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Clinical Outcome and Glycemic Control among Type 2 Diabetic Covid-19 Positive Patients With and Without Steroids

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ABSTRACT

Background: Severe acute respiratory syndrome corona virus 2 (SARS CoV-2) is the pathogen causing coronavirus disease. ACE2 is the surface receptor for SARS CoV-2 invasion in human cell and it is more abundant in the endocrine pancreas than in type 1 and 2 alveoli in the lungs, and there is probability that beta cell destruction can occur during an attack of COVID-19. There have been few studies on the possible consequence of beta cell destruction leading to an increase in the need for diabetic medication in post COVID status. **Objective**: In this study our main aim is to study glycemic control using HbA1c in covid positive diabetic patients and compare at admission and follow up after 6 months. And to study Clinical outcome in terms of mortality, ICU admission and stay, duration of hospital stay and the requirement of anti-diabetic medications at discharge and after 6 months of follow up and compare between pre covid and post covid requirements in non-steroid and steroid treated diabetic patients. **Materials and Methods**: This was a Comparative observational study conducted from March 2020 to June 2021 in AJ Institute of Medical Sciences, Mangalore. Total of 88 Covid 19 positive diabetic patients were enrolled in this study. Informed consent was taken. Patients were categorized into 2 groups based on AIIMS/ICMR Clinical guidance for management of adult COVID-19 patients. Group 1 were diabetic patients treated with steroids and group 2 were diabetic patients not treated with steroids. Between the 2 groups, HbA1c was compared at admission and follow up after 6 months and clinical outcome was analysed in terms of duration of hospital stay, ICU admission and stay, mortality and requirements of anti-diabetic medication at discharge and after 6 months of follow up and compared between pre covid and post covid requirements in non-steroid group and steroid group. **Results**: The mean HbA1c level showed statistically very high significant difference at admission and follow up among non-steroid group ($p<0.001$) and steroid group ($p<0.001$). Adverse clinical outcome seen more among diabetic patients with steroid compared to non-steroid group. The requirement of anti-diabetic medication was found to have increased among 48.3% patients in the steroid group and among 46.2% in the non-steroid group when compared at the time of discharge and follow up. But statistically no significant difference was observed between 2 groups ($p>0.05$), however clinically the difference was seen. The increase in requirement of anti-diabetic medication among non-steroid and steroid group was 56.8% and 52.3% respectively with significant statistical difference ($p<0.05$) when compared before and after COVID. **Conclusion**: Glycemic control in terms of HbA1c was good among both groups when compared at admission and follow up after 6 months. The clinical outcome in terms of duration of hospital stay, ICU admission and stay, mortality is seen more among covid positive diabetic patients treated with steroids compared to non-steroid group. The requirement of anti- diabetic medication has increased in both steroid and non-steroid group when compared at the time of discharge and follow up after 6 months but between the groups statistical significant difference was not observed but clinically difference was seen. We also compared the requirement of anti-diabetic medications before and after covid which is found to have increased in both the groups with significant statistical difference indicating the possibility of pancreatic beta cell damage persisting in post covid status among diabetic patients irrespective of treatment with steroids. But further studies are required on large scale to prove the possibility of pancreatic beta cell damage in post covid diabetic patients.

Key Words: *SARS-CoV-2, COVID-19, ACE2, Diabetes Mellitus, clinical outcome, Glycemic control, HbA1c, anti-diabetic medication, non-steroid group, steroid Group*

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INTRODUCTION

Coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) pathogen that emerged from Wuhan in China which quickly spread across most of the nation's worldwide. The disease had varied presentation which range from an asymptomatic state toa severe pneumonia leading to acute lung failure [1]. The incubation period may range from 2 to 14 days. The usual presentation in COVID-19-positive patients has been fever, cough, dyspnea, fatigue, loss of appetite, sputum production, joint pain, nausea, vomiting, and diarrhea. A severe disease could be related to serious problems like pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure, septic shock, disseminated intravascular coagulation, and ultimately leading to death [2, 3].

Angiotensin-converting enzyme 2 (ACE2) is a surface receptor responsible for SARS coronavirus (SARS-Co-V) invasion in human cells with direct interaction with its spike glycoprotein (S protein) [4, 5]. Diabetes Mellitus known to have deregulated immune system, predisposing to numerous infections [6]. ACE2 has anti-inflammatory effects, and its expression is decreased in diabetic patientsprobably due to glycosylation. This explains the occurrence of a severe acute lung injury and ARDS indiabetic patients. It is also important to know that ACE2 receptors, through which SARS-CoV-2 attaches to the cells, is also present on the cells of endocrine pancreas, at a greater density than in the Type 1 and 2 alveoli in lungs [7]. It is, therefore, possible (but not proven) that beta cell destruction may occur due to COVID19 attack on pancreatic beta cells, similar to alveolar injury in lungs. It is found that 17% patients having extreme COVID19 is shown to have pancreatic injury in one study [8]. There is probability that injury to beta cells, already under attack from cytokines (cytokine-induced apoptosis) [9], could cause acute insulinopenia, and ketoacidosis [10]. Viral 'sepsis' could induce resistance to action of insulin, posing additional challenges to management including high insulin requirement. Insulin is mandatory to control surge of blood glucose which may also occur due to steroid therapy and/or sepsis. It is also found that in diabetic patients, the vascular permeability is increased followed by collapse of alveolar epithelium are responsible for higher mortality and they also show higher levels of IL-6, ferritin, hsCRP, and D-dimer which indicates cytokine storm, hypercoagulable state causing rapid deterioration [11, 12]. The correlation of glycemic control and clinical outcomes, including mortality in diabetic patients with COVID-19 and post covid sequelae due to pancreatic beta cell damage has been demonstrated recently in the literature, but not well established.

Therefore, in this present study, our main aim is to study glycemic control in terms of HbA1c in covid positive diabetic patients at admission and follow up after 6 months. And also study the clinical outcome in terms of mortality, ICU admission and duration of hospital stay and requirements of anti- diabetic medications at discharge and after 6 months of follow up and compare between pre covid and post covid requirements in diabetic patients treated with and without steroids.

AIMS AND OBJECTIVES

1) To study glycemic control in terms of HbA1c at admission and follow up after 6 months in COVID- 19 positive diabetic patients with and without steroids.
2) To study clinical outcome in terms of mortality, ICU Admission and stay, duration of hospital stay in COVID-19 positive Diabetic patients with and without steroids and the requirements of anti- diabetic medications at discharge and after 6 months of follow up and compare between pre covid and post covid requirements in diabetic patients treated with and without steroids

MATERIALS AND METHODS

This was a Comparative observational study conducted from March 2020 to June 2021 in AJ Institute of Medical Sciences and Research Centre, Mangalore .Patients enrolled in this study are known case of type 2 diabetes mellitus with laboratory confirmed covid 19 positive were categorized in to 2 groups based on AIIMS/ICMR Clinical guidance for management of adult COVID-19 patients. Total of 88 patients were recruited for the study based on inclusion and exclusion criteria .Group 1 were moderate to severe category covid 19 positive diabetic patients treated with steroids (n-44) and group 2 were mild category covid positive diabetic patients not treated with steroids (n-44).

Informed consent was taken. Information from medical records was extracted for evaluation, interpretation, and association among both groups regarding medical history, clinical manifestations, laboratory findings, management, and outcome.

The following parameters were considered

1) FBS,+/-PPBS,HbA1C at the time of admission
2) Duration of hospital stay
3) ICU Admission and length of stay
4) Mortality in the hospital
5) Anti-diabetic medications before covid and at the time of discharge
6) After 6 months, HbA1c, FBS/RBS, Anti-diabetic medications noted.

ETHICS COMMITTEE APPROVAL: Approved by AJ Institute of Medical Sciences ethics committee

INCLUSION CRITERIA

- Age >18 years
- Known case of type 2 Diabetes mellitus with Laboratory confirmed RTPCR/Rapid antigen test positive Covid -19 patients.

EXCLUSION CRITERIA

- CKD/nephrotic syndrome
- Malignancy
- Patients less than 18 years of age
- Pregnancy

STATISTICAL ANALYSIS

1) Descriptive statistics was used to summarize the data.
2) Categorical variables were represented as percentage.
3) Diagrammatic representation such as simple bar diagram, multiple bar diagram was used torepresent the data.
4) Normality of the data was checked using Kolmogorov-Smirnov test and the observations which follow normal distribution where subjected to parametric tests such as paired t test, unpaired t test and variables which did not follow normal distribution were subjected to non-parametric tests suchas Mann Whitney U test.
5) Chi square test was used to test the association of the selected variables of interest for clinical outcome between steroid and non-steroid groups.
6) Scatter diagram was used to get visual idea regarding correlation between variables.
7) To measure the strength of relationship between variables, Karl Pearson's correlation coefficient (r) was used.
8) The value of r lies between -1 and +1.
9) The value of r >0 implies positive correlation between variables and r<0 implies negative correlation between variables.
10) P<0.05 will be considered to be statistically significant.

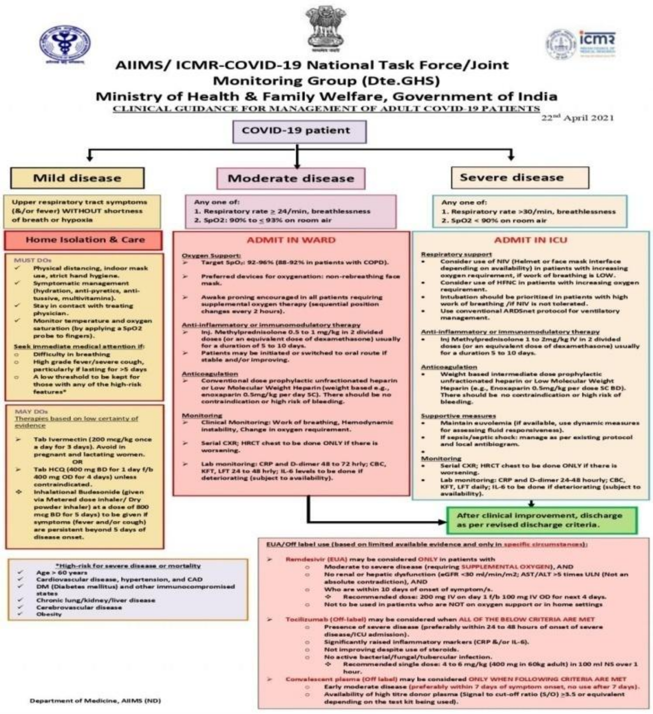

Figure 1: Clinical guidance for management of adult COVID-19 patients according to AIIMS/ICMR

RESULTS

Table 1: Comparison of HbA1c levels at admission among patients with andwithout steroids

HbA1c	Numbe	Mean	Std.	Minimu	Maximu	Percentiles			Mann Whitney	P valu
						25th	50th	75t h		

	r		Deviation	m	m		(Median)		Utest value	e
Without Steroids	44	9.775	2.9336	6.3	20.0	8.000	8.800	10.950	802.5	0.137
With Steroids	44	10.111	2.5752	5.5	17.5	8.800	9.350	11.483		

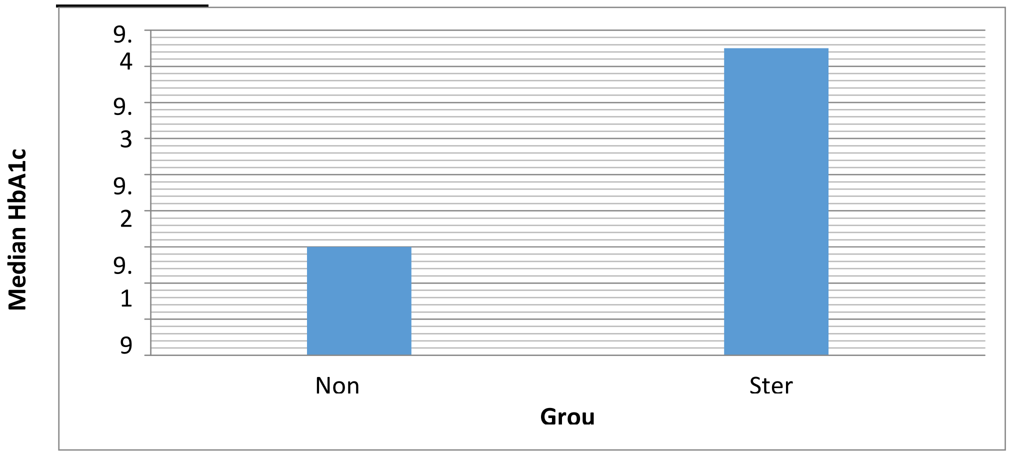

Figure 2: Comparison of Hba1c levels at admission among patients with andwithout steroids

From the above Table and Figure it may be observed that the median HbA1c levels among COVID 19 patients without steroids and with steroids is 8.80 with IQR (8.00- 10.95) and 9.35 with IQR(8.80- 11.48) respectively. On using Mann Whitney U test statistically no significant difference was observed in HbA1c levels among COVID patients without andwith steroid (p>0.05)

Table 2: Comparison of HbA1c at admission and follow up between 2 groups

	Mean	N	Std. Deviation	t test value	P value
Non HbA1c at Steroid admission group	9.775	44	2.9336	4.497	.000
HbA1c at follow up	7.01	44	2.683		
Steroid HbA1c at					
Group admission	10.111	44	2.5752	6.801	.000
HbA1c atfollow up	5.47	44	4.397		

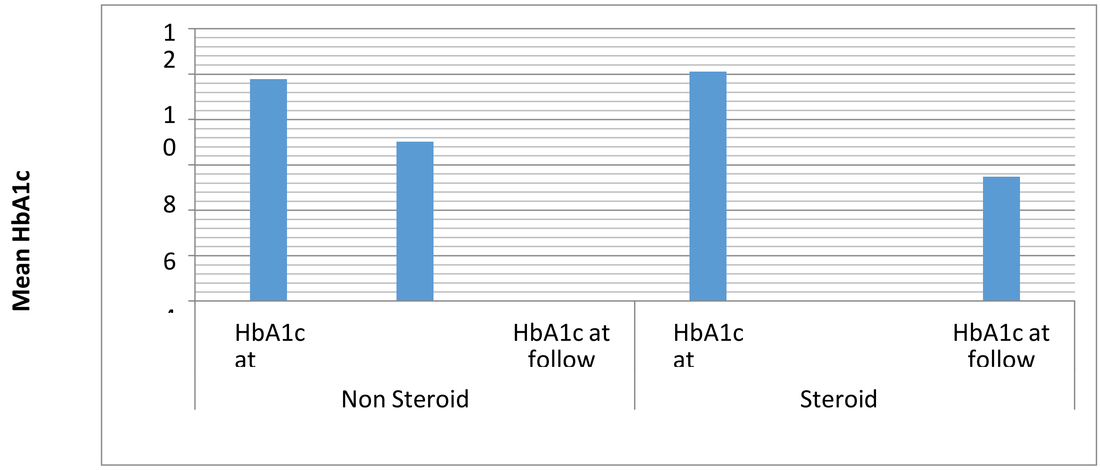

Figure 3: Comparison of Hba1c at admission and follow up between 2 groups

Among patients who were not on steroids, the mean HbA1c level at admission and at follow up is found to be 9.775±2.9 and 7.01 ±2.68 respectively. Also among patients who were on steroids, the mean HbA1c at admission and at follow up is found to be 10.11 ±2.57 and 5.47 ± 4.397 respectively. On applying Paired t test, statistically very high significant differencewas observed in HbA1c level at admission and follow up among patients who were not onsteroids (p<0.001) and also among patients who were on steroids (p<0.001).

Table 3: Comparison of improvement in HbA1c levels among patients with andwithout steroids

Difference inHbA1c	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles			Mann whitney U test value	P value
						25th	50th (Median)	75th		
Non steroid group	44	-2.7614	4.07341	-17.80	1.10	-4.6500	-1.000	-.200	2.233	.026
Steroid Group	44	-4.6382	4.52407	-17.50	3.40	-8.2875	-4.550	-.8250		

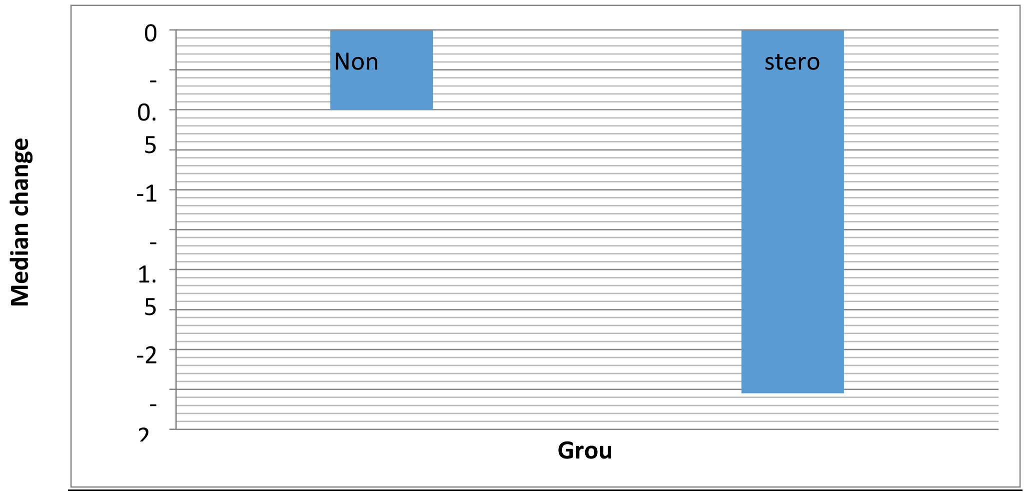

Figure 4: Comparison of improvement in HbA1c levels among patients with and without steroids

The above table reveals that the median change in HbA1c levels from admission to follow upamong patients without and with steroids is found to be 1.00 with IQR (4.65 -0.200) and 4.550 with IQR (8.287 – 0.8250)respectively. Mann Whitney U test shows statistically significant difference in the reduction of HbA1c levels among patients without and withsteroids (p<0.05)

Table 4: Comparison of the outcome- duration of hospital stay & ICU stay (in days)between the groups

Duration of hospital stay (indays)	Group	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles			P value
							25^{th}	50^{th} (Median)	75^{th}	
	Steroid	44	12.07	6.529	2	30	6.25	10.50	16.50	.375
	Non steroid	44	10.39	4.260	3	20	7.00	10.00	12.00	
ICU stay (in days)	**Steroid**	44	5.34	6.473	0	22	.00	3.00	9.75	.000
	Non Steroid	44	.45	1.355	0	6	.00	.00	.00	

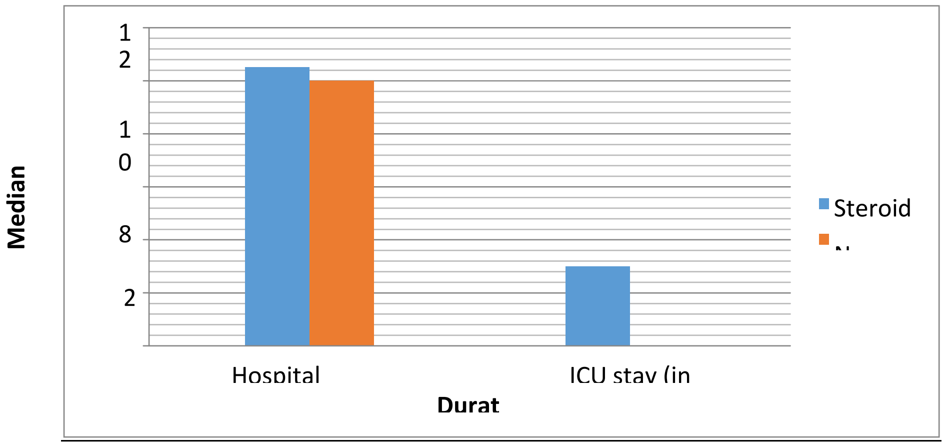

Figure 5: Comparison of the outcome- duration of hospital stay & ICU stay (in days) between the groups

Using Mann Whitney U test statistically very high significant difference was observed in the duration of ICU stay between the groups (p<0.001) The median duration of hospital stay was 10.50 days among steroid group and 10.0 days among non-steroid group. Therefore no statistical significant difference observed in duration of hospital stay between 2 groups.

Table No. 5: Comparison of the outcomes between the groups

			Group		Total	P value
			Non Steroid	**Steroid**		
Clinical outcome	**Died**	**Count** **%**	0 0.0%	12 27.3%	12 13.6%	.000
	Discharged	**Count** **%**	44 100.0%	32 72.7%	76 86.4%	
Total		**Count** **%**	44 100.0%	44 100.0%	88 100.0%	

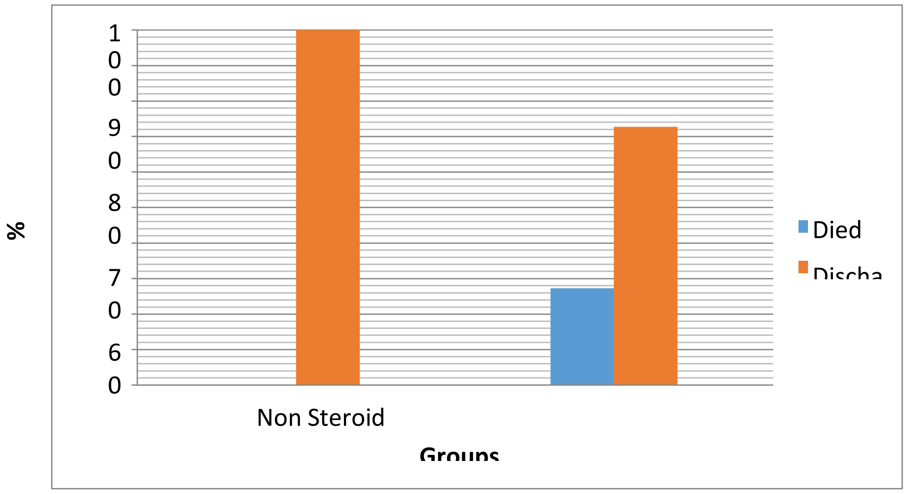

Figure 6: Comparison of the outcomes between the groups

Using Chi Square test, statistically very high significant difference has been observed in the outcomes in terms of mortality in the steroid and non-steroid group (p<0.001)

Table 6: Comparison of anti diabetic medications given before COVID

			Group		Total	Chi Square test	P value
			Non Steroid	**Steroid**			
OHA insulin before COVID	OHA	Count	38	33	71	1.885	.390#
		% within Group	86.4%	75.0%	80.7%		
	Insulin	Count	1	0	1		
		% within Group	2.3%	0.0%	1.1%		
	OHA+Insulin	Count	1	3	4		
		% within Group	2.3%	6.8%	4.5%		
	No medication	Count	4	8	12		
		% within Group	9.1%	18.2%	13.6%		
Total		Count	44	44	88		
		% within Group	100.0%	100.0%	100.0%		

Cell frequencies were pooled

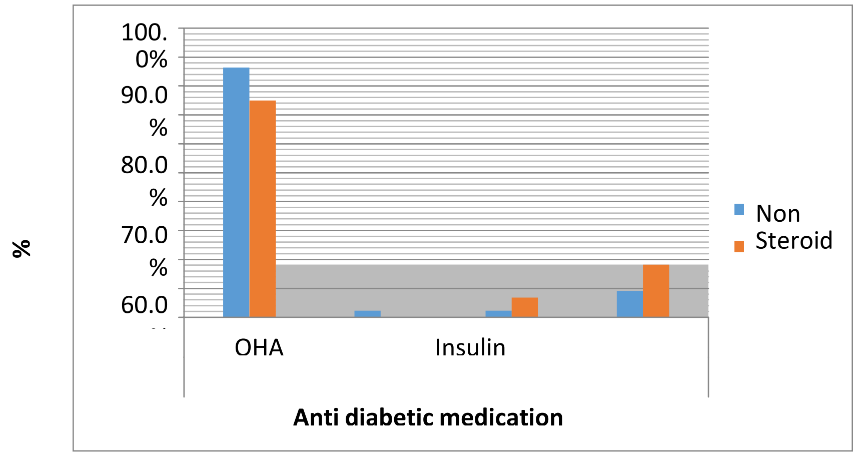

Figure 7: Comparison of anti-diabetic medications given before COVID

Using Chi square test, statistically no significant difference was observed in the anti-diabetic medications given before COVID between the groups (p>0.05). In both groups, 86.4% and 75% patients were on OHA among non-steroid and steroid group respectively before COVID.

Table 7: Comparison of anti-diabetic medications on discharge

			Group		Total	Chi Square test	P value
			Non Steroid	Steroid			
OHA insulin on discharge %	Expired	Count %	0 0.0%	12 27.3%	12 13.6%	21.106	.000
	OHA	Count %	38 86.4%	19 43.2%	57 64.8%		
	Insulin %	Count %	3 6.8%	8 18.2%	11 12.5%		
	OHA+Insulin	Count %	3 6.8%	5 11.4%	8 9.1%		
Total		Count %	44 100.0%	44 100.0%	88 100.0%		

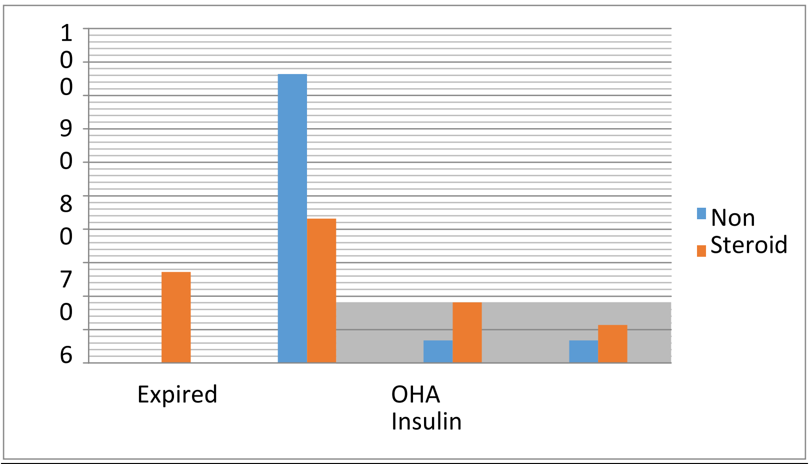

Figure 8: Comparison of anti-diabetic medications on discharge

Using Chi square test, statistically very high significant difference was observed in the anti-diabetic medications on discharge between the groups (p<0.01)

Among non-steroid group, 86.4% were on OHA and 6.8% were on insulin and combination of insulin and OHA on discharge. Among steroid group, 43.2% were on OHA, 18.2% on insulin and 11.4% on combination of OHA and insulin on discharge.

Table 8: Comparison of anti-diabetic medications on follow up

			Group		Total	Chi Square test	P value
			Non Steroid	Steroid			
	Expired	Count	4	13	17	9.249	.026#
		% within Group	9.1%	29.5%	19.3%		
	OHA	Count	30	17	47		
		% within Group	68.2%	38.6%	53.4%		
	Insulin	Count	4	1	5		
		% within Group	9.1%	2.3%	5.7%		
	OHA+Insulin	Count	3	10	13		
		% within Group	6.8%	22.7%	14.8%		
	No medication	Count	2	1	3		
		% within Group	4.5%	2.3%	3.4%		
	Lost to follow up	Count	1	2	3		
		% within Group	2.3%	4.5%	3.4%		
Total		Count	44	44	88		
		% within Group	100.0%	100.0%	100.0%		

cell frequencies were pooled

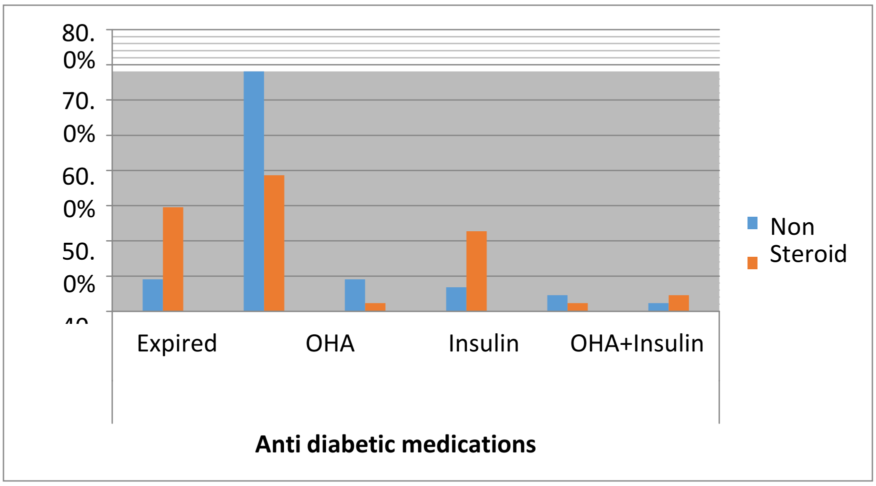

Figure no-9: Comparison of anti-diabetic medications on follow up

Using Chi square test, statistically significant difference was observed in the anti-diabetic medications given on follow up between the groups ($p<0.05$).On follow up after 6 months, among non-steroid group 68.2% were on OHA , 9.1% on insulin and 6.8% on combination of OHA and insulin. Among steroid group, 38.6% on OHA, 22.7% on combination of OHA andinsulin and 2.3% were only on insulin.

Table 9: Comparison of the requirements of antidiabetic medications (n=68) atdischarge and follow up

Requirement of antidiabetic medication			Group		Total	Chi Square test value	P value
			Non Steroid	Steroid			
	Increased	Count	18	14	32	2.534	0.282
		%	46.2%	48.3%	47.1%		
	Decreased	Count	7	9	16		
		%	17.9%	31.0%	23.5%		
	Same	Count	14	6	20		
		%	35.9%	20.7%	29.4%		
Total		Count	39	29	68		
		%	100.0%	100.0%	100.0%		

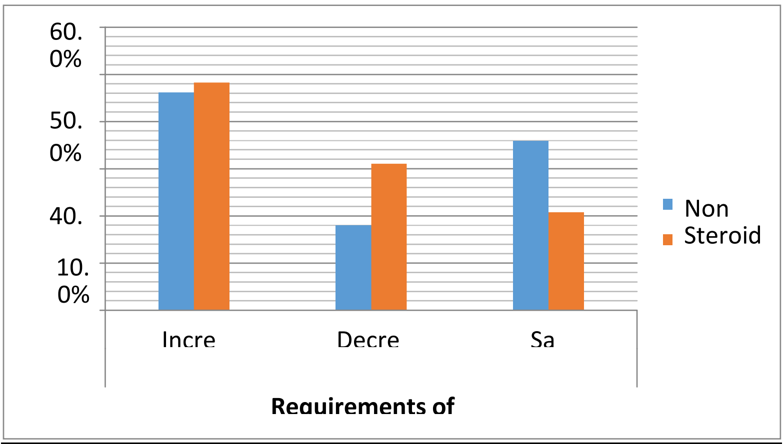

Figure 10: Comparison of the requirements of antidiabetic medications (n=68) atdischarge and follow up.

From the above table it may be seen that the requirement of anti-diabetic medication was found to have increased among 14 (48.3%) patients in the steroid group and among 18(46.2%) in the non-steroid group. On applying Chi Square test, statistically no significant difference was observed ($p>0.05$) between 2 groups, however clinically the difference may be observed between 2 groups. There is significant increase in requirement in both groups (47.1%) when compared at the time of discharge and follow up.

Table 10: Requirements of anti-diabetic medications in terms of frequencydistribution among steroid and non steroid groups before and after COVID

Non steroid	Frequency	Percent
Expired	4	9.1
Increased	25	56.8
Decreased	3	6.8
Same	11	25.0
Lost to follow up	1	2.3
Total	44	100.0

Steroid	Frequency	Percent
Expired	13	29.5
Increased	23	52.3
Decreased	3	6.8
Same	3	6.8
Lost to follow up	2	4.5
Total	44	100.0

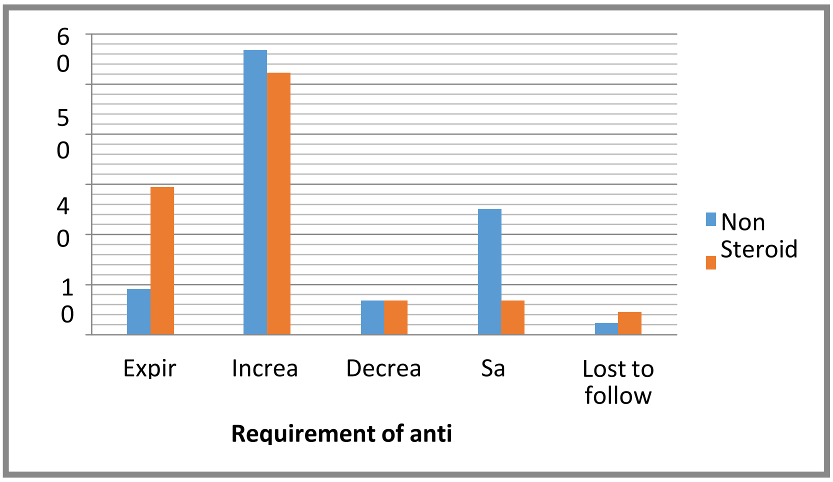

Figure 11: Requirements of anti-diabetic medications in terms of frequencydistribution among steroid and non steroid groups before and after COVID.

From the above table it may be seen that the requirement of anti-diabetic medication when compared before COVID and after 6 months post covid status was increased in steroid and non-steroid groups were 52.3% and 56.8% respectively whereas decrease in requirement ofanti-diabetic medication was 6.8% in both groups.

Table 11: Distribution of anti-diabetic medications before and after COVID amongnon-steroid group

Non Steroid group			Anti diabetic medications after COVID						Total
			Expired	OHA	Insulin	OHA+Insulin	No medication	Lostto follow up	
Anti diabetic medications before COVID	OHA	Count	4	26	2	3	2	1	38
		%	100.0%	86.7%	50.0%	100.0%	100.0%	100.0%	86.4%
	Insulin	Count	0	0	1	0	0	0	1
		%	0.0%	0.0%	25.0%	0.0%	0.0%	0.0%	2.3%
	OHA+Insulin	Count	0	0	1	0	0	0	1
		%	0.0%	0.0%	25.0%	0.0%	0.0%	0.0%	2.3%
	No Medication	Count	0	4	0	0	0	0	4
		%	0.0%	13.3%	0.0%	0.0%	0.0%	0.0%	9.1%
Total		Count	4	30	4	3	2	1	44
		%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

From the above table it is found among non-steroid group, 86.4% were on OHA before COVID among which 68.42% continued on OHA, 5.26% were started on insulin and 7.89%were started on combination of OHA and insulin. It is also seen that 13.3% of k/c/o type 2 diabetes mellitus who were not on medication before covid were started on OHA in post covid status.

Table 12: Distribution of anti-diabetic medications before and after COVID amongsteroid group

Steroid			Anti diabetic medications after COVID						Total
			Expired	OHA	Insulin	OHA+Insulin	No medication	Lost to follow up	
Anti diabetic medications befoere COVID	OHA	Count	10	14	1	6	1	1	33
		%	76.9%	82.4%	100.0%	60.0%	100.0%	50.0%	75.0%
	OHA+Insulin	Count	1	0	0	1	0	1	3
		%	7.7%	0.0%	0.0%	10.0%	0.0%	50.0%	6.8%
	No medication	Count	2	3	0	3	0	0	8
		%	15.4%	17.6%	0.0%	30.0%	0.0%	0.0%	18.2%
Total		Count	13	17	1	10	1	2	44
		%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.%

From the above table it is found that among steroid group, 75% were on OHA before COVIDamong which 42.42% continued on OHA, 3.03% were started only on insulin and 18.18% were started on combination of insulin and OHA.

Table 13: Comparison of requirement of anti-diabetic medications before and afterCOVID

Requirements of medications before andafter COVID		Groups		Total	Chi Square value	P value
		Non Steroid	Steroid			
Expired	Count	4	13	17	9.655	.022#
	%	9.1%	29.5%	19.3%		
Increased	Count	25	23	48		
	%	56.8%	52.3%	54.5%		
Decreased	Count	3	3	6		
	%	6.8%	6.8%	6.8%		
Same	Count	11	3	14		
	%	25.0%	6.8%	15.9%		
Lost to follow up	Count	1	2	3		
	%	2.3%	4.5%	3.4%		
Total	Count	44	44	88		
	%	100.0%	100.0%	100.0%		

cell frequencies were pooled

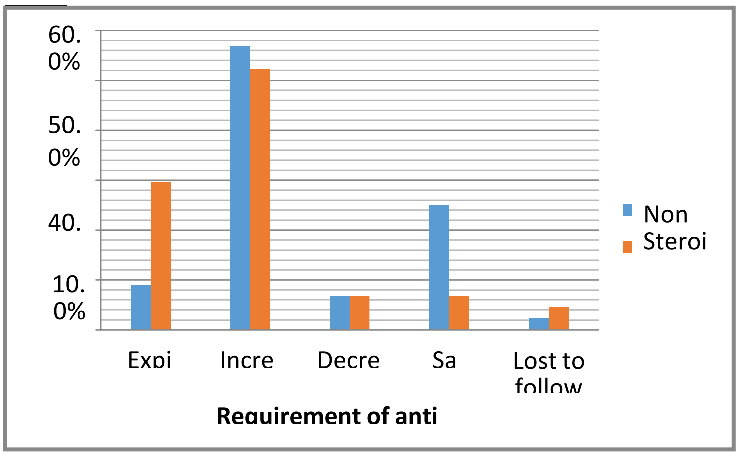

Figure 15: Comparison of requirement of anti-diabetic medications before and afterCOVID

From the above table it is seen that the increase in requirement of anti-diabetic medication was 56.8% and 52.3% among non-steroid and steroid group respectively when compared before and after COVID. Using Chi square test statistically significant difference was observed in the requirement of anti diabetic medications before and after COVID ($p<0.05$)

DISCUSSION

In our study, 88 Covid positive diabetic patients were enrolled and they were categorized into 2 groups based on AIIMS/ICMR Clinical guidance for the management of COVID-19 patients. Group 1 were moderate to severe category covid 19 positive diabetic patients treated with steroids (n-44) and group 2 were mild category covid positive diabetic patients not treated with steroids (n-44).

Medical records were analysed for information on medical history, laboratory findings, management, and outcome. Study done by Bhandari et al [13] studied Impact of glycemic control in diabetes mellitus on management of COVID-19 infection where 80 COVID-19 patients were enrolled to assess the difference between uncontrolled and controlled diabetes for COVID-19 manifestations. Patients were divided into two groups: those with uncontrolled diabetes (HbA1c > 8 g%) and those with controlled diabetes (HbA1c 8g%). COVID-19 patients with uncontrolled diabetes had severe symptomatic presentation, excessive uncontrolled inflammatory responses, and a hypercoagulable state. When compared to the controlled diabetes group, patients with uncontrolled diabetes had a higher mortality rate ($p = 0.0375$) and required more hospitalization ($p = 0.0479$).

Another study by Bode et al [14] studied Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States where uncontrolled hyperglycemia was defined as two blood glucoses greater than 180 mg/dL in a 24-hour period. The mortality rate in 184 diabetes and/or uncontrolled hyperglycemia patients was 28.8% compared to 6.2% in 386 patients without diabetes or hyperglycemia (P.001). Patients with diabetes and/or uncontrolled hyperglycemia had a significantly longer LOS and higher mortality than patients without diabetes or uncontrolled hyperglycemia.

In our study, we studied glycemic control in terms of HbA1c at admission and follow up after 6 months. It was found that good glycemic control was observed to have achieved on follow up in both the groups. Among the 2 groups, reduction was more among steroid group (-4.6382) comparedto non-steroid group (-2.7614) which could be attributed for aggressive blood glucose control with increased anti-diabetic medication at the time of discharge.

In South Korea, Moon et al [15] investigated the link between diabetes and COVID-19 severity. Patients with laboratory-confirmed COVID-19 aged 30 years were enrolled in this study. The numberof patient's hospitalised 94.0%, receiving oxygen16.7%, requiring ventilator support2.3%, and dying 4.0%. Among which, proportion of diabetic patients in outcome groups hospitalized 14.7%, receiving oxygen28.1%, requiring ventilator support 41.3%, and dying 44.6%, with an increasing trend based on outcome severity. Diabetes, regardless of other comorbidities, was associated with worse clinicaloutcomes in Korean patients with COVID-19.

In our study clinical outcome was assessed between 2 groups based on duration of hospital stay, ICU Admission and stay, mortality. The median duration of hospital stay was 10.50 days among steroid group and 10.0 days among non-steroid group. Therefore no statistical significant difference observed in duration of hospital stay between 2 groups. ICU Admission among the diabetic patients with steroids (n-44), 26 patients (59%) were admitted in ICU with average duration of 11 days and among diabetic patients without steroids, 5 patients (11.36%) were admitted in ICU with average duration of 4 days. Very high statistical significant difference was observed in the duration of ICU stay between the groups (p<0.001). Among diabetic patients with steroids (n-44), 27% (n-12) mortality noted whereas in non-steroid group (n-44) no mortality seen. Therefore statistically very high significant difference has been observed in the outcome between steroid and non- steroid group (p<0.001). Since steroid were given in more severe subgroup increased mortality could havehappened.

Very few studies have shown correlation between covid associated pancreatic injury and hyperglycemia. As a result, attention to pancreatic injury is lacking, which may have an impact on patients' prognosis. The following two studies have shown that covid 19 disease can cause pancreatic damage. Liu et al. [8] investigated the expression and distribution of angiotensin- converting enzyme 2 (ACE2), a SARS-CoV-2 receptor, in normal pancreases, as well as patients diagnosed with COVID19 in Wuhan Tongji Hospital and Wuhan Jin Yin-tan Hospital between January 1, 2020, and February 15, 2020. They discovered that the pancreas had higher levels of ACE2 messenger RNA than the lung (P.001, Wilcoxon signed-rank test). They discovered that ACE2 was expressed in both exocrine glands and islets after identifying different types of pancreatic cells.

There were 121 COVID-19 patients in the study cohort. In mild cases, 1.85% (1 of 54) had elevated amylase and lipase levels. 17.91% (12 of 64) of patients with severe COVID-19 had elevated amylase levels, while 16.41% (11 of 64) had elevated lipase levels. A computed tomography scan revealed changes in the pancreas in 5 patients with severe COVID-19 (7.46%), primarily focal enlargement of the pancreas or dilatation of the pancreatic duct, but no acute necrosis. They focused on the expression of ACE2 in the pancreas and pancreatic damage in a subset of SARS-CoV-2 patients in thisstudy. Therefore, ACE2 was expressed in normal people's pancreas, and that this expression was slightly higher in the pancreas than in the lungs, implying that SARS-CoV-2 could bind to ACE2 in the pancreas and cause pancreatic injury. Pancreatic injury occurred in approximately 1% to 2% of non- severe and 17% of severe COVID-19 patients in our study cohort.

According to Yang et al. [7] patients infected with SARS-CoV experienced hyperglycemia, whichcould be caused by SARS-CoV damaging the pancreatic islets via ACE2.

The findings of the above two studies suggest that the pancreas should be given special attention in patients with SARS-CoV-2 infection, particularly in severe cases. In our study, we observed that the requirement of anti-diabetic medication was found to have increased among 48.3% patients in the steroid group and among 46.2% in the non-steroid group at the time of discharge. But statistically no significant difference was observed between 2 groups (p>0.05), however clinically the difference was seen. The increase in requirement of anti-diabetic medication among non-steroid and steroid group was 56.8% and 52.3% respectively with significant statistical difference (p<0.05) when compared before and after COVID indicating the possibility of pancreatic beta cell damage persisting in post covid status among diabetic patients irrespective of treatment with or without steroids. But further large scale studies are required to prove the possibility of pancreatic beta cell damage in post covid diabetic patients.

CONCLUSIONS

- Glycemic control in terms of HbA1c was good among both steroid and non-steroid group after 6 month of follow up when compared from the time of admission. The reduction in HbA1c was more among steroid group compared to non-steroid group. This can be attributed to the increased requirement of anti- diabetic medication seen in steroid groupthan non-steroid group for strict control of blood glucose levels.
- The clinical outcome in terms of duration of hospital stay, ICU admission and stay, mortality was seen more among covid positive diabetic patients treated with steroids compared to non-steroid group. Since steroids were given in more severesubgroup increased mortality could have happened.
- The requirement of anti-diabetic medication has increased in both steroid and non-steroid group at the time of discharge and also after 6 months at follow up when compared from pre covid anti diabetic requirement indicating the possibility of pancreatic beta cell damage persisting in post covid status among diabetic patients irrespective of treatment with or without steroids.
- But further studies are required on large scale to prove the possibility of pancreatic beta cell damage in post covid diabetic patients.

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