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Research article

A COMPARATIVE STUDY ON COMBINATIONAL DRUGS LIKE METFORMIN PLUS TENELIGLIPTIN AND METFORMIN PLUS GLIMEPIRIDE

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ABSTRACT

Diabetes mellitus is a metabolic disorder of multiple aetiology characterized by sustained hyperglycaemia with disturbances of carbohydrate, fat, and protein homeostasis resulting from defects in insulin secretion , insulin action or both. The defects in insulin secretion are the result of inappropriate functioning of the β cells of the pancreas while those in insulin action are generally associated with resistance of the peripheral tissues to insulin. In all cases, the end result is a defective availability of insulin. Biguanides and sulphonyl ureas are the most commonly prescribed drugs due to their safety and efficacy. They were divided into two groups based on their treatment plan – Group A and Group B. The Group A exhibited a significantly greater reduction inHbA1C as compared to Group B. The reductions in FBS and PPBS were also found to be significantly more in the Group A. In this present study we observed that the patients on Metformin plus Teneligliptin combination exhibited better control over glycemic profile when compared to patients who are on Metformin plus Glimepiride combination. Since, this study was conducted in less number of patients, to make consecutive remarks about the superiority of either of the treatment regimen, furthermore analysis of clinical trials is required for appropriate selection of best combination of anti – diabetic medication.

Key Words:- Surgery, Prophylaxis, Therapeutic Efficacy, Adverse Effects.

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INTRODUCTION

The key factors to promote and maintain good health throughout the life are diet and nutrition. Diabetes, cardiovascular disease, stroke, obesity, cancer, osteoporosis, and dental diseases are all chronic diseases linked to a diet and nutrition imbalance [Alberti, K.G.M.M. and Zimmet, P.Z. (1998)] [A. Ramachandran, 2014]. Chronic diseases accounted for 60% of total fatalities among 56.5 million persons in 2001, accounting for approximately 46% of the global burden of disease [Miriam Cnop, et. al. 2005]. Diabetes mellitus was diagnosed in 285 million people worldwide in 2010, a prevalence of 6.4 percent. By 2030, this number is expected to rise to 439 million, representing a prevalence of 7.7% [J. E. Shaw, et. al. 2010]. According to the latest 2019 data from the International Diabetes Federation, 463 million persons worldwide are projected to have diabetes when compared to developed countries, chronic disease is more prevalent in developing countries like India. Chronic diseases such as Diabetes Mellitus are expected to account for nearly three-quarters of all deaths by 2025, with 70% of diabetes-related deaths occurring in developing countries [Ravindranath Aathira, Vandana Jain, 2014] [Mohan V, et. al., 2007]. Diabetes mellitus (DM) is a metabolic condition defined by hyperglycaemia, which is caused primarily by disruptions in carbohydrate, protein, and lipid metabolism, resulting

in organ dysfunction and failure [Abdulfatai B. Olokoba, et.al., 2012] [Viollet B., et. al., 2012].

According to estimates, India will have 65.1 million adult diabetes mellitus patients by 2015, placing it second among the top ten countries with the highest number of diabetic patients, with the figure likely to rise to 109 million by 2035[Floris Alexander van de Laar, Vasc Health Risk Manag]. WHO has categorised diabetes mellitus as TYPE1 DIABETES MELLITUS (insulin dependent diabetes mellitus) and TYPE2 DIABETES MELLITUS (non insulin dependent diabetes mellitus) based on the aetiology [Abdulfatai B. Olokoba, et. al., 2012]. However, these classifications have vanished, and a new one has been proposed that explains four forms of diabetes: TYPE I, TYPE II, additional specialised types, and gestational diabetes[. Campbell LK., et. al., 1996]. By invading pancreatic islets with mononuclear cells, Type 1 DM primarily attacks pancreatic beta cells. Insulitis is an inflammatory process in which beta cells die as a result of direct interaction with macrophages and T cells, which might result in an initial lack of first-phase insulin production to glucose [Wachters-Hagedoorn RE, et. Al., 2007] [Ulrike Gottwald-Hostalek, et.al., 2016]

Diabetes mellitus type I: Dietary variables, genetics, anti and perinatal risk factors, stress filled life events, and environmental risk factors are all key causes of type I DM [Giuseppe Derosa and Salvadeo Sibilla, 2007].Because Type 1 DM is primarily caused by an insulin shortage, rapid acting insulin can be utilised when the patient demands a quick onset and short duration of action. Type 1 DM symptoms include polyuria, hyperglycemia, polyphagia, and polydipsia

METHODS:

Study Population and Design :

This research was carried out for 5 months in an ASHRAYA MULTI SPECIALTY HOSPITAL in Chittoor, Andhra Pradesh, India, from DECEMBER 2021 to APRIL 2022. The study enlisted both male and female patients with type 2 diabetes mellitus. Before beginning the investigation, the subjects were provided information about the framework of the study. Sensitive information about the subjects has been secured for the aim of maintaining the confidentiality of those who took part in the study. After discussing the study's risks and advantages to the patients, they signed informed consent forms. The latest study has enlisted the help of 200 volunteers. A total of 200 people were divided into two groups and studied in a prospective cohort study. - Patients aged 35 to 75 years are enrolled in this study, and both genders are participating.

- Patients with diabetes mellitus who are not taking metformin, glimepiride, or teneligliptin are excluded from the trial.
- The study will not include pregnant or lactating mothers.
- Patients with negative social behaviours, such as alcohol intake during and 6 months before to the trial, were eliminated.
- People who have had severe hypersensitivity or idiosyncratic reactions to Metformin, Glimepiride, or Teneligliptin in the past.
- Patients with renal failure or congestive heart failure are not eligible for the trial since they are contraindicated with the medications of our choice.
- Patients with underlying medical issues that jeopardise their safety or make participation in the trial impossible.

Enrolled patients gave informed consent and were divided into 2 groups. Group A was taking combinational therapy of Metformin (500mg) and Teneligliptin (20mg) . Group B was taking Metformin (500mg) and Glimepiride (2mg) .Total 200 patients were included for the study i.e., 100 subject in each group from baseline to 3 months after treatment. Estimation of Fasting blood sugar, postprandial blood sugar and glycated haemoglobin was measured in clinical laboratory of AASHRAYA MULTISPECIALITY HOSPITAL, CHITTOOR.

RESULTS:

The study enrolled two hundred and eight patients who matched the eligibility requirements. A total of 200 patients attended all of the follow-up appointments. Patients were known to have type 2 diabetes, had no concomitant illnesses, and had been treated with one of the medication combinations in our trial. The participants in the research had an average age of 53.519.4920795. In group 1, females have a higher mean SD age than males, but in group 2, males have a higher mean SD age than females. Table 1 shows the demographic characteristics of the study population as a whole.

The average age of group A patients is 52.5, while that of group B patients is 54.5. In group-B, the percentage of male patients is higher, but in group-A, the percentage of female patients is higher.

R0 denotes the baseline review, R1 denotes the first month review, R2 denotes the second month review, and R3 denotes the third month review data in group - A patients.

The mean fasting blood sugar (FBS) of group A patients (Metformin + Teneligliptin) at baseline was 189.06 66.17, while it was 92.62 15.09 at the final evaluation. Within one month of starting therapy, the blood sugar levels had stabilised. Figure 1 depicts the FBS levels on each evaluation of group A.

R0 denotes the baseline review, R1 denotes the first month review, R2 denotes the second month review, and R3 denotes the third month review data in group - A patients.

Group – A patients' mean postprandial blood glucose (PPBS) levels are 279.36 96.89, with a final review R3 of 138.59 18.39.

Within one month of starting treatment, the blood sugar levels had stabilised. In fig.2, the PPBS levels on each review of group – A patients are presented.

R0* denotes the baseline review, R1* denotes the first month review, R2* denotes the second month review, and R3* denotes the third month review data in group B patients.

The mean FBS concentration in group B patients is 176.6866.60, which is lower than the FBS concentration in group A. However, it is 94.82 15.13 at the final evaluation (R3*). Despite being under control in both groups, group A's FBS levels are better regulated than group B's. The concentration of FBS in each review of group B patients is depicted in fig 3.

R0* denotes the baseline review, R1* denotes the first month review, R2* denotes the second month review, and R3* denotes the third month review data in group B patients.

The mean PPBS of group – B patients was 258.54 83.30 at baseline and 139.76 20.87 at the conclusion of the final evaluation (R3*). Despite being under control in both groups, group A's PPBS levels are more regulated than group B's. The concentration of PPBS in each evaluation of group – B patients is depicted in fig 4.

Values are given as Mean SD, and R0, R1, R2, R3 values are compared in both groups; reviews from group 1 are compared to reviews from group 2. ANOVA and unpaired t test were used to find a significant difference.

Group –A had better management of fasting blood glucose levels than Group –B. At the end of the study, there was a significant difference in mean FBS levels between Group A and Group B patients (P0.0001) (R3). During the first (R1) and second (R2) reviews, however, there is no significant difference between the groups, with P values of 0.1430 and 0.0696, respectively.

Values are reported as Mean SD, and R0, R1, R2, R3 values are compared in both groups. When group 1 reviews are compared to group 2 reviews, a significant difference is discovered using ANOVA and an unpaired t test.

By the completion of the final review, the mean SD of PPBS was 279.3696.89 in group – A patients and 138.5918.39 in group – B patients (R3). At R3, there is a statistically significant difference in PPBS concentrations across the groups (P0.0001). During the first (R1) and second (R2) reviews, however, there is no significant difference between the groups, with P values of 0.1583 and 0.0818, respectively. Table 5 shows the results of PPBS level analyses within and between groups.

R0 denotes the baseline review of group A (Metformin + Teneligliptin) and R0* denotes the baseline review of group B (Metformin + Glimepiride) in this diagram.

The mean baseline FBS of patients in group A is 189.06 66.17, while the mean baseline Fasting blood glucose of patients in group B is 176.62 57.60, which is lower than group A. The mean baseline PPBS in group A is 279.36 96.89, while group B's mean baseline is 258.5483.30, which is lower than group A's.

R1 represents the first month review of group A (Metformin + Teneligliptin) and R1* represents the first month review of group B (Metformin + Glimepiride) in this diagram.

Group A and B FBS have mean SDs of R1 of 144.05 36.97 and 160.63 46.26, respectively. When compared to R1*, R1 had better control of fasting blood glucose levels.

The mean SD of PPBS in group R1 is 213.89 56.06, while the mean SD in group B's R1* is 237.87 78.08. When comparing R1 of group A to R1* of group B, the PPBS levels are better regulated in R1.

R2 denotes the second month review of group A (Metformin + Teneligliptin) and R2* denotes the second month review of group B (Metformin + Glimepiride) in this diagram.

The mean SD of fasting blood glucose in R2 of group – A is 108.82 16.80 and in R2* of group – B is 112.63 18.62.

When compared to R2* of group B, R2 of group A has better management of fasting blood glucose levels.

The mean SD of PPBS in group A's R2 is 176.65 46.61, and the mean SD of group B's R2 is 191.76 49.81. The PPBS level is better controlled in R2 of group A when compared to R2* of group B.

R3 represents the third month review of group A (Metformin + Teneligliptin) and R3* represents the third month review of group B (Metformin + Glimepiride) in this diagram.

In R3 of group A, the mean SD of fasting blood glucose is 92.62 15.13, while in R3 of group B, the mean SD of fasting blood glucose is 94.82 15.13. When compared to R3 of group B, the fasting blood glucose level is better managed in R3 of group A.

PPBS in R3* of group – A has a mean SD of 138.59 20.87, while PPBS in R3 of group B has a mean SD of 139.76 20.87.

R0 denotes baseline data, while R3 denotes the third month evaluation of group A.

R0 of group A has a mean SD of 9.913.695, while R3 has a mean SD of 6.121.486. When comparing R3 of group A patients to R0 of group A patients, the HbA1C level is dramatically controlled in R3.

R0* denotes baseline data, while R3* denotes data from group B's third month review.

R0* of group – B has a mean SD of 9.423.267, while R3* has a mean SD of 6.341.523. When comparing R3 of group A patients to R0* of group B patients, the HbA1C level is significantly controlled in R3

In this diagram, R0 represents baseline data and R3 represents the third month review of group A, whereas R0* represents baseline data and R3* represents the third month review of group B.

The mean SD of HbA1C in group A's R0 is 9.913.695, and the mean SD of HbA1C in group A's R3 is 6.121.486. The mean SD of HbA1C in group B's R0* is 9.42 3.695, while the mean SD of HbA1C in group B's R3* is 6.34 1.523. Both groups' HbA1C levels are significantly controlled in R3. When comparing the HbA1C levels of both groups, R3 of group A patients has much better control than R3 of group B patients.

TABLE 1: Comparision on fasting blood sugar reviews between and within groups

S.No	R0	R1	R2	R3	P
GROUP 1	189.06± 66.17	144.05± 36.97	108.82±16.80	92.62±15.09	<0.0001
GROUP 2	176.68±46.61	160.63±46.26	112.62±18.62	94.82±15.13	<0.0001
P	0.2517	0.1430	0.0696	<0.0001	

TABLE 2: Comparision of post prandial blood sugar reviews between and with in groups

S.No	R0	R1	R2	R3	P
GROUP 1	279.36± 96.89	213.89± 56.06	176.65± 46.61	138.59± 18.39	<0.0001
GROUP 2	258.54± 83.30	237.87± 77.08	191.76± 48.81	139.76± 19.875	<0.0001
P	0.2992	0.1583	0.0818	<0.001	

TABLE 3: Comparision of HbA1C reviews within and between groups

S.No	R0	R3	P
GROUP 1	9.91± 3.695	6.12± 1.486	<0.0001
GROUP 2	9.42± 3.267	6.34± 1.523	<0.0001
P	0.3021	<0.0001	

Figure 1: FBS levels in group-A patients compared from baseline (R0) to final review (R3).

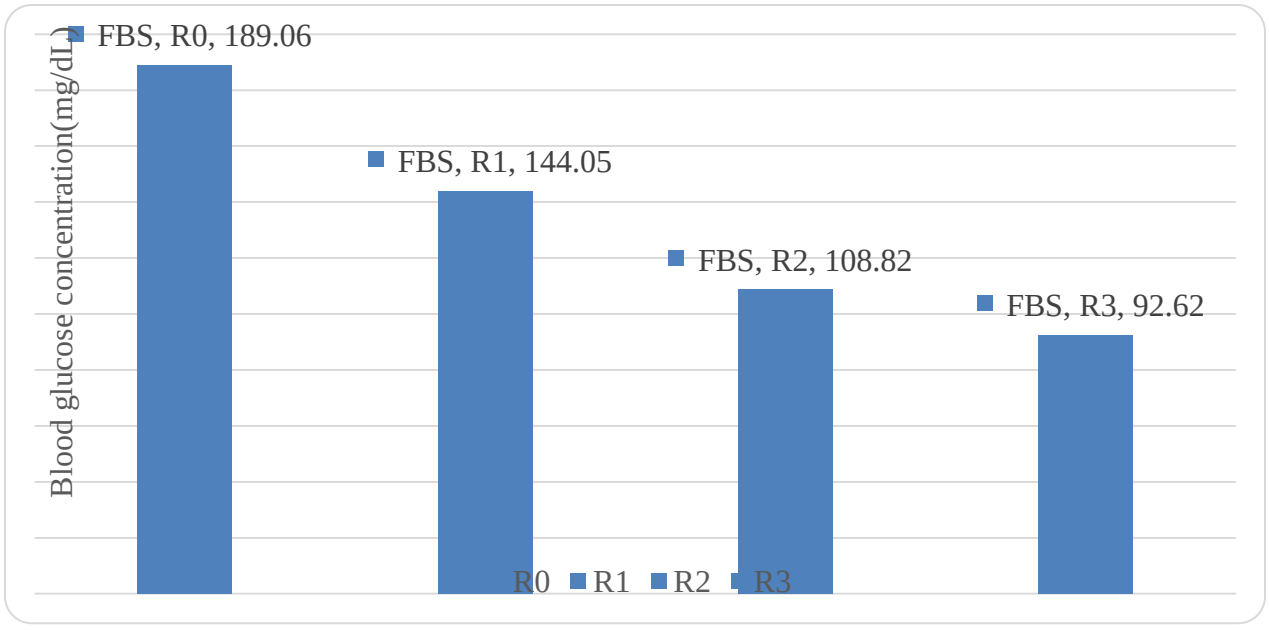
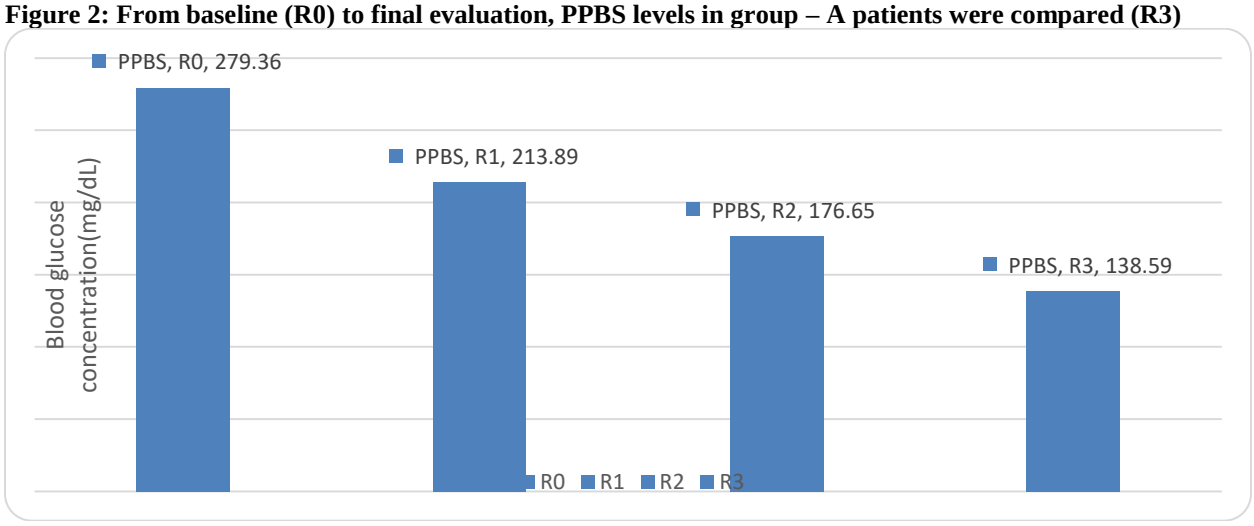


Figure 2: From baseline (R0) to final evaluation, PPBS levels in group – A patients were compared (R3)



Figuer 3: FBS levels in Group B patients compared from baseline (R0*) to final review (R3*).

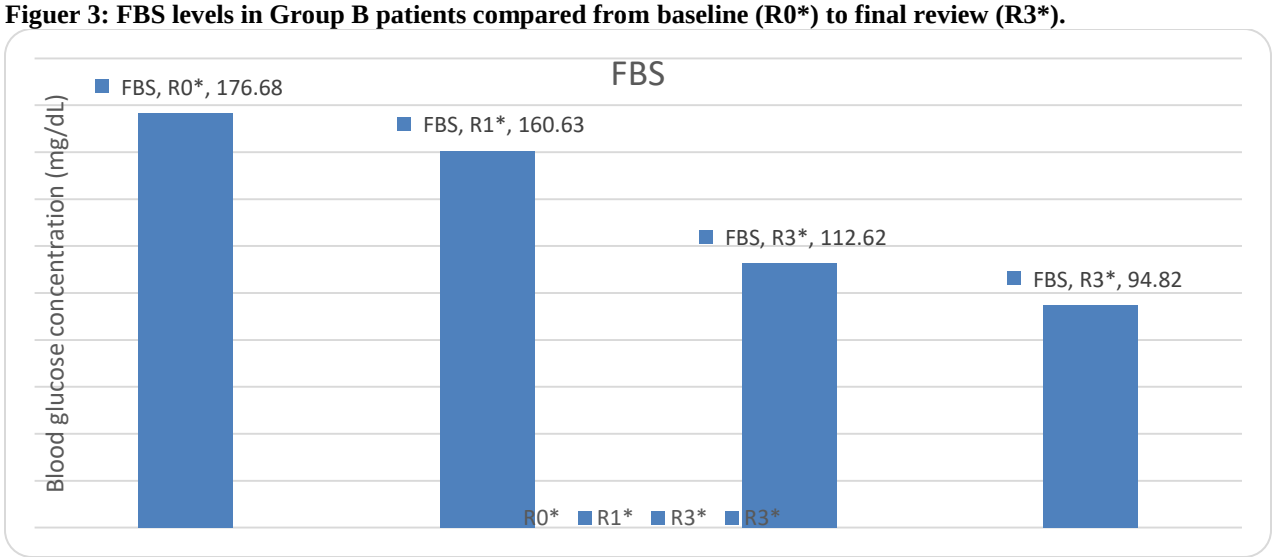


Figure 4: PPBS levels in group B patients compared from baseline (R0*) to final review (R3*).

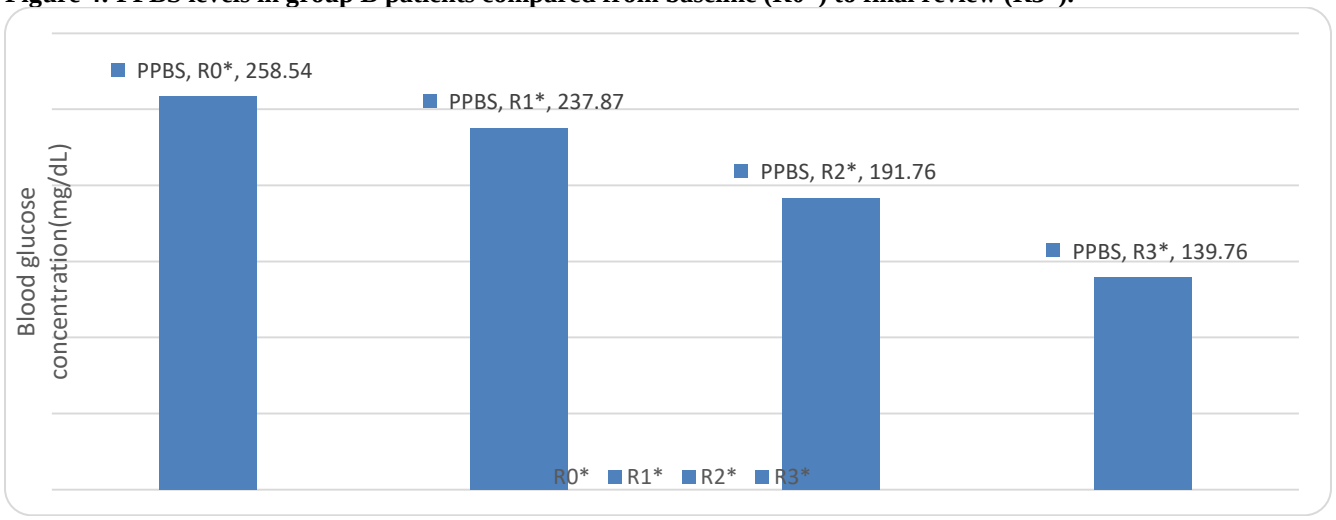


Figure 5: Blood glucose levels for baseline review data comparison between groups

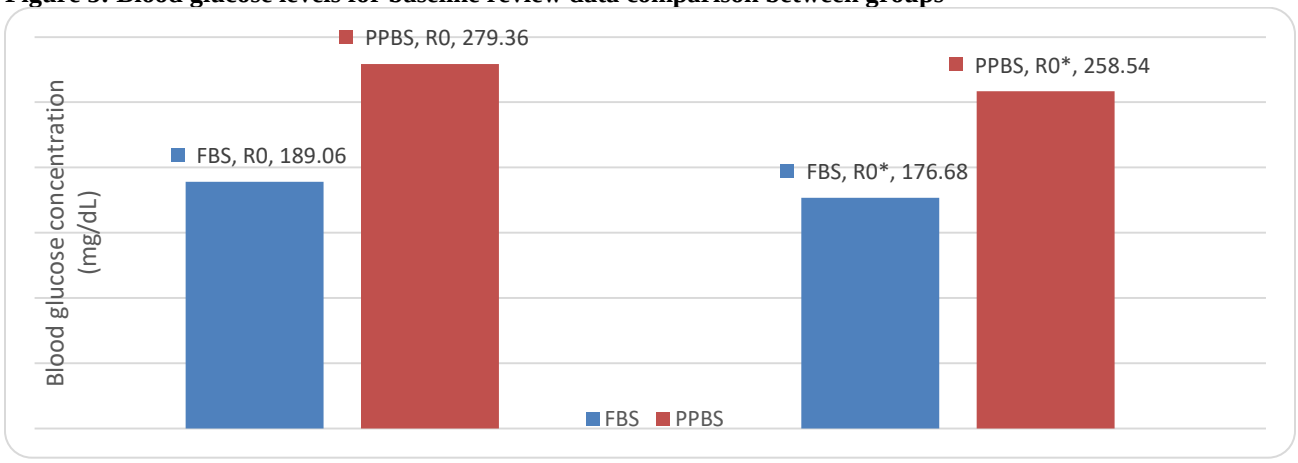


Figure 6: Comparison of blood glucose parameters between groups for the first review data.

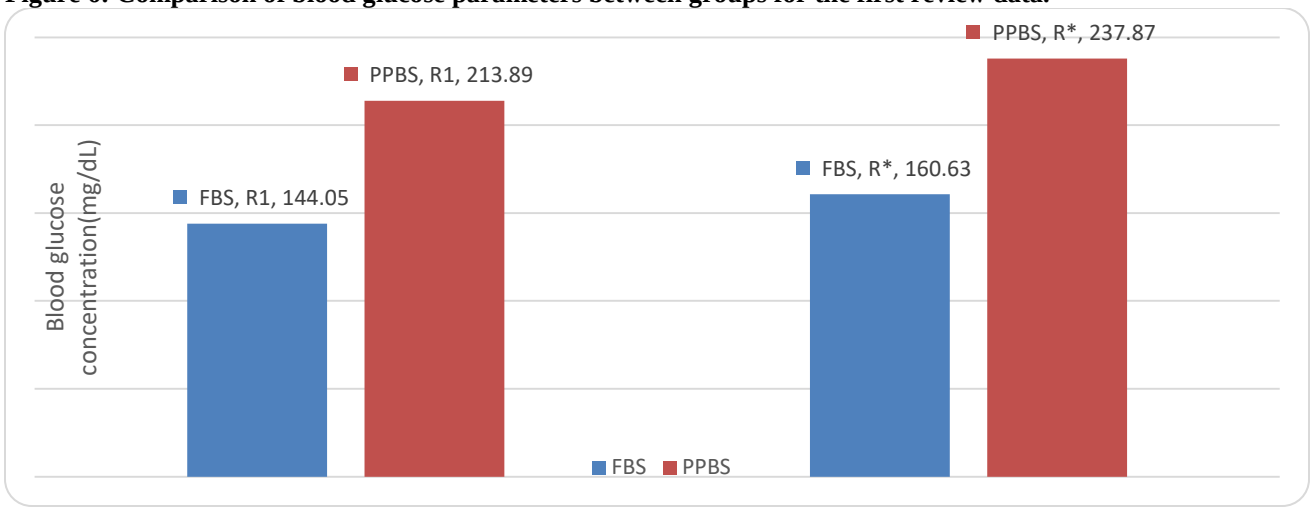


Figure 7: Comparison of blood glucose values between groups for the second review data

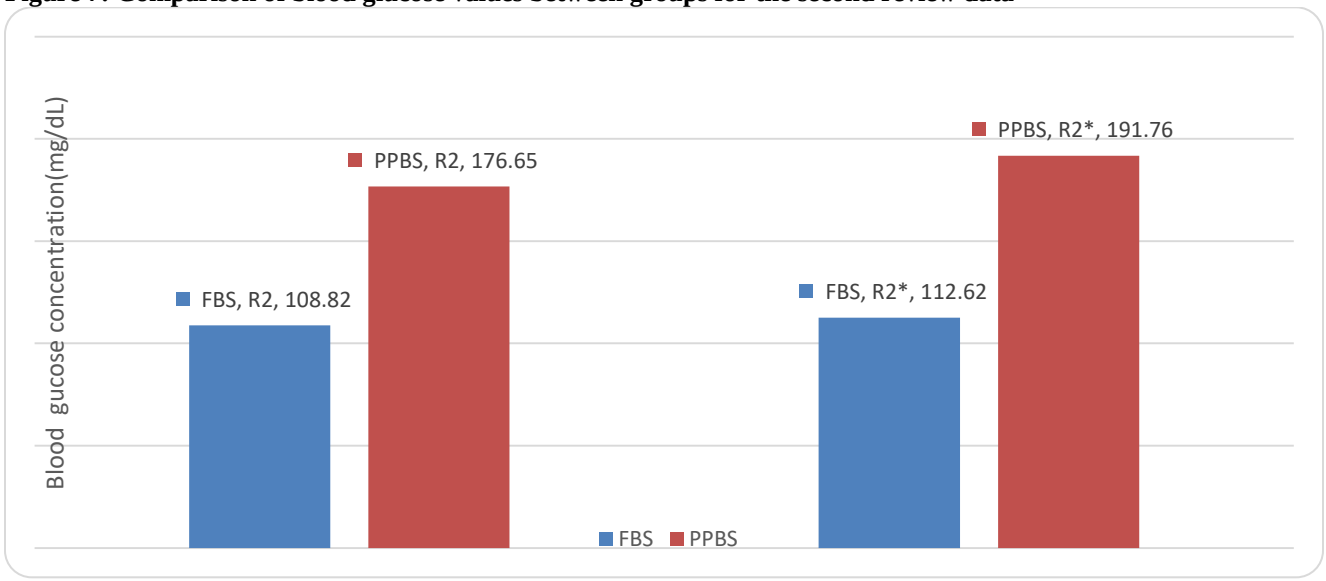


Figure 8: Comparison of blood glucose parameters between groups during the third review data.

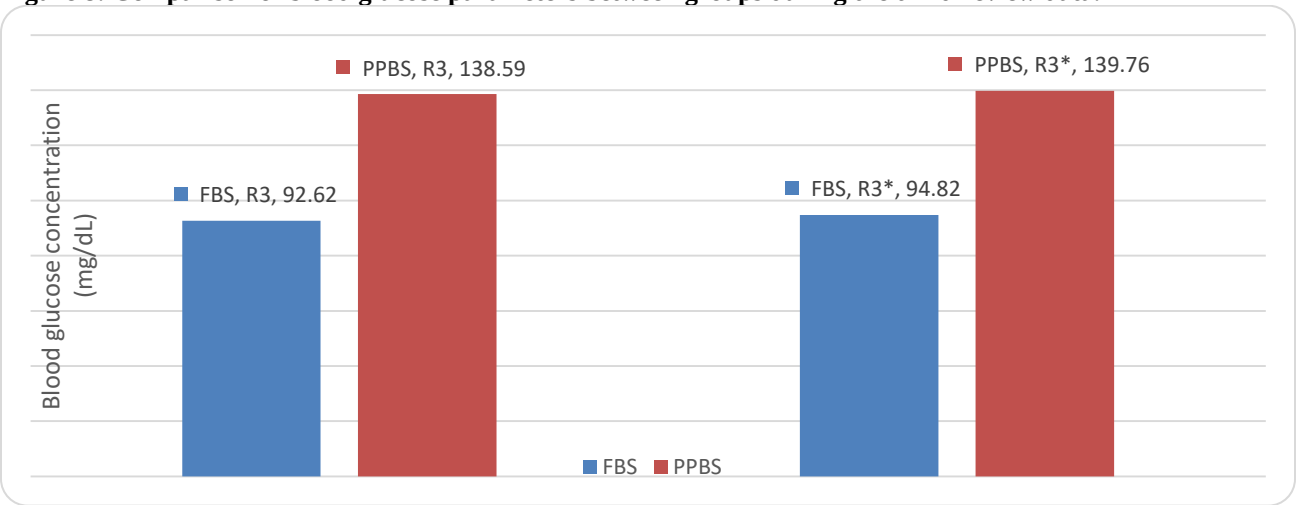


Figure 9: HbA1C review data comparison with participants in group A

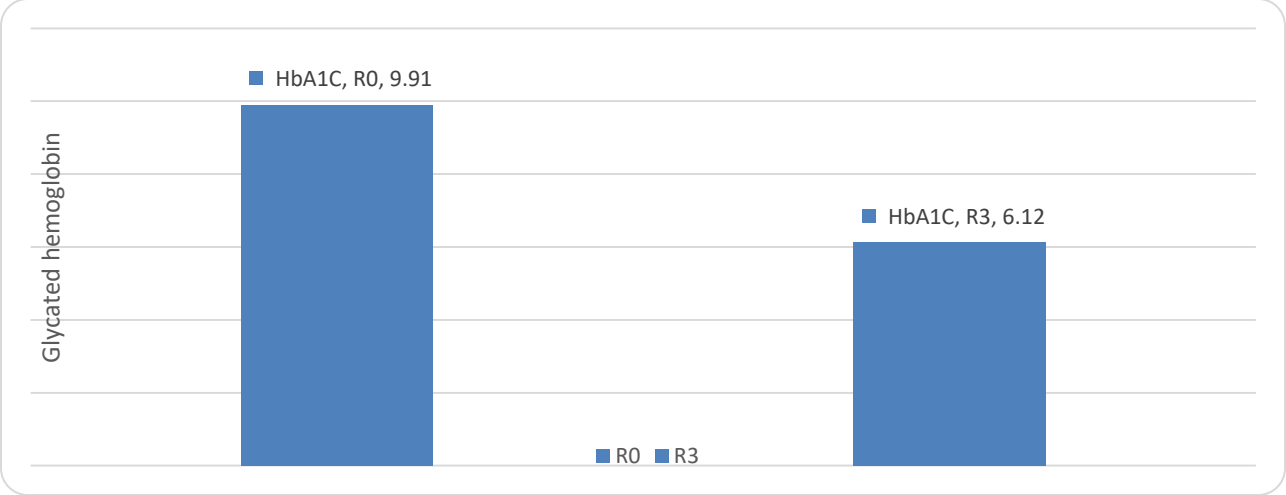


Figure 10: HbA1C review data compared to patients in group B.

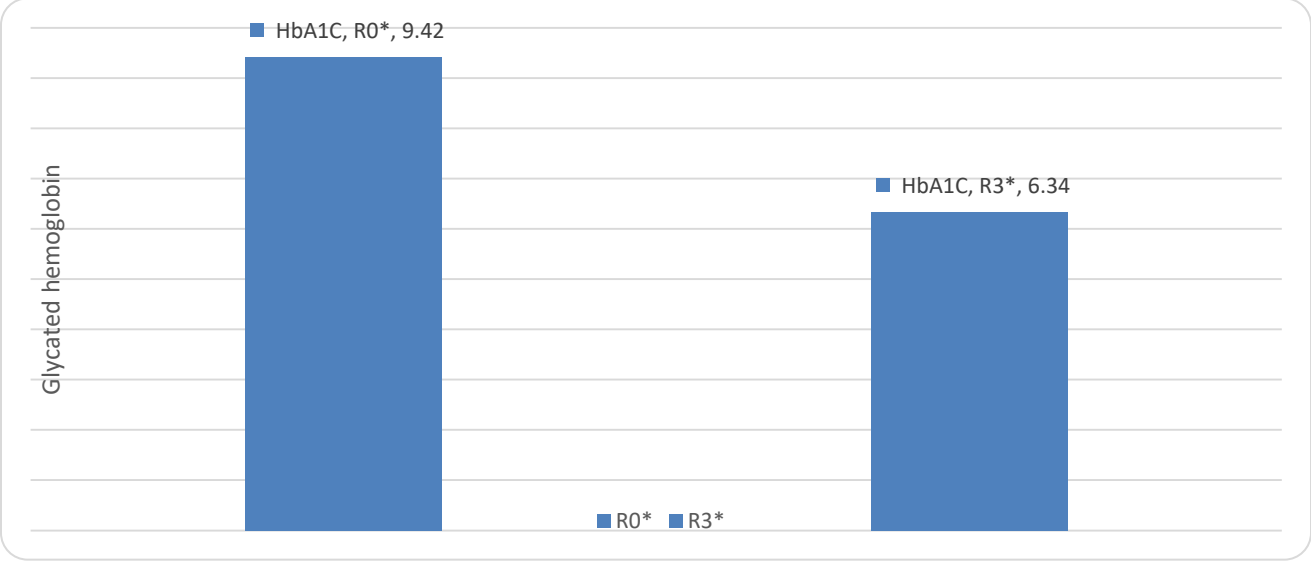
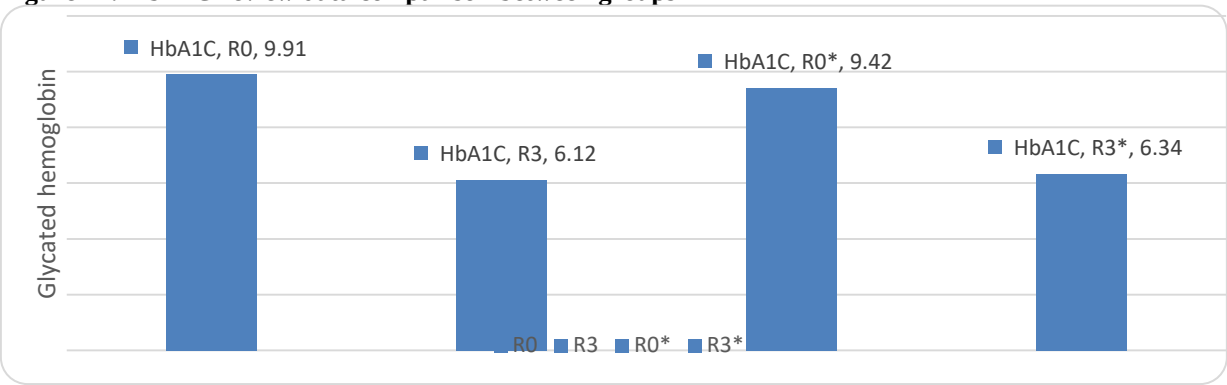


Figure 11: HbA1C review data comparison between groups



DISCUSSION:

Hyperglycemia caused by abnormalities in insulin secretion, insulin action, or both characterises diabetes mellitus. Diabetes-related chronic hyperglycemia is linked to long-term damage, dysfunction, and failure of a variety of organs, including the eyes, kidneys, nerves, heart, and blood vessels. Despite multiple evidences that various co morbid diseases contribute to diabetes mellitus, the interaction between hypertension and diabetes appears to be bidirectional. Despite the fact that people with chronic diabetes mellitus can acquire hypertension, those who have a history of hypertension should be cautious about obtaining diabetes. Depending on the severity of the underlying illness condition, the degree of hyperglycemia may alter over time. The severity of the underlying metabolic process and its therapy, rather than the nature of the process, determines the degree of hyperglycemia. For a patient to achieve optimistic efficacy and controlled glucose levels, a readable assessment of treatment regimen is required. Patients who received metformin plus teneligliptin had a better outcome than those who received metformin plus glimepiride. Despite the fact that the mechanisms of action of both combinations are distinct, no group appears to have any specific credibility in decreasing glucose levels based on the mechanism of action. . When compared to the other combination, Metformin plus teneligliptin exhibited improved control of hyperglycemia regardless of gender. There is no substantial difference between the two groups after one to two months of therapy, although a noticeable change can be detected after extended periods of use. Patients taking metformin plus teneligliptin had lower blood glucose levels than those on metformin plus glimepiride. The combination of metformin and glimepiride reduced blood glucose levels more effectively in obese and overweight patients than in the other group. As a result, metformin with teneligliptin is more effective than metformin plus glimipiride in treating type 2 diabetes mellitus. However, studies show that both groups are equally effective in terms of drug safety and short-term use. For more accurate and visible data, studies concentrating on geriatrics and obese individuals should be undertaken with a larger sample size.

SUMMARY AND CONCLUSION:

Diabetes mellitus has become a global concern, with 1.2 million new cases diagnosed in the continents of South Asia. It has a substantial impact on people's quality of life (QOL), which has a negative impact on public health. To begin treating diabetes mellitus type II, a proper examination of the patient's glucose profile is essential. When patients on metformin plus teneligliptin and metformin plus glimepiride were examined, patients on metformin plus teneligliptin had greater control over their glycemic profile than those on metformin plus glimepiride. Because of its efficacy and many other advantages, teneligliptin is a preferable choice as an add-on medicine to metformin in type 2 diabetic patients. Regardless of the therapy regimen, careful monitoring is required to ensure that the patient is not hypoglycemia, especially when using sulfonylureas.

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