Introduction

There is a strong evidence to indicate that active smoking during pregnancy is one of the main causes of preterm labor, premature rupture of membranes, placental abruption, placenta previa and delayed intrauterine growth ***(Pichler et al., 2008).***

Passive smoking is defined as an involuntary exposure to environmental tobacco smoke ***(Krisela et al., 2006).***

Intra uterine growth retardation (IUGR) means, infant not reached his/her genetic growth potential due to an insult that has occurred in utero. An IUGR fetus may or may not be small for gestational age (SGA) but it always implies a pathological process ***(Bamberg et al., 2004).***

IUGR lead to fetal morbidity and mortality if not properly diagnosed and managed. The condition is most commonly caused by inadequate maternal-fetal circulation. Less common causes include intrauterine infections such as cytomegalovirus and rubella, and congenital anomalies such as trisomy 21 and trisomy 18 ***(Gardosi et al., 1998).***

A significant negative correlation has been observed between numbers of cigarettes smoked per day by pregnant women and newborns weight, body mass index, length and head circumference ***(Anastasia et al., 2008)***

Etiology of growth delay in fetuses exposed to tobacco smoke is due to intermittent periods of intrauterine hypoxia, hence causing a significant decrease in fetal body weight and length. Maternal smoking increases cord blood erythropoietin concentrations, a finding that indicates chronic fetal hypoxia ***(Djin-Karlsson et al., 1998).***

Aim of the Work

The aim of the present study is to evaluate the role of maternal smoking whether (active or passive) on newborn's growth parameters including birth (weight, Length, skull circumferences, chest circumference and mid arm circumference). These parameters are tested for their interaction effect on fetal growth

Smoking

Introduction

Smoking is a major world wide public health problem. The period from early teens to early twenties is a critical period in which the majority of individuals begin to develop the social pattern that will cause them to start smoking or to become smoker later on their lives ***(Azab et al., 1995).***

Tobacco use is one of the leading preventable causes of premature death, disease, and disability around the world. Nearly five million deaths every year can be attributed to tobacco use, and many more suffer from smoking-related morbidity, while the number of fatalities is expected to more than double by the year 2020, if the current epidemic continues, More than 70 % of these deaths are expected to occur in developing countries ***(Ljaljvi et al,2008).***

The risks of active smoking were assumed to be higher than that of passive one, ***Rebagtiliato and Florey (1995)*** reported that 41% of pregnant women were being exposed to environmental tobacco smoke (ETS) by their husbands and 42% reported working in a smoking environment.

In addition, passively inhaled smoke adversely affects the functioning of the oviduct and increases the risk of ectopic pregnancy in women. There is strong evidence to indicate that active smoking during pregnancy is associated with increased risk of preterm labor, intrauterine growth retardation, premature rupture of membranes, placental abruption, and placenta previa. All of which, carry a high risk of perinatal loss ***(Mumtaz et al.,2003).***

Cigarette consumption in Egypt:

Tobacco consumption has scored many records and it is still progressing. Egypt is the highest consumer of tobacco in the Middle East and North Africa (MENA) region ***(Islam and Johnson, 2005).*** Egypt has the highest rate of tobacco consumption in the Arab world. Cigarettes consumption increased 12,027 million sticks in 1997 the number of smokers in Egypt have increased over the 30 years ***(World Bank, 2001).***

The median age of smoking initiation in many countries is below the age of 15, and smoking prevalence rates are rising among children and adolescents. If we do not deal with this problem effectively, tobacco use will result in the deaths of 250 million children and adolescents alive today, mostly in developing countries ***(Dous, 2003).***

In Egypt, the number of smokers is steadily increasing by 8% every year, with a declining age of initiation ***(Islam and Johnson, 2005).***

Epidemiology of smoking in Egypt:

In The national survey done in 1998 revealed the prevalence of smoking among out of school children to be double the prevalence of in-school children; which is 15.4% and 7.6% respectively ***(Dous, 2003).***

Studies have shown that initiating smoking at a younger age increases the possibility of continuing smoking during adulthood and makes it even harder to quit, in other words creating addicts. This leads to profound health hazards when it continues to adulthood ***(Gadalla et al., 2003).***

Smoking prevalence among adult men in Egypt is 43.4 %, and it is 4.7% among women ***(Islam and Johnson, 2005).*** Others estimated it to be 47% among males over 15 years old ***(Mohamed et al., 2006).***

Women from low socioeconomic classes had more intense and longer exposure than women from high socioeconomic classes mainly because of work exposure ***(Curtin et al., 1998)***

World *Consumption*

Approximately 5.5 trillion cigarettes are produced globally each year and are smoked by over 1.1 off or declined in developed nations, they continue to rise in developing parts of the world. Smoking rates in the United States have dropped by half from 1965 to 2006 falling from 42% to 20.8% of adults. In the developing world, tobacco consumption is rising by 3.4% per year ***(Hammond et al., 2006).***

Table (1): Smoking prevalence by gender:

	Percent smoking	
Region	**Men**	**Women**
Africa	29	4
United States	35	22
Eastern Mediterranean	35	4
Europe	46	26
Southeast Asia	44	4
Western Pacific	60	8

(World Health Organization, 2000)

Types of smoking:

Active smoker:

An active smoker is any one who reports during the first clinic visit that he or she smoked any number of cigarettes ***(Ahluwalia et al., 1997).***

Anastasia and his colleagues (2008) defined active smoker as those who smoked one or more cigarettes per day.

Passive smoker:

Passive smoking is defined as an involuntary exposure to environmental tobacco smoke ***(Krisela et al., 2006).***

Passive smokers are defined as those who had been exposed to tobacco smoke for minimum daily duration 2 hours starting from the period at least before conception (so as to include the impact of harmful impact of smoke exposure in early pregnancy ***(Mumtaz et al., 2003).***

Passive smoking has been shown to adversely affect the health of infants and children. Black children and adults appear to be more susceptible to a variety of tobacco smoke health hazards for unknown reason ***(Jennifer et al., 1996).***

Passive smoking results in inhalation of nicotine by children in amounts equivalent to their actively smoking 60 to 150 cigarettes yearly ***(Jennifer et al.,1996).***

Table (2): Exposure to passive smoking in public places.

Methods of tobacco smoking

SNUFF:

Snuff consists of ground dried tobacco leaves of the tobacco species Nicotina tobacum and frequently contains additives ***(Krisela et al., 2006).***

Prolonged use cause atrophy of the nasal mucous membrane with replacement of ciliated columnar by squamous epithelium ***(Laurence and Bennett, 1992).***

Cigars and pipes:

They have alkaline PH (8.5) and nicotine is relatively unionized and lipid soluble so that is readily absorbed in the mouth .Cigar and pipes smoker thus

obtain nicotine without inhaling (they also have a slower death rate from lung cancer) ***(Laurence and Bennett, 1992).***

Cigarettes:

A **cigarette** (French "small cigar", from *cigar* + *-ette*) is a product consumed through smoking and manufactured out of cured and finely cut tobacco leaves and reconstituted tobacco, often combined with other additives, then rolled or stuffed into a paper-wrapped cylinder (generally less than 120 mm in length and 10 mm in diameter). The cigarette is ignited at one end and allowed to smolder for the purpose of inhalation of its smoke from the other (usually filtered) end, which is inserted in the mouth. They are sometimes smoked with a cigarette holder. The term cigarette, as commonly used, refers to a tobacco cigarette but can apply to similar devices containing other herbs, such as cannabis ***(Wigand, 2006).***

They are acidic (ph 5.3) and nicotine is ionized and insoluble in lipids most cigarettes contain 6 to 8 mg of nicotine ***(Herfindal and Gourley, 2000).***

Fig. (1): Diagram of a cigarette. **(1)** Filter made of 95% cellulose acetate. **(2)** Tipping paper to cover the filter. **(3)** Rolling paper to cover the tobacco. **(4)** Tobacco blend ***(Pbroks, 2008).***

Chewing tobacco:

Nicotine in chewing tobacco is more slowly absorbed than inhaled nicotine, so it has a longer duration of effect ***(Goodman and Gilman, 1996).***

Narghil (hubble-bubble) smoking:

The waterpipe (also known as gouza, narghile, hubble-bubble, hookah or shisha, depending on the local tradition) has been used for smoking tobacco for centuries in the Eastern Mediterranean Region.

There are three distinct types of water pipe . The gouza is the oldest form of water pipe. It has a small water container (about 200–500 ml**)** that is made of metal; coconut shell was formerly used. The bouri has a water container made of brass (about 200–500 ml). The authentic shisha is a larger **(**about 1000–2000

ml) and more decorated form of water pipe, usually with a glass water contain It's reported that 11% of Egyptian men and women smoke shisha ***(Lancaster, 1996)*** **(**Fig. 2).

Fig. (2): Different types of waterpipe.

Earlier studies have reported an association between shisha smoking and oral cancer ***(Gupta et al., 1996)*** and decreased fertility ***(Inhorn and Buss, 1994),*** these effects may be due to higher carboxyhemoglobin **(COHb)** compared to cigarette smoking ***(Zahran and Al Fayez, 1985).***

Chemical composition of tobacco:

Cigarette smoke is composed of volatile and particulate phases. Some 500 gaseous compounds including nitrogen, carbon monoxide (CO), carbon dioxide(C02), ammonia(NH3), hydrogen cyanide and benzene, have been identified in the volatile phase which accounts for about 95% of the weight of cigarette smoke; the other 5% is accounted for by particulates. There are about 3,500 different compounds in the particulate phase, of which the major one is the alkaloid nicotine. Other alkaloids include nornicotine, anatabine, and anabasine**.** The particulate matter without its alkaloid and water content is called tar. Many carcinogens, including polynuclear aromatic hydrocarbons, N-nitrosamines and aromatic amines, have been identified in cigarette tar ***(Hoffman et al., 1997).***

Main stream and side stream smoke:

Main stream smoke:

Mainstream smoke was defined as the smoke that is inhaled by the smoker *(**Michael** et al.,2005)* emerges into the environment after having been drawn through the cigarettes filtered by the smokers on lungs and then exhaled ***(Brunneman et al., 1978).***

Side stream smoke:

Arises from the burning end of the cigarette and enters directly into the environment ***(Brunneman et al.,1978)***, while patients with side stream smoke exposure were defined as those women self-identifying that they live with a partner who regularly smokes ***(Michael et al.,2005).***

Fig. (3): Schematic of smoke extraction methods. **(A)** In mainstream extraction, all smoke passes through cigarette filter. **(B)** In sidestream extraction, no smoke passes through filter. Other details are given in methods ***(Michael et al.,2005).***

Both active and passive smokers may be similarly side stream smoke. Obviously, main stream smoke is inhaled directly into the lungs and is diluted by the volume of air breathed in by the smokers when he/she inhales. Side stream smoke is generally diluted in a considerably large volume of air. Thus, passive smokers are exposed to a quantitatively smaller and potentially qualitatively different smoke exposure than active smokers ***(Weiss et al., 1983).***

Nicotine is distilled from burning tobacco. Selected constituents of cigarette smoke:

1. Nicotine:

Chemistry of nicotine in tobacco smoke:

Nicotine is a tertiary amine consisting of a pyridine and a pyrrolidine ring. There are two stereoisomer of nicotine: (S)-nicotine is the active isomer which binds to nicotinic cholinergic receptors and is found in tobacco. During smoking, some racemisation takes place, and small quantities of (R)-nicotine, a weak agonist of cholinergic receptors, are found in cigarette smoke ***(Hoffman et al., 1997).***

Absorption of nicotine from tobacco products:

Nicotine is a weak base, and thus its absorption across cell membranes depends on the pH. The pH of smoke from most American cigarettes (blonde tobacco) is acidic (pH 5.5). At this pH, nicotine is mostly ionized and does not freely cross cell membranes. Consequently, nicotine from the blonde tobacco cigarette smoke is not absorbed through the buccal mucosa. However, the pH of smoke from tobacco in pipes and cigars is alkaline (pH 8.5), at which pH nicotine is mostly unionized and well absorbed from the mouth ***(Gourlay and Benowitz et al., 1997).***

When nicotine from cigarette smoke reaches the small airways and the alveoli of the lung, it is buffered to physiological pH and rapidly absorbed into the pulmonary alveolar capillary and venous circulation, and hence directly into systemic arterial blood. From here, nicotine is distributed quickly throughout the body. It takes about 10-19 seconds for nicotine to reach the brain. The arterial blood perfusing the brain contains levels of nicotine following cigarette smoking which exceed venous levels by a factor of two- to six folds**,** mostly unionized and well absorbed from the mouth ***(Gourlay et al., 1997).***

Fig. (4): Schematic diagram showing rise in venous blood nicotine levels after smoking a cigarette and after using different nicotine replacement therapy products, following overnight abstinence from cigarette ***(Micheal et al.,2005).***

Cotinine:

Cotinine is the principal metabolite of nicotine and has a half-life of about 17 hours ***(Benowitz, 1996).***

An indirect measure of recent exposure to cigarette smoke is the concentration of cotinine in the blood, urine, or saliva ***(Glasgow et al.,1993).***

Table (3): Concentration of saliva cotinine in nonsmokers and indicators of exposure to environmental tobacco smoke, Geneva, Switzerland, 1995.

* P.value based on the Mann-Whitney U test.

Carbon monoxide (CO):

It is a colorless odorless gas resulting from incomplete combustion of organic matters. CO is the most abundant pollutant found in the lower atmosphere ***(National Research Council, 1986).***

CO produces its adverse effects by reducing the amount of available oxyhemoglobin and myoglobulin, and by displacing the oxygen-Hb dissociation curve to the left ***(Gritz, 1988).***

Acrolin:

Acrolin is major contributor to the irritative quality of cigarette smoke, it irritates mucous membrane of the nose upper respiratory tract and eyes producing running nose, sorethroat, headache and cough ***(Wood-Bury and Zenz,1983).***

Toluene:

Is an aromatic substance present in the gas phase of cigarette smoke, it is chemically related to Benzene, it is CNS depressants and low concentration produce fatigue, weakness and confusion ***(Jernia and Daley, 1974).***

Hazards of Smoking

Effect of Smoking on pregnancy:

The negative impact of cigarette smoking on fetal health is well established. Cigarette smoking has been associated with numerous adverse outcomes, including spontaneous pregnancy loss, placental abruption, PROM, placenta previa, preterm labor and delivery, low birth weight (LBW), and ectopic pregnancy. While the pathophysiology is not completely understood, several possible mechanisms related to impaired gas exchange, direct toxicity, and sympathetic activation have been proposed ***(Rodriquez et al., 2009).***

Subfertility:

As much as 13 percent of subfertility and delay in time to conception has been attributed to smoking ***(Fertil et al.,2008)***. Chemicals in cigarette smoke appear to accelerate follicular depletion and may impede gametogenesis ***(Zenzes et al., 2000)***.

Low birth weight:

LBW (<2500 grams) is the best-studied complication of smoking and/or being exposed to second hand smoke during pregnancy. Women who smoke are 1.5 to 3.5 times more likely to have a LBW infant. The risk increases with increasing cigarette consumption. Birth weight is influenced greatly by gestational age at delivery, and smoking modestly increases the risk of preterm delivery ***(Martin, 2006).***

Spontaneous pregnancy loss:

Multiple studies have evaluated the association between cigarette smoking and spontaneous pregnancy losses, with conflicting results being found. While some reports have suggested that smokers may not have an increased risk, there is significant evidence that heavy smoking (>10 cigarettes per day) may be associated with increased pregnancy loss (relative risk 1.2 to 3.4) ***(Dominguez et al.,1994).*** In addition, cigarette smoking has been associated with early pregnancy loss after assisted reproductive technology treatment ***(Winter et al.,2002).***

Stillbirth:

Although it had been thought that cigarette smoking did not increase the risk of stillbirth, defined as fetal death after 28 weeks of gestation, large case control and cohort studies have shown a relative risk ranging from 1.2 to 1.4 in smokers. A dose response curve has been reported, with heavy smokers having the greatest risk ***(Burguet et al., 2004).***

Placental abruption/placenta previa:

Cigarette smoking increases the risk of placental abruption because PROM is associated with both cigarette smoking and placental abruption, the relationship between cigarette smoking and abruption may be partially explained by the increased risk of PROM. However, cigarette smoking appears to be a risk factor for placental abruption, independent of PROM ***(Cnattingius, 1997).***

Congenital malformations:

In theory, it's plausible that smoking may increase the risk of congenital abnormalities due to fetal exposure to over 2500 chemicals found in cigarette smoke. As an example, the vasoactive effects of nicotine may result in vascular

disruption and the subsequent development of malformations ***(U.S. Department of Health and Human Services, 2001)***

Postnatal morbidities:

The risk of neonatal death (death within 28 days of birth) appears to be increased in smokers ***(Schramm,1997).*** Other postnatal morbidities that have been associated with maternal smoking include sudden infant death syndrome (SIDS), respiratory infections (e.g, bronchitis, pneumonia), asthma, atopy, otitis media, infantile colic, bronchiolitis, short stature, lower reading and spelling scores, shorter attention spans, hyperactivity, childhood obesity, and decreased school performance ***(Skorge et al., 2005).***

However, studies that have adjusted for measured and unmeasured confounders have often found these adverse outcomes are not present or are related to familial factors associated with maternal smoking ***(Mennella et al., 2007).***

Maternal cigarette smoking is also associated with lower rates of breast-feeding and early weaning from breast milk Breast-fed infants of smoking mothers slept less when fed after their mothers smoked recently than when she had abstained, they have urinary cotinine levels up to 10-fold higher than bottle-fed infants of smoking mothers, and up to 50 times higher than infants of nonsmoking mothers ***(Mascola et al., 1998).***

Effects in childhood:

Sudden infant death syndrome:

SIDS refers to the unexpected death of a seemingly healthy infant while asleep. Maternal smoking during pregnancy has been causally associated with SIDS. An estimated 25 to 40 percent of SIDS cases are related to smoking during pregnancy ***(Pollack, 2001).***

Pregnancy complications associated with an increased risk of SIDS include placenta previa, abruptio placenta, premature rupture of membranes, and elevated maternal alpha-fetoprotein. The increased risk associated with these complications appears to be independent of their relationship with preterm birth ***(Getahun et al., 2004).***

Respiratory symptoms and illness:

Numerous surveys demonstrate a greater frequency of the most common respiratory symptoms, cough, phlegm, and wheeze, in the children of smokers ***(Cook and Strachan, 1997).***

The highest risks for these symptoms occurred in children with two parents who smoked **(Table 4).**

Table (4): Pooled random effects (odds ratios) (0R) for respiratory symptoms in children associated with parental smoking.

	Either parent smokes			One parent smokes			Both parents smoke		
	OR	**95 percent**	**N**	**OR**	**95 percent**	**N**	**OR**	**95 percent**	**N**
Asthma	1.23	(1.14 to 1.33)	(31)	1.01	(0.84 to 1.22)	(7)	1.42	(1.30 to 1.56)	(10)
Wheeze .	1.26	(1.20 to 1.33)	(45)	1.18	(1.10 to 1.26)	(13)	1.41	(1.23 to 1.63)	(14)
Cough	1.35	(1.27 to 1.43)	(39)	1.27	(1.14 to 1.41)	(18)	1.64	(1.48 to 1.81)	(18)
Phlegm .	1.35	(1.30 to 1.41)	(10)	1.24	(1.10 to 1.39)	(7)	1.42	(1.19 to 1.70)	(6)
Breathlessness .	1.31	(1.14 to 1.50)	(6)						

Note: Number of studies in parentheses.

. Excluding EC study, in which the pooled odds ratio was 1.20.

. Data for phlegm and breathlessness restricted as several comparisons are based on fewer than five studies. ***(The Surgeon General's Report, 2006).***

Lower respiratory tract illnesses:

Infants with parents who smoke have an increased risk of lower respiratory tract illness, including a significantly increased frequency of bronchitis and pneumonia during the first year of life ***(Carroll et al., 2007).*** Presumably, this association represents an increase in frequency or severity of illnesses that are infectious in etiology, perhaps related to increased nasopharyngeal and oropharyngeal colonization with respiratory pathogens ***(Greenberg et al.,2006)*** and not a direct response of the lung to the toxic components of second hand smoke (SHS). Effects of exposure in utero on the airways also may play a role in the effect of postnatal exposure on risk for lower respiratory illnesses ***(U.S. Department of Health and Human Services, 2006).*** Although measures of health outcome have varied somewhat among the various studies, the relative risks associated with involuntary smoking were similar, and dose-response relationships with the extent of parental smoking were demonstrable.

Lung growth and development:

During childhood, measures of lung function increase are more or less parallel to increase in height. Parental smoking adversely affects growth of lung function during childhood ***(Kauffmann,1989).***

Middle ear disease:

The US Surgeon General's Office, the National Research Council and the US Environmental Protection Agency all have reviewed the literature on SHS and otitis media and concluded that an association exists between SHS exposure and otitis media in children, Exposure to SHS has been associated most consistently with recurrent otitis media and not with incident or single episodes ***(Lieu and Feinstein, 2002).***

Dental caries:

Exposure to SHS may be associated with an increased risk of dental caries in children ***(Aligne et al.,2003).***

Childhood cancers:

Secondhand smoke (SHS), including maternal smoking during pregnancy, has been evaluated as a risk factor for the major childhood cancers, most recently in the 2006 Surgeon General's Report . The evidence is limited and is currently inadequate to infer the presence or absence of a causal relationship between prenatal and postnatal exposure to SHS and childhood cancers. For the specific cases of childhood leukemias, lymphomas, and brain tumors, the evidence was suggestive but not strong enough to infer a causal association ***(Pang et al.,2003).***

Effects in adulthood:

Chronic obstructive pulmonary disease (COPD):

Smoking is a major risk factor for respiratory disorders, especially COPD, often diagnosed in advanced stages, when lung function impairment has already reached less than 50% of its normal value. Presently, all diagnostic and therapeutic guidelines mention relationship between tobacco consumption and COPD and strongly recommend smoking cessation as mandatory and benefic in COPD, Most of these exacerbations are caused by Pneumococus, Haemophylus influenza or Moraxela catharalis and express chronic inflammation.

Consequently, mucocilliary clearance is imbalanced as oxidative stress due to tobacco smoke exposure and irreversible bronchial structure changes progress. Severity and evolution of COPD in smokers are related to early smoking intake, gender, number of packs-year, type of tobacco product used, precocity of giving up smoking ***(Trofor and Frasila, 2007).***

Lung cancer:

The primary risk factor for the development of lung cancer is cigarette smoking, which is estimated to account for approximately 90 percent of all lung cancers ***(Alberg and Samet, 2003).***

The risk of developing lung cancer for a current smoker of one pack per day for 40 years is approximately 20 times that of someone who has never smoked. Factors that increase the risk of developing lung cancer in smokers include the extent of smoking and exposure to other carcinogenic factors, such as asbestos ***(Alberg and Samet, 2003).***

Esophageal cancer (EC):

Smoking probably increases the risk of EC, particularly in patients with Barrett's esophagus ***(Pandeya et al., 2008).***

Head and neck cancer (HNC):

It has been estimated that the use of tobacco and alcohol accounts for up to 80 percent of cases of HNC, both act throughout the upper aero digestive tract, contributing to the field cancerization effect, and both can induce genetic alterations, such as mutations in the p53 tumor suppressor gene, Other risk factors include viral infection (particularly Epstein-Barr virus (EBV) and human papillomavirus (HPV), occupational exposure, radiation, dietary factors, and genetic susceptibility ***(Sankaranarayanan et al., 1998).***

Cardiovascular disease:

Causal associations between active smoking and fatal and nonfatal coronary heart disease (CHD) outcomes have long been demonstrated. The risk of CHD in active smokers increases with amount and duration of cigarette smoking and decreases quickly with cessation, Active cigarette smoking is considered to**:**

1. Increase the risk of cardiovascular disease by promoting atherosclerosis