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Fetomaternal Outcome of Exacerbation of Bronchial Asthama in Pregnancy

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ABSTRACT
Bronchial asthma is a chronic inflammatory disease of the airways characterized by bronchial hyper reactivity and a variable degree of airway obstruction. The exacerbation of asthama in pregnancy and labouris common due to theimmunological and physiological changes of pregnancy itself. However, the adverse consequences are preventable by following proper guidelines regarding its control. The study was conducted in the department of obstetrics and gynaecology SKIMS soura over a period of two years. A total of 240 pregnant women were included in the study after taking a proper informed consent. Fetomaternal outcome was evaluated. Pregnancy is adversely affected by exacerbations of asthama. There is increased risk of hypertensive disorders (35.8%) of pregnancy, preterm labour (19.58%), use of additional drugs for asthama control (66.66%). Exacerbation of asthama in pregnancy and labour can be avoided by lifestyle modification and strict drug control throughout pregnancy. In absence of exacerbations fetomaternal outcome is good.

INTRODUCTION

Exacerbations of asthamaare a major clinical problem during pregnancy. Kwon *et al*.[1] reported an Increase in the prevalence of asthma during pregnancy from 3.7% in 1997 to 8.4% in 2001. More recent reports from the USA found a prevalence of 5.5% in 2001, increasing to 7.8% in 2007[2]. A prevalence of 9.3% has been reported in Ireland and 12.7% in Australia[3,4].

Pregnancy is an immunocompromised state and is also characterized by decrease in total lung capacity, residual volumes, functional residual capacity and expiratory reserve volume, which further add to the burden of the disease in pregnancy. As a result up to 45% of women need to seek medical help and have poor outcomes for mothers and their babies, including low birth weight and preterm delivery[5]. Maternal asthma is associated with an increased risk of adverse perinatal outcomes. The changes in the course of the disease are to be expected due to the physiological and immunological response of pregnancy, which at times can be unpredictable. Optimising the management of asthama and preventing exacerbations in pregnancy is essential for protecting the health of both mother and baby. This is achieved by aiming to prevent day- and night-time symptoms and maintain lung function and normal activity.

Since the histopathological findings of asthma include, inflammatory mediator infiltration, airway remodeling (epithelial shedding and basement membrane thickening), eosinophilic infiltration, T-helper cell involvement and IL-5 production, therefore the goals of it's management also need to prevent this inflammatory cascade. During pregnancy, there is the additional goal to maintain fetal oxygenation by preventing episodes of maternal hypoxia[6]. Achieving this requires regular monitoring of clinical symptoms, provision of self-management education and the correct use of pharmacotherapies. Multidisciplinary management by all health professionals involved in a woman's care is encouraged[6].

Lifestyle modification avoiding cold exposure and allergens, treating comorbidities also has a pivotal role in the management of asthama. However, pharmacotherapy is the main stay of treatment in asthama.

A stepwise approach to asthma treatment is recommended during pregnancy as for other adults with asthma. Guidelines recommend the use of short acting β-agonists (SABA) as reliever medication and the use of inhaled corticosteroids (ICS) for women with persistent asthma. There is much reassuring data concerning the safety of ICS medication use in pregnancy, particularly for budesonide, which has the best safety rating during pregnancy. Guidelines recommend the continued use of ICS medication that has been effective in controlling asthma prior to pregnancy[5,6].

Various drugs available for asthama are listed below, however the permissibility of drug use in pregnancy is to be taken care of. Some of the drugs are mentioned below.

B2-agonists: SABAs are effective bronchodilators for quick-acting relief of asthma symptoms and are generally considered safe for use during pregnancy and breastfeeding. While SABA use was associated with a small increased risk of congenital malformation in some of the large studies described above, most studies evaluating maternal SABA use during pregnancy have not shown significant increases in adverse maternal or fetal outcomes associated with drug use[7,8].

Inhaled and systemic corticosteroids: Due to potent and predictable anti-inflammatory effects, ICS form the foundation of maintenance therapy in patients with persistent asthma. As a drug class, ICS have generally been shown to decrease the risk of asthma exacerbations among pregnant women, with no increased rate in adverse maternal or fetal outcomes[9,10]. Systemic absorption of an ICS is typically very low, with data demonstrating very low to undetectable plasma concentrations of triamcinolone, fluticasone, ciclesonide and becolmethasone after inhalation[11]. Inhaled budesonide has approximately 39% bioavailability but results of studies of inhaled budesonide in lactation demonstrated a negligible amount transferred to the breastfeeding infant[12].

Concerns regarding the safety of corticosteroids in pregnancy have been specifically addressed in a number of studies. Data from most studies support the safety of ICS use for asthma during pregnancy[13-19].

There is no compelling evidence to substantiate a correlation between the use of an ICS during pregnancy and an increased risk of adverse infant outcomes, currently, these agents should be used when necessary to maintain asthma control.

Systemic corticosteroids should be reserved for use in acute exacerbations for all asthma patients or in those patients unable to achieve disease control using other agents. In contrast to ICS, oral corticosteroids have been associated with a higher incidence of maternal adverse effects, including preeclampsia and gestational diabetes[17,19-21].

Leukotriene receptor antagonists: Leukotrienes are potent mediators in the signaling pathways of allergic inflammation and thus play a central role in the pathophysiology of asthma. Leukotriene antagonists (LTRAs) function to reduce inflammation through this

pathway and can reduce asthma exacerbations and improve lung function in persistent asthma. Few studies have been conducted to analyze the effects of this medication class exclusively and large, well-designed studies of LTRA use in pregnancy are lacking.

Theophylline: Theophylline is a drug with mild bronchial anti-inflammatory effects. While it is not a preferred agent in the treatment of asthma due to prevalent adverse effects, drug-drug interactions and the need for monitoring of serum concentrations, theophylline may be beneficial in selected patients. In a prospective study, 153 women with asthma including 85 receiving theophylline were followed throughout the course of their pregnancy. Results of the study demonstrated a significantly reduced risk of preeclampsia in patients treated with compared to those not receiving theophylline. Investigators suggested that theophylline's ability to increase cAMP levels and thereby reduce vascular reactivity and platelet aggregation may result in the decreased incidence of preeclampsia[22].

Available evidence suggests that use of theophylline in pregnancy is likely safe, the drug is currently classified as a category C medication by the United States FDA.

Mast-cell stabilizers: Mast-cell stabilizers prevent mast-cell release of histamine and other inflammatory mediators during allergic response. Although, they are not commonly compared to other asthma medications, they are considered effective second-line agents for asthma control. Very few studies have evaluated the use of mast-cell stabilizers for asthma during pregnancy and major limitations of available studies include small patient sample size, concurrent use of other medications and comparison of treatment groups to healthy, non-asthmatic controls. Nevertheless, cromolyns are considered safe for use during pregnancy due to limited systemic bioavailability and could be an appropriate adjunctive therapy in some patients[6].

Omalizumab: Omalizumab is a recombinant monoclonal anti-IgE therapy that works by binding and neutralizing the effects of IgE in basophils and mast cells, thereby preventing downstream allergic inflammation. The biologic therapy is reserved for patients with moderate to severe persistent asthma who are unable to be controlled by medium- to high-dose ICS plus LABA therapy. As a relatively new therapy, evidence for safety of omalizumab use in pregnancy is very limited.

Human gestational studies were identified for the inhaled corticosteroids (ICSs) beclomethasone, budesonide and triamcinolone and for cromolyn sodium, theophylline and salmeterol. Human pregnancy data support an FDA Pregnancy Category B rating for budesonide. Pregnancy category B ratings for cromolyn, nedocromil, montelukast and zafirlukast are based primarily on safety in animal reproduction studies. ICSs other than budesonide, theophylline, zileuton and long-acting β2-adrenergic agonists are pregnancy category C.

Aims and objectives:

- To study the fetomaternal outcome of exacerbations of asthama in pregnancy
- To study the effect on dosage of drugs for asthama in pregnancy
- To study the goals for management of asthama in pregnancy

MATERIALS AND METHODS

The study was conducted in the department of obstetrics and gynaecology SKIMS Soura over a period of two years. A total of 240 pregnant women were included in the study after taking a proper informed consent. Patients were observed for various variables like age, parity, residence. They were divided into two groups A (with exacerbation) and group B (without exacerbations). Maternal and fetal adverse effects of exacerbation of asthama on pregnancy was studied. Also any increase in dose and the number of drugs used were noted.

Inclusion criteria was pregnant women with asthama. However, patients with placenta previa and accreta, heart diseases, IVF conceptions, autoimmune disorders were excluded from the study.

Statistical analysis: Statistical package for social sciences version 22 was used for data analysis. The result was expressed in percentages or mean SD, as specified. Categorical data was analysed by using Pearson's Chi- square test and quantitative data by using two sample independent t-tests, $p<0.05$ was taken as statistically significant.

RESULTS

Table 1 shows that 240 patients were enrolled in the study aged between 20-39 years with a mean age of 29.3+4.01 years. Majority of patients i.e., 101 (42.1%) were between age group of 30-34 years followed by 80 (33.3%) patients who were between 25-29 years. 32 (13.3%) patients were between 20-24 years of age group while 27 (11.3%) patients were 35-39 years of age.

Table 2 shows 174 (72.5%) women were primigravidae and 66 (27.5%) were multigravida.

Table 3 shows that Majority of patients i.e., 192 (80%) were rural and only 20% were urban.

Table 1: Age distribution of study patients

Age (years)	No.	Percentage
20-24	32	13.3
25-29	80	33.3
30-34	101	42.1
35-39	27	11.3
Total	240	100.0

Mean±SD (range): 29.3±4.01 (20-39)

Table 2: Parity distribution of study patients

Parity	No.	Percentage
Primi	174	72.5
Multi	66	27.5
Total	240	100.0

Table 3: Demographic variables

Location	No.	Percentage
Urban	48	20.0
Rural	192	80.0
Total	240	100.0

Table 4 :Additional dose of drugs required in the study patients

	Group A		Group B	
Drugs	No.	Percentage	No.	Percentage
SABA frequency (increased)	None	None	46	19.16
SABA+ICS	25	10.41	34	14.16
LABA+ICS	92	38	None	None
ICS+ORAL CS	40	16	None	None
Intubation/mechanical ventilation	3	1.25	None	None
Total	160	66.66	80	33.33

Table 5: complications in groupwhich had exacerbations [a] versus the group which did not have exacerbations [b]

	Group A		Group B		
Complications	No.	Percentage	No.	Percentage	p-value
Anaemia	20	8.30	12	5	0.029
Hypertensive Disorder in pregnancy	86	35.80	7	2.9	0.025
Recurrent hospitalization	34	14.16	NONE	NIL	
Antepartum haemorrhage	2	0.83	1	0.4	0.619
Preterm labour	47	19.58	3	1.25	0.025
Gestational DM	5	2.08	4	1.6	0.420
Postpartum heamorrhage	10	4.10	4	1.6	0.025
Total	160		27	0	0.021

Table 6: Foetal and neonatal outcome in the study

	Group A		Group B		
Outcomes	No.	Percentage	No.	Percentage	p-value
Apgar score <7 at 5 min	32	13.30	6	2.50	0.012
NICU admissions	24	10.00	4	1.66	0.329
Perinatal morality	3	1.25	1	0.41	0.824
Low birth weight	28	11.60	6	2.50	

Table 4 shows that out of 240, 160 (66.66%) patients had exacerbation. In group A, 10.41% required SABA+ICS, 38% required LABA+ICS, 16% required ICS+oralcs, 1.25% required intubation. While in group B none was intubated, majority were controlled by SABA (19.16%), though the frequency of use was increased, 14.16% were controlled on SABA+ICS.

Table 5 shows there was increase in complications in Group A as compared to Group B and the difference between the two was statistically significant. Total 35.8% patients in Group A had hypertensive disorders of pregnancy as compared to 2.9% in Group B. Recurrent hospitalization was seen in 14.16% in group A while none in group B. Preterm labour was seen in 19.58% in group A and 1.25% in group B.

Table 6 shows Apgar score of <7 was present in 32 (13.3%) babies in study group A and 6 (2.5%) in group B the difference was statistically significant. In study group A (10%) babies had NICU admissions out of which 3 (1.25%) babies had perinatal mortality. In comparative group B (1.66%) went to NICU and only 1 (0.41%) baby had perinatal mortality. The difference in the data regarding the perinatal mortality in both the groups was statistically significant.

DISCUSSIONS

The study was conducted in the department of obstetrics and gynaecology SKIMS Soura over a period of two years. A total of 240 pregnant women were included in the study after taking a proper informed consent.Fetomaternal outcome was evaluated.

The total 240 patients enrolled in the study, aged between 20 to 39 years with a mean age of 29.3+4.01 years. Majority of patients i.e., 101 (42.1%) were between age group of 30-34 years. 174 (72.5%) women were primigravidae and 66 (27.5%) were

multigravida. Majority of patients i.e., 192 (80%) were rural and only 20% were urban. In our study, out of 240, 160 (66.66%) patients had exacerbation i.e, group A. This group required higher drugs and in increased dosage. While only 10.45% continued to use SABA+ICS, majority of them, 38% required LABA+ICS and 16% required ICS+ oral CS. Also 1.25% had the need for intubation.While in group B none was intubated, majority were controlled by SABA (19.16%) only, though the frequency of use was increased, 14.16% were controlled on SABA+ICS.

It was seen that there was increase in complications in group A as compared to group B and the difference between the two was statistically significant. Total 35.8% patients in group A had hypertensive disorders of pregnancy as compared to 2.9% in group B. Recurrent hospitalization was seen in 14.16% in group A while none in groupB. Preterm labour was seen in 19.58% in group A and 1.25% in group B.

Majority of neonates had low birth weight (11.6%) in group A, while in group B only 2.5 had low birth weight. In group A majority of the babies had low Apgar score of <7 (13.3%) and only (2.5%) in group B. In study group A (10%) babies had NICU admissions out of which 3 (1.25%) babies had perinatal mortality. In group B (1.66%) went to NICU and only 1 (0.41%) baby had perinatal mortality. The difference in the data regarding the perinatal mortality in both the groups was statistically significant.

Thus it was seen that the women with exacerbations of asthma are more likely to have fetal and maternal complications like low birth weight baby, NICU admissions, hypertensive disorders of pregnancy, preterm birth and need of additional drugs to control asthama, as compared to asthmatic women without exacerbations, Namazy *et al*.[23] suggesting that prevention of exacerbations during pregnancy may also lead to improvements in perinatal outcome. Preconception care is also needed, with recommendations to offer advice about the uncontrolled asthma or asthma exacerbations.

CONCLUSION

Exacerbations of asthama adversely affects the fetomaternal outcome. Asthamatic pregnant women who did not have exacerbations did not have much complications, thus by following proper guidelines asthama should be managed properly in pregnancy. Allergins, cold exposure and bronchoconstrictive drugs should be avaoided in them. Exacerbation free asthama in pregnancy has better outcome.

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