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ORIGINAL ARTICLE

Incidence of Steroid-induced Diabetes in COVID-19 patients

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ABSTRACT

Background: Since the COVID-19 pandemic has started, glucocorticoids have been proved to be one of the most effective lifesaving treatments for respiratory complications associated with SARS CoV-2.
Aim: To review the incidence of steroid induced diabetes and the associated risk factors in COVID-19 patients.
Study Design: Retrospective cohort study
Place and duration of the study: Bahria International Hospital Lahore from 15th April 2020 to 31st December 2020
Methodology: Two hundred and thirty patients of COVID-19 cases treated with glucocorticoids (Dexamethasone 4mg BID) were enrolled. All known cases of pre-existing diabetes mellitus and with initial (admission) random blood glucose levels of more than 200 mg/dl were excluded. Patients labelled as glucocorticoid induced diabetes mellitus (GI-DM)met the following criteria, fasting blood glucose level of more than 126 mg/dl or a random glucose level of more than200 mg/dlon two occasions after starting these patients on steroids.
Results: The glucocorticoid induced diabetes mellitus was 36 (15.65%). Multivariate logistic regression analysis revealed that older age (odds ratio 1.19, 95% confidence interval (1.02-1.36) was found to be the most profound risk factor for GI-DM.
Conclusion: Glucocorticoid induced diabetes mellitus found to be associated with glucocorticoid used among COVID-19 patients especially in older ages. So, it is recommended that the treating physicians should consider this side effect of steroids especially when dealing with geriatric cases.
Keywords: Hyperglycaemia, COVID-19, Steroids, SARS-CoV-2, Diabetes mellitus, Steroids induced diabetes, Glucocorticoids

INTRODUCTION

Since their emergence at the surface of medicine in the last century (1950s), glucocorticoids have been bearing a central role in the management of different inflammatory diseases by decreasing inflammation and minimizing tissue damage[1].. This includes respiratory diseases, but not limited to, chronic obstructive pulmonary disease (COPD), interstitial and hypersensitivity pneumonitis, sarcoidosis, endo-bronchial and extra-pulmonary tuberculosis. This anti-inflammatory benefit of steroids comes with some price in the form of various adverse effects like fluid accumulation leading to edema, increased blood pressure, menstrual disorders, weight gain, Cushing's syndrome, gastric ulceration, insomnia, and recurrent infections due to suppression of immunity. Impaired metabolism of glucose is the most common untoward effect encountered. Glucocorticoids not only increase the episodes of high blood glucose levels in already known diabetic patients but can also cause elevated blood glucose levels leading to diabetes in patients with no prior history of high blood glucose levels[2]. Mostly, this condition of raising blood sugar levelsis temporary, but some cases may develop clinical manifestations of diabetes like persistent polydipsia, polyuria, and repeated infections where the treatment with glucocorticoids merely seem to uncover the hidden diabetes. When starting a patient on steroids, especially in geriatric patients, there is a chance of causing non-ketotic hyperosmolar and hyperglycaemic state which may progress to coma. If persistent, increases in blood glucose can increase the risks of developing cardiovascular disease[3,4] and microvascular complications[5].

We reviewed the incidence and associated risk factors leading to steroid-induced diabetes mellitus (GI-DM) in COVID-19 patients with respiratory complications.

MATERIALS AND METHODS

This is a retrospective cohort where we reviewed charts of all the adult cases (ages 15 years onwards) admitted and treated for COVID-19 in Bahria International Hospital, Lahore from 15th April 2020 to 31st December 2020 after permission from IRB. All the admitted patients with moderate to severe disease received glucocorticoids (dexamethasone) as a part of standard treatment protocol. The starting dose was 4 mg BID dexamethasone. doses varied in some cases depending upon the treating consultant preferences and included pulse steroids up to 500 mg daily of methylprednisolone for 3 to 5 days. These cases were excluded from the study along with the pre-existing diabetes, having random sugar levels greater than 200mg/dl at the time of ICU admission and patients who were already taking steroids because of other medical conditions like malignancy, rheumatoid arthritis, renal transplant or nephrotic syndrome. We also excluded those patients received dexamethasone less than 21 days. During the period of 21 days, we check the frequency of occurrence of GI-DM. Patients' data including demographicsand laboratory findings were collected from their medical records retrospectively. We recorded daily andtotal dose of steroids along with the total duration of treatment.

Student's 't' test was used to compare and analyze continuous variables between two groups of patients (with and without GI-DM) while Chi-square test was applied on categorical variables. To find outthe predicting factorsfor GI-DM, we used multiple logistic regression models. Statistical significance was considered if $p<0.05$. All statistical analyses were performed using SPSS-20.

RESULTS

The median age was 56 years (23–86 years) and 141 were males (61.30%). The median glucose level checked at random before starting steroids in all 230 patients was 105 mg/dl (80-188 mg/dl). GI-DM was diagnosed in 36 (15.65 %).The age was found to be an obvious predisposing factor as the patients who developed GI-DM were older than those who did not (67 vs 52 years, $p<0.001$). Additionally, severe pneumonitis secondary to SARS-CoV2 infection was found to be significantly associated with the GI-DM (78.6% vs 48.9%, $P = 0.001$) [Table 1]. It was only the age (odds ratio 1.19, 95% confidence interval 1.01-1.26) that came up as a risk factor for developing GI-DM (Table 2).

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Table 1: Demographic data, clinical characteristics of patients and steroids dosage and duration

Variable	Patients with steroid-induced diabetes (n=36)	Patients without steroid induced diabetes (n=194)	P value
Age (years) median range	67 (50-81)	52 (23-85)	<0.001
Male	19 (13.47%)	122 (86.52%)	0.09
Female	17 (19.10%)	72 (80.89%)	0.05
Body mass index (kg/m^2)	22.6±4.2	23.1±3.8	0.54
Hypertension	12(33.33%)	43 (78.18%)	0.11
Dyslipidemia	4 (11.11%)	8 (4.1%)	0.07
Chronic kidney disease	1 (2.7%)	10 (5.1%)	> 0.99
Severity of pneumonitis	11 (78.6%)	3 (48.9%)	<0.001
Random glucose (mg/dl)	118 (76-190)	100 (59-198)	0.11

Table 2: Multivariable analysis describing predictors of steroid-induced diabetes mellitus

Parameters	Odds ratio	95% confidence interval	p-value
Age* (years)	1.19	(1.02-1.36)	0.006
Male	1.70	(0.48-5.99)	0.41
Severity of pneumonitis	1.19	(0.36-3.86)	0.78

*(year X + 1 vs year X).

GI-DM onset time was 7.4 days (6-21 days); 19 patients (52.7%) developed GI-DM in the first week, while 5 (13.8%) in the second week of treatment. The remaining 12 cases were diagnosed after first two weeks.All patients have been advised follow-upondiagnosis of GI-DM was established, 26 were treated with oral medication (Vildagliptin plus Metformin) and 8 received insulin.

DISCUSSION

Steroids induce hyperglycaemia by causing insulin resistance which leads to hepatic gluconeogenesis and decreases peripheral uptake of glucose in muscles and fat.[2,6] Due to the above-mentioned mechanism, a varied glucose metabolism is seen in patients on glucocorticoid therapy. In our study of 230 patients with COVID-19 pneumonia who received glucocorticoids, 36 (15.65%) patients developed GI-DM. International literature has demonstrated, GI-DM in other conditions treated with glucocorticoids, like connective tissue diseases, from 0.4% to 54%.[7-9] The percentage of COVID-19 patients who developed GI-DM after steroid therapy in our study is comparable to the observations ofKimet al.[9]

The wide variability in the available literature is probably due to the differences in study populations and sample sizes, different glucocorticoid types and dosages, and perhaps different criterion used to label GI-DM. Different suggested risk factors to develop GI-DM included old age, high body mass index (BMI), impaired glucose tolerance before initiation of steroids, cumulative dose and the time duration of steroid use. However, detailed literature search indicates that these risk factors for developing GI-DM are not the same in all studies.[7-10] In our study, only old age turned out to be an independent risk factor for the development of GI-DM. It is well known that glucose tolerance declines with advancing age, and this results in a higher chance of developing type 2 diabetes (T2DM) and impaired glucose tolerance in geriatric patients.[11,12]

In addition, there are several other factors associated with aging that play their role in the altered glucose metabolism, includingobesity, less physical activity, addition of daily medications and systemic diseases.[12,13] Considering these factors, the association of increasing age with the development of GI-DM in our study can be easily understood. There are certain limitations to our study. We have monitored fasting blood sugar levels (BSF) rather than the postprandial glucose though the effects of steroids on glucose metabolism are more prominent after meals.[14]

In this context, the incidence of GI-DM could be underestimated, secondly, this is a single center study and multi-centered data will be more helpful in understanding the disease and thirdly, the pathophysiology of COVID-19 disease is still under investigation and a lot more has to be understood yet. More robust data analyses with larger number of cases are needed to establish the relationship of steroid induced Diabetes in COVID-19 patients.

CONCLUSION

Glucocorticoid induced diabetes mellitus occurs commonly in COVID-19 patients who are treated with steroids for respiratory complications. The treating physicians should considerthis fact especially when they are dealing with elderly patients with SARS CoV-2 infection to avoid the more complications induced by glucocorticoid induced diabetes mellitus.

Conflict of interest: Nil

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