Association between Maternal Smoking during Pregnancy and Low Birth Weight among Syrian Refugees in RHUH from 2015 to 2016

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Abstract

**Introduction:** Maternal smoking during pregnancy has long been proposed to be one of the most critical and preventable factor that can affect the intrauterine environment. Tobacco consumption when associated with pregnancy can lead to numerous adverse maternal and fetal outcomes. One of a particular significance is the low birth weight (LBW). **Objectives:** Our main objective was to study the association between maternal smoking during pregnancy in LBW versus normal birth weight babies of Syrian refugees at Rafic Hariri University Hospital (RHUH) from 2015 to 2016. **Methods:** This was a retrospective case-control study. Four hundred newborns were recruited from RHUH. One hundred LBW and three hundred normal birth weight (BW) Syrian newborns were recruited from RHUH during a twelve months period time between 2015 and 2016 and were considered as case and control, respectively. **Results:** The prevalence of smoking among the mothers of cases and controls was 22.3%. In our study population, smoking during pregnancy was associated with LBW (p < 0.05). Increased maternal weight, absence of economic support and inadequate iron intake during pregnancy were also found to be associated with LBW. **Conclusion:** Tobacco consumption during pregnancy was significantly associated (p < 0.05) with LBW in our study. This result suggests that specific interventions and screening for smoking during pregnancy can be powerful tools to educate pregnant women on the benefits of tobacco cessation.

**Keywords:** Low Birth Weight (LBW), Maternal Smoking, Smoking Cessation, Pregnancy.

INTRODUCTION

Smoking of tobacco products, including water-pipe and cigarette, during pregnancy has been associated with numerous adverse pregnancy outcomes, namely, LBW, stillbirth, fetal death, etc. LBW is defined as newborn’s weight at birth less than 2500g regardless of gestational age while the normal birth weight (BW) at term should be between 2500-4200g. LBW continues to be a significant public health problem globally. Moreover, it is associated with both short and long term consequences. Thus, it is estimated that 14.6% of all babies born globally in 2015 suffered from low birth weight [1]. Water-pipe also called narguile or Hubble Bubble is a way of smoking tobacco. The special ingredient used is a mix of tobacco, fruits’ flavors and sugar molasses through a bowl and hose tube. However, the cigarette is made from pure tobacco. The unit used to measure the amount a person has smoked over a period of time is pack-year where one packs equal 20 cigarettes. It is calculated by multiplying the numbers of packs of cigarettes smoked per day by the number of years the person has smoked. Due to an increase of public health education, smoking rates during pregnancy are declining. However, good numbers of women continue smoking while pregnant. In a recent study published in 2018, the global prevalence of smoking during pregnancy was estimated to be 1.7% [2]. The highest prevalence of smoking during pregnancy was in the European region (8.1%) while the lowest prevalence was in the African region (0.8%); in the Eastern Mediterranean region the prevalence was 0.9% [2]. According to new data from the Centers for Disease Control (CDC), about 8.4% of pregnant women smoke despite the risks for the developing fetus. The habit is most prevalent during the first 2 trimesters with 20.6% of women who smoked during pregnancy quitting by the third trimester [3]. The CDC and several public health organizations warn that smoking during
pregnancy raises the risk of premature deliveries, placental abruption (placenta previa), prolonged rupture of membrane (PPROM), stillbirth and neonatal death, miscarriage, congenital malformations and certain birth defects such as cleft lip, LBW, and other long term effects: sudden infant death syndrome (SIDS) [3]. The aim of this thesis is to study the impact of maternal smoking on the BW among a special population: Syrian refugees in Beirut who have fled from their country since the onset of the Syrian Civil War in 2011 and gave sought asylum in other countries. To note that over one million Syrian refugees are currently registered with United Nations High Commission for Refugees (UNCHR) in Lebanon. Nevertheless, the government has estimated that the number is closer to 1.5 million. Recent media reports that there are 300,000 Syrian refugee women currently pregnant in Lebanon. Despite the prenatal care provided by the UNHCR and the awareness campaigns about smoking during pregnancy, a large group remains non-compliant. Moreover, many other risk factors for LBW will be discussed in our thesis such as mother age, nutritional status, socioeconomic status, education, alcohol, coffee, mother co-morbidities and insufficient prenatal care.

**LITERATURE REVIEW**

**Pathophysiological Effects of Smoking on Pregnancy**

Adverse pregnancy outcomes associated with maternal smoking were explained through several mechanisms. These include toxin exposure, altered fetal development and physiologic response as well as impaired fetal oxygenation. Nicotine exposure leads to a reduction in fetal breathing movement and an acceleration of fetal heart rate. However, the aforementioned parameters are important indicators of fetal well-being in the antenatal fetal assessment tests. Beyond nicotine, more than 2500 potential toxins are found in cigarettes such as nitrogen oxide, hydrogen cyanide, polycyclic aromatic hydrocarbons and vinyl chloride. In addition, more than 100,000 compounds are emitted in tobacco smoke. De La Chica et al., concluded that toxin exposure can cause direct damage to fetal genetic material, more specifically an increased incidence of structural chromosomal abnormalities in fetuses of women who smoked regularly [4]. Most of these chromosomal abnormalities were translocations or deletions, mainly in the 11q23 region, which is linked to several hematologic malignancies. Moreover, maternal smoking during pregnancy impacts fetal development. Nicotine reduces uterine blood flow and increases vascular resistance in animal models. Furthermore, nicotine directly impairs lung development by its interaction with nicotinic acetylcholine receptors (nAChR). This was observed in a primate model where nAChR were abundantly expressed in fetal lung tissue [5]. In addition, nicotine exposure on sheep was found to blunt the cardio-respiratory response to postnatal hypoxemia. Similarly, a limited ability to maximize and vary heart rate (HR) during the first 4 hours of life was noted in term infants with high levels of cotinine at delivery. Furthermore, impaired fetal oxygen delivery was explained by several mechanisms. Structural changes in the placentas of smokers including an increased thickness of the villous membranes and a reduction in the fraction of capillary volume which lead to abnormal gas exchange within the placenta. These changes were noted when compared with non-smokers. During smoking the release of carbon oxide (CO) leads to carboxyhemoglobin formation, which is known to have several adverse effects on systemic and also on fetal oxygen delivery. Carboxyhemoglobin causes a left-shift of the oxyhemoglobin dissociation curve due to its slow clearance from the fetal circulation and its competitive inhibition with oxyhemoglobin. In addition, smoking may increase placental production of nitric oxide as well as mitochondrial reactive oxygen species. Nitric oxide can damage placental function when it reacts with superoxide radicals.

![Fig-1: Smoking during Pregnancy](image)

**Maternal Adverse Outcomes**

- **Subfertility:** Smoking has been linked to a delay in time of conception as well as subfertility (13% of the cases). Follicular depletion and gametogenesis were strongly affected by many of the toxins found in cigarette [6]. Several studies done on sub fertile women undergoing in vitro fertilization (IVF) have shown that the majority of oocytes retrieved from smoker women were immature with increased levels of oxidative stress markers and increased thickness of the zona pellucida.

- **Smoking-related conditions:** Asthma, lung cancer and hypertension (HTN) negatively affect the pregnancy with significant fetal and maternal mortality rate.

- **Miscarriage:** Although many studies have shown a modest effect of smoking on miscarriage, there are several limitations to these data due to variation in study designs and a lack of ascertainment of smoking status during pregnancy.

- **PPROM:** Even when other risk factors for PPROM were controlled, the risk persisted in heavy smokers (>10 cigarettes/day) making
smoking a consistent risk factor for PPROM. However, smoking less than ten cigarettes per day was not found to increase the risk at any gestational age (GA) [7].

- **Placental abruption and Placenta Previa:** Smoking has been consistently associated with placental abruption and placenta Previa (reported relative risks up to 3.5 and 4.4 respectively) [8].
- **Preterm Birth (PTB):** PTB (<37 weeks of gestation) has many well-known etiologies. Smoking was found to increase the RR of PTB [9].
- **Preeclampsia:** Despite of all the negative effects of smoking on pregnancy, one benefit was noted by a meta-analysis showing a significant decrease (p < 0.05) of preeclampsia risk among smoker women. This was explained by an increase in serum placenta growth factor (PIGF) and it is well known to be decreased in preeclampsia [10].
- **Breastfeeding:** A shorter duration of lactation was observed among a smoker woman due to decrease milk volume production and lower milk fat concentrations [11].

**Fetal and Neonatal Adverse Outcomes**

- **Low Birth Weight:** Smoking increases the risk of LBW (< 2500 g) and SGA infants [12]. Several studies showed that cessation of smoking in the first trimester resulted in a decrease in the rate of LBW infants. However, the greatest impact of smoking on birth weight appeared in the third trimester. Thus, mothers who quit smoking by the third trimester had infants with higher birth weight [13].
- **Intrauterine Fetal Death (IUFD) and neonatal death:** The risk of stillbirth and neonatal death among active smoker mothers were increased by nearly 50% and 20%, respectively. It was the end result of a meta-analysis of 142 studies [14].
- **Congenital Malformations:** A study has reported a correlation between smoking during pregnancy and increased risk of developing specific anomalies such as gastroschisis. Cleft lip with or without cleft palate, anal atresia, cardiac defects, bilateral renal agenesis or hypoplasia, transverse limb reduction defects and digital anomalies (polydactyly, syndactyly or adactyly). Many other studies showed that the amount and timing of exposure were important factors in the development of specific congenital malformations. A case-control study showed an increased risk of CHD for infants exposed to cigarette smoking during the first trimester of pregnancy [15].
- **Changes in the neonate’s neurobehavioral:** Multiple studies have demonstrated that neonates exposed to in-utero maternal smoking had increased signs of stress, excitability, hyper tonicity and the greatest degree of irritability. This degree was assessed by the graham-Rosenblatt behavioral examination of the neonate [16].

**Postnatal and long-term effects**

Several postnatal morbidities have been linked to maternal smoking including asthma, SIDS, respiratory infections, otitis media, Atopy, short stature, decreased attention, decreased school performance, lower reading and spelling scores, hyperactivity, and childhood obesity [17].

- **Diabetes Mellitus (DM):** Based on data from the British national child development study, the risk of DM type 2 was increased (x4) among young adults who were exposed prenatally to heavy maternal smoking (>10 cigarettes/day) [18].
- **Pulmonary function:** Genome wide DNA methylation changes have been noted in the offspring of smoker mothers and these changes were associated with regions contributing to pulmonary function [19].
- **Behavioral problems:** A meta-analysis of 15 cohort and 5 case control studies concluded that the risk of attention deficit hyperactivity disorder (ADHD) among off springs of smoker mothers was increased by 60% [20]. However, there are many potential risk factors for ADHD; this meta-analysis has succeeded to confirm association but not causality.
- **Cognitive ability:** Cognitive development is affected by several variables (maternal socio-economic status, maternal education level, maternal cognitive ability, exposure to drugs, alcohol, etc.). Nevertheless, the impact of smoking by itself on the child cognitive ability needs adequate studies where these confounding variables must be well controlled. In an unadjusted analysis, intelligence quotient scores (IQ) of children whose mothers smoked were 2.9 points lower than children whose mothers did not smoke during pregnancy. However, no difference in IQ score was noted between the two groups of children when maternal IQ and education levels were controlled [21].
- **Neurologic disorders:** Based on data from Danish National Birth Cohort, an increase of 66% in the risk of Tourette syndrome (TS) was observed in children born, to heavy smoker mothers [22].
- **Other effects:** Sleep problems, childhood hearing loss, decreased sperm volume and count in adult male offspring, increased risk of polycystic ovarian syndrome (PCOS) in female offspring [23], decreased neonatal serum parathyroid hormone (PTH) and 25-hydroxy vitamin D and increased serum phosphorus.
Low Birth Weight
Definition and Epidemiology
LBW is defined as weight at birth < 2500 g (5.5 lb.) regardless of GA; subcategories include very LBW < 1500g and ELBW < 1000g while normal weight at term delivery should be 2500-4200g [24]. LBW is the result of preterm labor or IUGR. Based on WHO researches, out of 120 million child births annually worldwide, 20 millions are LBW; 70% of newborns mortality was found to be caused by LBW especially in developing countries. In comparison with infants of normal birth weight, mortality rates were found to be 24 times higher in infants with LBW and 100 times higher in infants with VLBW (< 1500g). ELBW infants are more prone to have complications of preterm birth in neonatal period. However, the use of surfactants leads to a significant decrease (p < 0.05) in mortality rates but severe squeal persist such as cerebral palsy, chronic lung disease, sensor neural hearing loss, blindness and cognitive delays. On the other hand, LBW is not only the leading cause of mortality but also causes increased risk of infections, nutritional and hematological diseases.

Risk factors for LBW
Many maternal and fetal factors are known as risk factors of LBW [25]: previous history of a child of LBW, nutritional status and the weight gained by the mother during pregnancy, alcohol and tobacco use, chronic underlying diseases in the mother: hypertensive disorders, thyroid diseases, diabetes mellitus, anemia during pregnancy, etc., absence of antenatal care, socioeconomic situation: monthly income, economic support, mother’s activity during pregnancy, demographic factors : Maternal age at delivery <20 years , maternal body mass index < 18kg/m2, lack of formal education, residing in rural area, inter-pregnancy interval < 2 years.

OBJECTIVES
The main objective is to evaluate the presence of an association between maternal smoking during pregnancy and LBW among LBW and normal birth weight babies born to Syrian Refugees in RHUH-Beirut during 2015-2016. The secondary objectives are to determine the presence of other risk factors such as mother’s weight and age, gestational age, economic status, absence of prenatal care, iron intake, coffee intake, stressful life events and baby genetics.

MATERIAL AND METHODS
MATERIAL
The inclusion criteria were all newborn babies born to smoker and non-smoker Syrian refugee mothers aged between 18 and 34 years delivered at term in RHUH between 2015 and 2016. All newborns were delivered at term and from singleton pregnancy. The total number of neonates included was 400, divided into 100 LBW and 300 normal weight neonates. The data were identified and collected, then an Excel spread sheet (Microsoft) was created for data management and descriptive analysis while SPSS software was used for further statistical analysis (logistic regression statistical analysis). The exclusion criteria for cases and controls were all preterm babies, babies born to mothers of extreme ages (<18 years or > 34 y), babies delivered from multiple gestation pregnancy, those born with a birth defect and stillborn infants.

METHODS
Data Collection
The Methodological Approach was a retrospective review of data base of the Syrian newborns collected from RHUH (in great Beirut)archives between the year 2015 and 2016, to assess the impact of maternal smoking on their birth weight. This is a case-control study of patients including all LBW Syrian newborns versus those with a normal BW. 400 patients were recruited retrospectively. In our study, we have used a modified version of a standardized checklist to collect information about dependent and all independent variables that can influence on birth weight. This checklist included: socio-demographic data (maternal weight, maternal age, education, occupation, and marital status, place of residence, OB-GYN data, lifestyle data (alcohol, tobacco…), smoking habits and neonatal data.

Data Analysis
Exposure Variables
In our study, maternal age was divided into 3 groups: < 18, between 18-34 and > 35. We selected maternal age of 18-34 as a reference group, maternal education was categorized as none or primary,
secondary, and high school, vocational school and university by marital status all mothers were divided into 4 groups: unmarried, married, widowed and divorced. Concerning maternal occupation status, it was divided into 2 categories unemployed and employed/self-employed or student. Place of mother’s residence was categorized into urban and rural; with urban residence serving as reference group mother’s weight was recorded in Kg. Other information were obtained including the obstetrical history (number of gestation, parity, abortions, gestational age at delivery), adequate prenatal care recorded as yes or no with the number of visits, the previous mode of deliveries (Cesarean section and/or NVD), presence of stressful life events, psychiatric diseases, economic support (all recorded as yes or no). In addition, answers to many questions about maternal smoking habits were recorded retrospectively. These questions include current and previous smoking status, smoking pattern which was assessed by the number of cigarettes consumed, also attempting to quit smoking was addressed by other questions. Evidence of alcohol abuse or coffee consumption during pregnancy was recorded by yes or no. Past medical and surgical history, as well the complications during pregnancy (including anemia, DM, HTN.) were documented. Regarding neonatal data, birth weight was classified into 4 categories: < 1000; < 1500; < 2500 and > 2500. Gender of baby, mode of delivery, Apgar score at 1 and 10 min were all registered.

Statistical Analysis
Each of these parameters from the checklist: socio demographic characteristics, OB-GYN history, lifestyle and neonatal data were defined as potential risk factors in order to identify their association with birth weight. A p-value < 0.05 was considered statistically significant. The SPSS statistical software was used for statistical analysis.

RESULTS
A total of 400 pregnant Syrian refugees were recruited in our study, their smoking status was presented in Graph-1. Almost one quarter of them were smokers (22.3%). Socio-demographic data on maternal education level, occupation, marital status and their place of residence were shown in Graph 2, 3, 4 and 5 respectively.
Concerning the education level, approximately half of the mothers (47.8%) were non-educated and less than 1% went to high school (Graph-2). Almost all of the mothers were unemployed (92.5%) (Graph-3), married (99.8%) (Graph 4) and living in the urban area (99.5%) (Graph-5).

OB-GYN data including the gestational age at time of delivery, the adequate prenatal care with the number of visits, the mother's obstetric history (previous NVD and/or C-section), the presence of stressful life events and economic support were all presented in Graph-6 till 11.

Regarding the time of delivery, more than one third of the recruited mothers delivered in their 38th week of gestation (37%) (Graph-6).

As shown in Graph-7, only one third as 37.8% of the mothers reported having a prenatal care, with a maximum number of visits reaching 2 to 3 times throughout the pregnancy (25.8%). Their previous mode of delivery is presented in Graph 8, and 9 respectively.

Since our selected population was Syrian refugees, almost all of them reported stressful life events (94.8%) (Graph-10). Most of them (88.2%) reported receiving an adequate economic support (Graph-11).
Also, data on smoking habits during pregnancy were registered and shown in figure-15 till 20. More than three quarter (77.5%) of mothers was non-smokers and 22% of these smoker mothers were smoking on a daily basis (Graph-12).

Concerning the tobacco products smoked per day, the vast majority of smoker mothers (93.3%) reported smoking cigarettes (Graph-12).

From all the smoker mothers, 77% of them reported having attempted to quit smoking (Graph-13), nearly 90 % had received cessation advice from their doctors (Graph-14) and more than the half had noticed anti-cigarette information on TV as well as on cigarette packs (Graph-15).

Most of our study population as 72.3% of the smoker mothers was thinking about quitting smoking (Graph-16).
Graph-16: Thinking about Quitting Smoking

Thinking about quitting because of health warnings on cigarette packs

Graph-17: Alcohol and Coffee Intake during Pregnancy

Graph-18: Past Medical History

Graph-19: Medications during Pregnancy

Graph-20: Past Surgical History

Graph-21: Baby Gender

Fig-22: Current Mode of Delivery

Other life style data such as alcohol and coffee intake, the mothers past medical history with their medications and their past surgical history were shown in Graph 17, 18, 19 and 20 respectively.

All of our recruited women were non-alcoholic while 76.5% of them reported drinking coffee during pregnancy (Graph-17). Almost all of them as 94% were previously healthy (Graph-18) and 62.3% were taking iron and multivitamins during their pregnancy (Graph-19). More than two thirds as 69% of the selected population didn’t report any past surgical history (Graph-20).

Some neonatal data including the baby gender and the current mode of delivery were reported and shown in Graph 21 and 22.

**DISCUSSION**

Our selected population was Syrian women refugees hospitalized in RHUH-Beirut during 2015-2016. In our study, almost one quarter as 22.3% of Syrian women surveyed in RHUH reported smoking cigarettes during pregnancy and 36% of them gave birth to LBW babies, while worldwide, the global prevalence of smoking during pregnancy was estimated to be 1.7% [2]. This huge difference may be due to the fact that our population is refugees with very low socio-economic status knowing to hold high prevalence of smoking [26]. Moreover, our study confirmed the strength of the association between smoking during pregnancy and baby’s birth weight with an Odds Ratio approaching 3 (OR=2.447). This crucial finding was similar to previous studies findings done in Switzerland as well as Americas [24, 27, 28]. In addition, our multiple
regression analysis showed three other potential risk factors that had significant impact on birth weight: maternal weight, iron intake and economic support. High maternal weight at time of delivery did result in lower birth weight infants (OR =1.044) in our study while this finding was not the case in other studies [29]; this difference may be due to the fact that increase weight in our pregnant refugees mothers must be a resultant of low quality diet (high carbohydrates and high fats) in these refugees which might have influenced the baby’s birth weight. On the other hand, iron intake during pregnancy (OR=0.012) and the presence of economic support (0.313) were found to be very significant protective factors on birth weight in our study. Indeed, these results were similar to other studies results [30, 31]. Although the stressful life events during pregnancy and its known influence on LBW have been reported previously [32], we could not prove this relation in our study due to the presence of stressful life events among all our studied population.

Strengths and Limitations
Some limitations of this study needed to be mentioned, first the absence of accuracy on second hand smoking during pregnancy in our questionnaire may limit the validity of this study findings because passive exposure to tobacco smoke (non- investigated) was not well documented which could result in some under estimation of the smoking effect on birth weight. Second, our studied population was nearly homogenous concerning maternal education level and living conditions (e.g. stressful life events) which limits the availability of the comparison between low and high educational level as well as the presence or absence of stressful life events and their influence on birth weight. Nevertheless, one of the hardest limitation a study can face is retrieving data from only one hospital or center but since the majority of Syrian refugees pregnant women living in Beirut delivered in RHUH which is considered a referral center for Syrian refugees and high risk pregnant women, so this is turned into a strength point in our study. Also many other strengths support the validity of our results: the adequate sample size coupled with the absence of selection bias as well as the similar magnitude of our result compared to other international studies findings.

Perspectives
Syrian refugees are more likely to continue smoking during pregnancy in an attempt to relieve their stress and to deal with the strains due to limited financial resources. Accordingly, pregnant women should be encouraged to quit smoking, through concerted counseling about the risks of smoking to fetus and mother during prenatal medical visits. The findings in our study show that actions to promote smoking cessation during pregnancy are definitely necessary, but for women who are unable to quit smoking, other studies must needed to discuss the use of nicotine replacement therapy and its safety during pregnancy and the number of cigarettes allowed to be smoked per day to minimize the negative effects of smoking on newborn weight.

Conclusion
The present study reveals a strong and significant relationship between LBW and maternal smoking during pregnancy. Accordingly tobacco use during pregnancy remains a significant public health challenge. The findings of our study emphasize the importance of smoking cessation during one of the most important phases of a woman’s reproductive lifetime. Pregnancy can be considered a golden opportunity to intercept smoking for the welfare of the mother and the fetus altogether. In order to prevent postpartum relapses, interventions should continue beyond the perinatal period. Furthermore, a significant relationship between LBW and several other maternal factors such as low socioeconomic status and inadequate iron intake was found in our study. Most of these factors are preventable with educational programs, regular prenatal care and economic support. The added knowledge from this study would help in establishing prevention of smoking during pregnancy. Moreover, it would raise awareness by screening and intervention for tobacco use to achieve smoking cessation in pregnant refugee women, thus, improving fetal health. Finally, this study should emphasize medical doctors to ask regularly all pregnant women about tobacco use in order to advise them to quit smoking. Additionally, smoking cessation helps to limit the healthcare cost by reducing hospitalization, morbidity, mortality and medications for both mother and baby.

References


