



# **Effect of Sitagliptin and Glimepiride on Pancreatic Beta-Cells during the Treatment of Type-2 Diabetic Mellitus by Statistical Analysis**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author BJ designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author PY managed the literature searches. Author AGB supervised this research, which includes conception, design, analysis, interpretation of the data and organizing the article. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Aim:** The study aimed to analyze the effect of Sitagliptin with Glimepiride during the treatment to improve pancreatic beta-cells in T2DM patients. Beta cells are type of cell found in pancreatic islet and also synthesize, secrete the insulin and amylin. Sitagliptin is found to be maintaining the beta-cells function and glycaemic control in T2DM patients.

**Place and Duration of Study:** Sample: This study open label randomized T2DM patients, study was conducted at the, Felix multi-specialty hospital, Noida U.P with enrolled patients from 1<sup>st</sup> Oct, 2017 to 30<sup>st</sup> Sept, 2019.

**Methodology:** Randomly diabetes mellitus type-2 (T2DM) patients' data is collected (110patients) for statistical analysis. For this study T2DM patients enrolled with age of 30-60 years, treated with

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Sitagliptin and Glimepiride once a day. The baseline of HbA1c >7.0% to <10.5% thus, the performed student t-test is to find out the significance role.

**Results:** The 110 patients are distributed in two groups: one Sitagliptin user group (n=62) and second Glimepiride user group (n=43). The sitagliptin treatments may also protect also beta cells as pancreas may not able to regenerate beta cell.

**Conclusion:** The sitagliptin treatments may also protect beta cells as pancreas may not able to regenerate beta cell.

*Keywords: Beta-cells; diabetes mellitus type-2; glimepiride; sitagliptin.*

## 1. INTRODUCTION

Type-2 Diabetes mellitus (T2DM) is a metabolic disorder to hyperglycemia and dysfunction of pancreas and insulin resistance or deficiency of insulin. T2DM is a serious public health disease and globally increases in number by year over year. Metformin is a first-line of treatment for diabetes patients, on the other hand single anti-hyperglycemic agents are unsuccessful at achieving the target results in patients, so clinician preferred combination therapies [1] for effective T2DM treatment. Insulin resistance is a cause of hyperglycemic so mono-therapy with metformin is the most commonly used oral hypoglycemic agent regimen to treat patient with type-2 diabetes mellitus. The usage of sitagliptin is in regular practice to improve blood glucose level by stimulating insulin secretion from pancreatic beta-cells in a non-glucose dependents manner [2]. Sitagliptin is practiced as a single dosage medicine in a day and highly selective to dipeptidyl peptidase-4 (DPP-4) in many of countries for the diabetes mellitus patients treatment [3]. According to the report of UKPDS16 [4] the type-2 diabetes mellitus patients is treated with combination or add-on drug to improve insulin pancreatic beta cell function gradually. Sitagliptin treatment promising effect to reduce anti-inflammatory effect due to multiple actions and also effect the T-Lymphocyte and monocyte clinical usefulness of the add-on therapy with sitagliptin for T2DM would be decrease glycaemic [5].

In addition, DPP-4 inhibitor effect of pancreatic beta cell has been demonstrated in animal models [6] to show the effect and indicators of beta-cell function. A high P/I ratio suggests that there is a high proportion of proinsulin (pre-stage peptide of insulin) among the secreted insulin, which may indicate beta-cell dysfunction. Recently, Terauchi et al. [7] reported that sitagliptin exhibited a lowering the effect in P/I whereas glimepiride had no such effect in Japanese elderly type-2 diabetes patients. The present study is aimed the statistical analysis

over T2DM patients treated with sitagliptin with glimepiride to improve pancreatic beta cells in type-2 diabetes patients and compared the study to examine glucose levels with irrespective to age groups.

## 2. METHODOLOGY

The patients data having the diabetic history for last 2 years to 8 months with the age group between <30 years to <60 years data is collected for analysis. All patients are under the treatment with combination oral agents or without insulin therapy. This study open label randomized T2DM patients, study was conducted at the, Felix multi-specialty hospital, Noida U.P with enrolled patients from 1<sup>st</sup> Oct, 2017 to 30<sup>st</sup> Sept, 2019. This patient's blood glucose level is noted at the starting time of study and found to be from <125 mg/dl to 400 mg/dl. The complete methodology of patient selection is shown in Fig. 1.

The inclusion criteria parameters are (i) all patients diagnosed diabetic history (ii) age between 30 years to 60 years (iii) HbA1c > 6.9 % to < 10.5 %. The exclusion criteria parameter are (i) patients were already diagnosed Retinopathy, neuropathy, malignancy (ii) upper age >70 years excluded in the inclusion criteria, (iii) if patients history of ketosis, (iv) surgical treatment for severe infection, (v) symptoms of renal disease (serum creatinine level >1.6 mg/dl), (vi) history of Hepatic and malignancy and (vii) pregnancy, history of allergy. Only these are patients enrolled the study when full file the inclusion criteria.

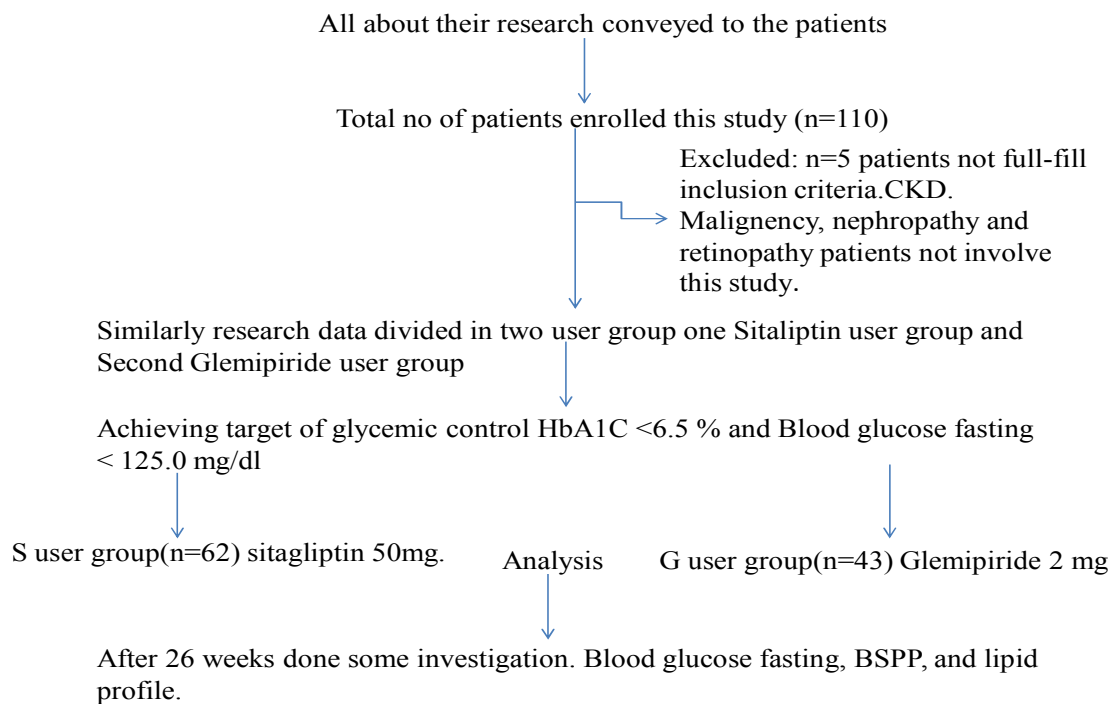
## 3. RESULTS

The patients were randomly divided two user groups: sitagliptin user group which patients use sitagliptin 50mg once a daily and second glimepiride user group which patients use glimepiride 2mg once a daily. The target glycaemic control was set HbA1c < 6.5 % and fasting glucose <125 mg/dl. After 26 weeks treatment we are done fasting glucose, 2h post-

meal, HbA1c, lipid profile data show in Tables 1 and 2. The primary hypothesis for the study was that sitagliptin (50mg) is non-inferior to glimepiride and improvement of pancreatic beta cell and glycemic control in 26 weeks of combination therapy. The chi-square test was used to analyze the patients data and perform the 'p' test. SD Mean calculated by mathematical formulas and level of significance analyzed by null hypothesis.

The primary characteristics of the patients are shown in Table 1. The total number of patients n=105 and sitagliptin user group n=62 and

glimepiride user group n=43 and done to calculate mean & standard deviation (SD) and p-value, after diagnosis of diabetes mellitus by HbA1c respectively, Mean age (54.88 ± 5.67 years in sitagliptin and 55.61 ± 5.17 years in glimepiride, respectively and p-value is 1.0), blood glucose fasting-BGF (187.39 ± 65.94 mg/dl in sitagliptin and 155.50 ± 48.79 mg/dl in glimepiride, respectively), blood glucose postprandial-BGPP (218.32 ± 78.0 mg/dl in sitagliptin and 166.0 ± 48.08 mg/dl in glimepiride, respectively), HbA1c % (8.25 ± 1.48% in sitagliptin and 8.65 ± 1.91% in glimepiride and p-value is (0.63), respectively. The treatment after



**Fig. 1. Methodology of selection parameters**

**Table 1. Clinical characteristics and demographical data of patients**

Tests	<sup>a</sup> S user group n=62	<sup>b</sup> G user group n=43	'p' value
	Mean ± SD	Mean ± SD	
Age(years)	55.61 ± 5.17	54.88 ± 5.67	1
Blood glucose fasting(mg/dl)	183.25 ± 56.44	167.46 ± 30.12	0
Blood glucose pp(mg/dl)	218.98 ± 65.32	205.19 ± 41.66	0
HbA1c %	8.16 ± 0.86	7.92 ± 0.84	0.63
<sup>c</sup> SGOT	32.47 ± 21.27	39.53 ± 26.46	0
<sup>d</sup> SGPT	32.81 ± 14.21	43.44 ± 22.24	0
Total cholesterol(mg/dl)	173.0 ± 35.85	185.12 ± 32.12	0
Triglyceride(mg/dl)	154.2 ± 48.62	199.30 ± 50.01	0
HDL-cholesterol(mg/dl)	43.76 ± 7.33	42.88 ± 5.88	0.2

<sup>a</sup>S user group: Sitagliptin; <sup>b</sup>G user group: Glimepiride; n: number of patients, <sup>c</sup>SGOT: Aspartate aminotransferase, <sup>d</sup>SGPT: Alanine aminotransferase

**Table 2. After 26 weeks treatment of sitagliptin (50mg) and glimepiride (2mg) HbA1c (%) and other parameters value change from dataset**

Test	<sup>a</sup> S user group n=62 Mean ± SD	<sup>b</sup> G user group n=43 Mean ± SD	'p' value
Blood glucose fasting(mg/dl)	123.39 ± 21.88	134.49 ± 17.44	0
Blood glucose pp(mg/dl)	157.60 ± 25.99	168.02 ± 22.57	0
HbA1c %	6.29 ± 0.30	6.54 ± 0.27	1
Total cholesterol(mg/dl)	162.50 ± 26.11	172.09 ± 26.20	0
Triglyceride(mg/dl)	150.06 ± 38.32	182.74 ± 35.12	0
HDL-cholesterol(mg/dl)	44.47 ± 4.06	43.19 ± 3.62	1

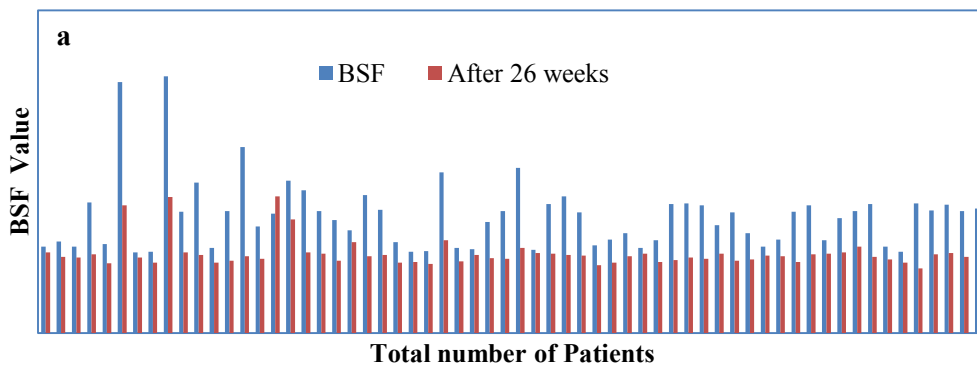
<sup>a</sup>S user group: sitagliptin; <sup>b</sup>G user group: glimepiride; n: number of patients. All values for HbA1c expressed as %

26 weeks, the percentage of HbA1c, blood glucose fasting and lipid profile level is found to be decrease significantly as showed in Table 2, respectively. Data indicates the DPP-4 inhibitors present in sitagliptin influence the insulin secretion by enhancing the glycogen like peptide-1 (GLP-1). The DPP-4 enzyme activity is inhibited by GLP-1 incretin function continue for insulin production. Insulin level increases in blood glucose level will be come down significantly. The treatment with sitagliptin glycosylated hemoglobin level in body maintained. DPP-4 inhibitor do not increase body weight, sitagliptin also decrease postprandial level, and triglyceride level.

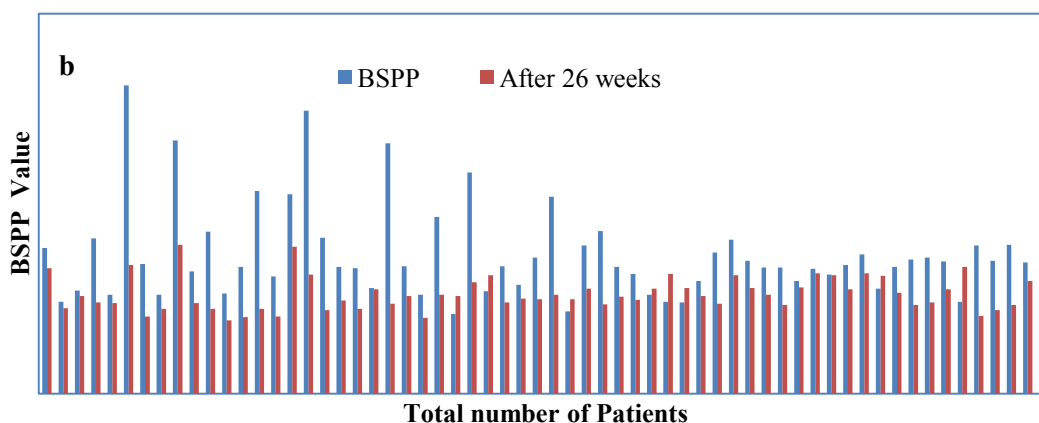
The Fig. 2(b) blood glucose level after 2h duration of post meal significant the effect on glycaemic control by treatment of 26 weeks with sitagliptin (50mg). Diabetes awareness programs help the patients to reduced fear a discourage option, which provide a potential for poorly glycaemic control. Diabetes treatment with insulin is at risk by developing hypoglycemic. The treatment with sitagliptin DPP-4 inhibitor inhibited plasma DPP-4 activity, inhibition of plasma DPP-4 activity sitagliptin increases in active GLP-1

and gastric inhibitory polypeptide levels influence to increase the insulin and C-peptide index level also reduced the blood glucagon level and reduced glycemic excursion [8] was found in an animal experiment with the treatment of sitagliptin. This data analysis also observed the significant improvement on pancreatic beta cells protecting and growth-promoting effects in the patient body [9]. The significant difference in data was found from the test values of the treatment beginning and after treatment of sitagliptin (50mg) regimen.

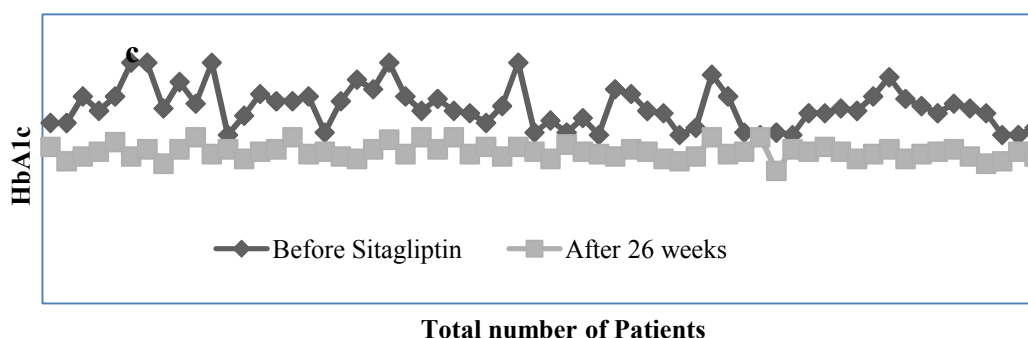
Fig. 2(c) confirms the HbA1c % value after 26 weeks treatments of sitagliptin (50mg) shows significant effect on glycaemic control. This is may be due to DPP-4 in inhibited the DPP-4 enzyme activity therefore insulin production increase inside the body and reduce the glucose level. Fig. 3a shows the variation in blood glucose fasting level over the 26 weeks of treatments of glimepiride regimen. The glimepiride directly out on ATP dependent K<sup>+</sup> channel of pancreatic beta-cells. This cause positive ion increase in side beta cells and the action potential, active potential enhance the Ca<sup>++</sup> channel of beta-cells for the moment of



**Fig. 2a. Graphical presentation of blood glucose fasting results before and after treatment of sitagliptin (50 mg)**



**Fig. 2b. Graphical presentation of blood glucose pp (2 h post meal) results before and after treatment of sitagliptin (50 mg)**



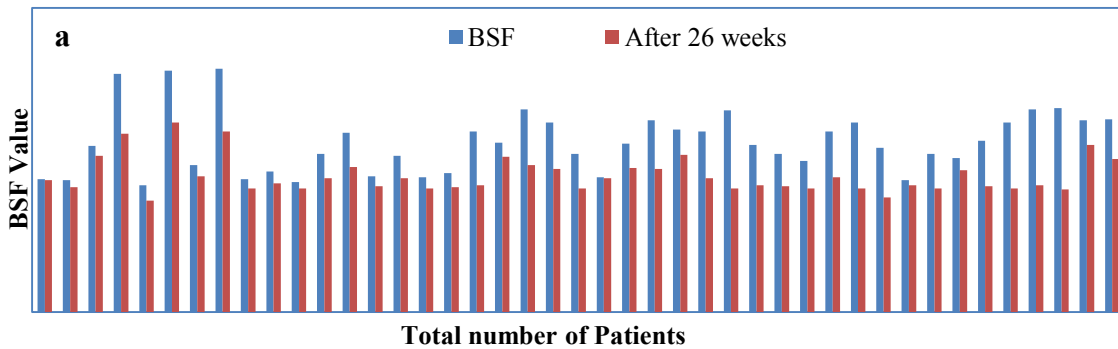
**Fig. 2c. Graphical presentation glycosylated haemoglobin (HbA1c) results of before and after treatment of sitagliptin (50 mg)**

Ca<sup>++</sup> ion inside from the outside. These Ca<sup>++</sup> ions bind with stored insulin and reduce it from beta cells released insulin reduced continues of glycosylated hemoglobin and blood glucose level. As shown in Fig. 3b, the change in HbA1c % level over the 26 weeks treatment period of glimepiride. Glimepiride inhibited the ATP dependent K<sup>+</sup> channel of beta cells to generated positive action potential to activate Ca<sup>++</sup> channel by which outside Ca<sup>++</sup> moves inside beta cells. These Ca<sup>++</sup> release stored insulin from beta cells. At 26 weeks, the primary goal of treatment is to target glycemic control by maintaining the HbA1c level near 6% to 6.5% shown in Table 1. The study expected and found that without any sort of side effect to control the blood sugar level by using combination therapy.

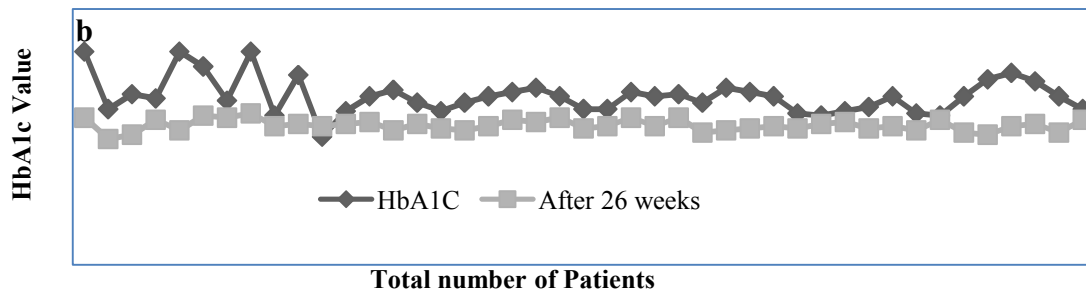
#### 4. DISCUSSION

Data were compared between the two groups using unpaired 't' test for measurement data the

'p' value and mean, standard deviation calculate after 26 weeks treatment with sitagliptin and glimepiride anti-hyperglycemic oral agents. The results of after 26 weeks data were found to be mean is 123.39 and SD-21.88 value of blood glucose fasting treated by sitagliptin and mean-134.49 and SD-17.44 is glimepiride, respectively. The value of HbA1c for same patients has drop down from baseline in comparison of starting values. After 26 weeks the HbA1c (6.29 ± 0.30 % in sitagliptin and 6.54 ± 0.27 % in glimepiride and p-value is 1.0), respectively. At 26 weeks, the patients achieving target HbA1c of <6.5 % with sitagliptin (50mg) were significantly higher compared to glimepiride (2 mg) therapy. However, there was a significant effect on the change in HbA1c percentage at 26 weeks is due to DPP-4 inhibitor activity of DPP-4 enzyme blockage and GLP-1 incretin is actively help in production of insulin and glucagon [10].



**Fig. 3a. Graphical presentation of blood glucose fasting results of before and after treatment of glimepiride (2 mg)**



**Fig. 3b. Graphical presentation of HbA1c results of before and after treatment with glimepiride (2 mg)**

Parameters of patient selection criteria is made on the basis of HbA1c because blood sugar levels of the most of the people is use to fluctuated depend upon individual physical condition like stress level and intake meal composition. The best parameter of HbA1c is from  $\geq 6.9\%$  -  $\leq 10.5\%$  to selected among the data of diabetic patients. The Fig. 2(a) reflects the blood glucose fasting graph of the drugs effect on clinical data after 26 weeks of sitagliptin (50mg) treatments [11]. This graph also clearly showing the considerable the effect on glycaemic control level. Diabetes is a progressive disease, glycaemic control directly associated with the onset and progression of retinopathy and nephropathy. The antidiabetic oral drugs and DDP-4 inhibitors influence endogenous incretin function and control with help of glucose homeostasis without increase the risk of unexpected weight gain and hypoglycemia [12,13]. Sitagliptin such as anti-inflammatory, effect on monocytes and T-lymphocytes, the clinical usefulness of the addition of sitagliptin in T2DM could improve beyond glycaemic reduction, secondary effects like prevention of weight gain, may be expected from the addition of sitagliptin to diabetes treatment [8,9]. Herman et al. [14]

used an animal experiment for evaluated the effect of sitagliptin, which shows the effect of protecting and promoting the growth of pancreatic beta cells in the body [15]. Pasquel et al. [16] also found that the metformin as an add-on therapy with Sitagliptin is found to be controlled levels of glycaemic over type-2 patients and also indicates low risk with control of hypoglycemia. In nutshell, the treatment with sitagliptin (100 mg) is more than effectively compared to glimepiride (1-3 mg) for T2DM patients in terms of achieving greater glycaemic control and most significant reduction in total daily dose required in insulin.

## 5. CONCLUSION

The present study intended on analyses the collected data of sitagliptin (50 mg) with metformin treatment over type-2 diabetes mellitus. The increase inadequate efficiency with better tolerance is seen in type-2 patients that result shows control glucose level. The comparison to glimepiride with sitagliptin (50 mg) found more effective to T2DM patients in treatments of achieving greater glycosylated hemoglobin. In nutshell, the present study

concludes the for better beta-cell function of protectiveness DDP-4 inhibitor protective effect has satisfaction outcome.

## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT

As per international standard or university standard, patients written consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

The study requirement, study protocol was conducted with the approval of the ethic committee of the Noida International University, U.P (NERB/SOS/CHEM/18/106) as per requirements of on need.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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