SEVERITY OF ASTHMA DURING PREGNANCY AND INFANT AND MATERNAL OUTCOMES

Kamal A. Ata*, Salah R. Ahmed, and Moustafa M. Abo Sedira*****

Departments of Chest Diseases, Obstetrics/Gynecology**, and Pediatrics****
Sohag Faculty of Medicine, South Valley University

SUMMARY

Prior studies have found an increased incidence of adverse perinatal outcomes of pregnancies in asthmatic mothers, however, these studies are limited by lacking of categorization of asthma severity. This study prospectively examined the relationship between severity of asthma during pregnancy and infant and maternal outcomes. A total of 82 pregnant asthmatic women (32 with mild asthma, 26 with moderate asthma and 24 with severe asthma) and 95 pregnant non-asthmatic control women were finally included in the study. All women were subjected to thorough history taking, complete clinical examination, routine investigations, abdominal sonography, pulmo- nary function tests and Doppler ultrasound of the umbilical artery. The asthmatic and control groups were well matched with regard to age, weight, height, smoking, gravidity and parity. The forced expiratory volume in one second was significantly reduced in women with severe asthma when compared with mild asthmatic and control groups ($p < 0.05$). Women with severe asthma were significantly more likely to have gestational diabetes and pre-eclampsia than were controls ($p = 0.02$ and 0.04, respectively). Compared with controls, patients with moderate and severe asthma were significantly more likely to be admitted for preterm labor ($p = 0.02$ and 0.002, respectively), to have their pregnancies complicated by premature rupture of membranes ($p = 0.03$ and 0.004, respectively), and to deliver by cesarean section ($p = 0.005$ and 0.0005, respectively). The occurrence of antepartum hemorrhage was significantly increased in severe asthmatics compared with controls ($p = 0.04$), however, the frequency of postpartum hemorrhage was comparable between groups. The neonates born to patients with moderate and severe asthma, were at significantly increased risk for intrauterine growth restriction ($p = 0.03$ and 0.02, respectively) and low birth weight ($p = 0.02$ and 0.01, respectively) compared to those of the control group. Also, preterm birth, low 5-minutes Apgar score and perinatal death were significantly more frequent in neonates born to severe asthmatics than in those born to the control group ($p = 0.03$, 0.04 and 0.004, respectively). There were statistically insignificant differences in the occurrence of congenital anomalies and respiratory distress syndrome in the neonates of the asthmatic and control groups ($p > 0.05$). From this study, it can be concluded that pregnant asthmatic women are at risk for adverse perinatal outcomes. The extent is variable and is related to the severity of the disease.

INTRODUCTION

Asthma is a relatively common disorder, affecting approximately 3 to 4% of the general population. It is the most frequent respiratory disorder complicating pregnancy, affecting between 0.4 and 1.3% of pregnant women. Despite considerable research on the causes and treatment of this condition, there has been relatively little attention given to the growing problem of asthma in pregnancy [1, 2].

The reported effect of pregnancy on asthma is variable. One study reported a significant improvement in asthma severity during pregnancy as demonstrated by a reduction in medication requirements [3]. Overall the results vary significantly from study to study because of differences in the groups studied. Generally, it appears that asthma improves, worsens or stays the same with equal frequency during pregnancy [4]. However, the course of asthma is often consistent in an individual woman's successive pregnancies [5].

Less clear, however, are the effects of asthma on perinatal outcome. Previous studies reported that uncontrolled asthma can have an adverse effect on pregnancy or the fetus. Uncontrolled pregnant asthmatics have an increase in preterm births and infants with low birth weights, decreased mean birth weight, increased neonatal mortality, increased neonatal hypoxia, hyperemesis gravidarum, vaginal hemorrhage, toxemia, and induced and complicated labors [6]. These problems are most often associated with maternal hypoxemia, hypocapnia, alkalosis or combination of these abnormalities [7,8]. Severe asthma during pregnancy also may cause maternal mortality [9]. Deaths are usually from mucus impaction causing asphyxiation or from tension pneumothorax[10].

These earlier studies, however, have been limited mainly by little or no information about asthma management and lacking of categorization of disease severity within the population studied.

AIM OF THE WORK

The aim of this study was to examine prospectively the relationship between severity of asthma during pregnancy and infant and maternal outcomes.

PATIENTS AND METHODS

A case-control study design was used. Both asthmatic pregnant women and control non-asthmatic pregnant women were recruited to the study from the antenatal clinic of Obstetrics/Gynecology Department and the asthma management clinic of Chest Department at Sohag University Hospital during the period from February 2000 to January 2004. Written, informed consent was obtained from all women for participation in the study.

All women were subjected to thorough history taking, complete clinical examination, routine investigations, abdominal sonography, pulmonary functionn tests, and Doppler ultrasound of the umbilical artery.

Asthmatic Group

Women reporting a history of asthma or asthma symptoms were evaluated in the asthma management clinic by the respiratory physician. A clinical diagnosis of asthma was made in patients who reported having had chest wheezing, tightness or cough within the prior 6 months that resolved spontaneously or with bronchodilator medication, in association with one or more of the following: (1) triggering of symptoms by allergies, infection or exercise; (2) wheezing during tidal breathing or chest auscultation; or (3) an abnormal age-related forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) ratio or peak expiratory flow rate (PEFR). Such patients were considered to be asthmatic pending complete documentation of their pulmonary function testing [(2)].

Control Group

Women who gave no history of asthma or asthma symptoms and who matched the asthmatic group on the basis of age, parity and smoking status were recruited to enter the study as controls.

Final Documentation of Asthmatic and Control Status

All subjects underwent complete pulmonary function testing using a computerized pulmonary functions apparatus (Medizintechnik mit System, JAEGER, TOENNIES, Hoechberg/Germany). Control subjects had spirometry monitored at 18 wk gestation whereas asthmatic women received 2 to 8 visits at the asthma management clinic depending on severity of asthma and individual needs. Pre- and post-bronchodilator testing were performed. Lung volumes and flows were measured and the normal values were considered according to the European Respiratory Society references[(11)]. To be included in the final data analysis, asthmatic and control subjects required the following objective documentation of their asthmatic and control (non-asthmatic) status:

(1) Asthmatic group: documentation of reversible airway obstruction from Pre- and post-bronchodilator spirometry or from serial spirometry.
(2) Control group: absence of airway obstruction.

Assessment of Asthma Severity

Clinical asthma severity was rated as mild, moderate, or severe using the integrated severity score described in the National Heart, Lung, and Blood Institute Guidelines[(12)]. Measurements of current daytime symptoms, nocturnal and morning symptoms due to asthma, bronchodilator use, FEV_1, peak expiratory flow (PEF), and hospitalizations were used to assign the patient a severity rating of either mild, moderate, or severe. The patient was assigned to

the most severe grade in which any feature occurred during her pregnancy. Subjects with mild persistent asthma exhibited any of the following characteristics: daytime symptoms > once a week but < once a day, exacerbations may affect activity and sleep, nocturnal symptoms > twice a month, infrequent use of inhaled short-acting β_2-agonist, FEV1 or PEF ≥ 80% predicted and PEF or FEV1 variability 20-30%. Moderate asthma was defined by daily symptoms, exacerbations that may affect activity and sleep, nocturnal symptoms > once a week, daily use of inhaled short-acting β_2-agonist, FEV1 or PEF > 60-< 80% predicted and PEF or FEV1 variability > 30%. In severe asthma, there were daily symptoms, frequent exacerbations, frequent nocturnal asthma symptoms, limitation of physical activities, FEV1 or PEF ≤ 60% predicted and PEF or FEV1 variability > 30%.

Clinical Management

All subjects received routine obstetric care in the antenatal clinic. Asthmatic subjects were managed in the asthma management clinic according to the standard treatment protocol of the National Heart, Lung, and Blood Institute Guidelines[12]. Patients with acute asthmatic exacerbations were admitted to the hospital and treated according to the same guidelines.

Perinatal Outcome Variables

Length of gestation was based on the reliable last menstrual period supplemented when clinically indicated by ultrasonography. Maternal, fetal and neonatal outcomes variables were studied in each pregnancy. Definitions of perinatal outcome variables investigated were based on standard textbook definitions [13]. The maternal variables comprised gestational diabetes mellitus; hypertensive disorders of pregnancy (pre-eclampsia, transient hypertension of pregnancy); preterm labor; antepartum hemorrhage (placenta previa, premature separation of placenta); membrane-related disorders (premature rupture of membranes, infection of the amniotic cavity); mode of delivery (forceps, vacuum or cesarean); and postpartum hemorrhage.

The fetal and neonatal variables comprised: (1) preterm birth; (2) low-birth weight; (3) intrauterine growth restriction (IUGR); (4) congenital malformations; (5) Apgar score at 5 minutes; (6) infant respiratory distress syndrome; (7) fetal death; (8) neonatal death; and (9) perinatal death.

Doppler Ultrasound

All women participating in the study were screened by Doppler ultrasound of the umbilical arteries as part of the routine fetal assessment at 20 wk of gestation. Abdominal circumference was recorded as a measure of fetal growth. Umbilical artery flow velocity waveforms were assessed by Duplex Doppler ultrasound (Acuson 128 XP/4; Acuson Corporation Company, USA) with color flow mapping using a 5-MHZ linear transducer. Abnormal

umbilical artery blood flow was defined as a systolic to diastolic flow ratio (SD ratio) greater than the 95th centile for gestational age [14].

Statistical Analysis

Subjects were excluded from final data analysis if they: (1) aborted (<20 weeks); (2) voluntarily withdrew from the study before delivery; (3) presented with a multiple gestation; (4) did not exhibit pulmonary function criteria for documentation of their asthmatic or control status; or (5) showed a pulmonary dysfunction pattern of a restrictive lung disease on pulmonary function testing.

Selected maternal, fetal and neonatal outcomes variables were compared in asthmatic cases and controls using Statistica for windows statistical software (Release 4.5 A, StatSoft, Inc.). The tests used were χ^2, Fisher's exact and one-way analysis of variance (ANOVA). A p value of < 0.05 was considered statistically significant.

RESULTS

A total of 82 pregnant asthmatic women (32 with mild asthma, 26 with moderate asthma and 24 with severe asthma) and 95 pregnant non-asthmatic control women were finally included in the analysis. Evaluation of the demographic characteristics of asthmatics and control subjects revealed well matched groups with insignificant differences with regard to age, weight, height, smoking, gravidity and parity. The pulmonary function tests showed that FEV_1 were significantly reduced in women with severe asthma when compared with mild asthmatic and control groups ($p < 0.05$). (Table 1)

Table (1): Maternal characteristics in the control and asthmatic groups*.

	Control group (n = 95)	**Asthmatic group**		
		Mild (n = 32)	**Moderate (n = 26)**	**Severe (n = 24)**
Age, years	28.1±0.6	27.6±0.8	26.9±1.32	27.9±0.85
Weight at beginning of pregnancy, kg	71.33±4.30	72.69±4.33	71.93±5.16	72.84±5.02
Height, cm	163.24±0.96	162.56±1.19	161.86±1.31	162.90±1.18
Smoking	0	0	0	0
Gravidity	3.68±0.28	3.56±0.35	4.00±0.36	4.15±0.32
Parity	2.5±1.6	2.08±0.35	2.83±0.57	3.13±0.22
Weight gain during pregnancy, kg	8.9±2.9	9.1±3.1	8.2±3.41	8.7±3.61
FEV1**, L	3.24±0.09	3.06±0.08	2.52±0.07	2.12±0.10

* All values are expressed as means ± SD. ** Forced expiratory volume in one second.

Women with severe asthma were significantly more likely to have gestational diabetes and pre-eclampsia than were controls ($p = 0.02$ and 0.04, respectively), whereas mild and moderate asthmatics did not show a significantly increased occurrence of these complications ($p > 0.05$). Compared with controls, patients with moderate and severe asthma were significantly more likely to be admitted for preterm labor ($p = 0.02$ and 0.002, respectively), to have their pregnancies complicated by premature rupture of membranes ($p = 0.03$ and 0.004, respectively), and to deliver by cesarean section ($p = 0.005$ and 0.0005, respectively). The occurrence of antepartum hemorrhage was significantly increased in severe asthmatics compared with controls ($p = 0.04$), however, the frequency of postpartum hemorrhage was comparable between groups. (Table 2)

Table (2): Maternal outcome variables in the control and asthmatic groups.

Variable, %	Control group (n = 95)	Asthmatic group		
		Mild (n = 32)	Moderate (n = 26)	Severe (n = 24)
Gestational diabetes	2.10	6.25	7.69	12.50
Pre-eclampsia	1.05	3.12	3.85	8.33
Preterm labor	3.16	9.37	15.38	20.83
Antepartum hemorrhage	0	0	3.85	4.17
PROM*	2.10	9.37	11.54	16.67
Cesarean section	5.26	18.75	23.08	29.17
Postpartum hemorrhage	2.10	3.12	3.85	4.17

*Premature rupture of membranes.

The neonates born to patients with moderate and severe asthma were at significantly increased risk for IUGR ($p = 0.03$ and 0.02, respectively) and low birth weight ($p = 0.02$ and 0.01, respectively) compared to those of the control group. Also, preterm birth, low 5-minutes Apgar score and perinatal death were significantly more frequent in neonates born to severe asthmatics than in those born to the control group ($p = 0.03$, 0.04 and 0.004, respectively). The neonates born to patients with mild asthma did not show a significantly increased occurrence of any of these complications ($p > 0.05$). There were statistically insignificant differences in the occurrence of congenital anomalies and respiratory distress syndrome in the neonates of the asthmatic and control groups ($p > 0.05$). (Table 3)

Table (3): Fetal and neonatal outcomes variables in the control and asthmatic groups.

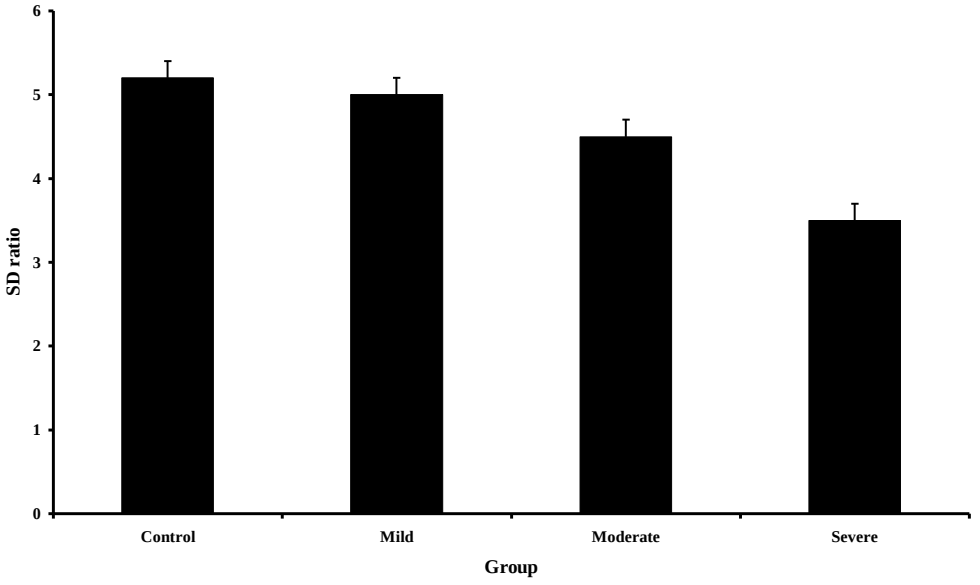
Variable, %	Control group (n = 95)	Asthmatic group		
		Mild (n = 32)	Moderate (n = 26)	Severe (n = 24)
Preterm birth*	4.21	9.37	11.54	16.67
Low birth weight**	5.26	12.50	19.23	20.83
IUGR***	2.10	9.37	11.54	12.50
Congenital anomalies	0	0	0	4.17
Apgar score at 5 min. < 7	1.05	3.12	7.69	8.33
RDS#	0	0	3.85	4.17
Perinatal death	0	0	3.85	8.33

* Delivery < 37 wk gestation ** Birth weight < 2500 gm *** Intrauterine growth restriction

Respiratory distress syndrome.

Umbilical artery waveforms as demonstrated by Doppler ultrasound and expressed as SD ratio, were significantly reduced in moderate and severe asthmatic groups when compared with mild asthmatics and control subjects ($p < 0.05$) (Figure 1).

Figure (1): Comparison of SD ratio of the umbilical artery flow velocity waveforms as measured by Doppler ultrasound in control and asthmatic groups.



DISCUSSION

Asthma, probably the most common medical condition occurring during pregnancy, can increase maternal and fetal morbidity and mortality. Conversely, the mechanical, hormonal, and metabolic stresses imposed by pregnancy might exacerbate asthma in the expectant mother. Accordingly, a knowledge of the complex interaction between these two conditions is essential if the health of the mother and fetus is to be maintained [(15)].

In evaluating investigations on perinatal outcome of asthma during pregnancy, it was found that categorization of disease severity is lacking [(16)]. In this study, we examined the relationship between asthma severity (as classified in the National Heart, Lung, and Blood Institute Guidelines) and infant and maternal outcomes.

In the present study, it was found that the frequency of gestational diabetes mellitus was significantly increased in women with severe asthma when compared with controls. Because many of these patients were concurrently treated with β-sympathomimetics, this finding may be consistent with the occurrence of carbohydrate intolerance with this therapy and with the diabetogenic effects of prolonged glucocorticoid administration [(16)]. Fitzsimons et al. [(17)] and Perlow et al. [(16)] found a similar frequency of gestational diabetes in severe asthmatics receiving steroid therapy. Also, the occurrence of pre-eclampsia was significantly higher in severe asthmatics than in controls. This finding is consistent with those of other investigators [(18-21)].

There was a significantly increased risk of preterm labor, premature rupture of membranes, and delivery by cesarean section for moderate and severe asthmatics compared with controls. Also, antepartum hemorrhage was a significantly more common occurrence for severe asthmatics. These results are in agreement with those of previous studies [(16,19-23)].

Beyond its effects on the mother, the importance of maternal asthma lies in its effects on fetal health. Abnormalities in lung gas exchange produced by worsening asthma can cause fetal hypoxia. It was reported that the well-being of the fetus depends on the severity of asthma and the fetal birth weight, a global index of fetal growth and development, correlates with the mother's FEV_1. Babies of women with the lowest percent predicted FEV_1 tend to have the lowest birth weights [(24)].

In this study it was found that neonates born to asthmatic patients especially moderate and severe asthmatics were at significantly increased risk for IUGR and low birth weight and those born to severe asthmatics were at significantly increased risk for preterm birth, low 5-minutes Apgar score and perinatal death. These findings are in accordance with those of other studies[(16,18,20-22)].The occurrence of respiratory distress syndrome and

congenital anomalies was comparable among control and asthmatic groups. This result is consistent with those of previous investigators [2, 16].

In normal pregnancy, the SD ratio of the umbilical artery flow velocity waveforms as demonstrated by Doppler ultrasound, is high in early gestation and decreases as diastolic flow increases with gestational age [14,25]. A high SD ratio is indicative of increased placental vascular resistance which creates a low-oxygen environment that promotes placental development and growth during early gestation [26]. Reductions of vascular resistance early in gestation may not be beneficial to placental development and fetal growth as it may create hyperoxic conditions that are inhibitory upon terminal villous development and angiogenesis [27]. In the present study it was found that the SD ratio of umbilical artery flow velocity was significantly reduced in moderate and severe asthmatics, suggesting that vascular resistance may be prematurely decreased. This finding is consistent with that of Clifton et al. [28]. Hitschold and coworkers [29] have described an association between reduced umbilical artery vascular resistance as demonstrated by Doppler ultrasound and IUGR.

Asthma severity is a likely cause of alterations in placental vascular function and the adverse outcome of low birth weight at term. Previous studies show that low birth weight neonates were associated with pregnancies complicated by severe asthma that required hospitalization versus asthmatics who did not require emergency care [2, 17, 30]. In our study, there was a significantly decreased birth weight in women with moderate and severe asthma during pregnancy. In pregnancies associated with deficient asthma control and status asthmaticus there are risks of development of maternal alkalosis [31] and subsequent reductions in uterine blood flow and fetal oxygenation leading to fetal hypoxia, hypercapnia, or acidosis under extreme conditions [32].

Earlier studies of the relationship between maternal asthma and adverse infant and maternal outcomes have yielded conflicting results. The most obvious difference between those reporting an association and those who did not is that in the latter group, the asthma was aggressively managed. However, most of these studies did not control for important confounding variables, making interpretation somewhat uncertain [20].

The study by Schatz et al. [2] failed to demonstrate an association between any of the infant and maternal outcomes and asthma complicating pregnancy. Asthma in that study population was well managed and aggressively controlled. However, the results of such a study with controlled asthma may not be generalizable to the broader population of pregnant asthmatics. Moreover, a close inspection of the numbers reported in their article reveals that asthmatic women as compared with the control women were more likely to develop pre-eclampsia, and to have a preterm, low-birth weight, or small-for-gestational-age

infant (odds ratios around 1.6), though the results did not achieve statistical significance with the smaller number of subjects in the study.

The pathophysiologic mechanisms that could explain the relationships between maternal asthma and adverse infant and maternal outcomes include (1) a common underlying etiology for the irritability or hyperactivity of both uterine and bronchial smooth muscles, (2) hypoxia secondary to maternal asthma, (3) release of bioactive mediators, and/or (4) medications used to treat asthma during pregnancy [21].

Irritability or hyperactivity of both uterine and bronchial smooth muscle could be common manifestations of an underlying diathesis in the mothers (atopic or otherwise) that increases intramuscular resistance in the myometrial vessels, which could also be related to a heightened myometrial tension. Such a hypothesis is further supported by the similarity of pharmacologic agents, particularly β_2-agonists, used to treat asthma and some of the adverse infant and maternal outcomes (e.g., preterm labor). Moreover, agents that cause constriction of airway smooth muscle (e.g., prostaglandin $F_{2\alpha}$) also cause contraction of uterine smooth muscle [23].

The hyperreactivity model, although intuitively attractive, seems to be inadequate in explaining all of the observed associations between adverse infant and maternal outcomes and maternal asthma. For example, if this model operates singly, one would expect an association of maternal asthma with preterm labor but not with IUGR. However, it was reported that maternal asthma was found to be associated with both preterm infant and IUGR and this suggests that an additional mechanism (probably hypoxia) plays a role in the pathogenesis of low birth weight [20]. This study supports this suggestion where the incidences of both preterm birth and IUGR were significantly increased among the neonates born to women with severe asthma.

The association between maternal asthma and congenital anomalies other than deformations could be due to hypoxic effects on organogenesis. However, this finding needs to be confirmed by other studies since organogenesis takes place early in life. If confirmed, the possible teratogenicity of commonly used drugs might need further investigation. It is notable that the relative risk is small, and to date no specific malformation syndrome has been identified [20].

The proposed pathogenesis of pre-eclampsia or hypertensive disorders of pregnancy in relation to asthma is more complex and highly speculative. Constriction of airway smooth muscle during asthma attacks may be caused by the local release of bioactive mediators. Among the substances implicated are histamine, platelet-activating factor, kinins and leukotrienes [33]. Of interest is the fact that leukotrienes are also implicated in the genesis of pregnancy-induced hypertension [34, 35].

Medications used to treat asthma during pregnancy have been suggested as a responsible agent for the probable adverse infant and maternal outcomes attributable to maternal asthma [19,36,37]. However, data from well designed and well executed studies showed, if anything, that asthmatic pregnant women who were treated with antiasthmatic drugs (β_2-agonists, theophylline, or steroids) had lower adverse infant and maternal outcomes than did those without treatment or those in the non-asthmatic control groups[38,39,40].

Prior studies reported that patients with severe asthma more often had adverse perinatal outcomes than did subjects with milder asthma even when asthma was actively managed [16, 19,41]. The present study supports these reports. However, it is not clear whether the mechanism of this relationship would involve inadequate asthma control or any of the previously mentioned pathogenetic factors. Further studies will be needed to clarify the existence and potential mechanisms of a relationship between adverse perinatal outcomes and more severe asthma, despite active asthma management.

In conclusion, the results of this study strongly suggest that maternal asthma complicating pregnancy is a significant risk factor for several adverse pregnancy outcomes. Although all asthma groups are at risk, the severe asthmatics seem to be at even greater risk than mild and moderate asthmatics. Physicians caring for mothers with asthma or their neonates should be aware of these risks. Further work is needed to confirm the specific risks and to elucidate their underlying pathogenesis.

REFERENCES

1. **Weinstein AM, Dubin BD, Podleski WK, et al (1979).** Asthma and pregnancy. JAMA; 241: 1161-1165 .
2. **Schatz M, Zeiger RS, Hoffman CP, et al (1995).** Perinatal outcomes in the pregnancies of asthmatic women: a prospective controlled analysis. Am J Respir Crit Care Med; 151: 1170-1174 .
3. **Juniper E, Daniel E, Roberts R, et al (1989).** Improvement in airway responsiveness and asthma severity during pregnancy: a prospective study. Am Rev Respir Dis; 140: 924-931.
4. **White RJ, Coutts CJ and MacIntyre C (1989).** A prospective study of asthma during pregnancy and puerperium. Respir Med; 83: 103-107.
5. **Schatz M, Harden K, Forsythe A, et al (1988).** The course of asthma during pregnancy, postpartum and with successive pregnancies: a prospective study. J Allergy Clin Immunol; 81: 509-517.
6. **Bahna SL and Bjerkedal T (1972).** The course and outcome of pregnancy in women with bronchial asthma. Acta Allergol; 27: 397-406.

7. **Schatz M and Hoffman C (1987).** Interrelationships between asthma and pregnancy: clinical and mechanistic considerations. Clin Rev Allergy; 5: 301-305.
8. **Greenberger PA and Patterson R (1987).** The management of asthma during pregnancy and lactation. Clin Rev Allergy; 5: 317-321.
9. **Schatz M, Hoffman CP, Zeiger RS et al (1988).** The course and management of asthma and allergic diseases during pregnancy, In Middleton E Jr, Reed CE, Ellis RF, Adkinson NF Jr., Yunginger JW (eds) *Allergy:* Principles and Practice, Vol 2, 3rd ed., St. Louis: C V Mosby, 1093-1155 .
10. **Huff RW (1989).** Asthma in pregnancy. Med Clin North Am; 73: 653-657.
11. **Qanjer PH, Tammeling GJ, Cotes JE, et al (1993).** Lung volumes, and forced ventilatory flows. Eur Respir J; 6(suppl.16):15-40.
12. **National Heart, Lung, and Blood Institute (1997).** National Institutes of Health. Guidelines for the diagnosis and management of asthma.
13. **Pritchard JA, MacDonald PC and Gant NF (1989).** Williams Obstetrics, 18th ed. Appleton-Century-Crofts, Norwalk, CT.
14. **Thompson RS, Trudinger BJ, Cook CM, et al (1988).** Umbilical artery velocity waveforms: normal reference values for A/B ratio and Pourcelot ratio. Br J Obstet Gynaecol; 95: 589-591 .
15. **Kelsen SG (2003).** Asthma and pregnancy. J Allergy Clin Immunol; 112: 268-270 .
16. **Perlow JH, Montgomery D, Morgan MA, et al (1992).** Severity of asthma and perinatal outcome. Am J Obstet Gynecol; 167: 963-967 .
17. **Fitzsimons R, Greenberger PA and Patterson R (1986).** Outcome of pregnancy in women requiring corticosteroids for severe asthma. J Allergy Clin Immunol; 78: 349-353 .
18. **Bahna SL and Bjerkedal T (1972).** The course and outcome of pregnancy in women with bronchial asthma. Acta Allergol; 27: 397-406 .
19. **Stenius-Aarniala B, Piirila P, and Teramo K (1988).** Asthma and pregnancy: a prospective study of 198 pregnancies. Thorax; 43: 12-18 .
20. **Demissie K, Breckenridge MB and Rhoads GG (1998).** Infant and maternal outcomes in the pregnancies of asthmatic women. Am J Respir Crit Care Med; 158: 1091-1095 .
21. **Liu S, Wen SW, Demissie K, et al (2001).** Maternal asthma and pregnancy outcomes: A retrospective cohort study. Am J Obstet Gynecol; 184: 90-96.
22. **Lao T and Huengsburg M (1990).** Labor and delivery in mothers with asthma. Eur J Obstet Gynecol Reprod Biol; 35: 183-190 .

23. **Kramer MS, Coates AL, and Michoud MC (1995).** Maternal asthma and idiopathic preterm labor. Am J Epidemiol; 142: 1078-1088 .
24. **Schatz M, Zeiger RS and Hoffman CP (1990).** Intrauterine growth is related to gestational pulmonary function in pregnant asthmatic women. Chest; 98: 389-392 .
25. **Hendricks SK, Sorensen TK, Wang KY, et al (1989).** Doppler umbilical artery waveform indices: normal values from fourteen to forty-two weeks. Am J Obstet Gynecol; 161: 761-765 .
26. **Kingdom JC and Kaufmann P (1997).** Oxygen and placental villous development: origins of fetal hypoxia. [Review]. Placenta;18: 613-621 ; discussion 623-626 .
27. **Khaliq A, Dunk C, Jiang J, et al (1999).** Hypoxia down-regulates placenta growth factor, whereas fetal growth restriction upregulates placenta growth factor expression. Lab Invest; 79: 151-170 .
28. **Clifton VL, Giles WB, Smith R, et al (2001).** Alterations of placental vascular function in asthmatic pregnancies. Am J Respir Crit Care Med; 164: 546-553 .
29. **Hitschold T, Weiss E, Beck T, et al (1993).** Low target birth weight or growth retardation? Umbilical Doppler flow. Am J Obstet Gynecol; 168: 1260-1264 .
30. **Greenberger PA and Patterson R (1988).** The outcome of pregnancy complicated by severe asthma. Allergy Proc; 9: 539-543 .
31. **Sachs BP, Brown RS, Yeh J, et al (1987).** Is maternal alkalosis harmful to the fetus? Int J Gynaecol Obstet; 25: 65-68 .
32. **Cousins L (1999).** Fetal oxygenation, assessment of fetal well-being, and obstetric management of the pregnant patient with asthma. J Allergy Clin Immunol; 103: S343-S349 .
33. **Haslett C (2000).** Asthma: Cellular and Humoral Mechanisms. In Crofton and Douglas's Respiratory Diseases, edited by Seaton A, Seaton D and Leitch AG. 5th ed. Vol. III. Oxford: Blackwell Science Ltd., p. 907-921 .
34. **Mitchell MD and Koenig JM (1991).** Increase production of 15-hydroxyeico-satetraenoic acid by placentae from pregnancies complicated by pregnancy-induced hypertension. Prostaglandins Leukot Essent Fatty Acids; 43: 61-62 .
35. **Biagi G, De Rosa V, Pelusi G, et al (1990).** Increased placental production of leukotriene B_4 in gestational hypertension. Thromb Res; 60: 377-384 .
36. **Stenius-Aarniala, B, Riikonen S and Teramo K (1995).** Slow release theophylline in pregnant asthmatics. Chest; 107: 642-647 .
37. **Schatz M, Zeiger RS, Harden K, et al (1997).** The safety of asthma and allergy medications during pregnancy. J Allergy Clin Immunol; 100: 301-306.

38. **Schatz M, Zeiger RS, Harden KM, et al (1988).** The safety of inhaled β-agonist bronchodilator during pregnancy. J Allergy Clin Immunol; 82: 686-695.
39. **Dombrowski MP, Bottoms SF, Boike GM, et al (1986).** Incidence of pre-eclampsia among asthmatic patients lower with theophylline. Am J Obstet Gynecol; 155: 265-267 .
40. **Fitzsimons R, Grammar LC, Halwig JM, et al (1988).** Prevalence of adverse effects in corticosteroid dependent asthmatics. N Engl Reg Allergy Proc; 9: 157-162 .
41. **Mabie WC, Barton JR, Wasserstrum N, et al (1992).** Clinical observations on asthma in pregnancy. J Maternal Fetal Med; 1: 45-50 .

الملخص العربي

شدة الربو الشعبي أثناء الحمل و علاقتها بصحة الأم و الطفل

كمال عبد الستار عطا* و صلاح رشدي احمد** و مصطفى محمد أبو سد يره***

أقسام الأمراض الصدرية و التوليد و أمراض النساء** و الأطفال****

كلية طب سوهاج - جامعة جنوب الوادي

اجريت هذه ا لدراسة المستقبلية في مستشفى سوهاج الجامعي في الفترة ما بين فبراير 2000 الى يناير 2004 و كان الهدف منها هو معرفة العلاقة بين شدة الربو الشعبي أثناء الحمل و صحة الأم و الطفل. تضمنت الدراسة 82 سيدة حوامل كن مصابات بالربو الشعبي بدرجات مختلفة (32 حالة ربو بسيط، 26 حالة ربو متوسط، 24 حالة ربو شديد) و كذلك 95 سيدة حوامل غير مصابات بالربو الشعبي كمجموعة ضابطة. و قد تم اخذ تاريخ مرضى مفصل لكل السيدات و تم عمل فحص اكلينيكى كامل و التحاليل الروتينية و فحص بالموجات فوق الصوتية و اختبار وظائف التنفس و فحص دوبلر للشريان السري الجينى لكل منهم. و تبين من الدراسة أن مجموعة الربو الشعبي و المجموعة الضابطة كانتا متطابقتين من حيث العمر و الوزن و الطول و عدم التدخين و عدد مرات الحمل و الولادة. و كان حجم الهواء في الثانية الاولى من الزفير القسرى اقل بقدر ذو دلالة إحصائية في مرضى الربو الشديد منه في مرضى الربو البسيط و سيدات المجموعة الضابطة.

و قد وجد أن نسبة حدوث مرضى البول السكري الناتج عن الحمل و ما قبل الاكلامبسيا كانت أعلى بقدر ذو دلالة إحصائية في مرضى الربو الشديد منها في سيدات المجموعة الضابطة. و كذلك كانت نسبة حدوث الولادة المبكرة و الانفجار المبكر في جيب المياه و الولادة القيصرية أعلى بقدر ذو دلالة إحصائية في مرضى الربو الشديد و المتوسط منها في سيدات المجموعة الضابطة. و كانت نسبة حدوث نزيف ما قبل الولادة أعلى بقدر ذو دلالة إحصائية في مرضى الربو الشديد منها في سيدات المجموعة الضابطة و لكن لم يكن هناك فرق ذو دلالة إحصائية في حدوث نزيف ما بعد الولادة في المجموعات الأربعة.

و لقد وجد أن أطفال مرضى الربو الشديد و المتوسط كانوا أكثر عرضة بقدر ذو دلالة إحصائية لتأخر النمو داخل الرحم و نقص الوزن عند الولادة من أطفال سيدات المجموعة الضابطة. و كذلك كان أطفال مرضى الربو الشديد أكثر عرضة بقدر ذو دلالة إحصائية للولادة قبل الميعاد و الوفاة بعد الولادة من أطفال سيدات المجموعة الضابطة. و لكن لم يكن هناك فروق ذو دلالة إحصائية في حدوث التشوهات الخلقية و متلازمة التأزم التنفسي في أطفال المجموعات الأربعة.

و نستخلص من هذه الدراسة أن مرض الربو الشعبي أثناء الحمل و خاصة الحالات الشديدة منه له خطورة و تأثير سلبي على صحة الأم و الطفل معا و يجب مرعاة ذلك عند التعامل مع هؤلاء المرضى و أطفالهم.