



INTERNATIONAL JOURNAL OF PAEDIATRICS AND GERIATRICS

P-ISSN: 2664-3685

E-ISSN: 2664-3693

www.paediatricjournal.com

IJPG 2019; 2(2): 18-23

Received: 10-05-2019

Accepted: 12-06-2019

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Maternal and infants outcomes in asthmatic pregnant women in Mosul

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DOI: <https://doi.org/10.33545/26643685.2019.v2.i2a.29>

Abstract

Background: Asthma affects between 3% and 12% of pregnant women worldwide and the prevalence among pregnant women is rising, it's often unrecognized and suboptimal treated. The course of asthma during pregnancy varies; it improves, remains stable, or worsens in similar proportion of women. The risk of an asthma exacerbation is high immediately postpartum, but the severity of asthma usually returns to the preconception level after delivery and often follows a similar course during subsequent pregnancies. Good control of asthma is essential for maternal and fetal wellbeing.

Patients and Methods: A prospective cohort study was adopted to achieve the study aim. The study conducted from January 2003 through September 2003. Asthmatic and non-asthmatic pregnant women were randomly selected from the outpatient clinics, in patient clinics and emergency department of Al-Razi Teaching Hospital in Mosul city, the data obtained including age, height and weight, parity and gravid, history with a clinical examination of respiratory system and history of maternal and fetal complications. These points were recorded in an especially designed collection form for all women examined after they were consent a form 102 asthmatics pregnant and 115 non-asthmatics pregnant were enrolled in the study; 92 and 93 of them respectively were followed to delivery by researcher and the assessment of maternal and fetal outcomes was done. Percentages, relative risk ratio, p-value and 95% confidence interval were calculated with SPSS version 18.

Results: The age interval (25-34) represents 58.7% of the asthmatic pregnant. The first, second and third trimesters correspond to 6.2%, 32.6% and 60.8% of asthmatic pregnant respectively. Regarding the symptoms, the study shows that Dyspnoae is the most common symptoms among them follows by wheeze, cough and chest tightness and lastly expectoration with percentage of 65.2%. Moreover finds out that 59 (64.2%) had worsening of symptoms during the three trimesters of pregnancy, 28 (30.4%) had No change in the severity of asthma and remainder 5 (5.4%) of them show improvement. The adverse maternal outcomes; hyperemesis gravid arum (RR of 1.43), recurrent hospital admission (RR= 2.26) and the severity of asthma in pregnant women with boys (RR= 2.29) occurs with high significant association. Also the infant outcomes; that the wheezy chest, fetal death and congenital anomalies occur in high significant statistical association among the asthmatic pregnant group with RR (1.66, 1.72, and 1.66 respectively).

Conclusion: Symptoms of asthmatic patients during the pregnancy are more severe than without pregnancy. The symptoms are more sever in third trimester, which are caused by mechanical factors and the severity of asthma is more in mothers bearing boys. More over some adverse maternal and infant outcomes were significant statistically associated with asthma.

Keywords: Asthmatic pregnant, maternal outcomes, infant outcomes, cohort study

1. Introduction

Asthma (which is also known as reversible obstructive airway disease) is characterized by hyper-responsiveness of the trachea-bronchial tree to respiratory irritant and bronchoconstriction chemicals producing attack of wheezing, dyspnoea, chest tightness and cough. These are reversible spontaneously or with treatment ^[1]. Asthma affects between 3% and 12% of pregnant women worldwide and the prevalence among pregnant women is rising ^[2], it's often unrecognized and suboptimally treated. The course of asthma during pregnancy varies; it improves, remains stable, or worsens in similar proportion of women. The risk of an asthma exacerbation is high immediately postpartum, but the severity of asthma usually returns to the preconception level after delivery and often follows a similar course during subsequent pregnancies. Good control of asthma is essential for maternal and fetal wellbeing ^[3]. Literature addressing the effect of pregnancy on asthma is conflicting, with no consistent trend to improvement or worsening of disease severity. Discrepant results between studies related to methodology and whether the outcome measure is objective or relies on patient

recall or reporting of symptoms. Patient selection, effect of medication and the control population also influence the results of such studies [4]. Overall, the data indicated that the clinical severity of asthma during pregnancy improved in about 30% of women, remains stable in about 50% and worsens in about 20%. The course of asthma in pregnancy in an individual woman is largely unpredictable. Women with mild disease are unlikely to experience problems, whereas those with severe asthma are at greater risk of deterioration, particularly late in pregnancy [5]. Physiological changes that may improve asthma during pregnancy include progesterone mediated bronchodilation and increased serum free cortisol level. While those changes may explain deterioration includes increased stress and gastro-esophageal reflux [6]. Other factors like exposure to fetal antigens and alteration in cell-mediated immunity may worsen asthma symptom. Many asthmatic patients experience worsening of their symptoms during pregnancy because they stop or reduce medication due to fear (either their own or those of medical advisers) about its safety [7]. The physiological respiratory changes that occur during pregnancy may affect asthma control. Changes in blood gases secondary to acute asthma will be superimposed on the physiological respiratory alkalosis of pregnancy. Therefore, a normal or elevated PCO₂ associated with acute asthma will indicate respiratory compromise of greater severity in pregnancy than in the non-pregnant state. The dyspnoea of pregnancy must be differentiated from dyspnoea caused by asthma. Indeed, the patients who develop asthma during pregnancy may wrongly attribute dyspnoea to the pregnancy, which can lead to under medication and severe maternal and fetal hypoxaemia [4]. It is difficult to predict which women will experience worsening of their asthma during pregnancy, but the severity of the condition before pregnancy and an absence of the expected decrease in IgE concentration during pregnancy, should alert the clinician to this possibility. If asthma is going to worsen, IgE will usually do so between 24 and 36 weeks gestation. Symptoms are likely to be less troubling some in peri-partum period. In most women, asthma severity returns to the pre-pregnant state within three months of delivery, but in rare cases it may be worse than before the pregnancy [8]. In most women, asthma has no effect upon the outcome of pregnancy. However, severe asthmatic attacks or poorly controlled asthma may have an adverse effect on fetal outcomes as a result of chronic or intermittent maternal hypoxaemia and diminution of the uterine artery blood flow secondary to the hypocapnic vasoconstriction [4]. The pregnant women with asthma are at substantially increased risk for several adverse infant and maternal outcomes [9]. For this reason, pregnant women with asthma are particularly at high risk group to both mother and infants to which extra attention, including increased efforts at education, monitoring, and optimal asthma management may be appropriate [10]. Uncontrolled asthma during pregnancy posed many more hazards to mother that occurred either during pregnancy or after delivery [11]. These complications include hypertensive disorder of pregnancy, which is included preeclampsia [4, 9, 10]. Transient hypertension of pregnancy and pregnancy-induced hypertension especially in the asthmatic women taking steroids those at high risk [4, 12]. The risk of cesarean section is increased among poor controlled asthma [4, 12, 13]. This rate was significantly more in the steroid-dependent group

(38.7%) in primigravida woman delivered by cesarean section [14]. Regarding the uterus related complications of pregnancy in asthmatic women included antepartum haemorrhage [10, 15], preterm contraction, insufficient placenta, restricted growth of uterus [15] and postpartum haemorrhage [12] which increased in poor controlled asthma independent of medication usage [10]. Other complications included gestational diabetes [10, 12] in steroid-dependent asthmatic patients, those were at significant increased risk for development insulin requiring diabetes [16], hyperemesis gravidarum [13], placenta previa [11], premature rupture membrane occurred more significantly often in both steroid and non-steroid dependent asthma group [16], chorioamnionitis [9, 10], preterm labour [9, 10, 12] occurred more significantly in both asthmatic groups [16] and increased the hospital stay [11]. Complications during labour, perinatal [13, 15, 17], and maternal mortality is increased [13, 15]. Perlow *et al.* (1992) reported significantly the impact of asthma and severity, as determined by medication requirement on prenatal outcome [16]. The magnitude of any effect on adverse prenatal outcome is small and related to the degree of the control of the asthma. There have been reports of increased incidence of low birth weight (< 2500gm) [3, 4, 6, 18] in both steroid and non-steroid-medication-dependent asthmatic women [12, 14], premature babies, prenatal death [6, 10, 15], small for gestational age [11], IUGR [3, 19], congenital anomalies [3, 4, 11, 12, 15], neonatal hypoxia [6], hyperbilirubinemia in infants of mother taking steroids and respiratory distress syndrome [12]. There have been reports of increased incidence of transient tachypnea of the newborn, neonatal hypoglycemia, neonatal seizures [4] and admission to the neonatal intensive care unit in babies born to both steroid-dependent and non-steroid medication dependent asthmatic mothers. No significant differences in minute APGAR scores found [3, 16]. The maternal asthma and pregnancy outcomes and their results clearly demonstrated in a study done using hospital discharge database in the Canadian province of Quebec in 2001, which showed that pregnant women with asthma are at substantially increased risk for several adverse infant and maternal outcomes and suggest the need for extra attention to mothers with asthma and their infants' [9]. Alexander-S; Dodds-L; Armson-BA, studied the adverse prenatal outcomes in 1998 among women with asthma during pregnancy which associated with asthma or asthma medications use during pregnancy. He found that the risk of antepartum and postpartum hemorrhage is increased in asthmatic women, independent of medication usage the increased incidence of neonatal hyperbilirubinemia and the borderline increased risk of pregnancy-induced hypertension may be complications of steroid use or may be related to poorly controlled asthma [12]. Asthma in woman has characteristic features related to hormone secretion. Classically, the prevalence of asthma is higher in boys than girls [20]. Milburn *et al.* in 1998 had noted that the course of asthma during pregnancy was variable but it might be worse when the fetus was female. Their prospective blind study of 34 pregnant asthmatic woman suggests that pregnant woman with girls are more likely than those pregnant with boys to have increased symptoms of asthma during pregnancy. Any psychological basis for this difference is unlikely as none knew the sex of her baby before delivery. This observation would have important clinical implications that asthmatic mother carrying girls need to be particularly

observed for deterioration during pregnancy. Several studies have suggested that exacerbation of asthma are more prevalent in second half of pregnancy this observation have important mechanistic implications that fetal hormones, especially androgens may influence gestational asthma course [21]. Acute exacerbation of asthma increased fourfold in women from day 26 to day 4 of the menstrual cycle and the injection of progesterone can reduce premenstrual asthma [22]. In the peri- and post- menopausal period, asthma may be worsening in women with prior disease. The rate of disease onset during this period is also higher than in other age groups [20].

1.1 Aim of the study

To assess the risk association between the adverse maternal and infant outcome and the asthma during pregnancy

1.2 Patients and Methods

A prospective cohort study was adopted to achieve the study aim. The study conducted from January 2003 through September 2003, asthmatic pregnant women were randomly selected from the outpatient clinics, in patient clinics and emergency department of Al-Razi Teaching Hospital in

Mosul city, the pregnant women were followed by the researcher. The inclusion criterion was any asthmatic pregnant women attendant to the hospital. Any pregnant women attended with no asthma also enrolled in the study with random sampling. The data obtained including age, height and weight, parity and gravid, history with a clinical examination of respiratory system and history of maternal and fetal complications. These points were recorded in an especially designed collection form for all women examined after they were consent a form 102 asthmatics pregnant and 115 non-asthmatics pregnant were enrolled in the study; 92 and 93 of them respectively were followed to delivery by researcher and the assessment of maternal and fetal outcomes was done. Percentages, relative risk ratio, p-value and 95% confidence interval were calculated with SPSS version 18.

2. Results

2.1 Demographical factors

Figure 1 shows the frequency distribution of asthmatic pregnant according to their age and reveals that, the age interval (25-34) is the most frequent one with 58.7%.

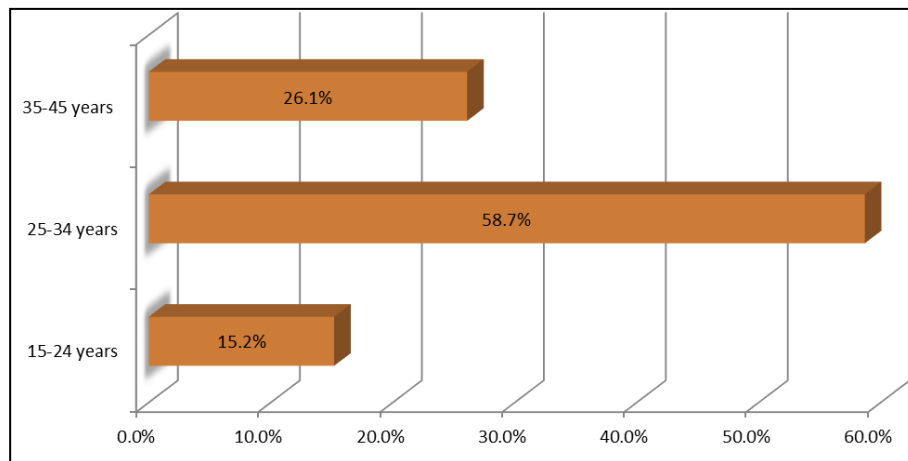


Fig 1: Frequency distribution of asthmatic pregnant according to their age.

Figure 2 shows the frequency distribution of asthmatic pregnant according to their age and illustrates that the first,

second and third trimesters represents 6.2%, 32.6% and 60.8% respectively.

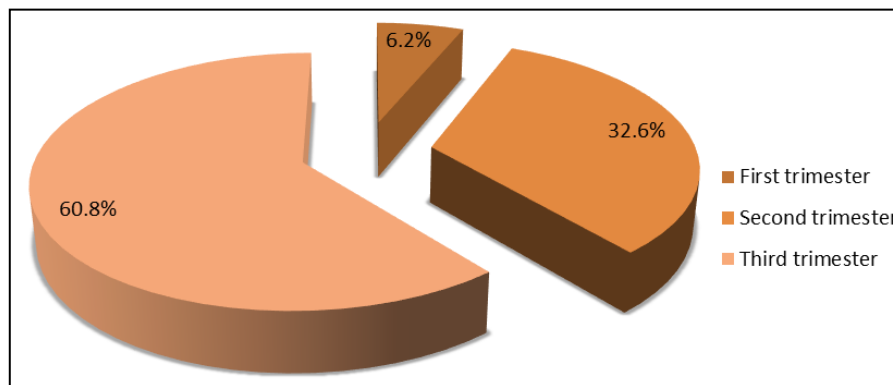


Fig 2: Frequency distribution of asthmatic pregnant according to their trimesters.

Figure 3 demonstrates the frequency distribution of asthmatic pregnant according to symptoms that they had and points up that Dyspnoae is the most common symptoms

among them follows by wheeze, cough and chest tightness and lastly expectoration with percentage of 65.2%.

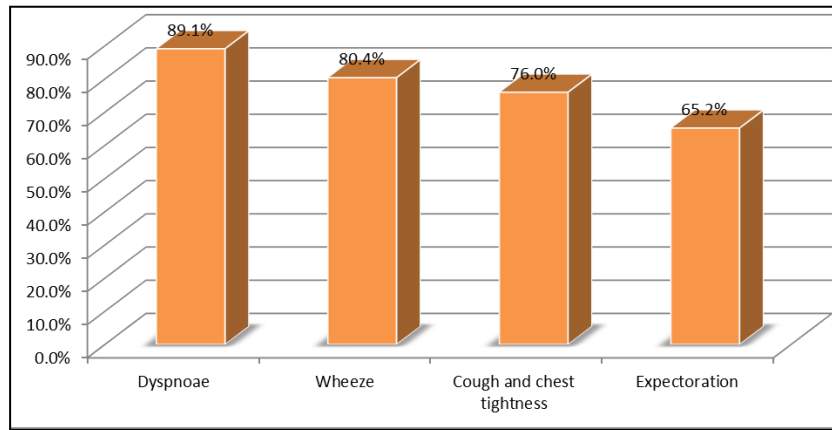


Fig 3: Frequency distribution of asthmatic pregnant according to their symptoms.

Figure 4 demonstrates the frequency distribution of asthmatic pregnant according the course of asthma during pregnancy and finds out that 59 (64.2%) had worsening of symptoms during the three trimesters of pregnancy, 28 (30.4%) had No change in the severity of asthma and

remainder 5 (5.4%) of them show improvement. Moreover during pregnancy, the worsening of symptoms of asthma is different; the worse trimester is third one, second is less and first is the least.

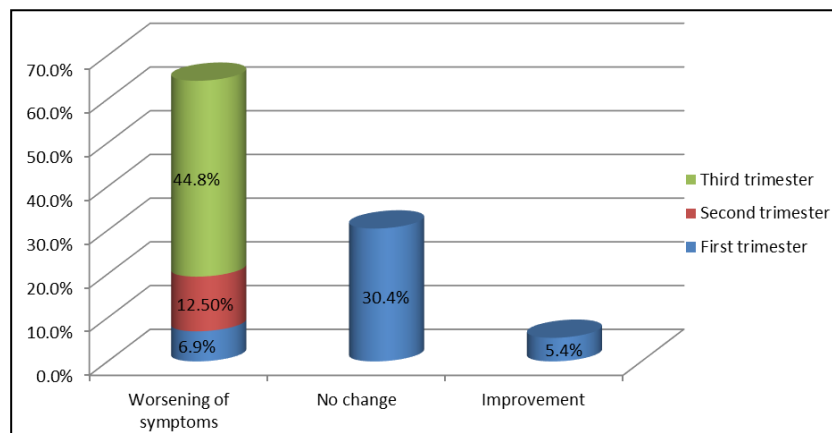


Fig 4: Frequency distribution of asthmatic pregnant according to course of asthma during pregnancy.

2.2 Maternal Outcomes

Table (1) shows the adverse maternal outcomes among the asthmatic pregnant group and the non-asthmatic pregnant, and reveals that hyperemesis gravid arum occurs with RR of 1.43 with high significant association (p= 0.015). Also

recurrent hospital admission and the severity of asthma in pregnant women with boys, both present with high statistical association p=0.000, (RR=2. 26, RR=2. 29 respectively). Regarding the normal vaginal delivery, although the RR is 0.93, there is no significant association.

Table 1: The association between the study population and the maternal outcomes.

maternal outcomes	Asthmatic pregnant No. (%)	Non-asthmatic Pregnant No. (%)	Relative risk	P value	95% CI
hyperemesis gravid arum	50 (54.3%)	34 (36.6%)	1.43	0.016	1.07- 1.91
recurrent hospital admission	64 (69.6%)	29 (31.2%)	2.26	0.000	1.61- 3.17
normal vaginal delivery	54 (58.7%)	58 (63.1%)	0.93	0.607	0.69 - 1.24
severity of asthma in pregnant women with boys	72 (78.3%)	41 (44.1%)	2.29	0.000	1.54- 3.41

2.3 Infant Outcomes

Table (2) demonstrates the infant outcomes among the study population and portrays that the wheezy chest, fetal death and congenital anomalies occur in high significant statistical

association among the asthmatic pregnant group with RR (1.66, 1.72, and 1.66 respectively), while the low birth weight shows no significant statistical association.

Table 2: The association between the study population and the infant outcomes.

Infants Outcomes	Asthmatic pregnant No. (%)	Non-asthmatic Pregnant No. (%)	Relative risk	P value	95% CI
wheezy chest	32 (34.8%)	13 (14.0%)	1.66	0.000	1.27- 2.17
low birth weight	21 (22.8%)	16 (17.2%)	1.18	0.314	0.85 - 1.64
fetal death	9 (9.8%)	2 (2.2%)	1.72	0.000	1.25 - 2.36
Congenital anomalies	5 (5.4%)	1 (1.1%)	1.71	0.001	1.16 - 2.53

4. Discussion

Asthma is the most common of potentially serious illness complicating pregnancy. About one of every hundred pregnant women suffers from asthma during pregnancy [23]. The course of asthma during pregnancy is largely unpredictable; it worsens, remains stable or improves. Changes in β -adrenoreceptors responsiveness and change in airway inflammation induced by high level of circulating progesterone have been proposed as possible explanations for the effects of asthma on pregnancy [3]. Other explanations for the variation of asthma severity during pregnancy include many factors like increase circulating free cortisol, a decrease in a bronchodilator tone and increase in serum concentration of cAMP. These changes would normally improve the asthma, but in pregnancy other competing factors including exposure to fetal antigens and alteration in cell-mediated immunity may worsen asthma symptoms [4]. The severity of asthma symptoms during pregnancy was (64.2%) in Mosul where the study was done which might be due to many factors like reduced or stopped medications taking during pregnancy especially in first trimester due to fear about their safety, stress and presence of electrical generators since War of 1991 which increase in numbers in all governorates of our country and environmental pollution specially after War of 20th of March 2003 like last air pollution by SO₂ at June 2003 that occurred in Mosul city and surround villages which exaggerated symptoms of asthmatic patients. Worsening of symptoms during pregnancy occurred mainly in third trimester (44.8%) more than second trimester (12.5%) and first trimester (9.6%); such results are obtained from this study. This severity of symptoms have important mechanistic implication due to increase abdominal girdle due to uterine enlargement, which caused diaphragmatic elevation which leads to reduction in both residual volume and functional residual capacity while total lung capacity is maintained by an increase in aspiratory capacity in later pregnancy [4, 6]. The asthmatic women pregnant with boy infants (78.3%) are more likely than with girl infants (21.7%) to have increased symptoms of asthma during the pregnancy. Any psychological basis for this difference is unlikely as none knew the sex of her baby before delivery. Minute hormonal differences may be implicated [21]. The maternal adverse outcomes especially hyperemesis gravidarum (54.3%) and preterm rupture of membrane among asthmatic pregnant patients and as in Table (1) were statistically significant ($p < 0.016$) in comparison with pregnant non-asthmatic patients, such results are due to poor controlled asthma especially in steroids depended-asthma which produced high rate of preterm rupture of membrane due to that steroids therapy in pregnancy increased risk of infection and Preterm rupture of membrane [2]. The rate of cesarean section was increased in poor controlled asthma or chronic severe asthma because of fear of gynecologist of complications of asthma of both mother and baby, but they can allow normal vaginal delivery under close medical supervision with continue their regular medical treatment during labor and delivery and treated any case of acute asthma like any case outside pregnancy by using Oxygen, nebulization and steroids. General anesthesia in asthmatic pregnant patients was risky because of chest infection and atelectasis [4]. Therefore; it was prefer to allow normal delivery with outside general anesthesia and in severe cases of asthma when indicated for cesarean section was high, it's

best to do spinal or regional anesthesia in order to avoid such complications. In addition, badly controlled asthma or unprepared asthmatic patients for operation by at least doing pulmonary function tests for one time during pregnancy make risk of bronchospasm and maternal hypoxia due to drugs those used during the operation [4]. Good control of asthma under regular medications and avoidance of trigger factors can result in normal labour and no complications and if there is an acute attack of bronchospasm although it is rare during labour, the patient can be treated usually as any case of acute asthma like in emergency unit by using bronchodilators and steroids. The infants adverse outcomes like attack of wheezy chest is high among asthmatic pregnant mothers ($P < 0.000$) in comparison with pregnant non-asthmatic mothers as in table (2). Maternal atopic seems to have important effect on the developing immune response of the infant and increases chances of the child developing allergy in later life. Maternal IgE, IgG and amniotic fluid cytokines combined with the presence of allergen in the fetomaternal environment are all possible factors involved in the ultimate outcomes in term of infants Th-1/Th-2 response to environmental allergens and thus increase chance of developing allergy in child later on [24]. Fetal death is high in asthmatic pregnant mothers and it is significant ($P < 0.000$) in comparison with pregnant non-asthmatic patients. This due to poor controlled asthma or severe asthmatic attack, which threaten fetus because of increased maternal hypoxaemia and diminish uterine blood flow secondary to vasoconstriction. Poor controlled asthma also produces high incidence of low birth weight, premature babies and neonatal hypoxia [13, 19], but in this study such incidence are not statistically significant. Congenital malformations are present in (5.4%) during this study and those malformations are not due to poor controlled asthma or use drugs in treatment of asthma, but such malformations are multi-factorial like hereditary, environmental, Trench infections and others. One retrospective study reported a high incidence of congenital anomalies in children of asthmatic women [24] but this has not been shown to occur in two large prospective studies [25] nor in any of the other studies of asthma in pregnancy [26-28], including a recent retrospective case control study of 101 pregnancies [29].

5. References

1. Abba I Terr MD. The atopic disease in: Tristram G. Parslow, MD, Ph D, Daneil P. sites, MD, Abba I. Terr, MD, John B. Imboden, MD. Medical Immunology 10thedn, U.S.A; McGraw-Hill companies, Inc, for manufacture and export, 2001, 359-360.
2. Kurinczuk JJ, Parsons DE, Dawes V *et al*. The relationship between asthma and smoking during pregnancy. *Women Health*. 1999; 29:31-47.
3. Tan KS, Thomson NC. Asthma in pregnancy. *Am-J-Med*. 2000; 109(9):727-33.
4. Nelson-Piercy C. Asthma in pregnancy. *Thorax*. 2001; 56(4):325-358.
5. Burdon JGW, Gross G. Asthma and pregnancy. *Aust NZJ Med*. 1994; 24:3-4.
6. Christine F Mc. Donald and Jonathan GW Burdon. Asthma in pregnancy and lactation. *MJA*. 1996; 165:485-488.
7. Pali-Schöll I, Motala C, Jensen-Jarolim E. Asthma and Allergic Diseases in Pregnancy: A Review. *World Allergy Organ J*. 2009; 2(3):26-36.

8. Murphy VE, Gibson PG, Smith R, Clifton VL. Asthma during pregnancy: mechanisms and treatment implications. *European Respiratory Journal*. 2005; 25:731-750.
9. Liu S, Wen SW, Demissie K, Marcoux S, Kramer MS. Maternal asthma and pregnancy outcomes: a retrospective cohort study. *Am-J Obstet-Gynecol*. 2001; 184(2):90-96.
10. Wen SW, Demissie K, Liu S. Adverse outcomes in pregnancies of asthmatic women: results from a Canadian population. *Ann-Epidemiol*. 2001; 11(1):7-21.
11. Demissie *et al*. Risks to fetus from asthma during pregnancy. *Am J Resp Crit Care Med*. 1998; 158:1091-1095.
12. Alexander S, Dodds L, Armson BA. Perinatal outcomes in women with asthma during pregnancy. *Obstet-Gynecol*. 1998; 92(3):430-440.
13. Hernandez E, Angell CS, Johnson JW. Asthma in pregnancy: current concepts. *Obstet-Gynecol*. 1980; 55:739-743.
14. Nafstad P, Magnus P, Jaakkola JJ. Risk of childhood asthma and allergic rhinitis in relation to pregnancy complications. *J Allergy-Clin-Immunol*. 2000; 106(5):867-873.
15. Sobande AA *et al*. Pregnancy outcome in asthmatic patients from High Altitudes. *International Journal of Gynecology and Obstetrics*. 2002; 77:117-121.
16. Perlow JH, Montgomery D, Morgan MA, Towers CV, Porto M. Severity of asthma and perinatal outcome. *Am J Obstet Gynecol*. 1992; 167(4-1):963-967.
17. Fitzsimons R, Greenberger PA, Patterson R. Outcome of pregnancy in women requiring corticosteroids for severe asthma. *J Allergy Clin Immunol*. 1986; 78:349-353.
18. Darlow BA, Horwood LJ, Moridge N. Very low birth weight and asthma by age seven years in national cohort. *Pediatr-pulmonol*. 2000; 30(4):291-296.
19. Zacharasiewicz *et al*. Indoor factors and their association to respiratory symptoms suggestive of asthma in Austrian children aged 6-9 years. *Wien-Klin-Wochenschr*. 1999; 111(21):882-886.
20. Prudhomme A. influence de sexe feminin sur l'asthme. *Rev-pneumol-Clin*. 1999; 55(5):296-300.
21. Beecroft N, Cochrane GM, Milburn HJ. Effect of sex of fetus on asthma during pregnancy: blind prospective study. *BMJ*. 1998; 317(7162):856-857.
22. Skobeloff EM, Spivey WH, Silverman R, Eskin BA, Harchelroad F, Alessi TV. The effect of the menstrual cycle on asthma presentations in the emergency department. *Arch Intern Med*. 1996; 156:1837-1840.
23. ACAAI. Executive office. Practical Tips for Pregnant Patients with Asthma or Other Allergic Conditions. Last modified, 1998, 6.
24. Bjorksten B. Environment and infant immunity. *Proc-Nutr-Soc*. 1999; 58(3):729-732.
25. Demissie K, Breckenridge MB, Rhoads GG. Infant and maternal outcomes in the pregnancies of asthmatic women. *Am J Respir Crit Care Med*. 1998; 158:1091-1096.
26. Schatz M, Patterson R, Zeitz S *et al*. Corticosteroid therapy for the pregnant asthmatic patient. *JAMA*. 1975; 233:804-807.
27. Fitzsimons R, Greenberger PA, Patterson R. Outcome of pregnancy in women requiring corticosteroids for severe asthma. *J Allergy Clin Immunol*. 1986; 78:349-353.
28. Schatz M, Zeiger RS, Harden K *et al*. The safety of asthma and allergy medications during pregnancy. *J Allergy Clin Immunol*. 1997; 100:301-306.
29. Minerbi-Codish I, Fraser D, Avnun L *et al*. Influence of asthma in pregnancy on labour and the newborn. *Respiration*. 1998; 65:130-135.