membranes*
pVHL	*Hippel–Lindau tumor suppressor protein*
SGA	*Small-for-gestational age*
SIDS	*sudden infant death syndrome*
SIDS	*Sudden infant death syndrome*
TUNEL	*Transferase dUTP nick end labeling*
UGT	*Uridine diphosphateglucuronosyltransferase*
US	*United states*
USDHHS	*U.S. Department of Health and Human Services*
VEGFs	*Vascular endothelial growth factors*
Xiap	*X-linked inhibitor of apoptosis protein*

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ABSTRACT

This study was designed to evaluate the acute effects of smoking cigarettes on uterine contractility and on fetal heart rate. The present study was carried out at Aim Shams University, in the period from 1st, March, 2009 to the 1st, March 2010. It included 120 pregnant women in their third trimester. They divided into two groups according to their habit of smoking: The first group (the study group; Group A): included 60 pregnant females in their third trimester who were smoking any type (smoking cigarette, cigar, pipe, or shisha). The second group (the control group; Group B): included 60 pregnant females in their third trimester who were not exposed to smoking. The purpose of the study was explained to all participants and an informed consent to participate in the study was taken. All included cases were submitted to the following: Full history taking, full clinical examination, and all participants completed a questionnaire containing demographic data, course of current pregnancy, and smoking habit The CTG after smoking 1 cigarette provided that she did not smoke for the past 12 hours for group A to evaluate uterine contraction, fetal heart rate and fetal movement

Results: smoking women had increased heart rate, systolic and diastolic blood pressure when compared to non smokers. In addition, maternal heart rate, systolic and diastolic blood pressure was increased after smoking one cigarette in comparison to their values before it. Furthermore, uterine contractility was decreased in smokers in comparison to non smokers, and after smoking one cigarette in comparison to their values before it. Fetal heart rate was increased and fetal movements and acceleration were decreased in smokers' women in comparison to non smokers. Also, after smoking one cigarette in comparison to their values before smoking it.

Conclusion: the results of the present study proved that there were adverse effects of chronic or acute cigarette smoking on maternal and fetal hemodynamics

Questionnaire

Personal history

Name:
Age:
Marital state:
Parity: Para Gravida

Past history of congenital anomaly

Special habit: Smoking:
For how long?
How many cigarette/day:

Fasting smoking for 10-12

Symptoms after smoking 10 minutes: ***Yes*** ***No.***

Headache:
Blurring of vision:
Tremor:
Sneezing:
Coughing:
Excessive sweating:
Increasing eyes tears:
Palpitation:
Nausea:
Vomiting:
Epigastric pain
Chest pain:
Abdominal colic:
Diarrhea:
Sense of happiness:

Vital data:

Pulse:
BIP:
Temperature:

INTRODUCTION

Cigarette smoking is the leading preventable cause of disease and death in the United States (**MMWR, 2005**).

With widespread use and exposure, tobacco is clearly the human development toxicant and teratogen with the greatest overall adverse impact on development in our population. Exposures to tobacco, both voluntary and involuntary, occur at all ages and come from multiple sources, resulting in deposition and disposition of thousands of chemicals in the body, and causing detrimental effects on virtually every stage and facet of development and survival of the neonate (**Difranza et al., 2004**).

Smoking prevalence among women of childbearing age has varied since the beginning of the 20th century, when a small minority of women smoked, as it was considered a male domain and very "unladylike." However, with the emancipation of women, cigarette smoking in women became more acceptable and was quite prevalent in the U.S. and throughout Europe in the 1960s and 1970s. Recently, with the advent of powerful messages against smoking, smoking rates among women have decreased in the U.S. and many European countries **(Stockholm**, **2002)**. Despite this, several studies have found that while the overall prevalence of smoking in women has decreased in the last two decades, smoking in young pregnant women has significantly increased **(Mohsin and Bauman, 2005)**.

In some Eastern European countries, the prevalence of smoking among all women continues to increase, particularly in very young women **(Andreeva and Krasovsky, 2007)**. Therefore, a substantial number of women of childbearing age continue to smoke cigarettes. The most recent statistics on the prevalence of smoking in pregnancy report that approximately 12–15% of all women continue to smoke during their pregnancy **(Goodwin et al., 2007).**

Smoking has anti-estrogenic effects that can lead to anovulation, a shorter luteal phase, and earlier menopausal age, all of which decrease the chance of becoming pregnant. Pelvic inflammatory disease (PID) is an important risk factor for ectopic pregnancy, and smoking is associated with increased risk of PID. Furthermore, smoking is also associated with increased risk of ectopic pregnancy independent of PID **(Kelly-Weeder and Cox, 2006)**.

The risk of miscarriage is 20-80% higher in women who smoke during pregnancy, and the increased risk is possibly due to decreased levels of human chorionic gonadotropin (hCG) in smoking women **(Castles et al., 1999). Cnattingius (2004)** suggested possible mechanisms for smoking leading to placental abruption include degenerative and inflammatory alterations in the placenta, decreased plasma ascorbic acid levels, and premature rupture of membranes A possible mechanism that has been suggested is that hypoxia leads to placental enlargement, enabling the placenta to reach the

cervical opening **(Shea and Steiner, 2008).** Women who quit smoking during the first trimester are at no greater risk of having a baby with low birth weight than women who do not smoke at all during pregnancy **(Jauniaux and Burton, 2007)**.

Risk may also be influenced by factors such as maternal age and genetic polymorphisms. Possible mechanisms that have been suggested are fetal hypoxemia and reduced blood flow across the placenta, as well as an increase in cadmium levels **(Collet and Beillard, 2005).**

A stronger association has been found with very early preterm delivery (<32 weeks) than moderate preterm delivery. Possible mechanisms that have been suggested include preterm rupture of membranes, intrauterine infection, and an increased production of prostaglandins **(Shah and Bracken, 2000).** Cigarette smoking has consistently been associated with a small increased risk in oral clefts across studies **(Little et al., 2004)**. Increased risk may be due to infant exposure to second-hand smoke and not prenatal exposure, as many women who smoke during pregnancy continue to smoke after their baby is born, therefore exposing the child (**Mitchell and Milerad, 2006).**

Studies have been conflicting for the following other risks:

- Craniosynostosis (**Kallen, 1999)**.
- Clubfoot **(Skelly et al., 2002)**.
- Childhood respiratory disease **(Carlsen and Carlsen, 2008)**.

- Attention deficit disorder **(Langley et al., 2005)**; and
- Childhood cancers **(Bluhm et al., 2006).**

A total of 20–40% of smokers quit during pregnancy, with spontaneous quitters representing the majority of successful quitters **(Pbert et al., 2004)**. However, most women who quit smoking during pregnancy will resume within 6 months after delivery, with up to an 80% relapse rate after 1 year **(Lawrence et al., 2005).**

AIM OF THE WORK

1- To evaluate the acute effects of smoking cigarettes on uterine contractility.

2- To evaluate the acute effects of smoking cigarettes on fetal heart rate and movement.

SMOKING

History of smoking:

Tobacco was cherished by the Mayans and other Native Americans long before Christopher Columbus brought back *nicotiana* seeds and leaves from the New World to Europe. Tobacco was smoked, chewed, or "drunk" in many different forms for hundreds of years with only limited health effects. The turning point from the perspective of world lung history does not come until the 19th century, however, when a series of social and technologic changes allowed "the golden leaf" to become far more popular and far more injurious. We can identify 6 principal stages in the rise of the modern cigarette: First was the invention of *flue curing*, a fermentation process chanced upon in the 1830s in the Piedmont region of North Carolina, allowing the production of a bright yellow tobacco leaf that, when smoked, could be drawn deeply into the lungs without coughing. Flue curing (heating by means of very hot air circulating through a flue or vent) increased the sugar content of the leaf, making it less harsh when smoked. The elevated temperature transforms the nicotine into a salt, allowing it to be dissolved in an aerosol form and delivered to the lungs with less of an alkali "sting." It is hard to overestimate the impact of this innovation: flue-curing made it possible for the first time to inhale tobacco smoke comfortably, producing a more profound level of addiction. (In comparison, smoke from pipes and cigars was normally not inhaled, and the health impacts were consequently much less dire) **(Tilley, 1948).**