Volume 29 / Issue 1 / January-June 2015

Indian Journal of Allergy, Asthma & Immunology

www.ijaai.in



Official Publication of Indian College of Allergy, Asthma and Applied Immunology (ICAAI)

Physicians' prescribing pattern, perceived safety of asthma medications and management of asthma during pregnancy in Nigeria

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Access this article online
Website: www.ijaai.in
DOI: 10.4103/0972-6691.162974
Quick Response Code:

ABSTRACT

Background: Under-treatment of asthma in pregnancy can result in adverse fetal and maternal outcomes. The potential risk of teratogenicity may limit prompt and adequate management of medical disorders in pregnancy. Objectives: The objective of this study was to investigate the physicians' prescribing pattern, their perceived safety of asthma medications and management of asthma during pregnancy in obstetric care units of a developing country. Materials and Methods: A self-administered questionnaire containing case vignettes and multiple choice questions were used to evaluate the physicians prescribing practices, their perceived safety of medications and approach to asthma management in pregnancy. Result: Of the 144 doctors that participated in the study; 76 (52.8%) would prefer inhaled long-acting β 2 agonist and inhaled corticosteroids combination (LABA/ICSs) while 10 (6.9%) would prefer leukotriene antagonists (LTA) as a controller medication in the first trimester of pregnancy. Short-acting β 2 agonists, LABA, and theophylline were perceived to be safest throughout pregnancy, corticosteroids and cromoglycates were considered unsafe in first trimester while LTA were considered unsafe in all the trimesters by a majority of respondents. To gain asthma control in a patient already on low dose LABA/ICS, 94 (65.3%) of the doctors would refer their to a respiratory specialist instead of increasing the dose of LABA/ICS. Less than half (42.3%) were willing to address medication compliance in nonconforming patients. The majority (72.2%) of the doctors' self-reported nonadherence to the asthma treatment guideline. Conclusion: Even though, most of the physicians caring for pregnant women seem to prefer LABA/ICS combination for asthma control, there exist a knowledge gap in the stepwise management of asthma, perceived safety of most asthma medications and tackling poor medication adherence.

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How to cite this article: Desalu OO, Adesina KT, Adeoti AO, Fadare JO, Sanya EO, Shorunmu T, et al. Physicians' prescribing pattern, perceived safety of asthma medications and management of asthma during pregnancy in Nigeria. Indian J Allergy Asthma Immunol 2015;29:18-23.

INTRODUCTION

Asthma is by far the most common respiratory disease in pregnancy with a prevalence ranging from 2.1% in India and 3.8–8% in USA.^[1,2] The burden of asthma has been growing over the past 30 years, particularly in the low and middle-income countries least able to absorb its impact.^[3] Among women, this illness is also becoming a cause for concern, as its prevalence has increased among all women over the past decade.^[4] The clinical course of asthma during pregnancy often changes, and patients may require close follow-up and adjustment of medications to achieve control. Nearly one-third of asthmatic patients experience worsening of symptoms in pregnancy; in one-third it becomes less severe, and the condition in the remaining one-third remains unchanged.^[3] The goal of asthma treatment in pregnant and nonpregnant state is to achieve and maintain clinical control. The step-wise management of asthma based on control in adults is recommended by Global Initiative for Asthma and other major respiratory society in the world.^[3,5-7] Failure to achieve optimal asthma control in pregnancy can result in adverse fetal outcomes such as increased perinatal mortality, increased prematurity, and low birth weight.^[3] This generalization has been contradicted in recent prospective studies.^[8,9] The overall pregnancy outcome for women and perinatal prognosis for children born to women with well-controlled asthma in pregnancy are similar.^[8-10] Inhaled glucocorticosteroids are the most effective anti-inflammatory and controller medications currently available.^[3,5-7] The American College of Obstetrics and Gynecology recommends that systemic steroids be used when clinically indicated and that benefits for maternal and fetal health are perceived to outweigh risks.^[11] Most controller medications used to achieve optimal asthma control in asthma treatment outside of pregnancy are also not contraindicated during pregnancy. There is little evidence to suggest an increased risk to the fetus with the use of most asthma medications in pregnancy notwithstanding, the safety concern still exists with the use of medications in pregnancy.^[3] Recent studies have revealed that there is low prescription of controller medication and under-treatment of asthma in pregnancy^[12-14] and in the nonpregnant state;^[15] this trend is due to physician knowledge gap, perceived safety concerns and their reluctance to weigh risks versus benefits of medication use in pregnancy in individual patients. Unlike in other regions of the world, there is a paucity of data on asthma management in pregnancy among physicians in sub-Saharan Africa. Data on the prescribing pattern of physicians caring for pregnant women with asthma would provide valuable information to improve asthma management during pregnancy and might also be useful in planning continuing professional development programs for physicians and other health professionals. The aim of this study was to investigate the physicians'

prescribing pattern, perceived safety of asthma medications and management of asthma during pregnancy in obstetric care units of a developing country.

MATERIALS AND METHODS

Study design

The study was a cross-sectional questionnaire-based study carried out among medical doctors caring for pregnant women in four hospitals located in South-West and North-Central Nigeria. The study was carried out from October 2013 to December 2013.

Study setting

The study was conducted in the Departments of Obstetrics and Gyneacology in three Tertiary Hospitals and one hospital that provides primary healthcare service. These hospitals have resident doctors (registrars and senior registrars), and consultants.

Participants' recruitment

Eligible physicians were approached and informed about the study; physicians who consented to participate in the study were requested to complete the questionnaire during their work-free period according to their own understanding of the subject. They were also asked to do so in a quiet environment without interference from their colleagues. The participants were reminded about questionnaire completion after a period of 1-week and those who failed to return the questionnaire were excluded from the study. The study design was approved by the Research Ethics Committee of the study centers.

Survey instrument

We used a pretested, self-administered structured questionnaire that was used in the previous study in Australia.^[16] Permission to use the questionnaire was granted by the authors of the previous study. The questionnaire was used to obtain demographics and the physicians prescribing practice, their perceived safety of different asthma medications in each trimester and their likely approach to asthma management in pregnant women with the help of three case vignettes.

Statistical analysis

The data obtained were analyzed using the Statistical Package for the Social Sciences, version 16.0 (SPSS Inc., Chicago, IL, USA), and descriptive statistics were performed to examine the general characteristics of the physicians. Pearson's Chi-square and Fisher's exact test were employed in order to test the significance of categorical variables. The data that had non-Gaussian distribution, their reference range was defined as the central 95% of the area under the distribution curve of values (i.e., from 2.5% to 97.5%), values of P < 0.05 were considered significant.

RESULTS

A total of 180 questionnaires were sent out, but 144 were completed and returned by the respondents giving a response rate of 80% in the study. The mean age of the respondents was 33 ± 5 years, 104 (72.2%) were males, 18 (12.5%) were general practitioners and 124 (86.1%) of the physicians were working in the urban areas. The median year of practice was 6 years (2.5th to 97.5th percentile range of 3–19 years). On average, 138 (95.8%) provide shared care in a year and 124 (86.1%) reported that <10% of these pregnant women have asthma and none of them had a nurse or asthma educator assisting in asthma management [Table 1]. One hundred and four (72.2%) of the respondents reported that they do not follow any guideline for managing asthma and 62 (43.0%) reported to a have a good knowledge of asthma.

Prescribing pattern of asthma medications

In a pregnant patient with worsening asthma in her first trimester, 76 (52.8%) of the respondents would prefer long-acting β 2 agonists and inhaled corticosteroid (LABA/ICS) combination and 56 (38.9%) would prefer ICS while 10 (6.9%) would prefer leukotriene antagonists (LTA) [Table 2].

Perceived safety of asthma medications in pregnancy

Most of the respondents considered the use of the ophylline, short-acting $\beta 2$ agonists (SABA) and inhaled LABA safe in a pregnant woman in all the three trimesters. Oral and ICSs and cromoglycates were considered safe to use except in first trimester. LTA were considered to be unsafe in all the three trimesters of pregnancy [Table 3].

Stepwise management of asthma based on control

When asked about intended action in the management of a woman who recently became pregnant and has been well controlled on $(250/25 \ \mu g)$ (fluticasone/salmeterol), which is a LABA/ICS combination. Majority (61.1%) intend to continue her on the same medications, 28 (19.4%) would refer her to another health professional (internist, respiratory specialist) and 10 (6.9%) would decrease the dose of LABA/ICS. If her asthma deteriorated few weeks later, 12 (8.3%) of the respondents would increase the dose of her LABA/ICS, while 94 (65.3%) of the respondents would refer her to respiratory specialist [Table 4].

Medication compliance in nonconforming patients

The respondents were given a scenario of a patient who is 18 weeks pregnant and frequently using a SABA inhaler and noncomplying with her LABA/ICS because she fears it will harm her unborn child. In response to the next intended action 62 (43.1%) of the physicians would give a prescription for SABA inhaler; discuss the importance and safety of LABA/ICS and reinforce the need for her to continue with it, 38 (26.4%) would give a prescription for SABA inhaler and refer her to a respiratory specialist. 30 (20.8%) would refer

Table 1: General characteristics of the respondents

Characteristic	п (%)
Median year of practice	33.0±6.0
Sex	
Male	104 (72.2)
Female	40 (27.8)
Current position in hospital	
Medical officer/SH0	18 (12.5)
Resident	94 (65.3)
SR	10 (6.9)
Consultants	22 (15.3)
Current location of practice	
Urban area	124 (86.1)
Rural area	20 (13.9)
Pregnant women you provide shared care per year	
None	4 (4.3)
<10	11 (12.0)
11-20	6 (6.5)
>20	71 (77.2)
Proportions of pregnant women with asthma (%)	
None	6 (4.2)
<10	16 (11.1)
11-20	4 (2.8)
20-30	114 (81.9)
>30	0 (0.0)
Availability of nurse educator	
Yes	40 (22.8)
No/don't know	104 (72.2)
Self-perceived knowledge of asthma*	
Very poor	0 (0.0)
Poor	2 (1.4)
Average	71 (51.4)
Good	54 (37.5)
Very good	8 (5.6)

*6 missing. SHO - Senior house officer, SR - Senior resident

Table 2: Respondents preference of asthma preventive medication in pregnancy (n = 144)

Types of asthma	n (%)			
controller medication	First preference	Second preference		
ICS				
With LABA	76 (52.8)	24 (16.7)		
Monotherapy	56 (38.9)	32 (22.2)		
LABA	52 (36.1)	30 (20.8)		
Cromolyns	34 (23.6)	22 (22.2)		
LKT	10 (6.9)	42 (29.2)		

Do not add up because more than one 1st or 2st preference is allowed. ICS - Inhaled corticosteroids, LABA - Long-acting β 2 agonists, LKT - Leukotriene inhibitors

her to a respiratory specialist without giving the prescription for the ventolin inhaler [Table 5].

The result of this study also revealed that 67 (72.8%) respondents had never intervened and promoted compliance with preventive asthma medication(s) during pregnancy.

DISCUSSION

Asthma is one of the medical conditions encountered during pregnancy, and many international asthma guidelines have been produced to ensure evidence based management of the condition during pregnancy.^[3,5-7,11] There are few studies in sub-Saharan Africa and developing countries that have

Asthma medication	п (%)					
	First trimester		Second trimester		Third trimester	
	Yes	No	Yes	No	Yes	No
Drugs						
Sodium cromoglycate	66 (45.8)	78 (54.2)	94 (65.3)	50 (34.7)	96 (66.7)	48 (33.3)
ICS						
Fluticasone	56 (38.9)	88 (61.1)	86 (59.7)	17 (18.5)	94 (65.3)	50 (34.7)
Budesonide	42 (29.2)	102 (70.8)	74 (51.4)	70 (48.6)	84 (58.3)	60 (41.7)
Beclomethasone	66 (45.8)	78 (54.2)	98 (68.1)	46 (31.9)	102 (70.8)	42 (21.2)
Leukotriene antagonist						
Monteleukast	20 (13.9)	124 (86.1)	58 (40.3)	86 (59.7)	66 (45.8)	78 (44.2)
Zafirlukast	28 (19.4)	106 (80.6)	58 (40.3)	86 (53.7)	64 (44.4)	80 (55.6)
LABA						
Salmeterol	82 (56.9)	62 (43.1)	92 (63.9)	54 (36.1)	92 (63.9)	54 (36.1)
Theophylline						
Aminophylline	74 (51.4)	70 (48.6)	92 (63.9)	54 (36.1)	102 (70.8)	42 (29.2)
Oral corticosteroids						
Prednisolone	64 (44.4)	80 (55.6)	84 (58.3)	58 (41.7)	94 (65.3)	50 (34.7)
SABA						
Salbutamol	124 (86.1)	20 (13.9)	126 (87.5)	18 (12.5)	124 (86.1)	20 (13.9)

Table 3: Perceived safety of asthma medications during pregnancy in the three trimesters (n=144)

ICS - Inhaled corticosteroids, LABA - Long-acting β 2 agonists, SABA - Short-acting β 2 agonists

Table 4: Management of asthma in pregnancy based on control $(n=144)$	
Respondents responses	n (%)
Clinical scenario: When respondent encounter a pregnant woman with well controlled asthma on seretide (250/25) (fluticasone/salmeterol) one puff twice daily and ventolin (salbutamol) inhaler as required. What is your intended action?	
Continue her on the same medications	88 (61.1)
Refer her to respiratory specialist	28 (19.4)
Decrease the dose of seretide	10 (6.9)
Change her to a different controller medication(s)	6 (4.2)
Stop seretide	6 (4.2)
Others/missing	6 (4.2)
Clinical scenario: A pregnant woman who was previously well controlled asthma on seretide (250/25) (fluticasone/salmeterol) now return with deteriorating asthma. What is your intended action?	
Refer her to respiratory specialist	94 (65.3)
Change her to another preventive medication	18 (12.5)
Increase the dose of seretide	12 (8.3)
Add another preventive medication	8 (5.6)
Continue with the seretide and simply monitor her closely	6 (4.2)
Others/missing	6 (4.2)

Table 5: Managing poor asthma medication compliance in pregnancy (n = 144)

Clinical scenario: One of your regular patients is 20 weeks pregnant	
and is, frequently using ventolin inhaler and noncomplying with her seretide because she fears it will harm her unborn child. She has no other medical conditions nor is she taking any other medications. What is your intended action?	
I would give a prescription for ventolin inhaler; discuss the importance and safety of seretide and reinforce the need for her to continue seretide	3.1
I would give a script for ventolin inhaler and refer her to a 38 (2 respiratory specialist	6.4
I would refer her to a respiratory specialist without giving the 30 (2 prescription for the ventolin inhaler	0.8
would give a script for ventolin inhaler and initiate her on 6 (4 another preventer/controller medication	.2)
I would give a script for ventolin inhaler and monitor her condition 4 (2	.8)
Missing/no response 4 (2	.8)

previously evaluated the prescribing pattern, perceived safety and management of asthma during pregnancy by physicians in this setting. This study demonstrated that the majority of the doctors would prefer LABA/ICS as controller medication in a pregnant patient with worsening asthma. Almost 60% would continue the LABA/ICS combination when a pregnant woman is well controlled on it, and if the asthma control deteriorated 15.9% would increase the dose. Most of the respondents perceived theophylline, SABA and LABA safe in a pregnant woman in all the three trimesters. In case of poor patients' compliance to LABA/ICS due to a safety concern, less than half of the doctors (42.3%) would discuss the importance and safety of asthma medication and compliance. The result of this study also revealed that a significant proportion of the physicians do not follow any guideline for managing asthma in pregnancy.

In this study, almost 53% preferred LABA/ICS as the controller medication in the first trimester. According to the asthma guidelines, ICS are the most effective treatment for asthma for adults and children of all ages.^[3,5-7] ICS was recommended as a monotherapy for the initial treatment for most treatment-naïve patients with persistent asthma symptoms or combined with inhaled long-acting inhaled β 2-agonists when symptoms at the initial consultation suggest that asthma is severely uncontrolled.[3,5-7,11] LTA was the least preferred medication in the first trimester for worsening asthma, and this finding is similar to the Australian study. This result of this study is in contrast to ICS monotherapy reported from Australia^[16] where most of the general practitioners providing shared maternity care preferred ICS. The differences of this result from our study might be due to the fact that in the last few years ICSs and LABA in combined form was the only readily available controller medication in the country and these two drugs were not readily or unavailable as a single pharmacological agent in most hospital. A previous study to assess the medication availability for asthma in Nigeria reported that ICS was available in 23.5% and inhaled LABA/ICS in 50.0% of the surveyed tertiary hospitals.^[17] This might have prompted most doctors to prescribe LABA/ICS instead of LABA or ICS when they were not indicated. The other reason might be due to the physician perception that the addition of a LABA to ICS is most likely to provide the greatest benefit as the next step in treatment. The ICS was gradually withdrawn from the market by the pharmaceutical company for commercial reasons and also because a lower dose of ICS in combination with LABA has been found to achieved better asthma control when compared with higher dose ICS monotherapy. Sixty percent of physicians in this study would continue the LABA/ICS combination when a pregnant woman is well controlled on it. This result is higher than 25% among the obstetricians, 47.5% of primary care physician in Spain^[18] and <71% among GPs in Australia.^[16] Unfortunately 4.2% of the physicians preferred to stop a winning therapy while 6.9% will reduce the dosage. The consequences of these intended action in the real world are loss of asthma control and poor outcome. This study also exposed their knowledge gap in the management of the deteriorating asthma case, whereas most of the doctors will refer the patients with deteriorating asthma to other health professional like internist and respiratory specialist. The referral to other professionals like the respiratory physician is due to their lack of knowledge asthma management. Referring to other doctors is not a bad action because management or co-management of these patients by a physician with sufficient experience in caring for pregnant asthmatics improves outcome,^[10] but it is not in conformity to the established guidelines. The following criteria are used to guide decisions about referrals; patients who experience a life-threatening exacerbation; who fail to meet treatment goals; with severe persistent symptoms, need immunotherapy; require continuous systemic corticosteroid therapy or more than one short course of corticosteroids per year; or have complicating comorbidities.^[19-21] It is an irony that only 15.9% would increase the dose of medication, which is in accordance with the recommendation of the treatment guidelines. Our observation contrasted sharply with the 67% found in another study^[16] and is a reflection of the knowledge of and adherence to asthma guidelines in the two different settings. In this study, 72% of the respondents did not follow any guideline for managing asthma, and this is <83.7% among obstetricians in Spain.^[18] The behaviors of physicians in this study are similar to what was reported in another study where 83.7% of obstetrician and gynecologists seldom or never use guideline for the treatment of pregnant asthmatic women. In this study, less than half of the participants (43.0%) reported to a have a good knowledge of asthma and this finding has implicated the need for more awareness and continuing professional development among physicians caring for pregnant women. Regarding the safety of asthma medications, only theophylline, SABA and LABA were considered safe throughout pregnancy. Most of the doctors will prefer to avoid oral and ICSs in the first trimester and leukotriene throughout the pregnancy. There is little evidence to suggest an increased risk to the fetus with most medications used to treat asthma in pregnancy. Appropriately monitored use of theophylline, inhaled glucocorticosteroids (budesonide has been most extensively studied) and leukotriene modifiers (specifically montelukast) are not associated with an increased incidence of fetal abnormalities.^[5-7] The avoidance of ICS, which is the most important asthma medication may be attributed to the limited access to safety data on these newer medications and/or prescribers' lesser familiarity with these drugs.^[16] It may also be due to lack of agreement with current guidelines by the prescriber or their inertia of previous practice. This also signifies that many health care professionals surveyed seem not to consider the concept of asthma control versus potential drug adverse effect as important. This conservative approach is very common among the obstetricians than other health care professionals managing patients with asthma.^[18] It is not encouraging that <50% of the physicians would address poor adherence when they encounter the situation; the result of our study is in contrast to 82.0% in a previous study.^[16] Literature has shown that pregnant women reduce their asthma medications during pregnancy either due to their attitude or to altered prescribing practices of their physicians.^[7,22,23]

Strengths and limitations

This study has provided information about physicians prescribing pattern and likely management of asthma in pregnant women in the obstetric unit in the setting of a developing country like Nigeria. All cadres of doctors providing care in an obstetric care unit of the participating hospitals were involved in the study. Another strength of the study is the fact that four hospitals were involved in the study. This study is limited by its relatively small sample size and nonprobability sampling. This study may implicate future national study on drug prescription pattern among primary care practitioners and obstetricians.

CONCLUSION

Even though most of the physicians caring for pregnant women seem to prefer LABA/ICS combination for asthma control, there exist a knowledge gap in the stepwise management of asthma, perceived safety of most asthma medications and tackling poor medication adherence.

Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

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