

# Incidence and Attributing Factors of Impaired Blood Glucose in Non-Diabetic Patients on Steroid Therapy

Hafsa Farooq<sup>1</sup>, Muhammad Awais Abid<sup>2</sup>, Hamna Farooq<sup>3</sup>, Madiha Fazil<sup>4</sup>, Ayesha Irshad<sup>5</sup>, Ambreen Butt<sup>6</sup>

<sup>1</sup>Senior Registrar, <sup>2,5</sup>Assistant Professor, <sup>3</sup>Medical officer, <sup>4</sup>Postgraduate resident, <sup>6</sup>Professor  
(Department of Medicine, Services Hospital Lahore)

## Author's Contribution

<sup>1</sup>Conception or design of the work, data collection

<sup>2</sup>Final approval of the version to be published

<sup>3,4</sup>Critical revision, analysis and

<sup>5</sup>Active Participation in active methodology

Funding Source: None

Conflict of Interest: None

Received: Dec 23, 2020

Accepted: Aug 07, 2021

## Address of Correspondent

Dr Hafsa Farooq

Senior Registrar, Department of Medicine, Services Hospital Lahore.

Email [hafsafarooq37@gmail.com](mailto:hafsafarooq37@gmail.com)

## ABSTRACT

**Objective:** To determine the incidence and attributing factors of impaired blood glucose in non-diabetic patients on steroid therapy.

**Methodology:** This descriptive study was conducted at the Department of Medicine, Sheikh Zayed Hospital Lahore during 6 months from April 2019 to September 2019. Patients of both genders with age of 18-70 years and receiving steroid therapy (at least 1 pulse) were included. After taking ethical approval, 371 patients were counseled and explained the details of the study. A bolus of 1 gram Methylprednisolone was given and blood was drawn after 2 hours and blood glucose levels were measured. All the labs were acquired from same lab (Hospital lab) and glucometer to eliminate bias and confounding variables were controlled by exclusion. Data was collected via study proforma.

**Results:** The average age of the patients was  $43.75 \pm 14.33$  years with a range of 18 to 70 years. There were 42% males and 57% females with a male to female ratio of 1:1.3. Average BMI of patients  $27.34 \pm 3.72$  kg/m<sup>2</sup>. Impaired blood glucose was observed in 55% of patients after steroid pulse therapy. Frequency of impaired blood glucose after steroid pulse therapy was statistically insignificant according to age and BMI ( $p > 0.05$ ). Positive family history was significantly higher in a patient with impaired blood glucose after pulse therapy ( $p = 0.001$ ).

**Conclusion:** Impaired blood glucose level was observed to be highly prevalent among non-diabetic patients receiving steroid pulse therapy. Female gender and positive family history of diabetes observed as attributing factors.

**Key words:** hyperglycemia, Steroids, incidence, factors

**Cite this article as:** Farooq H, Abid MA, Farooq H, Fazil M, Irshad A, Butt A. Incidence and Attributing Factors of Impaired Blood Glucose in Non-Diabetic Patients on Steroid Therapy. *Ann Pak Inst Med Sci.* 2021;17(3):232-235. doi: 10.48036/apims.v17i3.383

## Introduction

Drugs of the steroids have been utilized broadly in an assortment of conditions, both chronic and acute.<sup>1</sup> At the supraphysiological dose, they decrease the pro-inflammatory cytokines synthesis, function of the T-cells and expression of the antibody Fc receptor, which initiate the immunosuppressive and anti-inflammatory process, making them the foundation in the management of various inflammatory diseases.<sup>2-3</sup> These cases are weak to progress the worsen occasions of the prolonged treatment of *glucocorticoid*, like as, *glucocorticoid* induced glucose metabolism impairment in the others.<sup>4</sup> As per the American Diabetes Association and International Federation of Diabetes, cases those constantly treated with steroids therapies to be evaluated for diabetes as in

everybody. There are not measured as in a high-hazard group, although both RA and Steroid plus treatment increases the danger of diabetes. The insulin resistance development is principally postprandial and changes relying upon the kind of steroid utilized: middle and long-acting glucocorticoids. Prednisone and methylprednisolone are categorized as the steroid of intermediate-acting, with the highest of activity 4-6 h following the administration. Their impact on the levels of glucose is basically during the evening and night without impact in fasting glucose when managed with the single dose. Although they cause tenacious hyperglycemia after divided doses administration.

Dexamethasone fits in the long-acting glucocorticoids, with the hyperglycemia by steroid that goes on for in

excess of 24 hours, with a slight decrease during the fast overnight.<sup>2,5-7</sup> It has been showed that glucocorticoids modify the capacity of the beta cells of pancreas by the decrease of expression of GLUT2 and glucokinase receptor simultaneously expanding the action of glucose-6-phosphate dehydrogenase, with successive alteration in the  $\beta$ -oxidation. Furthermore, they decrease the synthesis of insulin and it is felt that they lessen cell mass by the enlistment of apoptosis of the beta cell. Similarly, because of the lessening in the sensitivity of the insulin, the beta cell of the pancreas regularly expands the secretion of insulin to keep up with glucose homeostasis, however on occasion this increment isn't adequate to balance the resistance of the insulin consequences in the hyperglycemia.<sup>2,8,10</sup> In light of the previously mentioned, Glucocorticoids raise the resistance of the insulin with the resulting condition of hyperinsulinism. Among healthy individuals, this mechanism is remunerated by the raises in the secretion of insulin from pancreas, causing the levels of serum glucose to stay in normal ordinary range.<sup>9</sup>

Nonetheless, in powerless populaces, like as individuals with normal glucose level with diminished sensitivity of the insulin and a lower production rate of the equivalent before steroid use, this balancing impact is lost, resulting in elevated glucose levels.<sup>2,8</sup> On other hand it is stated that the steroid is linked with increase hyperglycemia risk among individuals having diabetes or not.<sup>11,12</sup> Steroid interfere at many steps in the signaling cascade of the insulin, this inhibit signaling of the insulin in liver and skeletal muscles, causing in decreases glucose uptake and the synthesis of the glycogen, raised breakdown of the mass of the skeletal muscles, raises in the glucose production of the liver and additionally, steroid raise the lipolysis in whole body, subsequent in raised non-esterified fatty acids (NEFA) and the triglyceride.<sup>11</sup> This study has been conducted to evaluate the incidence and attributing factors of impaired blood glucose in non-diabetic patients on steroid therapy at tertiary care Hospital.

## Methodology

This descriptive study was conducted at Department of Medicine, Sheikh Zayed Hospital Lahore during 6 months from April 2019 to September 2019. Sample size of 371 was calculated with 95% confidence level and 5% margin error while taking expected frequency of steroid induced impaired blood glucose levels to be 40.6 %. Non probability consecutive sampling technique was used. Patients of both genders with age of 18-70 years receiving

steroid therapy (at least 1 pulse), patients who signed written informed consent to participate in the study were included. All he patients who had taken steroid in last year as per history and clinical record, patients who had taken Oral hypoglycemic drugs before and patients who were already diagnosed as having Diabetes mellitus were excluded. After approval from ethical review committee of the hospital, 371 patients who presented in the inpatient department of Hospital Lahore and who fulfilled the above criteria were counseled and explained the details of the study. Written informed consent and detailed history was taken from each patient. A bolus of 1 gram Methylprednisolone was given and blood was drawn after 2 hours and blood glucose levels were measured. All the labs were acquired from same lab (Hospital lab) and glucometer to eliminate bias and confounding variable were controlled by exclusion. All the data was collected via study proforma.

All the data was entered and analyzed through SPSS version 21. Numerical variables like age have been presented by mean  $\pm$  SD. Categorical variables i.e gender, impaired blood glucose and attributing factors (female gender, hypertension, and positive family history of diabetes) have been presented by frequency and percentage. Chi square test has been used and p value < 0.05 has been considered as significant.

## Results

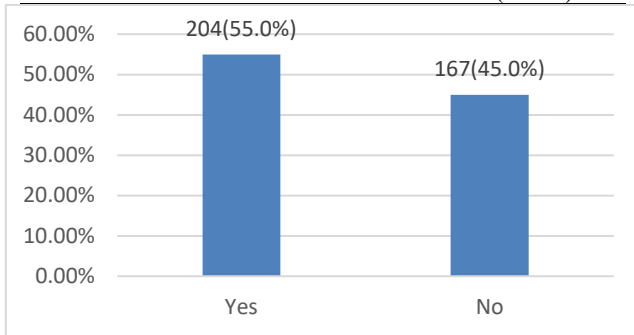
The age of the patients ranged from 18 years to 70 years with a mean of  $43.75 \pm 14.33$  years. Majority (n=177, 47.7%) of the patients were aged 45 years and above followed by 30-44 years (33.2%) and under 30 years of age (19.1 %). There were 159(42%) male and 212 (57%.1) female patients with male to female ratio nof1:1.3. The BMI of these patients ranged from 20.6kg/m<sup>2</sup> to 33.9 kg/m<sup>2</sup> with a mean of  $27.34 \pm 3.72$  kg/m<sup>2</sup>. 81 (21.8%) patients were hypertensive while 42 (11%) patients had positive family history of diabetes as shown in table I.

Impaired blood glucose was observed in 204 (55%) patients after steroid pulse therapy as shown in figure 1.

There was no statistically significant difference in frequency of impaired blood glucose after steroid pulse therapy across various age (p-0.997) and BMI (p-0.977) groups. The frequency of female gender and positive family history was significantly higher in patient with impaired blood glucose after pulse therapy (p-<0.05), while AG and BMI were found statistically insignificant (p->0.05). (Table III)

**Table no I: Descriptive statistics of demographic variables (n=371)**

Variables	Statistics
Age	43.75 ± 14.33 years
Gender	Males 159(42.9%)
	Females 212(57.1%)
BMI	27.34±3.72kg/m <sup>2</sup>
Hypertension	Yes 81(21.8%)
	No 290(78.2%)
Family history	Yes 42(11.3%)
	No 329(88.7%)



**Figure 1. Incidence of impaired glucose level (n=371)**

**Table III. Impaired glucose level as per age, gender and (BMI =371)**

Variables	Impaired glucose level		p-value	
	Yes	No		
Age groups	<30 years	39(10.5%)	32(8.6%)	0.997
	30-45 years	68(18.3%)	55(14.8%)	
	>45 years	97(26.1%)	80(21.6%)	
Gender	Males	63(17.0%)	97(25.9%)	0.001
	Females	141(38.0%)	71(19.1%)	
BMI	20-25 kg/m <sup>2</sup>	61(16.4%)	51(13.7%)	0.977
	26-30 kg/m <sup>2</sup>	89(24.0%)	71(19.1%)	
	>30 kg/m <sup>2</sup>	54(14.6%)	45(12.1%)	
Family history		33(16.2%)	09(5.4%)	0.001

## Discussion

Corticosteroids have proved to be extremely effective in the Treatment of many Acute and chronic inflammatory diseases like Inflammatory bowel disease, dermatological diseases, systemic lupus erythematosus.<sup>13</sup> Prolonged steroids use is associated with rise in blood sugar levels in diabetic and Non diabetic patients.<sup>14-17</sup> Risk factors are female gender, history of hypertension, and family history of diabetes However the available data was limited as there was no such local published material which necessitated the present study. In the present study, mean age of patients was 43.75 ± 14.3 years. A mean age of 43.8±10.6 years has been reported by Zafar et al.<sup>18</sup> Rais et al<sup>19</sup> also reported similar mean age of 43.7 ± 18 years among such

patients n Liaquat National hospital, Karachi, while shamim et al<sup>20</sup> reported mean age as 47.3 ± 2.9 years.

A similar mean age of 41± 14 years has been reported by Perez et al. 2011 among such patients in Mexico<sup>5</sup> while Bedi et al<sup>21</sup> reported to be 42 ± 13 years in India. We observed that Majority 47.7% of patients were aged 45 years and above followed by 30-44 years (33.2%) and under 30 years of age (19.9%). Our observation is in line with that of shamim et al. who reported similar distribution of < 30 years (20.0%), 33-44 years (36%) and > 45 years (44%) age groups among such patients at Jinnah postgraduate Medical Centre Karachi <sup>20</sup> Similar Results have also been reported by Zafar et al. < 30 yeas (14.6%), 30-44 years (40.4%) and > 45 years (45%) among such patients at Shaikh Zayed Hospital, Lahore.<sup>16</sup>

In the Present Study, impaired blood glucose was observed in 204(55%) patients after steroid pulse therapy and it significantly among females and those had positive family history. On other hand Tariq H et al<sup>22</sup> conducted a study to determine the incidence hyperglycemia caused by steroid treatment among individuals taking systemic steroids for the dermatological disorders and observed 18.7% hyperglycemia induced by steroid therapy out of all 150 cases. Furthermore, in their study steroid induced hyperglycemia was seen mostly among individuals aged more than 50 years and in the female’s gender. In another Indian study by Priti et al<sup>23</sup> demonstrated that the frequency of hyperglycemia was 62.5% after intake of steroid therapy and these findings were almost near to the our study. In another prospective international study conducted by Othman AS et al<sup>24</sup> reported that the Steroid-induced diabetes rate was observed among 64% of the cases during administration of therapy.

Although the present study is the first of its kind in local population and has found that a substantial proportion of non-diabetic patients receiving steroid pulse therapy had impaired blood glucose and female gender, hypertension and positive family history of diabetes were attributable to this steroid induced hyperglycemic state which advocate routine monitoring of blood sugar level among patients receiving steroid pulse therapy particularly female and hypertensive patients with positive family history so that timely identification and management can improve the patient outcome. A very strong limitation to the present study was that we did not stratify the results of underlying medical condition requiring steroid pulse therapy nor the dose of steroid pulse given which may attributable to impaired blood glucose. The relationship of these factors

is necessary to be investigated to give further insight into this phenomenon and management planning of such patients. Such a study is highly recommended in future research.

## Conclusion

Impaired blood glucose level was observed to be highly prevalent among non-diabetic patients receiving steroid pulse therapy. Female gender and positive family history were observed to be as risk factors. Routine monitoring of glucose levels should be done as timely identification & management can improve the patient outcome. Future large-scale studies are recommended on this subject.

## References

1. Trence DL. Management of patients on chronic glucocorticoid therapy: an endocrine perspective. *Prim Care*. 2003;30:593–605. [https://doi.org/10.1016/S0095-4543\(03\)00038-1](https://doi.org/10.1016/S0095-4543(03)00038-1)
2. Tamez-Pérez HE, Quintanilla-Flores DL, Rodríguez-Gutiérrez R, González-González JG, Tamez-Peña AL. Steroid hyperglycemia: prevalence, early detection and therapeutic recommendations: a narrative review. *World journal of diabetes*. 2015 Jul 25;6(8):1073. <https://doi.org/10.4239/wjd.v6.i8.1073>
3. Ha Y, Lee KH, Jung S, Lee SW, Lee SK, Park YB. Glucocorticoid-induced diabetes mellitus in patients with systemic lupus erythematosus treated with high-dose glucocorticoid therapy. *Lupus*. 2011;20:1027–34. <https://doi.org/10.1177/0961203311402246>
5. Saigí Ullastre I, Pérez PA: Hiperglucemia inducida por glucocorticoides. *Semin Fund Esp Reumatol* 2011;12:83–90
6. Schäcke H, Döcke WD, Asadullah K. Mechanisms involved in the side effects of glucocorticoids. *Pharmacol Ther*. 2002;96:23–43. [https://doi.org/10.1016/S0163-7258\(02\)00297-8](https://doi.org/10.1016/S0163-7258(02)00297-8)
7. Perez A, Jansen-Chaparro S, Saigí I, Bernal-Lopez MR, Miñambres I, Gomez-Huelgas R. Glucocorticoid-induced hyperglycemia. *J Diabetes*. 2014;6:9–20. <https://doi.org/10.1111/1753-0407.12090>
8. Galofre JC. Manejo de los corticoides en la práctica clínica. *Rev Med Univ Navarra*. 2009;53:9–18.
9. van Raalte DH, Ouwens DM, Diamant M. Novel insights into glucocorticoid-mediated diabetogenic effects: towards expansion of therapeutic options? *Eur J Clin Invest*. 2009;39:81–93.
10. Clore JN, Thurby-Hay L. Glucocorticoid-induced hyperglycemia. *Endocr Pract*. 2009;15:469–474.
11. Kang SH, Lee JY, Park HS, Sun IO, Choi SR, Chung BH et al. Hyperglycemic hyperosmolar syndrome caused by steroid therapy in a patient with lupus nephritis. *Journal of Korean medical science*. 2011 Mar 1;26(3):447-9.
12. Park SY, Kim SY, Kim DI, Kim HS, Yang SJ, Park JR, Kim DJ, Yoo HJ, Kwon SB, Baik SH. A case of hyperglycemic hyperosmolar syndrome induced by steroid treatment for idiopathic thrombocytopenic purpura. *J Korean Diabetes Assoc* 2005; 29: 571-3
13. Strohmayer EA, Krakoff LR. Glucocorticoids and cardiovascular risk factors. *Endocrinol Metab Clin North Am*. 2011;40:409–417.
14. Manson SC, Brown RE, Cerulli A, et al. The cumulative burden of oral corticosteroid side effects and the economic implications of steroid use. *Respir Med*. 2009;103:975–994.
15. Yang X, Lin X, Lu T, Chen P, Wang X, Hou FF. Fasting Plasma Glucose Levels Predict Steroid-Induced Abnormal Glucose Metabolism in Patients with Non-Diabetic Chronic Kidney Disease: A Prospective Cohort Study. *Am J Nephrol* 2015;41:107-15. <https://doi.org/10.1159/000377642>
16. Perez HET, de Ossio MDG, Flores DLQ, Coria MIH, Peña ALT, Pérez GJC, et al. Glucose disturbances in non-diabetic patients receiving acute treatment with methylprednisolone pulses. *Revista da Associação Médica Brasileira*. 2012;58:1258.
17. Gonzalez Gonzalez JG, Mireles Zavala LG, Gutierrez RR, Gomez Almaguer D, Lavella Gonzalez FJ, Tamez Perez HE, et al. Hyperglycemia related to high dose glucocorticoid use in non-critically ill patients. *Diabetol Metab Syndr*, 2013; 5(1): 18.
18. Zafar ZA, Mahmud TH, Rasheed A, Wagan AA, Frequency of metabolic syndrome in Pakistani cohort of patients with Rheumatoid arthritis. *J Pak Med Assoc* 2016;66(6):671-6.
19. Rais R, saeed M Haider R, Jassani Z, Riaz A parveen T. Rheumatoid arthritis clinical features and amangement strategies at an urban tertiary facility in Pakistan. *J pak Med Assoc* 2014; 64(12):1435-7
20. Shamim R, Jan MD, Zafar U. Prevalence of rheumatoid arthritis in population with arthralgia presenting to a tertiary care hospital. *J pak Med Assoc* 2015;65(11):1202-5.
21. Bedi GS, Gupta N, Handa R, pal H, pandey RM. Quality of life in indian patients with rheumatoid arthritis. *Qual life Res* 2005;14(8):1953-8
22. Tariq H, Malik LM, Azfar NA, Rashid T, Jahangir M. Frequency of steroid induced hyperglycemia in patients with dermatological disorders. *Journal of Pakistan Association of Dermatologists*. 2018 Jul 23;28(1):69-72.
23. Priti D, Asawari R, Arundhati D, Kushal G, Aeyna T. A prospective study of steroid induced hyperglycaemia. *J Med Sci Res* 2011;2(1):46-49
24. Othman AS, Salah-Eldin MA, Ebrahim MA, Abd EL-Aziz SM, Ramez AM. Impact of Steroid-Induced Diabetes on Prognosis of Patients with Aggressive Lymphoid Malignancies: A Prospective Study. *Research in Oncology*. 2021 Jun 1;17(1):31-7. <https://doi.org/10.21608/resoncol.2021.48233.1123>