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THE INTERACTION STUDY OF THE ORAL HYPOGLYCEMIC AGENTS WITH RIFAMPICIN IN TUBERCULOSIS PATIENTS WITH DIABETES MELLITUS

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ABSTRACT

Background: Tuberculosis remains a foremost cause of morbidity and mortality in developing countries. Diabetes mellitus boosts the risk of active tuberculosis. DM management in patients with TB is also problematic. TB drug rifampicin increases the consent of most oral antidiabetic drugs that are generally used in low-income to middle-income countries, sulfonylureas are metabolized in the liver by CYPP450 enzymes, from which rifampicin is a virtuous inducer. To overcome the properties of rifampicin in dealing with and maintaining glycaemic control, metformin has been recommended as a better choice over other oral hypoglycaemic agents for the reason that it is not metabolized in the liver. Moreover, metformin is the primary choice antidiabetic according to type 2 DM treatment strategies. There is very inadequate data on the concomitant use of metformin and rifampicin and the essential for dose modifications in patients with TB-DM. In healthy volunteers, rifampicin produced altered oral hypoglycaemic agents' absorption kinetics, foremost to higher exposure levels and improved glucose-lowering action. Hence there is a prerequisite to comprehend the effect of Oral hypoglycaemic agents when co-administered with rifampicin.

Method: The study is shown in the pulmonologist department. The study participants were included based on the study principles. The data is collected after obtaining the informed consent. Demographic data, clinical history, diagnosis, and investigations were documented in a pre-formed questionnaire. The subjects who are being treated with oral hypoglycaemic drugs and rifampicin were analysed for the

hypoglycaemic effect by unvarying blood glucose evaluations. The details of the management of these hypoglycaemic events with the required modification of the metformin are recorded.

Result: The drug interaction of Rifampicin with oral hypoglycaemic drugs is the foremost objective of our study. A total of 50 subjects were contained in our study and they were divided into groups based on the oral hypoglycaemic drugs that were prescribed. This study was performed for 6 months and their levels of RBS were detected every time they revisited for their ATT adjustment up to 5 times. In the 50 patients, it is observed that the 9 patients on metformin show drip in their RBS upon their 2nd visit after starting their ATT. The rest of the test groups show elevation in RBS from their 2nd visit and the dose of their oral hypoglycaemic is adjusted based on the rise or lowering of their RBS levels.

Conclusion: The study was led on the drug interaction of Rifampicin with oral hypoglycaemic drugs, it is concluded in the study that Rifampicin relates with oral hypoglycaemic drugs and reduces the efficacy of the oral hypoglycaemic drugs. It is also detected that the efficacy of metformin is increased as it reduced the RBS level when ATT was started.

Keywords: Tuberculosis, Diabetes mellitus, Hypoglycaemic agents, Rifampicin, Oral hypoglycaemic agents

INTRODUCTION:

Tuberculosis (TB) relics a leading cause of illness and mortality in emerging countries [1]. Diabetes mellitus upsurges the risk of active tuberculosis. DM management in patients with TB is also challenging [2]. TB drug Rifampicin dailies the clearance of most oral antidiabetic drugs that are normally castoff in low income to middle-income countries, sulfonylureas are metabolized in liver by CYPP450 enzymes, from which rifampicin is a virtuous inducer [3]. To overawed the paraphernalia of Rifampicin on managing and upholding glycaemic control, metformin has been recommended as a healthier choice over other oral hypoglycaemic agents for the purpose that it is not metabolized in the liver.

Moreover, metformin is the first-choice antidiabetic bestowing to type 2 DM treatment guidelines [4]. There is very partial data on the concomitant use of metformin and rifampicin and the prerequisite for dose adjustments in patients with TB-DM. In healthy volunteers, Rifampicin caused reformed oral hypoglycemic agents absorption kinetics, leading to sophisticated exposure levels and enhanced glucose-lowering action [5]. Hence there is a necessity to understand the outcome of Oral hypoglycemic agents when co-administered with Rifampicin.

Glimepiride an anti-diabetic agent wholly absorbs over oral administration, which is high to 100% and eliminated through metabolism by CYP2C9. Whereas, Rifampicin which is a strong inducer of cytochrome P_{450} decreases the plasma concentration. thereby finishing numerous

drugs. where Rifampicin persuades CYP_2C_9-mediated metabolism of glimepiride thereby slightly cumulating its systematic clearance. Hence Rifampicin and Glimepiride interaction leads to Rifampicin moderately decreasing the t½ of Glimepiride and slightly decreases C_{max} [6]. Rifampicin is an active hepatic enzyme inducer. It accelerates the metabolism of numerous oral antidiabetics, in specific sulfonylureas and biguanides, and reduces their plasma concentrations.

METHODS:

Study Participants: A Minimum of 50 patients was included in this study.

- INCLUSION CRITERIA:

Patient >18 years of age.

Patient with complete tuberculosis who are diabetics.

Patients must be specified with Oral hypoglycemic agents and Rifampicin collected.

- EXCLUSION CRITERIA:

Immunocompromised patients.

Patients who are oversensitive to Rifampicin

Multi-drug resistance tuberculosis patients.

Patients who are on adapted ATT for the full course of the treatment.

Study Procedure:

The study is conducted at the pulmonologist department. The study participants were comprised based on the criteria. The data is collected after obtaining of the informed consent. Demographic data, clinical history, diagnosis, investigations will be verified in a pre-formed questionnaire [7]. The subjects who are being treated with oral hypoglycemic drugs and rifampicin were analysed for the hypoglycaemic effect by stable blood glucose evaluations. The details of management of these hypoglycemic events with requisite adjustment of the metformin was recorded.

STATISTICAL ANALYSIS:

Statistical analysis was permitted out utilizing SPSS software. P values < 0.05 were considered statistically noteworthy. All outcomes were presented using descriptive statistics; typically, distributed data by the mean and standard deviation (SD) and skewed distributions by the median and interquartile range (IQR) [8]. Binary and categorical variables were accessible using count. Statistical test is used is Fisher exact test [9].

RESULTS:

In this prospective observational study, we have experiential 50 patients on ATT on oral antidiabetic treatment. We also observed the drug interaction of rifampicin with oral antidiabetic agent and its management.

Illustration: There are 34 Male patients and 16 female patients on dialysis. Among these 50 patients 68% are male patients and 32% are female patients. The figure shows that

male populations are most likely to contract TB compared to female **(Table 1, Figure 1)**.

Illustration: The **Figure 2** displays around 9 patients between the ages of 18-30 years, 24 patients in the age amongst 31-40 years of age, and 12 patients amid 41-50 years of age, and 5 patients with in 51-60 years of age. In our study we have also found that patients between the ages of 31-40 are more usually infected with tuberculosis

Illustration: As shown in the **Figure 3** above it is understood that 9 patients were on Metformin, 21 were on Glimepiride, 12 were on Gliclazide and 8 were on Dapagliflozin along with typical 600 MG of Rifampicin as their ATT.

Illustration: As seen in the **Table 4** given directly above, it is understood that the RBS of patient on Metformin while on rifampicin drips but when the dose of Metformin is reduced the RBS starts increasing. And the mean percentage difference between the first visit and 2nd visit was found to be 59.03 %.

Illustration: As seen in the **Table 5** it is understood that the RBS of 12 patients on Gliclazide, while on Rifampicin is elevated. But when the dose of gliclazide is augmented, then the RBS starts dropping and the mean percentage difference between the first visit and 2nd visit is found to be 24.24 %.

Illustration: As seen in the **Table 6** it is seen that the RBS of the 21 patients on Glimepiride, while on Rifampicin is elevated but when the dose of Gliclazide is increased the RBS starts plummeting. And the mean percentage difference between the first visit and 2nd visit is found to be 43.9 %.

Illustration: As seen in the **Table 7** it is seen that the RBS of the 8 patients on Dapagliflozin while on Rifampicin is elevated but when the dose of Gliclazide is augmented the RBS starts dropping. And the mean percentage difference between the initial visit and 2nd visit is found to be 36.75 %.

Table 1: Distribution Of Patients According To Gender

GENDER	NO. OF PATIENTS	PERCENTAGE
MALE	34	68%
FEMALE	16	32%
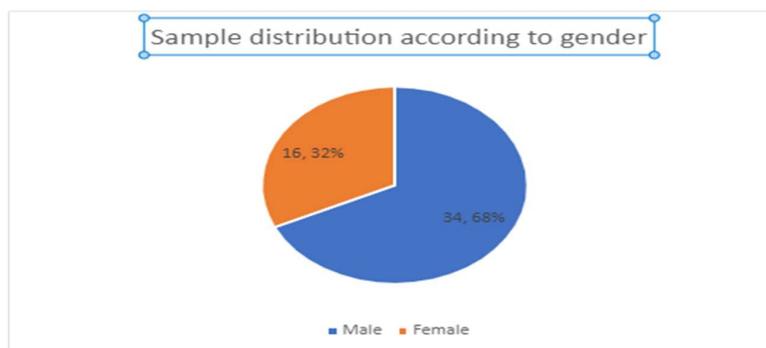
Figure 1: Distribution of sample according to Gender

Table 2: Distribution According To Age

AGE RANGE	PATIENT	PERCENTAGE
18- 30	9	18%
31-40	24	48%
41-50	12	24%
51-60	5	10%

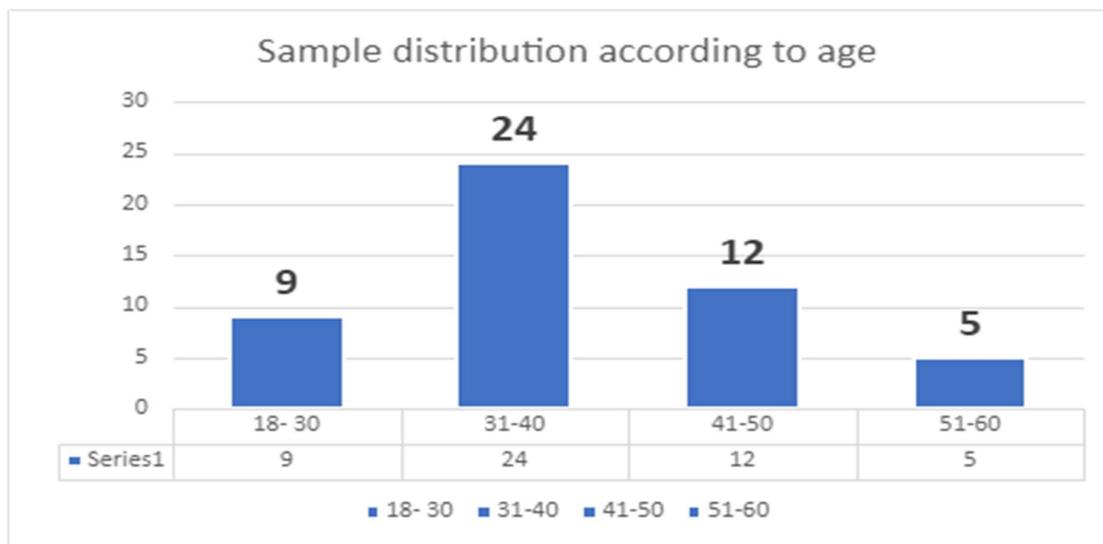**Figure 2: Sample distribution according to age**

Table 3: Sample Distribution According To Drugs

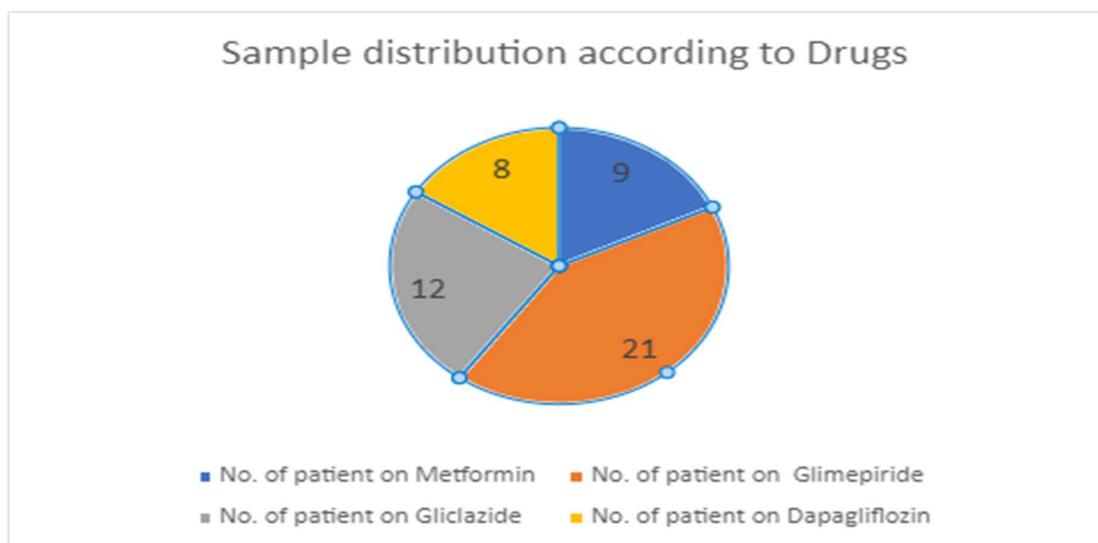| S. No	Patient Data	Total
1	No of patient on Metformin	9
2	No of patient on Glimepiride	21
3	No of patient on Gliclazide	12
4	No of patient on Dapagliflozin	8

Figure 3: Pie chart of sample distribution according to drug

Table 4: Level of RBS before and after Rifampicin therapy with metformin

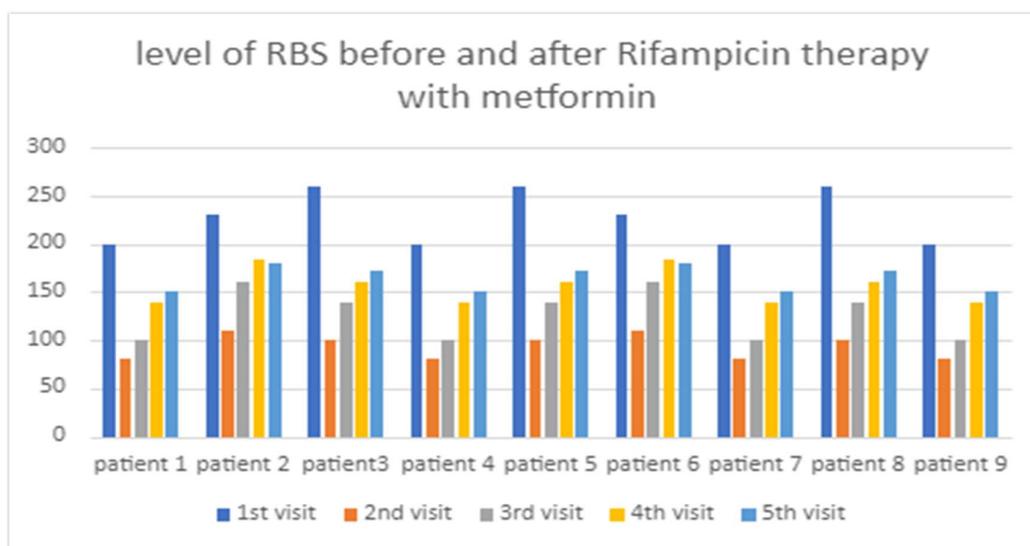| Patient Number	1st visit	2nd visit	3rd visit	4th visit	5th visit
patient 1	200	80	100	140	150
patient 2	230	110	160	184	180
patient3	260	100	140	160	173
patient 4	200	80	100	140	150
patient 5	260	100	140	160	173
patient 6	230	110	160	184	180
patient 7	200	80	100	140	150
patient 8	260	100	140	160	173
	200	80	100	140	150

Figure 4: Histogram of the RBS levels of 9 patients on their 1st visit to their 5th visit

Table 5: Level of RBS before and after Rifampicin therapy with gliclazide

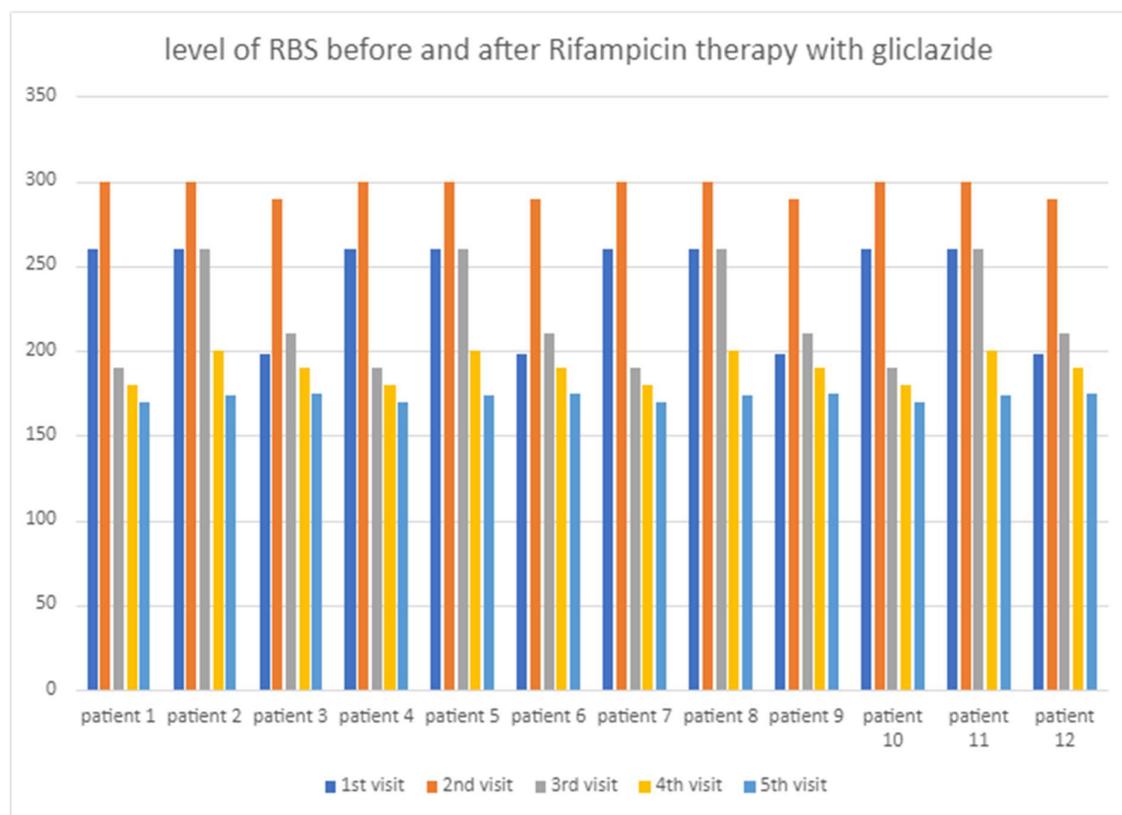| Patient Number	1st visit	2nd visit	3rd visit	4th visit	5th visit
patient 1	260	300	190	180	170
patient 2	260	300	260	200	174
patient 3	198	290	210	190	175
patient 4	260	300	190	180	170
patient 5	260	300	260	200	174
patient 6	198	290	210	190	175
patient 7	260	300	190	180	170
patient 8	260	300	260	200	174
patient 9	198	290	210	190	175
patient 10	260	300	190	180	170
patient 11	260	300	260	200	174
patient 12	198	290	210	190	175

Figure 5: Histogram of patients on gliclazide

Table 6: Level of RBS before and after Rifampicin therapy with glimepiride

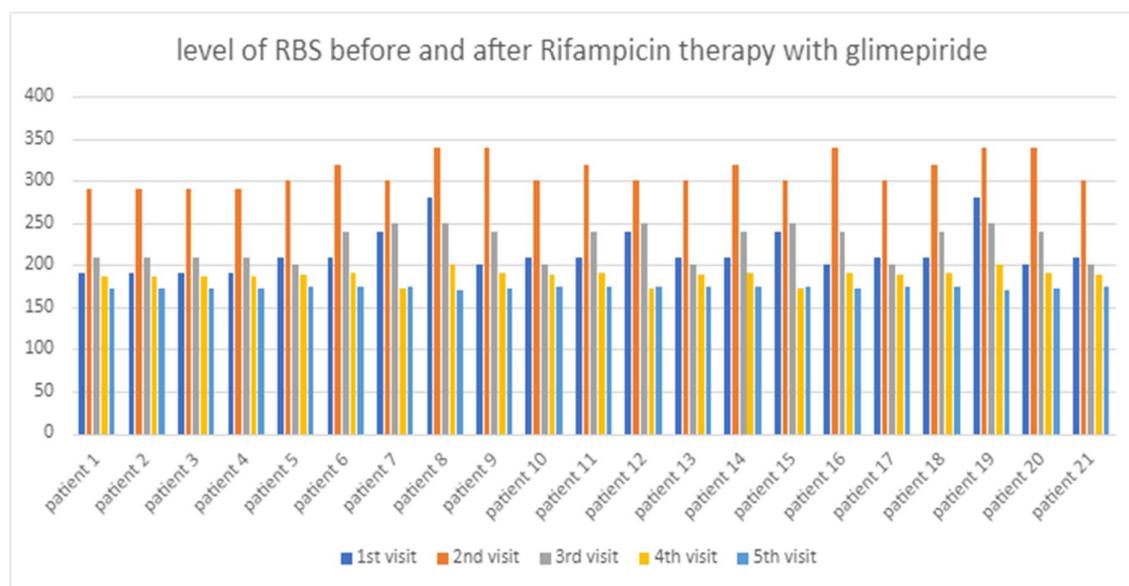| Patient Number	1st visit	2nd visit	3rd visit	4th visit	5th visit
patient 1	190	290	210	186	173
patient 2	190	290	210	186	173
patient 3	190	290	210	186	173
patient 4	190	290	210	186	173
patient 5	210	300	200	189	175
patient 6	210	320	240	190	174
patient 7	240	300	250	172	175
patient 8	280	340	250	200	170
patient 9	200	340	240	190	173
patient 10	210	300	200	189	175
patient 11	210	320	240	190	174
patient 12	240	300	250	172	175
patient 13	210	300	200	189	175
patient 14	210	320	240	190	174
patient 15	240	300	250	172	175
patient 16	200	340	240	190	173
patient 17	210	300	200	189	175
patient 18	210	320	240	190	174
patient 19	280	340	250	200	170
patient 20	200	340	240	190	173
patient 21	210	300	200	189	175

Figure 6: Histogram of patients on Glimepiride

Table 7: level of RBS before and after Rifampicin therapy with Dapagliflozin

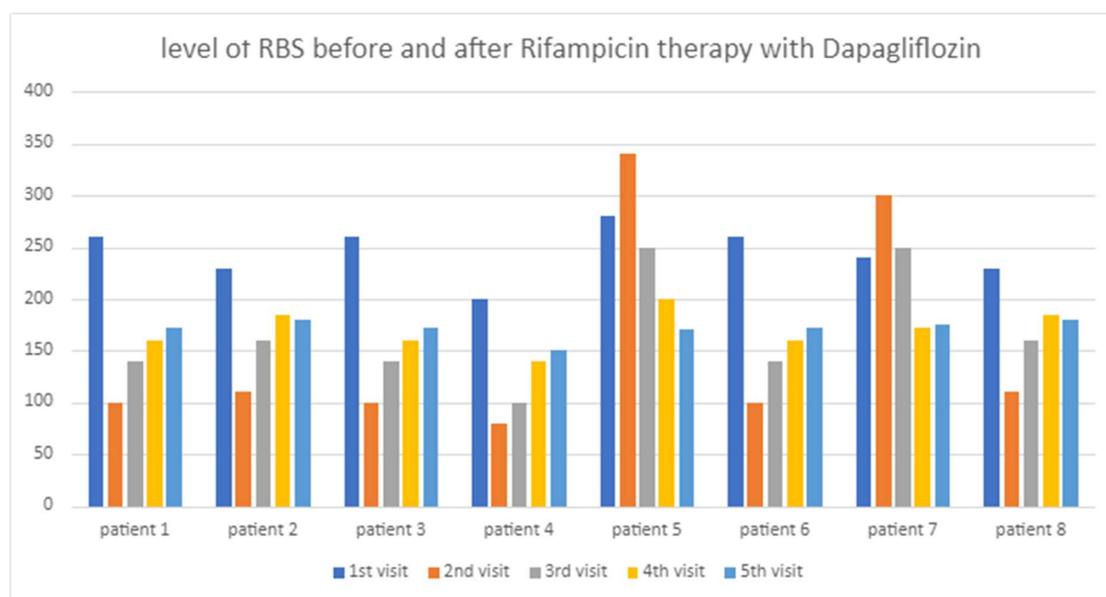| Patient Number	1st visit	2nd visit	3rd visit	4th visit	5th visit
patient 1	260	100	140	160	173
patient 2	230	110	160	184	180
patient 3	260	100	140	160	173
patient 4	200	80	100	140	150
patient 5	280	340	250	200	170
patient 6	260	100	140	160	173
patient 7	240	300	250	172	175
patient 8	230	110	160	184	180

Figure 7: Histogram of RBS levels of patient on Dapagliflozin

DISCUSSION:

The study connected to drug interaction of Rifampicin with other oral hypoglycaemic drug is the main objective of our study **[10]**. A total of 50 subjects were included in our study and they were divided into groups based upon their oral hypoglycemic drug they were prescribed **[11]**.

This study was achieved for 6 months and their levels of RBS were pragmatic on every time they re-entered for their ATT tuning up to 5 times **[12]**.

CONCLUSION:

In the 50 patients it is experiential that the 9 patients on metformin's show drops in their RBS upon their 2nd visit after preliminary task, their ATT while the rest of the test groups show increase in RBS from their 2nd visit and the quantity of their oral hypoglycaemic agents was attuned based on their increase or lowering of their RBS levels.

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