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Research Article

Prevalence and associated factors of steroid induced impaired glucose metabolism in obstructive lung diseases, Jimma, and Southwest Ethiopia, Africa

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ABSTRACT

Background: Impaired glucose metabolism is one of the complications of steroid therapy in patients with Obstructive lung diseases. Steroid induced impaired glucose metabolism is a serious, but often overlooked, metabolic disorder; it is largely remains under diagnosed. Although this has been reported from western countries, there is no study that evaluated the prevalence of impaired glucose metabolism and its associated factors in Ethiopia in general and in the study area in particular. Aim of the study was to determine the prevalence and associated factors of steroid induced impaired glucose metabolism in Obstructive lung diseases at Jimma University Specialized Hospital chest clinic from November 2014 to July 2015.
Methods: A hospital based cross-sectional study design was conducted. In this specific study Convenience sampling used. Data was collected through patient interview and chart review. Serum random glucose was determined during Hospital visit. Descriptive statistics and bivariatelogistic regression analysis were done. A P-vale of <0.05 was considered statistically significant.
Results: The study comprised of 90 patients with Asthma and COPD taking systemic steroids visited chest clinic during the study period were included in the analysis. 11.1% of the study subjects had impaired glucose metabolism. The level of RBS level was not associated with any of the independent variables studied (Age and sex of the patient, waist circumference, family history of DM and dose and duration of systemic steroid).
Conclusions: This study found that the prevalence of impaired glucose metabolism in obstructive lung diseases on systemic steroids is significant independent of the effect of dose and duration of steroids.

Keywords: Impaired glucose metabolism, Obstructive lung diseases, Steroid's (prednisolone), Ethiopia

INTRODUCTION

Asthma is a syndrome characterized by airflow obstruction that varies markedly, both spontaneously and with treatment. Asthmatics harbor a special type of inflammation in the airways that makes them more responsive than non-asthmatics to a wide range of triggers, leading to excessive narrowing with consequent reduced airflow and symptomatic wheezing and dyspnea.

Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by airflow limitation that is not fully reversible.[1] Since the introduction of glucocorticoids in the 1950s, they have played a pivotal role in the treatment of various inflammatory diseases, including respiratory diseases. As they decrease inflammation and minimize tissue damage, glucocorticoids have been used widely to treat idiopathic interstitial pneumonia, chronic obstructive pulmonary

disorders, endobronchial tuberculosis, sarcoidosis, hypersensitivity pneumonitis, and other respiratory diseases.[2,5] It is now well established that inflammation of the airway wall plays a central role in the pathophysiology of asthma.

Corticosteroids are the cornerstone of anti-inflammatory treatment in asthma. Oral corticosteroids are generally considered to be the standard for airway anti-inflammatory and clinical effects, with only occasional patients having marked systemic effects. Inhaled corticosteroids produce fewer systemic effects and exert their benefit locally within the airways, although an effect on bone marrow has been suggested.

Studies measuring the effects of oral prednisolone and/or inhaled corticosteroids on clinical parameters in asthma generally show a significant improvement in lung function, airway hyper responsiveness, rescue medication, and symptoms after treatment periods ranging from one to eight weeks. Few studies have made direct comparisons between oral and inhaled corticosteroids as initial treatment or during asthma exacerbations. The results have generally shown comparable effects on clinical parameters.[3,16]

However, glucocorticoids have various adverse effects. They can cause glaucoma, fluid retention, increased blood pressure, increased blood sugar, menstrual irregularities, weight gain, stomach pain, insomnia, and infection. Impaired glucose metabolism is one of the commonest adverse effects. Glucocorticoids not only exacerbate hyperglycemia in patients with known diabetes mellitus (DM), but also cause DM in patients without documented hyperglycemia before the initiation of glucocorticoid therapy.

The hyperglycemic condition is transient in many cases, but some patients may develop polydipsia, polyuria, and repeated infections. Especially in the elderly, there is a risk of precipitating hyperglycemic hyperosmolar states, including coma. In the long-term, the overall burden of repeated increases in blood glucose may increase cardiovascular risk and the risk of micro vascular complications.[16]

Diabetes mellitus, chronic obstructive pulmonary disease (COPD), and asthma are increasing in prevalence worldwide. The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 285 million in 2010. Based on current trends, the International Diabetes Federation projects that 438 million individuals will have diabetes by the year 2030.

In 2010, the prevalence of diabetes ranged from 11.6 to 30.9% in the 10 countries with the highest prevalence (Naurua, United Arab Emirates, Saudi Arabia, Mauritius, Bahrain, Reunion, Kuwait, Oman, Tonga, Malaysia—in descending order). In the most recent estimate for the United States (2010), the Centers for Disease Control and Prevention (CDC) estimated that 25.8 million persons, or 8.3% of the population, had diabetes.[1,16]

The prevalence of type 2 DM and its harbinger, IGT, is highest in certain Pacific islands and the Middle East and intermediate in countries such as India and the United States. Diabetes is a major cause of mortality, but several studies indicate that diabetes is likely underreported as a cause of death. In the United States, diabetes was listed as the seventh leading cause of death in 2007; a recent estimate suggested that diabetes was the fifth leading cause of death worldwide and was responsible for almost 4 million deaths in 2010 (6.8% of deaths were attributed to diabetes worldwide.[1]

In general, the prevalence of metabolic syndrome increases with age. The highest recorded prevalence worldwide is in Native Americans, with nearly 60% of women ages 45–49 and 45% of men ages 45–49 meeting National Cholesterol Education Program and Adult Treatment Panel III (NCEP: ATPIII) criteria.[1]

Diabetes mellitus is one of the most prominent non communicable diseases that are undermining the health of the people in sub-Saharan Africa and placing additional burdens on health systems that are often already strained. In 2011, 14.7 million adults in the African Region of the World Health Organization (WHO) were estimated to be living with diabetes mellitus. Of all of WHO's regions, the African Region is expected to have the largest proportional increase (90.5%) in the number of adult diabetics by 2030.[33]

In 2011, a systematic review summarized the prevalence and outcomes of diabetes in the Sub-Saharan Africa. It confirmed the increase in diabetes pre-valence and its complications in the Sub-Saharan Africa. In Ethiopia, few studies have evaluated the prevalence of hypertension and diabetes. For instance, a study conducted in 1982 among Ethiopian Bank employees attending a clinic in Addis Ababa found prevalence of 3.8% and 1.2% for hypertension and diabetes Respectively.[34]

Many researchers have investigated prevalence of steroid induced Diabetes mellitus and impaired glucose metabolism in obstructive lung diseases; however the studies conducted in Ethiopia on this group of patients are limited. This study will assess the prevalence, clinical risk factors and clinical characteristics of steroid-induced impaired glucose metabolism in patients treated with glucocorticoid therapy for various respiratory diseases.[16]

To our knowledge, this will be the first study on impaired glucose metabolism to be conducted in the country, to quantify the magnitude of this metabolic abnormality, and assess for potentially associated factors among Obstructive lung disease patients in JUSH. This study will help to assess the extent of impaired glucose

metabolism and its associated factors among Obstructive lung diseases, in JUSH, and pinpoint where we are in terms of our current practice of recognition, diagnosis, and prevention of the problem and how we should prepare our strategy for better intervention.

The identification of factors associated with this is important in determining preventive strategies. It also further helps for creating awareness among treating physicians in the consideration of impaired glucose metabolism during optimal management at chest referral clinic.

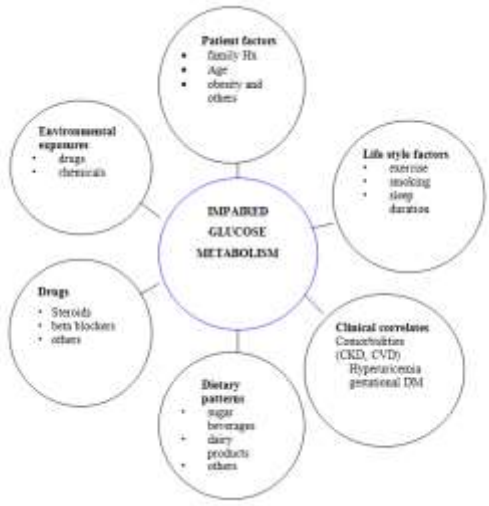

Figure 1: Conceptual frame work developed to depict factors related to impaired glucose metabolism after reviewing related literature, 2015.

METHODS

The study was conducted in JUSH which is found in Jimma town, 352 km Southwest of Addis Ababa. It provides services for approximately 9000 inpatient and 80000 outpatient attendances each year from the catchment population of about 15million people.

A total of 250 Asthma and COPD patients were visited chest clinic in 2006 E.C. The hospital has Medical, Pediatrics, OB/GYN, Surgery, Dental, Radiology, Ophthalmology, Anesthesiology and Psychiatry departments.

As of the outpatient service the hospital has specialty clinics where patients with problems like Asthma and COPD after discharge and from Medical OPDs are referred for follow up.

The actual number of Asthma and COPD patients having follow-up in the chest referral clinic is not known and there is only one day visit program per week by internists, residents, and medical interns. This study was conducted from November 10, 2014 to July 10, 2015. It is a hospital based Cross-sectional study.

Asthma and COPD patients taking steroids ≥18 years are included in this study. Whereas Already diagnosed Diabetic patients, Patients with cognitive impairment were excluded from this study. Data collection format containing individual patient characteristics was prepared before the data collection time.

The patients who were identified were assessed for inclusion into the study based on inclusion criteria. A structured questionnaire was used and patients were interviewed at JUSH chest follow up clinic during the study period to fill the data collection format with relevant information about patient socio-demographic characteristics, duration of the illness, number of previous symptoms over the day and night, related risk factors, and patient drug history.

Laboratory data like RBS and details of patient medications before interview and clinical characteristics of the patients were obtained from patient's medical record.

Serum glucose determination done at presentation to the hospital once the patients meet the inclusion criteria. A drop of blood was collected by lancet puncture from each patient. The blood samples analyzed within a minute at chest clinic. The normal range of the Laboratory for random blood glucose is <140 mg/dl.

Data collection was undertaken by total of three personnel one BSC Lab technologist and 2 internal medicine residents and two BSC nurses after they are trained for half day about impaired glucose metabolism associated with steroid therapy in asthma and COPD patients, objective of the study, variables on the questionnaire and its implication.

Then, they were assigned to fill the data collection format. All data collection activities were supervised by trained medical residents and principal investigator.

Each week, the investigator was checked the completeness and consistency of data collected by each data collector and the data was compiled. Each laboratory investigation was attached with the data collection format.

Then, the collected data will be organized, coded, entered, cleaned, and analyzed using SPSS version 20.0. A P-value of <0.05 was considered statistically significant in all tests of significance.

Operational definition

- *Impaired fasting glucose*-FBS between 100-125 mg/dl
- *Impaired glucose tolerance*-RBS between 140-199 mg/dl

- *Steroid induced IGM*-FBS≥100 mg/dl or RB≥because of steroid therapy in otherwise normal individuals.
- *Hyperglycemia*-an excess of glucose in the bloodstream, often associated with diabetes mellitus (FBS≥126 mg/dl or RBS≥200 mg/dl).
- *Obstructive lung diseases*-Asthma and/or COPD

RESULTS

A total of 90 patients with Asthma and COPD taking systemic steroids were included in the analysis. Forty six (51.1%) of them were males. The mean age (±14.8) of the study subjects was 48.41 years. Twenty six (28.9%) of them were in the age group of above 60 years. Thirty six (40%) of the patients were illiterate, whereas 27 (30%) and 10 (11.1%) of the respondents has completed primary and secondary school respectively.

Sixty nine (76.9%) of them were married. From the total study participants 28 (31.1%), 23 (25.6%), 23 (25.6%), 9 (10%) and two were farmers, housewife, government employee, merchants and students respectively. Half of the patients (50%) were from rural areas. The mean annual income is 15,340 birr (±13,664.56) (Table 1).

Table: 1. Socio demographic characteristics of obstructive lung disease patients who are on steroids at JUSH follow up chest clinic from November, 2014 to July 2015.

Socio demographic characteristics	Category	Frequency	Percentage
Age	≤19	1	1.1
	20-29	11	12.2
	30-39	9	10.0
	40-49	17	18.9
	50-59	26	28.9
	≥60	26	28.9
Sex	Male	46	51.1
	Female	44	48.9
Marital status	Single	12	13.3
	Married	69	76.7
	Divorced	1	1.1
	Widowed	8	8.9
Educational status	Not read or write	36	40
	1-4	12	13.3
	5-8	15	16.7
	9-12	10	11.1
	College/University	17	18.9
Occupation	Government employee	23	25.6
	Merchant	9	10.0
	Farmer	28	31.1
	Housewife	23	25.6
	Student	2	2.2
Annual income (In birr)	2000-4900	19	21.1
	≥5000	71	78.9
Residence	Urban	45	50
	Rural	45	50

Prevalence and factors associated with impaired glucose metabolism

Of the total 90 subjects in the study, 72 (80%) had Asthma and 18 (20%) COPD .There was no significant difference in glucose metabolism by gender (p=0.326), there is no effect of age on glucose metabolism (p=0.403). Thirty eight (42.2%) of them had prior hospital admissions and the majority with a frequency of not more than once the main reason being acute exacerbation (40%).

The majority stayed at hospital for recent hospitalization only for 24 hours. Sixty seven (74.4%) of them were adherent to their outpatient medications. Dual treatment with steroids and Beta agonists were the drugs used as outpatient (90%). Among 72 patients with Asthma the majority 28 (31.1%) patients are under category of Mild intermittent.

Half (50%), Fourty three (47.8%), Two (2.2%) were on average dose of steroid (prednisolone equivalent) less than 20 mg/dl, between 20 and 40 mg/dl and more than 40 mg/dl respectively and Fourty nine (54.4%) used steroids for more than four weeks.

Eighty eight (97.8%) has no family history of DM and among all women only one patient has history of gestational DM. Of the total study subjects visited JUSH chest clinic during the study period, Twenty four (26.7%) were with abnormal record of waist circumference and there was no strong association between waist circumference and glucose metabolism (p=0.363).

Ten (11.1%) had impaired glucose test results.

Table: 2. Clinical characteristics of Obstructive lung disease patients who are on steroids at JUSH follow up chest clinic from November, 2014 to July, 2015.

Clinical characteristics		Frequency	Percentage
Type of the disease	Asthma	72	80
	COPD	18	20
Prior asthma/COPD related admission	Yes	38	42.2
	No	52	57.8
Frequency of admission	Once	24	26.6
	More than once	14	15.6
Condition associated with recent admission	Acute Exacerbations	36	40
	Other comorbidities	2	2.2
Days of hospital stay for recent hospitalization	24 hr.	25	27.8
	24hr-7 days	12	13.3
	>7 days	1	1.1
History of drug interruption	Yes	23	25.6
	No	67	74.4
Drug adherence	100%	58	64.4
	Optimal	15	16.7
	Suboptimal	17	18.9
Outpatient medications	Steroids and Beta agonist	81	90
	Steroids	4	4.4
	Beta agonist	5	5.6
Severity of asthma	Mild Intermittent	28	31.1
	Mild Persistent	18	20
	Moderate Persistent	26	28.9

Table 3: Risk factors for impaired glucose metabolism related with Obstructive lung disease patients who are on steroids at JUSH follow up chest clinic from November, 2014 to July, 2015.

Risk Factors	Category	Frequency	Percentage
Dose (Prednisolone equivalent)	<20 mg	45	50
	20-40 mg	43	47.8
	>40 mg	2	2.2
Family history of diabetes	Yes	2	2.2
	No	88	97.8
History of gestational diabetes (Females)	Yes	43	47.8
	No	1	1.1
Total duration on steroids	2-4 weeks	41	45.6
	>4 weeks	49	54.4
Obesity (Waist circumference)	Normal (Male< 94 cm, Female<88 cm)	66	73.3
	Abnormal	24	26.7
Metabolic status(Glucose)	<140 mg/dl	80	88.9
	140-180 mg/dl	7	7.8
	>180 mg/dl	3	3.3

Factors associated with RBS level

The study undertook binary regression to assess the significance of variable association with RBS level; age and sex of patients, waist circumference, family history of DM, Dose and duration of steroids were analyzed. The level of RBS level was not associated with any of the independent variables studied (Table 4).

Table 4: Cross tabulation, binary logistic regression analysis of risk factors associated with RBS level.

Variables		Metabolic status		P-VALUE	OR	95% CI
		Normal (<140 mg/dl)	Impaired (≥140 mg/dl)			
Age	<60	56	8	0.54	0.726	(0.261-2.021)
	≥60	24	2			
Gender	Male	39	7	0.195	0.259	(0.034-1.995)
	Female	41	3			
Waist circumference	Normal	59	7	0.257	0.289	(0.034-2.479)
	Abnormal	21	3			
Family history	Yes	2	0	0.999	0.19	(0.000)
	No	78	10			
Dose of steroids	<20 mg	42	3	0.33	2.433	(0.406-14.571)
	20-40 mg	37	6			
	>40 mg	1	1			
Duration on steroids	2-4 weeks	41	0	0.997	0.000	(0.000)
	>4 weeks	39	10			

DISCUSSION

In this study 11.1% of the study subjects had impaired glucose metabolism. This finding goes in line with many studies done worldwide like Kim SY et al of Korea done in 2011 which found the prevalence of impaired glucose metabolism in steroid users among patients with respiratory diseases to be 14.3%.[16] Majority of the study subjects (51.1%) were males and 1/3rd were above the age of 60 years which are established risk factors for impaired glucose metabolism and related disorders. Majority of the study subjects were illiterate and farmers and had less risk for impaired glucose metabolism.

Of the total 90 subjects in the study, Ten (11.1%) had impaired glucose metabolism of which 7 were males. There was no significant difference in impaired glucose metabolism by sex (P=0.326). There was no effect of age on impaired glucose metabolism (P=0.403). Thirty eight (42.2%) of them had prior hospital admissions and the majority with a frequency of not more than once the main reason being acute exacerbation (40%) exacerbation and stayed for 2 or more days in hospital, the mean average hospital stay in days being 2.45+0.89, but there was no association between glucose metabolism and frequency of admission.

Among 72 patients with Asthma the majority 28 (31.1%) patients are under category of Mild intermittent and there was no association between severity of asthma and glucose metabolism. The majority (97.8%) has no family history of DM and there was no association between the two variables. Of the 10 patients who had impaired glucose metabolism, there was no strong association between dose and duration of steroids (p=0.572), (P=0.724) respectively. Many studies worldwide like Kim SY et al of Korea done in 2011 and Hwang JL et al of USA done in 2014 showed that patients with respiratory problems like chronic obstructive lung diseases on steroids the glucose metabolism mainly affected by the dose and total duration of steroids but there is no agreement between this study and other studies regarding the effect of steroid dose and duration on glucose metabolism.[16,36,37] This inconsistency can be explained by small sample size as compared with other studies.

CONCLUSION

This study found that the prevalence of impaired glucose metabolism in obstructive lung diseases on steroids is significant (11.1%) independent of the effect of dose and duration of steroids. Therefore, understanding all pathways and developing specific therapies only with indications along with periodic screening for impaired glucose metabolism, may reduce the mortality & morbidity.

Recommendations

Random blood sugar measurement should be done for all patients with obstructive lung diseases on steroids for

timely management of impaired glucose metabolism. Additional studies with HgA1c have to be done to distinguish patients with obstructive lung diseases on steroids who may have preexisting undiagnosed DM or impaired glucose metabolism. Additional studies with large sample size and multiple centers have to be done to show relation between impaired glucose metabolism and steroid and other risk factors.

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