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IMPACT OF CLINICAL PHARMACIST'S INTERVENTION IN THE MANAGEMENT OF TYPE 2 DIABETES MELLITUS: A COMPARATIVE STUDY

Shanmugapriya.S.K[1], Shashank.K[1], Subashini.S[1], Sujitha.G.S[1], Ashok Kumar.T.R[2], Dr. Karthikeyan. K[3], Dr. Shanmugasundaram. P[4]

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Abstract

Background: Diabetes is the one of the most prevalent metabolic disorder. At present, pharmacological therapy alone is considered for the treatment which results in higher possibility of adverse effect development with lesser expected benefit. Clinical pharmacist plays an important role in the reducing the possibility of developing the undesired event by analysing the prescription and also in framing the Medical Nutritional Therapy by considering the patient's preferences and dietician's recommendation. MNT is important as it can reduce the need for large number of medications to achieve the glycaemic control. This study is conducted as an attempt to emphasize the impact of clinical pharmacist's intervention in the management of Type 2 Diabetes Mellitus

AIM: The main aim of the study is to emphasize the role of clinical pharmacist's intervention in the management of Type 2 Diabetes Mellitus

OBJECTIVE: The primary objective is to achieve euglycemia and to reduce the HbA1C levels of the patients recruited in the study. The secondary objective is to reduce the possibility of developing any undesired effects in the patients recruited in the study.

RESULTS: 30 patients were recruited in both test and control group (60 in total). Mean of the FBG and PPBG of the test patients before intervention were 190.53 mg/dl and 311.43 mg/dl respectively. Mean of FBG and PPBG of the test patients after intervention were 128.8 mg/dl and 184.3 mg/dl respectively. Mean of the FBG and PPBG of the control group patients before interventions were 197.8 mg/dl and 309.9 mg/dl respectively. Mean of the FBG and PPBG of the control group after intervention were 187.9 mg/dl and 288.6 mg/dl respectively. Mean with standard deviation of the HbA1c of the test group before intervention was 8.64 $\pm$ 0.8 and after intervention was 7.37 $\pm$ 0.52 respectively. Mean with standard deviation of HbA1c of the control group before intervention was 8.91 $\pm$ 1.06 and after the intervention phase the mean with standard deviation was found to be 8.65 $\pm$ 1.03 respectively.

CONCLUSION: Significant reduction in the blood sugar parameters like Fasting Blood Glucose (FBG), Post Prandial Blood Glucose (PPBG), Glycated Haemoglobin (HbA1c) levels were observed in the test group patients after intervention when compared with the same blood sugar parameters of the control group patients. This proves that the conselling the patient regarding the condition, importance of the impact of lifestyle modification, inclusion of Medical Nutritional Therapy into treatment regimen and followup to assure the adherence of the patient to their treatment regimen has made a significant impact and aided a lot in reducing the blood sugar parameters of the patients. So the clinical pharmacist's intervention (in framing the medical nutritional therapy and educating the patients) has a significant impact in the management of diabetes mellitus.

KEYWORDS: Medical Nutritional Therapy, Pharmacological therapy, Clinical Pharmacist, Intervention

1. Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies, Chennai-117.

2. Assosiate Professor, Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai-117.

3. Head of the Department, Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies, Chennai-117.

4. Dean, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advenced Studies, Chennai-117.

Corresponding Author: Mr.Ashok Kumar.T.R, Assosiate Professor Department of Pharmacy Practise, Vels Institute of Science Technology And Advanced Studies, Chennai, Tamil Nadu.

trashokkumar.sps@velsuniv.ac.in

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INTRODUCTION:

Diabetes is a common metabolic condition. It causes hyperglycemia and insulin resistance. The majority of diabetes mellitus patients are type 1 and type 2. Type 1 diabetes is caused by autoimmune T-cell-mediated destruction of pancreatic β-cells (type 1A) or idiopathic damage (type 1B). Type 1 diabetes commonly develops in young people (under 30) and requires extrinsic insulin for survival.

Type 2 diabetes is more common in adults over 40, with a peak age of onset in developed countries between 60 and 70 years. It is also becoming more common in youngsters. Insulin resistance and relative insulin insufficiency cause it. Slower onset and milder symptoms than type 1. Type 2 diabetes may be accidental, especially in people with heart problems. Clinically, separating type 1 and type 2 diabetes is difficult. Treatment depends mostly on metabolic abnormalities.

The relationship between inherited and environmental factors in type 1 diabetes is unclear. Type 1 diabetes is immunologically linked to many organ-specific autoimmune diseases. 70% of type 1 diabetics had ICAs at diagnosis.

Despite widespread belief, type 1 diabetes is caused by slow immune damage. Cyclosporin, azathioprine, and prednisolone have been examined in newly diagnosed type 1 diabetics. These therapies improved clinical indices and remissions without insulin when started shortly after diagnosis. Their use is limited in healthy, young people due to toxicity and immunological suppression risks.

Insulin resistance and beta-cell malfunction cause the pancreas to generate too little insulin, resulting in type 2 diabetes. 85% of type 2 diabetics are obese. Fat causes insulin resistance, linking obesity with type 2 diabetes. Central obesity, which forms intra-abdominal fat, poses the greatest danger.

Type 1 and type 2 diabetes share symptoms, but severity differs. Type 1 diabetes causes more severe and earlier symptoms. Glucose's osmotic actions and energy partitioning abnormalities create symptoms. Symptoms include polyuria and polydipsia. Hyperglycemia causes osmotic diuresis. Due to an inability to utilise glucose, these symptoms are often accompanied by considerable weight loss and tiredness. Due to high urine glucose levels, patients may develop Candida and urinary tract infections.

Type 1 diabetics often show with severe metabolic problems. Diabetic ketoacidosis, nausea, vomiting, dehydration, shortness of breath from the respiratory system's attempt to offset metabolic acidosis are common symptoms. Type 2 diabetics often acquire hyperglycemia without symptoms. In obese adults, glycosuria or hyperglycemia may reveal diabetes. Because persistent hyperglycemia impairs phagocyte action and provides a bacteria-friendly environment, urinary tract and soft tissue infections are common. Long-term hyperglycemia often causes cardiovascular or renal problems. Standard ophthalmological exams can detect retinopathy. Infection, neuropathy, and PVD can cause foot ulcers or gangrene. Hyperosmolar hyperglycemia (HHS) is distinguished by glucose levels over 35 mmol/L and significant dehydration.

Pathophysiology:

In pancreatic beta-cells, preproinsulin is synthesised into insulin. The pancreas converts it to proinsulin. Insulin and C-peptide are produced equally by removing four amino acids. Two disulphide bridges connect the A and B chains of insulin, which include 21 and 30 amino acids, respectively. Islet granules contain insulin, C-peptide, and proinsulin. Insulin spontaneously creates a calcium-zinc hexamer. Insulin release starts with glucose. Nutrition and gastro-intestinal peptide hormones cause the response. After

intravenous glucose, insulin responds biphasically. After 2 minutes, a fast response is followed by a lesser but constant response after 5-10 minutes. The first phase releases stored insulin, while the second releases newly synthesised insulin. Pancreatic insulin enters portal circulation. Only 50% enters peripheral circulation because the liver rapidly degrades it. Food consumption immediately increases five- to tenfold. 40 units are secreted everyday. The liver and kidneys metabolise insulin, which circulates in the blood as a monomer with a half-life of 3-5 minutes. The glomeruli filter, tubules resorb, and kidneys eliminate insulin. Renal and hepatic disorders limit insulin clearance, requiring exogenous insulin dosage reduction.

Muscle and fat breakdown insulin, but this is not significant.Insulin binding to the cell surface receptor starts a messenger cascade. This moves glucose, amino acids, and electrolytes.

In type 1 diabetes, an acute insulin shortage promotes unrestricted hepatic glycogenolysis and gluconeogenesis, increasing hepatic glucose output. Insulin-sensitive tissues including adipose tissue and muscle absorb less glucose, causing hyperglycemia. Metabolic imbalance or severe illness causes increased production of the counter-regulatory hormones glucagon, cortisol, catecholamine, and growth hormone. All will boost hepatic glucose production. Type 2 diabetes reduces insulin production, making the procedure less severe. Hyperinsulinaemia can keep glucose levels stable for a while, but gradually -cell function deteriorates, resulting in hyperglycemia. Type 2 diabetes develops if this cycle is not broken. Those with type 2 diabetes may have already lost 50% of their -cell function at the time of diagnosis. Regardless of treatment, beta -cell function declines over time, frequently necessitating regular insulin administration.

Abdominal fat, found in abundance in the majority of those with type 2 diabetes, is physiologically different from subcutaneous fat and can induce 'lipotoxicity'. Abdominal fat is resistant to insulin's antilipolytic effects, leading in the production of excess free fatty acids, which leads to insulin resistance in the liver and muscle. The result is increased gluconeogenesis in the liver and decreased insulin-mediated glucose absorption in the muscle. Both of these cause a rise in circulating glucose levels. Excess fat may also contribute to insulin resistance because when adipocytes get too large, they are unable to store new fat, resulting in fat storage in the muscles, liver, and pancreas, which causes insulin resistance in these organs.

Treatment:

Treatment for people with diabetes includes Medical Nutritional Therapy (MNT), physical activity, weight loss, Oral Anti-Hyperglcaemic Agents (OHA) and Insulin therapy where ever required.

Medical Nutritional Therapy refers to the diet plan that is framed for achieving optimal glycaemic control (Euglycaemia) by considering the patient‟s preferences and usual diet routine and making the required changes in the diet plan. Dietary control is the cornerstone of type 2 diabetes treatment and also plays an important role in type 1 diabetes management. Dietary recommendations have been thoroughly reviewed in recent years, with significant revisions made. The recent considerations include increasing the amount of dietary fibre, substituting simple carbohydrates with complex carbohydrates, reduction in the amount of fatty acids, substituting trans fats and saturated fatty acids with unsaturated faty acids, increasing the fruit and vegetable consumption. Also 5-6 meal plan is considered (3 main meals and 2-3 snack meal) as an attempt to reduce the amount the sugar level in the blood.

All type 1 diabetics need insulin to survive. Exogenous insulin mimics each

patient's normal insulin secretion pattern. Insulin formulations vary by species, action, peak effect, and duration.

Insulin was developed from pig and cow pancreatic until the 1980s. Using recombinant DNA technology, human sequence insulins became the most popular. Animal insulins remain, however many animal-derived products have been withdrawn. Porcine insulin differs from human insulin by one amino acid at B30. Enzymatic modification of pig insulin (emp) produces semisynthetic human insulin. Genetic engineering and recombinant DNA produce most human insulin. In E. coli (crb, prb) or yeast cells (pyr), synthetic genes encoding the insulin A and B chains, proinsulin, and a proinsulin-like precursor are inserted. Fermentation produces a lot of recombinant protein, which is converted into insulin and purified. Genetic and protein engineering has produced human insulin mimics with different pharmacokinetics. All insulin-dependent individuals are started on human insulin. Insulin type and physical and chemical form determine initiation, peak effect, and persistence.

Oral Anti Hyperglycaemic Agents (OHAs):

To achieve long-term glycemic control, anti-diabetic drugs that repair the pathophysiological abnormalities found in T2DM are required **[1,2]**. Combination therapy has acquired universal acceptability and will continue to expand because no one medication can restore the many defects **[1-4].**

Biguanides:

Metformin is the most often prescribed diabetes drug in the world, and it works by decreasing hepatic glucose synthesis, resulting in lower fasting plasma glucose levels and HbA1c **[5].** Metformin's principal impact is to decrease hepatic glucose production, although the specific chemical mechanism is unknown. AMP kinase (AMPK) activity can be increased by either a direct agonist impact or through inhibition of hepatic mitochondrial oxidation, resulting in a greater AMP/ATP ratio and, as a result, secondary AMPK activation **[6,7]**. Metformin appears to have an insulin-sensitizing effect. The effect of lower endogenous glucose synthesis on muscle glucose absorption could simply represent an escape from the glucose toxicity phenomenon.

Sulphonylureas:

Sulfonylureas increase insulin secretion, resulting in hyperinsulinaemia, which overcomes insulin resistance, resulting in a decrease in fasting plasma glucose levels and HbA1c. However, HbA1c gradually climbs after the initial decrease because sulfonylureas have no long-term protective effect on cell function **[8-10]**. The mechanism of action of all SU drugs is based on binding to the pancreatic islet cell sulfonylurea receptor 1 (SUR1), which results in the closure of the cell membrane ATP-sensitive potassium channel (K1 ATP), causing membrane depolarization, calcium ion influx, and subsequent insulin release from storage vesicles **[11,12].** Sulfonylureas commonly cause hypoglycaemia and are associated with weight gain, and some retrospective studies suggest that they might increase cardiovascular events **[13,14].** Compared to the short-acting sulfonylurea glibenclamide, gliclazide has been linked to a lower risk of all-cause mortality and cardiovascular death, as well as a lower risk of weight gain and hypoglycemia **[15].** Stepwise addi- tion of sulfonylurea to metformin, or vice versa, is associ- ated with progressive failure of β-cell function and rise in HbA1c **[16].**

Meglitinides:

Meglitinides (repaglinide and nateglinide) are insulin secretagogues that

must be taken before each meal.Like SUs, these drugs work as agonists of the SUR1 receptor, but have extremely short durations of action.They are best regarded as non-SU SUs," and their usage is best reserved for those who are responsive to SU but are susceptible to fasting hypoglycemia, or for people who have real SU allergy **[17,18].** Despite being associated with less hypoglycemia than sulfonylureas, they do not prevent the progressive loss in cell function and rise in HbA1c associated with T2DM.

Thiazolidinediones:

Thiazolidinediones (pioglitazone and rosiglitazone) are the only true insulin-sensitizing agents. They enhance insulin action in skeletal and cardiac muscle, the liver and adipocytes **[16,19,20].** Rosiglitazone and pioglitazone produce heterodimers with peroxisome proliferator activating receptor gamma (PPARg) receptors with retinoid-X receptors, which subsequently bind to various response elements of the genome, resulting in transactivation of gene products that improve insulin action and transrepression of nuclear signal pathways that are generally detrimental to insulin action (particularly, nuclear factor kappa B [NF-kB] **[21,22]**. In adipose tissue, PPARg activation blocks release of free fatty acids (FFAs), reduces tumor necrosis factor alpha (TNF-a), and increases adiponectin. TZDs promote expansion of the subcutaneous adipose compartment, and contraction of the visceral adipose compartment **[23].** According to the lipid steal theory, enhanced adipose tissue FFA uptake permits FFAs to escape from muscle, liver, and islet cells, resulting in improved insulin action and greater insulin production **[21,22]**. Adverse events (including fluid retention, fat mass gain, and trauma-related fractures in post-menopausal women) are dose-related, and doses >30mg per day should be avoided **[24].** Weight gain is common with thiazolidinediones, but the greater the weight gain, the greater the decrease in HbA1c and the greater the improvements in insulin sensitivity and β-cell function **[25,26].**

Dipeptidyl Peptidase-4 Inhibitors (DPP-4 Inhibitors):

T2DM is associated with severe GLP1 resistance in β-cells **[27,28].**DPP4 inhibitors (sitagliptin, saxagliptin, linagliptin, alogliptin, and vildagliptin) increase the half-life of endogenously generated GLP1. Because DPP4 inhibitors do not raise (just prolong) plasma GLP1 levels, their ability to boost insulin production and lower HbA1c is limited **[29,30]**. Their major function is to enhance glycemic control by inhibiting glucagon secretion and decreasing baseline hepatic glucose synthesis **[31]**.DPP4 inhibitors have a very good safety profile **[32]**

GLP-1 Receptor Agonist:

GLP1 receptor agonists (exenatide, liraglutide, albiglutide, lixisenatide, and dulaglutide) raise plasma GLP1 levels, significantly boost insulin secretion, and suppress glucagon secretion **[33,34]**. Increased plasma insulin levels and decreased glucagon levels significantly limit hepatic glucose production **[33]** and promote a long-term reduction in HbA1c **[34,35]** (up to 3 years). GLP1 receptor agonists improve insulin sensitivity by promoting weight loss, delaying gastric emptying (accelerated in patients with new-onset diabetes), correcting endothelial dysfunction, lowering blood pressure, improving the plasma lipid profile, and lowering C-reactive protein levels **[35,36]**. Nausea and vomiting are the most common side effects of GLP1 receptor agonists, but these are usually mild and dissipate within 4–8 weeks.

Alpha-glucosidase Inhibitors (AGI):

AGIs (acarbose and voglibose) boost meal-stimulated GLP1 production while slowing carbohydrate absorption in the gut. The effect of AGIs on HbA1c is minimal and comparable to that of DPP4 inhibitors. Adverse effects of AGIs are related to the gastrointestinal tract (diarrhoea, abdominal pain, nausea, and vomiting). Based on its mechanism of action, it has little potential for drug-induced hypoglycemia, unless used in combination with exogenously administered insulin or insulin secretogogue (SU or glinides).

Sodium Glucose Transporter 2 Inhibitors (SGLT-2 Inhibitors):

SGLT2 inhibitors (dapagliflozin, canagliflozin, and empagliflozin) prevent glucose absorption in the proximal renal tubule **[37,38]**. They diminish the maximal renal glucose reabsorptive capacity and, more crucially, the blood glucose threshold at which glucose spills into the urine (to 40mg per dl). Increased glucose removal from the body by glucosuria results in a decrease in plasma glucose, which alleviates glucotoxicity, with improved cell function and insulin sensitivity as a result **[39,40]**. Their glucose-lowering efficacy is comparable to metformin, and urine calorie loss (4 calories per gramme glucose) produces a weight reduction of 2.5-3.0kg **[37]**. Because SGLT2 inhibitors also limit salt transport, they cause modest extracellular volume depletion and lower blood pressure (5-6 mmHg systolic and 1-2 mmHg diastolic). Their glucose-lowering action is offset by: increased glucose absorption by SGLT1, which can reabsorb 30-40% of filtered glucose after SGLT2 inhibition **[41].** Adverse effects include genital mycotic infections in female patients, balanitis in uncircumcised male patients, urinary tract infections, and volume-related side effects in older patients and individuals taking diuretics

METHODOLOGY

This is a prospective, interventional, uncontrolled, comparative study which was conducted in a private diabetic clinic on an attempt to emphasize the impact of clinical pharmacist's intervention in the management of Type 2 Diabetes Mellitus. 63 patients were recruited initially in the study, from which 3 patients withdrew from the study. After recruitment, the patients were categorised into two groups: Test group (interventions will be made to the patient's treatment regimen by the project team with the physician's approval) and the Control group (no interventions will be made to the treatment).

After recruitment, the prescription of the test group patients will be analysed for appropriateness i.e possible drug-drug, drug-food, drug-disease interactions and adverse effects caused by the prescribed drugs will be analysed and adequate changes will be suggested to the physician. Then the patient's usual lifestyle will be obatined by interview. Medical Nutritional Therapy (diet chart) will be framed on the basis of the base diet chart that is given by the dietician. Also, the patient's economic condition and preferences will be taken into consideration while framing the Medical Nutritional Therapy. This is done for improving the patient's adherence. Baseline data (initial data) of both the test group and control group patients will be recorded during the initial part of the study using the data collection form.

Once the pharmacological and dietary interventions are done to the patients, the patients will be followed for 3 months to assess the adherence and observe the impact of the intervention. Patients were adviced to check their blood glucose levels once a month and were asked to report to the project team. These monthly blood glucose values will be used as a measure to assess the patient's adherence to the interventions done by the project team.

STATISTICAL ANALYSIS

The final outcome of the intervention will be collected, reviewed for accuracy and will be entered as tabulated form in the Microsoft EXCEL. The tabulation will be exported to SPSS version 24.Mean, Standard Deviation and frequency are the statistical methods that will be used. The end outcome will be obtained after statistical treatment of the outcome data. The end data will be the Fasting Blood Glucose (FBG), Post Prandial Blood Glucose (PPBG), Glycated Haemoglobin (HbA1c) of the test group patients which will be compared with the end data of the control group patients. The comparison is to identify the impact of the intervention that has been done to the test patients therapy.

RESULTS

AGE:

VARIABLE	N	Minimum	Maximum	Mean	Std. Deviation
AGE	30	25	61	48.60	9.035

Table 1. Mean Age in the test group

VARIABLE	N	Minimum	Maximum	Mean	Std. Deviation
AGE	30	37	65	56.30	3.065

Table 2. Mean Age in the Control Group

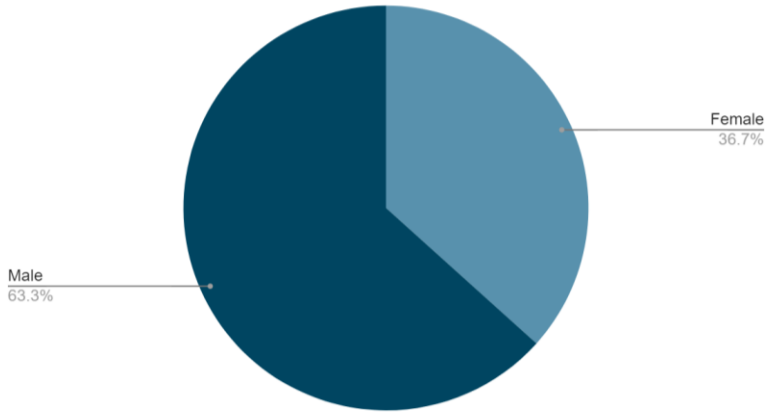
The mean of age of the participants in the test group is 48.6 $\pm$ 9.035 and the mean of age in the control group is 56.30 $\pm$ 3.065

GENDER:

	Frequency	Percent	Valid Percent	Cumulative Percent
FEMALE	11	36.7	36.7	36.7
MALE	19	63.3	63.3	100
TOTAL	30	100	100	100.0

Table 3. Gender Frequency in the Test Group (Interventional group)

11 female participants and 19 male participants are in the Test group. The gender frequency for the test group includes 36.7% for female and 63.3% for male.

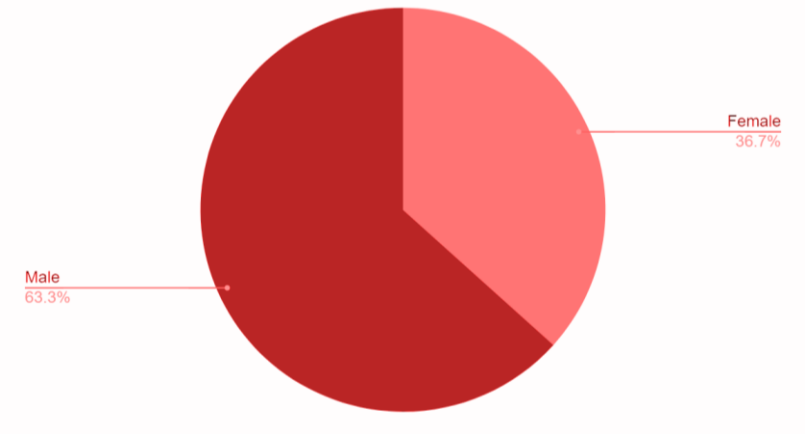


Gender Frequency In Test Group

VARIABLE	Frequency	Percent	Valid Percent	Cumulative Percent
FEMALE	11	36.7	36.7	36.7
MALE	19	63.3	63.3	100
TOTAL	30	100	100	100.0

Table 4. Gender Frequency in the Control Group

11 female participants and 19 male participants are in the control group. The gender frequency for the test group includes 36.7% for female and 63.3% for male.



Gender Frequency in Control Group

BLOOD GLUCOSE:

TEST GROUP VALUES

BLOOD GLUCOSE	N	Minimum	Maximum	Mean	Std. Deviation
FBG	30	75	270	190.53	48.134
PPBG	30	89	480	311.43	84.889
FBG - Fasting Blood Glucose; PPBG - Postprandial Blood Glucose Data was analysed using mean with standard deviation					

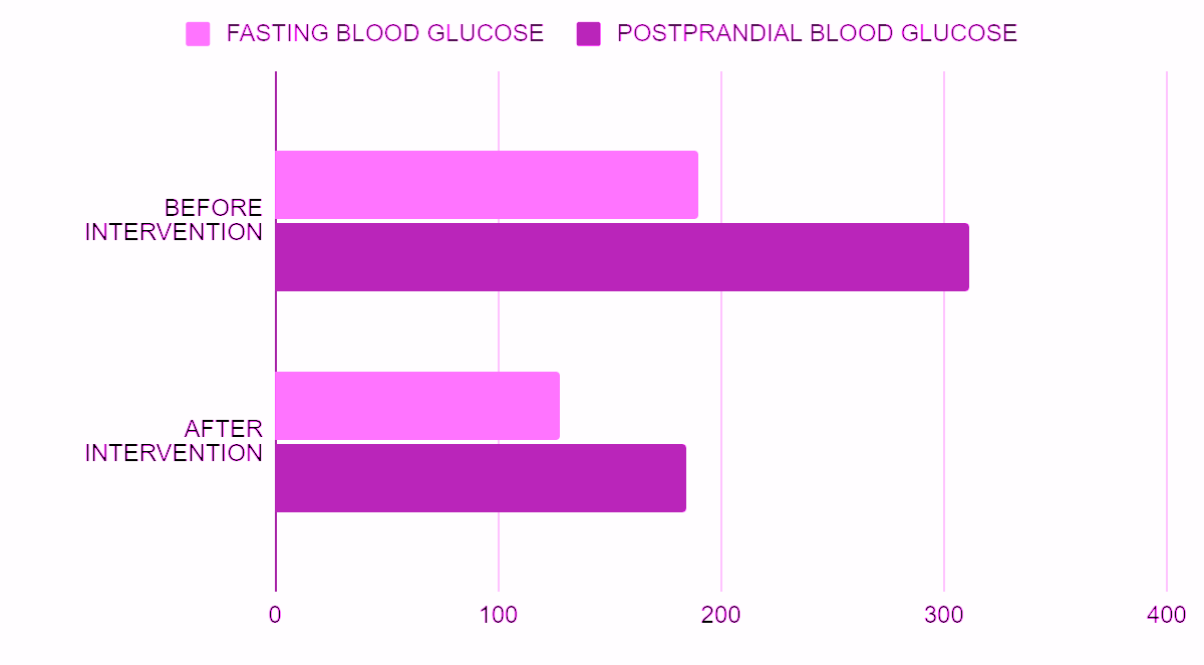
Table 5. Mean with Standard Deviation in the Test group (Before Intervention)

VARIABLE	N	Minimum	Maximum	Mean	Std. Deviation
FBG	30	80	231	128.8	33.598
PPBG	30	108	401	184.37	59.005
FBG - Fasting Blood Glucose; PPBG - Postprandial Blood Glucose Data was analysed using mean with standard deviation					

Table 6. Mean with Standard Deviation in the Test Group (After Intervention)

The mean with standard deviation of the Fasting Blood Glucose Value is 190.53 $\pm$ 48.134 mg/dl and Postprandial Blood Glucose value is 311.43 $\pm$ 84.89 mg/dl before the intervention

phase (initial value). The mean with standard deviation of the Fasting Blood Glucose is 128.8 ± 33.59 mg/dl and Postprandial Blood Glucose is 184.37 ± 59 mg/dl after the intervention phase (endpoint value)



Bar graph representing mean with standard deviation in test group

CONTROL GROUP VALUES

BLOOD GLUCOSE	N	Minimum	Maximum	Mean	Std. Deviation
FBG	30	91	337	197.8	56.375
PPBG	30	120	512	309.97	96.371

FBG - Fasting Blood Glucose; PPBG - Postprandial Blood Glucose

Data was analysed using mean with standard deviation

Table 7. Mean with Standard Deviation in Control Group (Before Intervention)

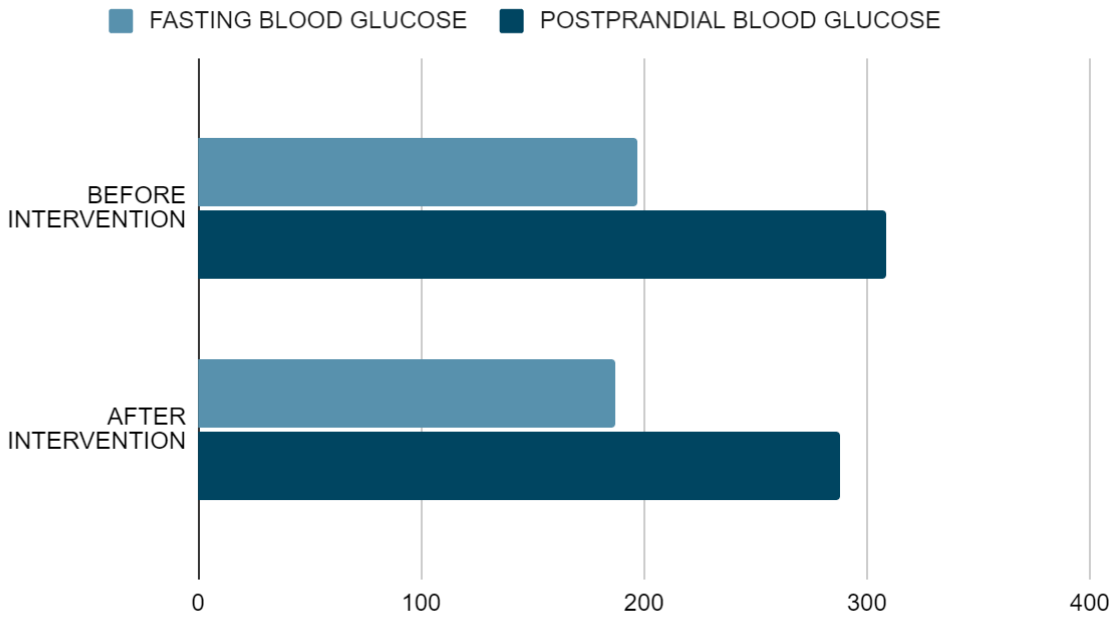
VARIABLE	N	Minimum	Maximum	Mean	Std. Deviation
FBG	30	86	298	187.90	50.867
PPBG	30	97	438	288.67	86.416

FBG - Fasting Blood Glucose; PPBG - Postprandial Blood Glucose

Data was analysed using mean with standard deviation

Table 8. Mean with Standard Deviation in Control group (After Intervention)

The mean with standard deviation of Fasting Blood Glucose is 197.8 ± 56.375 mg/dl and postprandial blood glucose is 309.97 ± 96.371 mg/dl before intervention phase (initial value). The mean with standard deviation of Fasting Blood Glucose is 187.9 ± 50.867 mg/dl and Postprandial blood glucose is 288.67 ± 86.416 mg/dl after the intervention phase (endpoint value).



Bar graph representing mean with standard deviation of control patients

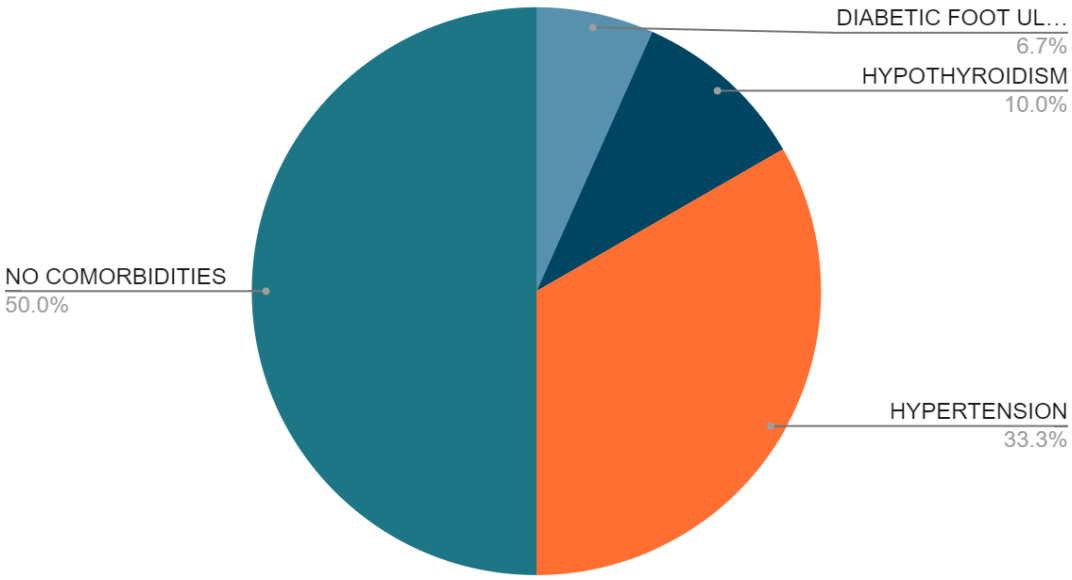
COMPLICATIONS:

COMORBIDITIES	FREQ	PERCENT	VALID PERCENT	CUM. PERCENT	
DIABETIC FOOT ULCER	2	6.7	6.7	6.7	
HYPOTHYROIDISM	3	10	10	16.7	
HYPERTENSION	10	33.3	33.3	50	
NO COMORBIDITIES	15	50	50	100	
TOTAL	30	30	100.0	100.0	

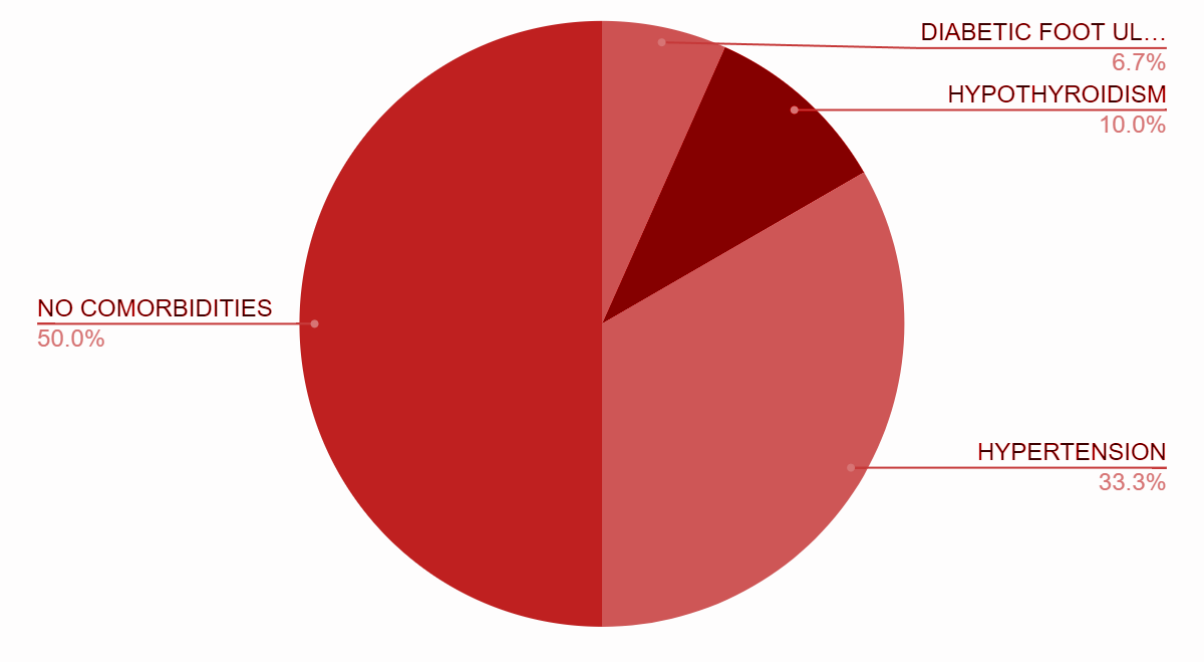
Table 9. Percentage of Comorbidities in the Control Group

COMORBIDITIES	FREQ	PERCENT	VALID PERCENT	CUM. PERCENT	
DIABETIC FOOT ULCER	2	6.7	6.7	6.7	
HYPOTHYROIDISM	3	10	10	16.7	
HYPERTENSION	10	33.3	33.3	50	
NO COMORBIDITIES	15	50	50	100	
TOTAL	30	30	100.0	100.0	

Table 10. Percentage of Comorbidities in the Test group



PIE CHART REPRESENTING COMORBIDITIES IN THE CONTROL GROUP



PIE CHART REPRESENTING COMORBIDITIES IN THE TEST GROUP

HbA1c (GLYCATED HAEMOGLOBIN):

PHASE	N	MINIMUM	MAXIMUM	MEAN	STD.DEV
BEFORE INTERVENTION	**30**	**6.50**	**10.30**	**8.64**	**0.80**
AFTER INTERVENTION	**30**	**6.40**	**8.50**	**7.37**	**0.52**

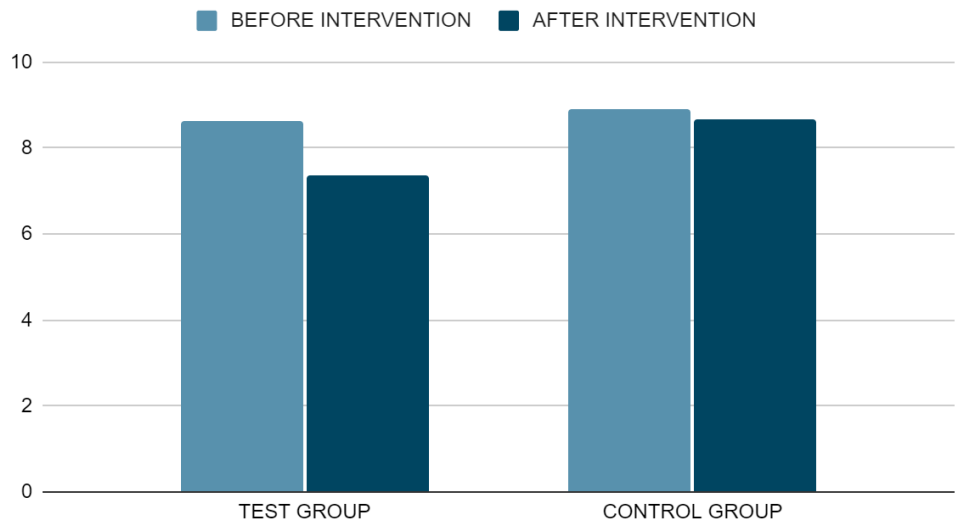
Table 11. Mean with Standard Deviation of the HbA1c of the Test Group (Before and After Intervention)

Mean with standard deviation of the HbA1c level of the test group is 8.64 $\pm$ 0.80 before intervention and 7.37 $\pm$ 0.52 after intervention.

PHASE	N	MINIMUM	MAXIMUM	MEAN	STD.DEV
BEFORE INTERVENTION	**30**	**6.10**	**11.10**	**8.91**	**1.06**
AFTER INTERVENTION	**30**	**6.00**	**10.80**	**8.65**	**1.03**

Table 12. Mean with Standard Deviation of the HbA1c levels of the Control group (Before and After Intervention)

Mean with standard deviation of the HbA1c levels of the control group is 8.91 $\pm$ 1.06 before intervention and 8.65 $\pm$ 1.03 after intervention.



Graph represents the difference in the HbA1c levels between the Test group and Control group

Difference in the biological parameters like Fasting Blood Glucose, Postprandial Blood Glucose and HbA1c levels were observed in the Test group (the group in which intervention were made by the project team in the dietary aspect by framing the Medical Nutritional Therapy and other necessary lifestyle modifications were made) when compared to the control group (no changes were made in the pharmacological and non pharmacological aspects of the therapy) which shows that the intervention by the project team has a significant beneficial effect in the patient's blood glucose level.

PARAMETERS	TEST GROUP (mean value)	CONTROL GROUP (mean value)
FASTING BLOOD GLUCOSE	128.8	187.9
POSTPRANDIAL BLOOD GLUCOSE	184.3	288.6
HbA1c	7.37	8.65

Table 13. A comparison table of the END VALUES of Fasting Blood Glucose, Post Prandial Blood Glucose and HbA1c levels

DISCUSSION:

30 patients were recruited in the test group and the mean age of the test group patients is 48.60 $\pm$ 9.035 and 30 patients were recruited in the control group patients is 56.30 $\pm$ 3.065 years. In both the groups 15 patients had no comorbidities (50%), 2 patients had Diabetic Foot Ulcer (6.7%), 3 patients had Hypothyroidism (9.9%), 10 patients had Hypertension (33.4%). Mean was applied for estimating the mean age and frequency was applied for estimating the percentage of comorbidities in the study population.

Mean with standard deviation was applied to estimate the final outcome of the fasting blood glucose and postprandial blood glucose of both the study groups. The average mean with standard deviation of the fasting blood glucose of the test group was 190.53 + 48.13 mg/dl and the mean with standard deviation of post prandial blood glucose was 311.43 + 84.89 mg/dl respectively before intervention (During the baseline data collection). The average mean with standard deviation of the fasting blood glucose of the control group was 197.80 + 56.37 mg/dl and the mean with standard deviation of post prandial blood glucose was 309.97 + 96.37 mg/dl respectively before intervention.

Mean with standard deviation of the fasting blood glucose of the test group was 128.80 + 33.60 mg/dl and the mean with standard deviation of the postprandial blood glucose was 184.37 + 59 mg/dl respectively after the intervention period (i.e after assuring the adherence to the Medical Nutritional Therapy). Mean with standard deviation of the fasting blood glucose of the control group was 187.9 + 50.86 mg/dl and the mean with standard deviation of the postprandial blood glucose was 288.67 + 86.41 mg/dl respectively after the intervention phase.

Average mean was applied for the HbA1c of both test and control group. Mean of HbA1c values of the test group before intervention was found to be 8.64 + 0.80 and the mean value after intervention (intervention phase) was found to be 7.37 + 0.52. Mean of HbA1c values of the control group before intervention was found to be 8.91 + 1.06 and the mean of the HbA1c after the intervention was found to be 8.65 + 1.03. This shows that intervention to the

test group patients (with Medical Nutritional Therapy) has resulted in significant reduction in the FBG, PPBG, HbA1c level of the test group patients when compared with control group patient's lab parameters. Also significant reduction in FBG, PPBG, HbA1c values were found after intervention when compared with their laboratory parameters before intervention.

A Prospective study conducted by *Ashwini Pande et.al* on the hypoglycaemic and hypolipidemic effects of low GI and medium GL Indian diets shows that mean blood glucose level was reduced from 173.6 mg/dl to 137.8 mg/dl and HbA1c was reduced from 8 to 7.1 (This study was conducted for 4 weeks). In our study, the mean reduction in the FBG of test group patients was from 190.5 mg/dl to 128.8 mg/dl, PPBG was reduced from 311.4 mg/dl to 184.3 mg/dl and the mean reduction in the HbA1c was from 8.64 to 7.37 (study duration is 3 months). This proves that complex carbohydrates with low glycaemic index and high fiber diet has a significant effect and hence can be considered for the treatment of the Diabetic patients.

Complex Carbohydrate with High Fibre diet was prescribed for the patients in the test group. Theoretically, the complex carbohydrate content takes a longer duration for digestion when compared to the simple carbohydrates (the nature of common staples consumed) and so the glycaemic load and the glycaemic index for the carbohydrate contents framed will help in reducing the blood sugar levels. Also, high fibre content will delay the gastric emptying time and results in the reduction in the glycaemic load in the blood. Prescription of the Medical Nutritional Therapy with Complex Carbohydrate and High Fibre Diet has played a significant role in the reduction of the blood glucose parameters of the test group patients.

While framing the Medical Nutritional Therapy, regional food content with complex carbohydrate should be considered as the level of acceptance and availability will be high and so this will result in better reduction in the blood glucose parameters when compared with the other diet. Hence, the outcome will be better when the diet is framed by considering the regional food available in that locality.

The initial plan of the study was to perform the prescription analysis and make the required changes in the drug therapy given to the patient in the control group. As per the plan the prescription analysis was conducted and the possible drug-drug, drug-food, drug-disease interactions within the prescribed medications of the patients were identified and reported to the physician in the study site. But no major changes were made in the prescription or the pharmacological therapy of the test group patients. Also there were no reports of the incidence of adverse events during the follow-up in the intervention phase (3 months). There were no adverse effects development during the therapy and so no major changes or interventions were made to the pharmacological therapy of the test group patients. If any adverse event was developed and reported, necessary intervention by the clinical pharmacist will ensure the significant reduction in the possibility of developing an adverse event in future.

CONCLUSION:

Significant reduction in the blood sugar parameters like Fasting Blood Glucose

(FBG), Post Prandial Blood Glucose (PPBG), Glycated Haemoglobin (HbA1c) levels were observed in the test group patients after intervention when compared with the same blood sugar parameters of the control group patients. This proves that the conselling the patient regarding the condition, importance of the impact of lifestyle modification, inclusion of Medical Nutritional Therapy into treatment regimen

and followup to assure the adherence of the patient to their treatment regimen has made a significant impact and aided a lot in reducing the blood sugar parameters of the patients. So the clinical pharmacist's intervention (in framing the medical nutritional therapy and educating the patients) has a significant impact in the management of diabetes mellitus.

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