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ASSESSMENT OF STEROID THERAPY ON GLYCEMIC STATUS IN COVID-19 PATIENTS.

Biochemistry

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ABSTRACT

Background: By April 2020, COVID-19 had spread to over 200 countries, causing over three million confirmed cases and 200,000 deaths. Observational studies show diabetes is linked to an increased risk of severe illness and death from COVID-19. Diabetic patients face higher chances of complications and ICU admission. **Objectives:** This study aims to know the glycemic status in non-diabetic COVID-19 patients and the effect of steroids on glycemic status in non-diabetic COVID-19 patients. **Materials and Methods:** This is a retrospective, single-center study. Data were obtained from the records of patients who were diagnosed with confirmed COVID-19 between January 2021 to December 2021. The HbA1c and Random Plasma Glucose(RPG) levels were recorded. A history of diabetes mellitus and steroid usage was also noted. Appropriate Statistical analysis was done. p value of <0.05 was taken as significant. **Results:** The median HbA1c(%) of steroid-treated group(n=56) was 6.2(6.67-5.6), non-steroid treated group(n=60) was 5.5(6.2-5.2) and healthy controls(n=40) was 4.98(5.3-4.67). The median Random Plasma Glucose(RPG)(mg/dL) levels of steroid-treated group was 107(143.3-89.25); non-steroid treated group was 94.5(110.5-83.75) and healthy controls was 91.38(105.34-81.63). The median HbA1c and RPG levels of steroid-treated COVID-19 patients were higher than the non-steroid-treated COVID-19 patients and healthy controls and the difference was statistically significant (P<0.0001). On Spearman correlation, a significant positive correlation was found between RPG and HbA1c. (ρ=0.5679) **Conclusion:** Glucose homeostasis is deranged in COVID-19 patients. This could occur due to steroid intake as well as COVID-19 infection itself. Hence there is a need to monitor the glycemic status continuously in COVID-19 patients irrespective of steroid usage.

KEYWORDS

COVID-19, HbA1c, Steroids.

INTRODUCTION

In, 2020, the World Health Organization [1] classified COVID-19 as a global pandemic, marking its worldwide spread. Diabetes mellitus is recognized as a risk factor for more severe clinical outcomes in individuals with COVID-19. Nevertheless, the connection between these two conditions appears to be mutually influential [2]. The COVID-19 pandemic has significantly affected blood glucose management in people with diabetes. These effects are classified as direct (due to the viral infection itself) and indirect (from changes in glucose management or treatments that affect glucose balance).

COVID-19 infection directly triggers notable metabolic shifts, causing significant spikes in blood glucose levels. This is due to heightened release of cytokines and inflammatory agents, resulting in increased insulin resistance and subsequent hyperglycemia [3].

Nasser M et al suggested that COVID-19 could contribute to the onset of acute diabetes mellitus in specific cases by targeting pancreatic islet ACE2 receptors, potentially causing pancreatic damage [4].

Research indicates that diabetes is a significant comorbidity associated with increased severity and mortality from COVID-19. The exact pathophysiological mechanisms underlying this heightened risk in diabetic individuals remain unclear. Numerous hypotheses have been proposed to understand why COVID-19 is more prevalent in diabetes and leads to poorer outcomes.

Typically, diabetes heightens the risk of several infections, including viral infections [5]. Hyperglycemia impairs various functions critical for fighting infections, such as neutrophil activity, phagocytosis, and bacterial killing [6].

Steroids, used to treat various diseases including COVID-19, can lead to hyperglycemia by boosting insulin resistance, hindering post-meal glucose uptake, and promoting liver glucose production [7]. While dexamethasone, as shown in the RECOVERY study, reduces mortality in COVID-19 patients needing oxygen or ventilation by dampening inflammation [8,9], it also heightens insulin resistance and blood glucose levels [10]. Hospitalized diabetic patients receiving corticosteroids often experience exacerbated glucose fluctuations and prolonged hyperglycemia [11,12]. Hospitalization stress further complicates glucose management in diabetic individuals.

Aims and Objectives

- To know the glycemic status in non-diabetic COVID-19 patients.
- The effect of steroids on glycemic status in non-diabetic COVID-19 patients.

MATERIALS AND METHODS

Study Design: Retrospective study.

Participant Recruitment Procedures

Data were obtained from the records of non-diabetic patients diagnosed with confirmed COVID-19 between January-December 2021 at Nizams Institute of Medical Sciences.

The Cases were Divided into Groups:

- Group 1- Steroid-treated COVID-19 patients
- Group 2- non-steroid-treated COVID-19 patients.
- Group 3- Healthy controls.

Inclusion Criteria

- Age 18-70years.
- Confirmed COVID-19, non-diabetic cases.
- Age and sex-matched healthy controls.

Exclusion Criteria

- Age below 18 years and above 70 years.
- Patients with a history of diabetes mellitus.

Methodology

Data regarding HbA1c, random plasma glucose, and history of diabetes mellitus and steroid usage were obtained from records. HbA1c was estimated on D-10 automated analyzer, Bio-Rad. Principal for estimating Glucose- Hexokinase method.

Statistical Analysis

Statistical analysis of data was done using GraphPad prism 9.4.1(681) version, MedCalc 20.115 version, and Microsoft Excel. The normality for all the variables in controls and cases was checked using the Kolmogorov-Smirnov test. The two groups were compared using the Mann-Whitney U test for non-parametric data. Kruskal Wallis test was applied to compare more than two groups and post hoc multiple comparisons were performed using Dunn's multiple comparison test procedure. All hypothesis testing was 2-tailed and $p<0.05$ was considered statistically significant. Spearman's Rank correlation analysis was done.

RESULTS

Demographics

A total of 156 subjects (116 cases and 40 controls) were included in the study. Among the 116 cases, 56 belonged to the Steroid-treated COVID-19 group and 60 belonged to the non-steroid-treated COVID-19 group.

Biochemical Investigations

The median HbA1c levels of steroid treated group was (n=56) was 6.2(6.67-5.6), non-steroid treated group(n=60) was 5.5(6.2-5.2) and healthy controls(n=40) was 4.98(5.3-4.67). The median Random Plasma Glucose(RPG)(mg/dL) levels of steroid-treated group was 107(143.3-89.25); non-steroid treated group was 94.5(110.5-83.75) and healthy controls was 91.38(105.34-81.63). The median HbA1c and RPG levels of steroid-treated Covid-19 patients were higher than the non-steroid-treated Covid-19 patients and healthy controls and the difference was statistically significant (P<0.0001).

On post hoc analysis, there was a significant difference in HbA1c(%) and RPG(mg/dL) levels in the Steroid-treated vs control group; Non-steroid treated vs control group; and Steroid-treated vs non-steroid-treated group.

DISCUSSION

Steroids raise blood sugar levels through multiple pathways:

1. Boost hepatic gluconeogenesis, increasing glucose production from the liver by intensifying the impact of counter-regulatory hormones [13].
2. Hinder insulin's function and heighten insulin resistance.
3. Steroid medications impede glucose uptake by muscles and adipose tissue [14,15].
4. Directly diminish the activity of Beta cells [16].
5. Inflammatory cytokine surges, as observed in COVID-19, exacerbate insulin resistance [17].
6. Illness-induced stress and the fear of mortality can trigger heightened stress hormone release, leading to elevated blood glucose levels.

In our study, the usage of steroid medication for reducing inflammation caused due to COVID-19 infection has the adverse effect of blood glucose derangements due to the above-given reasons. The blood glucose levels were deranged even in non-diabetic COVID-19 patients, thus emphasizing the importance of blood glucose monitoring in COVID-19 patients receiving steroids for therapy. Moreover, blood glucose levels were also deranged in COVID-19 patients who did not receive steroid therapy during treatment, showing that COVID-19 infection itself causes blood glucose derangement. Recent data indicates that new-onset hyperglycemia is common among hospitalized COVID-19 patients with no previous history of diabetes mellitus. Besides, hyperglycemia on hospital admission is a significant prognostic factor for COVID-19 patients without diabetes mellitus [18].

CONCLUSION

The COVID-19 pandemic and its treatment have opened our eyes to the importance of controlling glycemic status. Glucose homeostasis is deranged in COVID-19 patients. This could occur due to steroid intake as well as Covid-19 infection itself. Hence there is a need to monitor the glycemic status continuously in COVID-19 patients irrespective of steroid usage.

Table 1

Variable	Steroid-treated group (n=56)	Non-Steroid Treated group (n=60)	Controls (n=40)	p value
HbA1c (%)	6.2 (6.67-5.6)	5.5 (6.2-5.2)	4.98 (5.3-4.67)	<0.0001
RPG (mg/dL)	107 (143.3-89.25)	94.5 (110.5-83.75)	91.38 (105.34-81.63)	<0.0001

RPG- random plasma glucose

Table 2: Inter Group Analysis

Variable	Steroid-treated vs controls	Non-steroid treated Vs controls	Steroid-treated Vs non-steroid-treated
HbA1c(%)	<0.0001	<0.0001	0.0234
RPG (mg/dL)	<0.0001	0.0002	0.0306

Dunn's Multiple comparison test was done, p<0.05 was considered significant.

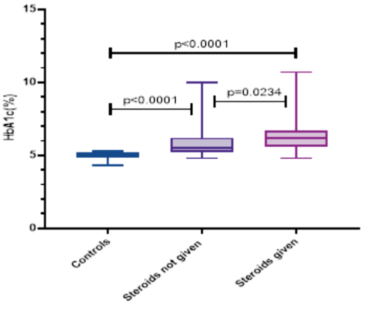

Figure 1: Median Value of HbA1c in Cases and Controls:

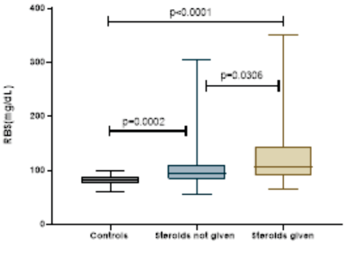

Figure 2: Median Values On Random Plasma Glucose(mg/dl) In Cases And Controls.

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