Egyptian Journal of Bronchology

Vol. 6, No 1, June, 2012

ORIGINAL ARTICLE

MATERNAL AND FETAL PERINATAL OUTCOMES AMONG PREGNANT WOMEN HOSPITALIZED WITH RESPIRATORY DISEASES IN ASSIUT UNIVERSITY HOSPITALS

Olfat M. El-Shinawy,[1] Raefat T. El-Sokkary,[1] Aliaë AR. Mohamed-Hussein,[1] Eman I. Tohamy,[1] Safwat Abdel Rady[2]

[1]Chest Department Assiut University, [2]Obstetric and Gynecology Department Assiut Woman Health Hospitals, Egypt

Correspondence to: Aliaë AR. Mohamed-Hussein, Email: massah_99@yahoo.com

Objectives: ***To assess the maternal and fetal perinatal morbidities related to respiratory diseases requiring hospitalization among pregnant women and to describe and quantify the impact of respiratory diseases during pregnancy on maternal and fetal health.***

Design: ***One year, hospital- based prospective study.***

Patients and Methods: ***The study included all pregnant women admitted with respiratory diseases in Chest Departments, Assiut University hospital and Assiut Women Health Hospital as well as similar number of normal pregnant women attending the Maternity out-patients clinic during the period from June 2010 to June 2011. All patients were followed during their pregnancy and one month after delivery. The detailed history and examination of their medical conditions were recorded as well as any associated complications in both the mother and her infant.***

Results: ***the study included 34 pregnant woman with respiratory diseases aged 19- 39 years old. The indications of hospitalization were: bronchial asthma (32.4%), pulmonary embolism (20.6%), tuberculosis, IPF, acute bronchitis (8.8% each), ARDS, H1N1 pneumonia, bacterial pneumonia (5.9% each), pulmonary hypertension (2.9%). The most common maternal complications were early rupture of membranes (17.6%), antepartum hemorrhage (placenta previa and placental abruption 11.7% and 2.9%), gestational diabetes (11.8%) and pre-eclampsia (5.8%). Mechanical ventilation was indicated in 11.7%. Fetal complications were low birth weight (14.6%), intrauterine growth retardation (8.8%) and intrauterine fetal death (5.8%). Uncontrolled bronchial asthma was the most common maternal respiratory illness associated with both maternal and fetal morbidities (31.8% - 61.5% respectively), followed by pulmonary embolism (21.8%- 15.4%).***

Conclusion: ***In this population of pregnant women, those with asthma accounted for one- third of maternal hospitalizations and morbidities and two- thirds of fetal morbidities followed by pulmonary embolism. Intervention efforts to increase awareness to improve respiratory care in pregnant women should be encouraged in our community.***

Keywords: ***Respiratory diseases, asthma, pulmonary embolism, pregnancy, maternal and fetal outcomes.***

INTRODUCTION

Pregnancy results in many changes in female body, which make it more susceptible to respiratory complications.[1,2] On the other hand, acute respiratory diseases are associated with many maternal complications during pregnancy like spontaneous premature rupture of membranes,[3] placental abruption,[4] preterm delivery,[5] placenta previa, preeclampsia, cesarean delivery and increased length of hospital stay.[6] Also, they are associated with fetal morbidities as prematurity, low birth weight, small- for gestational age, congenital anomalies.[6]

The most commonly studied respiratory emergency recorded during pregnancy is the poorly controlled asthma which has a definite adverse effect on both baby and mother; while most asthma medications have little or no adverse effect. The most common maternal and fetal morbidities are preterm labour,[7] preeclamsia,[8] transient tachypnoea in newborn,[9] oligohydramnious,[10] and increased risk of cesarean section.[6]

Pulmonary embolism is a leading cause of maternal mortality during pregnancy and up to 6 weeks postpartum compared with non-pregnant women. Women who are pregnant have a 5 fold increased risk for venous thromboembolism.[11] The incidence of pulmonary embolism in pregnancy varies between 1 per 1000 and 1 per 3000 deliveries.[12] Within the antenatal period, thromboembolism occurs equally within each trimester, and the postnatal period is the most dangerous time in terms of deaths per week but no period of pregnancy is without risk.[13] The major risk of heparin use is maternal hemorrhage especially in utero-placental junction.[14,15]

Pneumonia is the most common frequent cause of non-obstetric infection in pregnant subjects and the third most frequent cause of non-obstetric death.[16] It poses a special hazard for pregnant women possibly due to changes in a pregnant woman's immune system. Many complications can lead to premature labor, intrauterine growth retardation and perinatal death and increase the risk of maternal death during pregnancy. Extensive pneumonia with severe hypoxia may cause intrauterine fetal death.[17-19]

Untreated tuberculosis represents a far greater hazard to a pregnant woman and her fetus than does treatment of the disease. Maternal tuberculosis has been associated with an increased risk of spontaneous abortion, perinatal mortality and low birth weight in some studies and the outcome is unfavorably influenced by delays in diagnosis or treatment.[20,21]

Primary pulmonary hypertension (PPH) is a rare, progressive condition aggravated by the physiologic changes occurring during pregnancy and surgery. The maternal mortality rate associated with pregnancy and pulmonary hypertension range from 30 to 50%.[22]

Acute respiratory failure during pregnancy, although relatively uncommon, continues to be a prominent cause of maternal mortality, accounting for 30% of maternal deaths,[23] and is the most common reason for admission to the intensive care unit (ICU) of critically ill obstetric patients.[24]

The aim of this study was to assess the maternal and fetal perinatal complications related to respiratory diseases requiring hospitalization among pregnant women and to describe and quantify the impact of respiratory diseases during pregnancy on maternal and fetal health.

PATIENTS AND METHODS

This prospective, hospital-based, case-control study included 34 pregnant women admitted with respiratory diseases in Chest Department, Assiut University Hospital and Assiut Women Health Hospital during the period from June 2010 to June 2011 as well as 34 randomly selected pregnant women attending in outpatient Maternity Clinic as controls. All ladies were followed during their pregnancy and one week after delivery. The detailed demographic data including age, medical, gynecological and obstetric histories were reported. Complete physical and gynecological examinations were done, as well as the following investigations to confirm their gestational and pulmonary diagnosis: Abdominal and Pelvic Ultrasonography, Plain X ray chest if needed, Transthoracic Ultrasonography, Compression Doppler of lower limbs, Echocardiography, sputum gram stain, direct smear for acid-fast bacilli, PCR for H1N1 surface antigen and D-Dimer. These data were collected and any associated complications in both the mother and her infant were recorded.

Maternal outcomes were defined as: Preterm labor (pregnancies with 34 or less completed weeks of gestation), gestational diabetes, membrane–related disorders (premature rupture of membranes, infection of amniotic cavity, oligohydramnios and polyhydramnios), hypertensive disorders of pregnancy (pre eclampsia, transient hypertension and gestational hypertension), antepartum hemorrhage (placenta previa, premature separation of placenta), mode of delivery (normal or cesarean), post-partum hemorrhage, and increased length of hospital stay > 3 days.

Fetal and Infant outcomes: Low birth weight (<2500 gram), high birth weight (> 4000 grams), preterm birth (gestational age<37 completed weeks), post term birth (gestational age > 42 weeks), intra-uterine growth retardation (small-for- gestational age, fetal growth ratio <0.85), large for gestational age (>1.15), intrauterine fetal

death, any congenital anomalies and increased length of hospital stay > 3 days.

Exclusion criteria were: maternal smoking, previously diagnosed medical diseases as: hypertension, DM, rheumatic heart, chronic hepatic, collagen vascular, hematological diseases before pregnancy, maternal age > 40 years old, or mothers on anticoagulant therapy.

This study was approved by the Ethical Committee of Assiut University.

Statistical analysis: The data were analyzed using the statistical package Version 11; SPSS AG, USA. For multiple comparisons between the parametric variables, one way analysis of variance (ANOVA) tests was done, and P value < 0.05 was considered significant. Estimation of relative risk (odds ratio OD) was done by logistic regression using multivariate analysis and presented with 95% confidence interval (CI).

RESULTS

The study included 34 pregnant ladies with respiratory diseases hospitalized in Assiut University Hospitals, and 34 ladies with normal pregnancy as controls. Seventeen patients (50%) in the diseased group were < 25 years old, mean age 24.8±3.9, and range from 19 to 39 years old. The house wives were 76.5% and 79.4% were from Assiut Governorate. There was no statistical difference of medical importance between this group and controls (Table 1).

Table 1. Demographic data of the patients and controls.

Demographic data	Pregnant with respiratory diseases (n= 34)	Controls (n=34)	P value
Age			NS
< 25 yrs, n (%)	17 (50%)	15 (44.1%)	
≥ 25 yrs, n (%)	17(50%)	19 (55.9)	
Mean ±SD (Range)	24.8 ± 3.9 (19 – 36)	27.9±2.7 (19-38)	
Occupation			
Housewives	26 (76.5%)	23 (67.6%)	NS
Employee	3 (8.8%)	8 (23.5%)*	<0.05
Student	5 (14.7%)	3 (8.8%)	NS
Residence			NS
Assiut	27 (79.4%)	26 (76.5%)	
Al-Minia	4 (11.8%)	5 (14.7)	
Sohag	3 (8.8%)	3 (8.8%)	

Table 2. Obstetric and gynecological history of the studied population.

Clinical data	Pregnant with respiratory diseases (n= 34)	Controls (n=34)	P value
Gravidity			
Primigravida, n %	15 (44.1%)	14 (41.1%)	NS
Multi gravida, n %	19 (55.9%)	20 (58.8%)	NS
Number of previous deliveries			
0	15 (44.1%)	14 (41.1%)	
1	9 (26.4%)	11(32.3)	
2 or more	10 (29.4 %)	9 (26.4%)	
Number of CS	14 (41.1%)	10 (29.4)	
1	11 (78.6%)	5 (50%)	0.01
2 or more	3 (21.4%)	5 (50%)	0.01
Indication of CS	14	10	
Breech	2 (14.2)	5 (50%)	0.001
IUFD	2 (14.2)	0	-
Pre-eclampsia	2 (14.2)	2 (20%)	NS
Unspecified	8 (57.1%)	3(30%)	NS
Duration from last delivery	19	20	
≤ 1 year	12 (63.2%)	13 (65%)	NS
> 1 year	7 (36.8%)	7 (35%)	NS

Table 3. Indications of hospital admission in pregnant women with respiratory diseases (n=34).

Medical disease	n = 34	%
Bronchial asthma	11	32.4
Pulmonary embolism	7	20.6
Acute bronchitis	3	8.8
Tuberculosis	3	8.8
IPF	3	8.8
ARDS	2	5.9
H1N1 pneumonia	2	5.9
Bacterial pneumonia	2	5.9
Primary Pulmonary hypertension	1	2.9

IPF, interstitial pulmonary fibrosis; ARDS, acute respiratory distress syndrome; H_1N_1, Swine flu.

Table 4. Maternal and fetal complications in the studied groups.

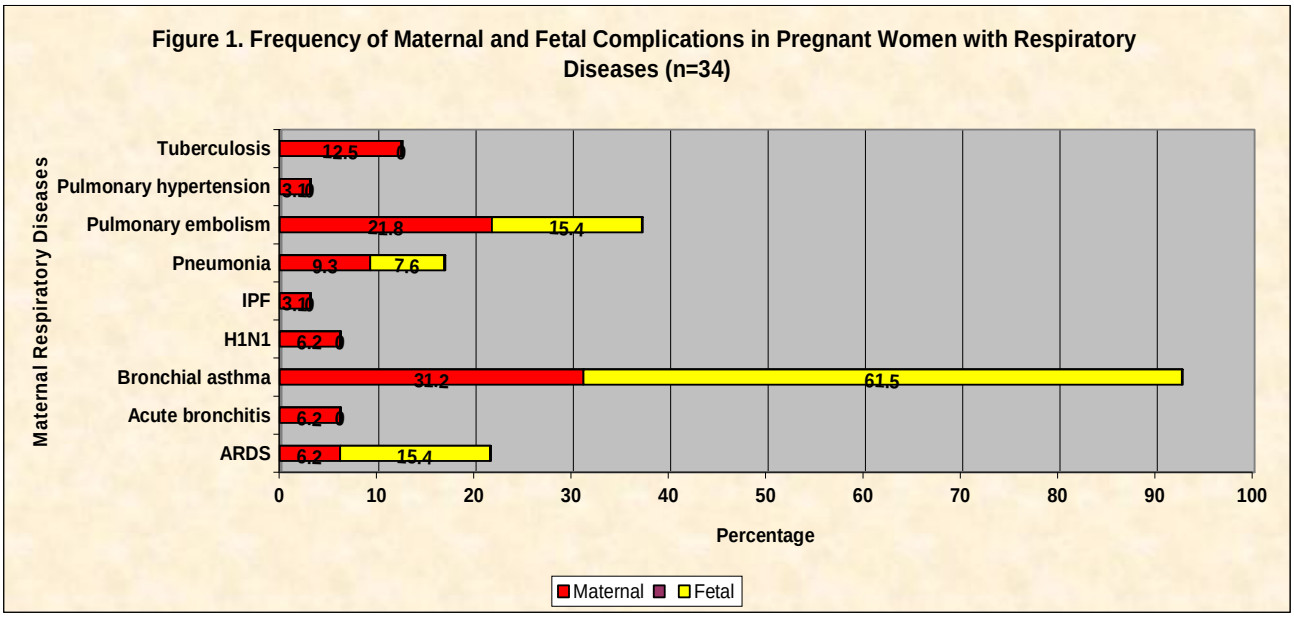
	Pregnant with respiratory diseases (n= 34)	Controls (n=34)	P value
Maternal complications, n %	32 (94.1%)	3 (8.8%)	<0.001
Pre-term labor (<37 weeks)	2 (5.8%)	0	
Membrane- related complications		0	
- PROM	6 (17.6%)		
- Infection of amniotic cavity	0 (0.0%)		
- Oligohydramnios	1 (2.9%)		
- Polyhydramnios	0(0.0%)		
Spontaneous abortion	2 (5.8%)		
Gestational DM	4 (11.7%)	2 (5.8%)	
Antepartum hemorrhage		0	
- Placenta previa	4 (11.7%)		
- Abruptio placenta	1 (2.9%)		
Hypertensive disorders of pregnancy			
- Gestational HTN	2 (5.8%)	1(2.9%)	
- Pre-eclampsia	2 (5.8%)		
Maternal hospital stay >3 days	4 (11.7%)	0	
Mechanical ventilation	4 (11.7%)	0	
Fetal complications:	13 (38.2%)	2 (5.8%)	<0.001
IUFD	2 (5.8%)	0	
IUGR	3 (8.8%)	0	
Low birth weight	4 (11.7%)	1(2.9%)	
Post term	0	0	
Congenital anomalies	0	0	
Infant hospital stay > 3 days	4 (11.7%)	1 (2.9%)	

PROM, Premature rupture of membranes; DM, Diabetes Mellitus; HTN, hypertension; IUFD, intra-uterine fetal death; IUGR, intra-uterine growth retardation.

Table 5. Multivariate analysis of relative risk of maternal and fetal complications in different maternal respiratory diseases.

Maternal respiratory diseases	Maternal complications Odd's ratio (95% ci)	P value	Fetal complications Odd's ratio (95% ci)	P value
ARDS	2.4 (1.1-5.1)	NS	5.5(1.8-11.5)	<0.01
Bronchial asthma	0.3(0.14-0.64)	<0.001	3.2(1.99-4.26)	0.001
Pneumonia	3.5(1.6-8.4)	<0.05	3.6(1.7-8.2)	NS
Pulmonary embolism	0.56 (0.2-1.5)	<0.01	0.39(0.14-0.65)	<0.01
Tuberculosis	6.02(1.08-3.7)	<0.05	5.1(1.9-12.5)	NS

Acute bronchitis, H1N1, IPF, Primary pulmonary hypertension were not significant by univariate analysis.



Univariate analysis of the maternal respiratory diseases during pregnancy as risk factors of bad maternal or fetal outcomes showed that acute bronchitis, H1N1, IPF and pulmonary hypertension were not significant. Further multivariate analysis with logistic regression showed that asthma, pulmonary embolisms are significantly important risk factors for maternal and fetal morbidities. Tuberculosis and pneumonia were significantly risky for mothers and ARDS for the fetus (Table 5).

DISCUSSION

In this study we found that pregnant women admitted with respiratory diseases had increased risk of adverse maternal and fetal outcomes. Maternal asthma and pulmonary embolism were the most common recorded causes of hospitalization and associated with higher risk of maternal and fetal complications.

As recorded in this study, asthma is the most common medical condition that can complicate pregnancy (32.4% in this group). The prevalence of asthma in USA is estimated to be 3.7%-8.4% and it affects 200.000-376.000 pregnancies annually. Episodes of acute asthma requiring emergency department visit or hospitalization have been reported in 9-11% of pregnant subjects managed by asthma specialists.[9]

Few studies found no significant difference in birth outcomes between asthmatic and non-asthmatic females.[25,26] However, initial observations of the relationship between maternal asthma and maternal and fetal outcomes were taken from the Norwegian Birth Registry in 1972, suggested increased risks from bronchial asthma of preterm birth, low birth weight, preeclampsia, and neonatal death.[27] Subsequently, Bertrand et al, 1985 proposed that the hyperreactivity of smooth muscle characteristic of asthma might lead to both bronchial and uterine complications.[28] Liu and colleagues suggested that the more common sequelae in pregnancies complicated by asthma or asthma medication include preterm delivery and low birth weight.[29] The most common maternal and fetal morbidities are preterm labor,[7] preeclamsia,[8,30] transient tachypnoea in newborn,[9] oligohydramnious,[10] and increased risk of cesarean section.[6] Increasing asthma severity and symptoms appeared to significantly decrease fetal growth, particularly when they occurred in the absence of an asthma diagnosis. A possible causal effect on these outcomes is due to a hypoxic effect from chronic reduced pulmonary function in the asthmatic pregnant mother has been suggested. These results are in agreement with the finding in the included group.

It is difficult to disentangle the influence of asthma from the effect of medications in many studies of treated women. Greenberger and Patterson, (1988), reported that avoiding acute asthma attacks by use of steroids and theophylline resulted in low birth weight rates equal to the normal population.[31] Schatz and colleagues, (1990), reported that inhaled or oral steroid therapy had no effect on birth weight.[32] In a later article, Schatz et al, (1995),

found that actively managed patients (which included the use of oral prednisone for the most severe cases) had no increased risk of intrauterine growth retardation (IUGR), low birth weight, or preterm delivery.[33] Moreover, Stenius Arniala et al, (1988), reported no increased risk of preterm delivery in patients managed with β2 agonists and theophylline for acute episodes.[34] Olesen et al, (2001), reported that Danish women who received prescription drugs for asthma during pregnancy had newborns with birth weight and birth length within expected ranges, but both outcomes worsened when the intensity of asthma therapy was reduced.[35]

However, Corchia and colleagues, 1995 reported a low birth weight rate of 5.6% in asthmatic women treated with β2 agonists and 18.2% in untreated women.[36] Interestingly, they did observe increased likelihood of preterm delivery with greater medication use, which appeared to be restricted to theophylline and oral steroids.[37] The effect of the asthma medications was not recorded in the present study.

The second most recorded maternal illness in this study was pulmonary embolism. Pulmonary embolism (PE) is the leading cause of maternal death.[38] The rate of PE in pregnancy is five times greater than that for non-pregnant women of the same age and is about 1 in 1500 deliveries; the risks are even higher in the perperium. The physiological changes during pregnancy, maternal age, parity, obesity, operative delivery and hypercoagulable state further increase the risk of venous thromboembolism (VTE) during pregnancy.[1,11,39-40]

Pregnant women with pulmonary embolus are usually otherwise healthy. They either die suddenly and unexpectedly or they have an illness that lasts several days or weeks where the diagnosis has not been considered. This emphasizes the need for prophylaxis in some cases and above all for correct diagnosis.[42] There were no recorded maternal deaths due to PE in the present study and this may be explained by the early diagnosis and treatment of PE.

In this study, 21.8% of maternal complications and 15.4% of fetal complications were recorded in patients with pulmonary embolism. The main cause of maternal morbidity was ante-partum hemorrhage. Ginsberg and Bates, 2003 stated that although Heparin (the mainstay of therapy for acute venous thromboembolism (VTE) in pregnancy) does not cross the placenta, and so does not carry risks of teratogenesis, fetal hemorrhage and bleeding at the uteroplacental junction is a possibility.[15]

The rate of major bleeding with various doses of un-fractionated heparin (UFH) was 2%,[43] Also, therapeutic doses of subcutaneous UFH (adjusted-dose UFH) can cause a persistent anticoagulant effect at the time of delivery, which can complicate its use prior to labor.[44,45] The mechanism for this prolonged effect is unclear. Bleeding complications appear to be very uncommon with low molecular weight heparin (LMWH).[46-48]

As regards fetal complications there are 2 potential fetal complications of maternal anticoagulant therapy: teratogenicity and bleeding.[16] IUFD was recorded in 5.8% of the studied group and both in patients wit PE. So it seems that anticoagulation therapy rather than the pulmonary embolism itself is the cause of both maternal and fetal outcomes.

We recorded 9.3% of maternal complications and 15.4% of fetal complications in pregnant patients admitted with pneumonia (preterm labor and low birth weight). These results were in agreement with many studies. Munn et al, 1999 stated that there is persuasive evidence to indicate that maternal and fetal outcomes are affected by maternal pneumonia. Mothers with pneumonia are significantly more likely to deliver before 34 weeks gestation, with preterm delivery occurring in up to 43% of cases. Prostaglandin production or the host's inflammatory response to infection may be responsible. In addition, infants born to mothers with pneumonia weigh significantly less.[49] A difference of 150 g in the birth weight of infants born to mothers with pneumonia compared with controls was recorded and the frequency of low birth weight infants (2500 g or less) was higher in cases than in controls (16% v 8%).[50] Mothers with pneumonia are more likely to deliver early and have infants of lower birth weight than other pregnant women.[50]

The most common complication of H1N1 influenza (swine-flu) is pneumonia. Other reported complications noted in pregnant women include disseminated intravascular coagulation, cognitive impairment post viraemia/encephalitis, and psychological effects after the recovery phase, requiring appropriate support, venous thromboembolism and pulmonary embolism.[51] There are no previous records of maternal and fetal morbidities in pregnant women with H1N1 pneumonia. During this study 2 pregnant ladies were admitted with H1N1 pneumonia, one of them required mechanical ventilation but weaned within 3 days without any fetal complications.

The effects of TB on pregnancy depend upon various factors such as type, site and extent of the disease, stage of pregnancy when management gets instituted, nutritional status of mother, presence of concomitant disease, immune status and co-existence of HIV infection, availability of facilities for early diagnosis and treatment, and so on.[52] If anti-tuberculosis treatment (ATT) is started early in pregnancy, the outcome is the same as that in non-pregnant patients, whereas late diagnosis and care is associated with 4-fold increase in obstetric morbidity and 9-fold increase in pre-term labor.[20] Poor nutritional states,

hypo-proteinaemia, anemia and associated medical conditions add to maternal morbidity and mortality. Co-existing HIV infection is known to augment progression of TB and worsens the immunosuppression.[53]

Maternal tuberculosis has been associated with an increased risk of spontaneous abortion, perinatal mortality and low birth weight in some studies and the outcome is unfavorably influenced by delays in diagnosis or treatment,[20,21] In agreement, it was found that TB was associated with increased relative risk of maternal complications in pregnant tuberculous mother (especially spontaneous abortion).

A fetus can get TB infection either by haematogenous spread through umbilical vein to fetal liver or by ingestion or aspiration of infected amniotic fluid.[54] True congenital TB is believed to be rare. The risk to neonate of getting TB infection shortly after the birth is greater.[55] No recorded cases of congenital TB were found in this study.

Primary pulmonary hypertension (PPH) is a rare, progressive condition aggravated by the physiologic changes occurring during pregnancy. The maternal mortality rate associated with pregnancy and pulmonary hypertension ranges from 30 to 50%.[22] Pulmonary hypertension has always been considered to be an indicator of poor prognosis in pregnancy[56] and is said to carry high morbidity and mortality to both the mother and the fetus. Also, pulmonary hypertension has always been a feature of cardiac disorders in which early termination of pregnancy is traditionally recommended. In certain instances, the severity of maternal pulmonary hypertension in rheumatic heart diseases can be higher than in congenital heart diseases.[57] Only one patient with PPH was included in this study and was associated with oligohydramnios.

Although less than 1 percent of women require admission to an intensive care unit (ICU) during pregnancy or the peri-partum period (the last month of gestation and the first few weeks after delivery), both maternal and fetal mortality are high when such care is required.[58]

Mirghani and colleagues have found that only 0.11 to 0.89 % of deliveries require maternal ICU admission.[59] The most common indications for ICU admission are postpartum hemorrhage and the hypertensive disorders (severe preeclampsia or eclampsia). Maternal mortality is high when critical care is required, with estimates ranging from 5 to 30 percent.[60] In the present study 11.7% needed ICU admission and mechanical ventilation. This is higher than the recorded results as the included mothers had already respiratory diseases requiring hospitalization.

Fetal mortality is also high when critical care is required. Early gestational age, severe maternal illness, the need for maternal blood transfusions, and the absence of prenatal care are associated with fetal mortality.[61] Only 4 patients were admitted to ICU in the studied group and 50% had IUFD.

The effect of maternal ARDS on neonatal outcomes is not well studied, but high rates of fetal death, spontaneous preterm labor, and fetal heart rate abnormalities are reported. A high rate of perinatal asphyxia among surviving infants is also reported. In one series of 13 patients with ARDS who reached viability (>24 wks), the perinatal fetal death rate was 23%.[62] More recently, in a series of ten antepartum patients in the third trimester ventilated for ARDS, only five of the neonates survived intact after delivery, data were not available for one infant.[23] This study supported that ARDS is a relative risk factor of fetal morbidities and was associated with 15.4% of fetal complications.

The mortality and morbidity rates of ARDS in the general population are high, with reported mortality ranging from 35% to 60%.[63] In a series of 83 obstetric patients with ARDS, the antepartum mortality rate was 23% and the postpartum mortality rate was 50%.[64] Similarly, in another series of 28 obstetric patients with ARDS, the mortality rate was 39% and three of the 17 survivors had long-term sequelae.[62] Multiple organ dysfunction syndrome has been reported as the most common cause of maternal death.[23,65,66] No maternal morbidities or mortalities due to ARDS were recorded in the present study.

The limitations of this study were in the small number of included subjects, lack of some databases concerning the detailed therapeutic regimens especially for asthmatic patients, arterial blood gas analysis, pulmonary function tests monitoring specially in those patients admitted in the Women Health Hospitals.

CONCLUSIONS

The key of successful management of respiratory diseases during pregnancy is early identification and treatment, stabilizing heamo-dynamics and oxygenation, close monitoring of both mother and fetus. Knowledge of normal maternal and fetal physiology and implementing strategy to maintain fetal oxygenation is important. A multidisciplinary team approach is required to ensure a successful outcome for both mother and fetus specially asthma and pulmonary embolism.

REFERENCES

1. Rizk NW, Kalassian KG, Gilligan T et al., Obstetric complications in pulmonary and critical care medicine. Chest. 1996;110:791-809.

2. Al-Suleiman, SA, Qutub, HO, Rahman, J, Rahman, MS. Obstetric admissions to the intensive care unit: a 12-year review. Arch Gynecol Obstet. 2006;274:4.

3. Getahun D, Ananth CV, Oyelese Y, et al., Acute and chronic respiratory diseases in pregnancy; association with spontaneous premature rupture of membranes. J matern fetal neonatal Med. 2007;20:669-75.

4. Getahun D, Ananth CV, Peltier MR, et al., Acute and chronic respiratory diseases in pregnancy; association with placental abruption. Am J Obstet Gynecol. 2006;195:1180-4.

5. Sorensen TK, Dempsey JC, Xiao R, et al. Maternal asthma and risk of preterm delivery. Ann Epidemiol. 2003;13:267-72.

6. Dimissie K, Breckenridge MB, Rhoads GG. Infant and maternal outcomes in the pregnancies of asthmatic women. Am J Respir Crit Care Med. 1998;158:1091-5.

7. Juniper EF and Newhouse, MT. Effect of pregnancy on asthma: a systematic review and meta-analysis. In: M Schatz, RS Zeiger and HC Claman, Editors, Asthma and immunological diseases in pregnancy and early infancy, Marcel Dekker, New York. 1993:401–27.

8. Schatz M. Asthma during pregnancy: Interrelationships and management. Ann Allergy. 1992;68:123-33.

9. Barken MB, Triche EW, Belanger K, et al., Asthma symptoms, severity, and drug therapy: a prospective study of effects on 2205 pregnancies.Obst Gynecol. 2003;102:739-52.

10. Lao TT, Huengsburg M. Labour and delivery in mothers with asthma. Eur J Obstet Gynecol Reprod Biol. 1990;35:183-90.

11. Pereira A, Krieger BP. Pulmonary complications of pregnancy. Clin Chest Med. 2004;25:299-310.

12. Macklon NS, Greer IA. Venous thromboembolic disease in obstetrics and gynaecology: the Scottish experience. Scott Med J. 1996;41:83–6.

13. Ginsberg JS, Brill-Edwards P, Burrows RF et al. Venous thrombosis during pregnancy: leg and trimester of presentation. Thromb Haemost. 1992;67:519–20.

14. Ginsberg JS, Greer I, Hirsh J. Use of antithrombotic agents during pregnancy. Chest. 2001;119:122S-131S.

15. Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. J Thromb Haemost. 2003;1:1435-42.

16. Ramsey PS, Ramin KD. Pneumonia in pregnancy.Obstet Gynecol Clin North Am. 2001;28:553-69.

17. Maccato M. Respiratory insufficiency due to pneumonia during pregnancy. Obstet Gynecolol Clin North Am. 1991;18:289-99.

18. Lim WS, Macfeerlane JT, Colthorpe CL. Pneumonia and pregnancy. Thorax. 2001;56:398-405.

19. Lim WS, Macfeerlane JT, Colthorpe CL, et al., Treatment of community acquired lower respiratory tract infection during pregnancy. Am J Respir Med. 2003;2:221-33.

20. Figueroa-Damien R., Arredondo–Garcia J.L.; Pregnancy and tuberculosis: influence of treatment on perinatal outcome; Am J Perinatol. 1998;15:303.

21. Ormerod P. Tuberculosis and pregnancy and the puerperium; Thorax. 2001;56:494.

22. Weiss B, Zemp L, Seifert B, Hess O M. Outcome of pulmonary vascular disease in pregnancy: A systemic overview from 1978 through 1996. J Am Coll Cardiol. 1998;31:1650–7.

23. Catanzarite V, Willms D, Wong D, Landers C, Cousins L, Schrimmer D. Acute respiratory distress syndrome in pregnancy and the puerperium: causes, courses, and outcomes. Obstet Gynecol. 2001;97:760–4.

24. Afessa B, Green B, Delke I, Koch K. Systemic inflammatory response syndrome, organ failure, and outcome in critically ill obstetric patients treated in an ICU. Chest. 2001;120:1271–7.

25. Jana N, Vasishta K, Saha SC, et al., effect of bronchial asthma on the course of pregnancy, labour and perinatal outcome. J obstet Gynacol. 1995;21:227-32.

26. Dombrowski MP,Schatz M, Wise R et al., Asthma during pregnancy.Ostet Gynecol. 2004;103:5-12.

27. Bahna S, Bjerkedal T. The course and outcome of pregnancy in women with bronchial asthma. Acta Allergol. 1972;27:397-406.

28. Bertrand J, Riley S, Popkin J, Coates A. The long term pulmonary sequelae of prematurity: The role of familial airway hyperreactivity and the respiratory disease syndrome. N Eng J Med. 1985;312:742-5.

29. Liu S, Wen S, Demissie K, Marcoux S, Kramer M. Maternal asthma and pregnancy outcomes: A retrospective cohort study. Am J Obstet Gynecol. 2001;184:90-6.

30. Schatz M, Dombrowski MP, Wise R, Thom EA, Landon M, Mabie W, et al. Asthma morbidity during pregnancy can be predicted by severity classification. J Allergy Clin Immunol. 2003;112:283-8.

31. Greenberger P, Patterson R. The outcome of pregnancy complicated by severe asthma. Allergy Proc. 1988;9:539-43.

32. Schatz M, Zeiger R, Hoffman C. Intrauterine growth is related to gestational pulmonary function in pregnant asthmatic women. Chest. 1990;98:389-92.

33. Schatz M, Zeiger R, Hoffman C, Harden K, Forsythe A, Chillinar L, et al. Perinatal outcomes in the pregnancies of asthmatic women: A prospective controlled analysis. Am J Respir Crit Care Med. 1995;151:1170-4.

34. Stenius-Aarniala B, Piirila P, Teramo K. Asthma and pregnancy: A prospective study of 198 pregnancies. Thorax. 1988;43:12-8.

35. Olesen C, Thrane N, Nielsen G, Sorensen H, Olsen J. A population-based prescription study of asthma drugs during pregnancy: Changing the intensity of asthma therapy and perinatal outcomes. Respiration. 2001;68:256-61.

36. Corchia C, Bertollini R, Forastiere F, Pistelli R, Perucci C. Is maternal asthma a risk factor for low birth weight? Results of an epidemiologic survey. Eur J Epidemiol. 1995;11:627-31.

37. Wen S, Demissie K, Liu S. Adverse outcomes in pregnancies of asthmatic women: Results from a Canadian population. Ann Epidemiol. 2001;11:7-12.

38. Pabinger I, Grafenhofer H. Thrombosis during pregnancy: risk factors, diagnosis and treatment. Pathophysiol Haemost Thromb. 2002;32:322–4.

39. Rubio ER, Alper B, Szerlip HM. Respiratory complications of pregnancy. Obst Gynecol Surv. 2002;57:39-46.

40. Stone SE, Morris TA .Pulmonary embolism and pregnancy. Crit care Clin. 2004;20:661-77.

41. Tan LK De Swiet M.Management of thromboembolic disease in pregnancy. Ann Acad Med Singapore. 2002;31: 311.

42. Carson JL, Kelley MA, Duff A et al. The clinical course of pulmonary embolism. N Engl J Med. 1992;326:1240–5.

43. Ginsberg JS, Kowalchuk G, Hirsh J, et al. Heparin therapy during pregnancy: risks to the fetus and mother. Arch Intern Med. 1989;149:2233-6.

44. Levine MN, Raskob G, Landefeld S, Kearon C. Hemorrhagic complications of anticoagulant treatment. Chest. 2001;119:108s-121s.

45. Anderson DR, Ginsberg JS, Burrows R, Brill-Edwards P. Subcutaneous heparin therapy during pregnancy: a need for concern at the time of delivery. Thromb Haemost. 1991;65:248-50.

46. Greer IA, Thomson AJ. Management of venous thromboembolism in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2001;15:583-603.

47. Devendra G, Morris T. Pulmonary Embolism and Deep Venous Thrombosis Treated With Either Low Molecular Weight Heparin Or Unfractionated Heparin Have The Same Incidence Of Thrombocytopenia. CHEST. 2000;118:262s.

48. Lindhoff-Last E, Nakov R, Misselwitz F, Breddin HK, Bauersachs R. Incidence and clinical relevance of heparin-induced antibodies in patients with deep vein thrombosis treated with unfractionated or low-molecular-weight heparin. Br J Haematol. 2002;118:1137-42.

49. Munn MB, Groome LJ, Atterbury JL, et al. Pneumonia as a complication of pregnancy. J Matern Fetal Med. 1999;8:151–4.

50. Yost NP, Bloom SL, Richey SD, et al. An appraisal of treatment guidelines for antepartum community-acquired pneumonia. Am J Obstet Gynecol. 2000;183:131–5.

51. Lim B H and. Mahmood T A, Pandemic H1N1 2009 (swine flu) and pregnancy. Obstet Gynaecol & Reproduc Med. 2010;20:101-6.

52. Good J.T., Iseman M.D., Davidson P.T., et al; Tuberculosis in association with pregnancy; Am J Obstet Gynecol. 1981;140: 492.

53. Saade G.R.; Human immunodeficiency virus (HIV) related pulmonary complications in pregnancy; Semin Perinatol. 1997;21:336.

54. Hamadeh M.A., Glassroth J.; Tuberculosis and pregnancy; Chest. 1992;101:1114.

55. Starke J. R. Tuberculosis. An old disease but a new threat to the mother, fetus and neonate; Clin Perinatol. 1997;24:107.

56. Ducey JP, Ellsworth SM. The hemodynamic effects of severe mitral stenosis and pulmonary hypertension during labor and delivery. Intensive Care Med. 1989;3:192.

57. Lin JH, Zhao WX, Su Y, Shi J, Jiang GJ, Wu ZM. Perinatal management and pregnancy outcome in pregnant women with pulmonary hypertension complicating cardiac disease. Zhonghua Fu Chan Ke Za Zhi. 2006;41:99–102.

58. Keizer, JL, Zwart, JJ, Meerman, RH, et al. Obstetric intensive care admissions: a 12-year review in a tertiary care centre. Eur J Obstet Gynecol Reprod Biol. 2006;128:152.

59. Mirghani, HM, Hamed, M, Ezimokhai, M, Weerasinghe, DS. Pregnancy-related admissions to the intensive care unit. Int J Obstet Anesth. 2004;13:82.

60. Zwart, JJ, Dupuis, JR, Richters, A, et al. Obstetric intensive care unit admission: a 2-year nationwide population-based cohort study. Intensive Care Med. 2010;36:256.

61. Leung, NY, Lau, AC, Chan, KC, Yan, W. Clinical characteristics and outcomes of obstetric patients admitted to the intensive care unit: a 10-year retrospective review. Hong Kong Med J. 2010;16:18.

62. Mabie WC, Barton JR, Sibai BM: Adult respiratory distress syndrome in pregnancy. Am J Obstet Gynecol. 1992;167:950–7.

63. Ware LB, Matthay MA: The acute respiratory distress syndrome. N Engl J Med. 2000;342:1334–49.

64. Catanzarite VA, Willms D. Adult respiratory distress syndrome in pregnancy: Report of three cases and review of the literature. Obstet Gynecol Surv. 1997;52:381–92.

65. Perry KG Jr, Martin RW, Blake PG, et al: Maternal mortality associated with adult respiratory distress syndrome. South Med J. 1998;91:441–4.

66. Clark, SL, Belfort, MA, Dildy, GA, et al. Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. Am J Obstet Gynecol. 2008;199:36.