



## A CLINICAL STUDY OF TYPE II DIABETES MELLITUS PATIENTS WITH PERSISTENT HYPERGLYCEMIA IN CENTRAL INDIA: AN OBSERVATIONAL STUDY.

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**ABSTRACT** **Background:** Diabetes is increasing day by day in Indian subcontinent at a very high rate and is associated with high morbidity and mortality. Various factors contribute to uncontrolled blood glucose levels and needs to be reassessed. **Materials and Methods:** The present study enrolled 50 patients presented in OPD/ Emergency with persistent dysglycemia were admitted in department of Medicine for evaluation and management of persistent hyperglycemia and hypoglycaemia at J K Hospital during the session 2023-2024. **Results:** Total 50 patients data was analysed with diabetes with significant hyperglycemia on multiple drugs. In our study we found that the incidence of dysglycemia, both hyperglycemia and hypoglycaemia were much higher. The patients were on multiple drug therapy of various combination but never in euglycemic state. **Conclusion:** Our study showed that diabetic patients presented earlier in life and with high insulin resistance and insulin deficiency, requiring multiple drugs, hence we conclude that the patients of Indian subcontinent may require insulin, preferably a basal insulin along with oral hypoglycaemic drugs from the day of diagnosis for better glycaemic control and preservation of residual pancreatic function.

**KEYWORDS :** Diabetes, hyperglycemia, OHAs : oral hypoglycemic agents, Insulin injection, LSM life style modification, MNT medical nutrition therapy.

### INTRODUCTION

The prevalence of secondary failure to OHAs among T2DM patients taking oral agents particularly late into the disease, in different populations, ranges from 30% to 60% over 5 years after initiation of therapy.<sup>1</sup>

Since the two OHA regimen has the potential to reduce the HbA1c levels on an average by only 1.2–2%, addition of a third agent either an oral agent or insulin is required in all patients in the future course of time with advancing T2DM.<sup>2,3</sup>

Despite the triple OHA regimen is found to be statistically and clinically more effective in reducing HbA1c<sup>4</sup>, patients with triple OHA were less likely to complete the regimen due to an additive risk of adverse effects, dose adjustments may become complex or intolerable side effects.<sup>5,6</sup>

On the other hand, insulin therapy has been shown to result in significant decreases in fasting plasma glucose (FPG) and HbA1c values<sup>7</sup>. However, large doses of insulin are often required to achieve near-normal blood glucose levels and are associated with weight gain and the risk of hypoglycemia<sup>8</sup>.

Since both approaches have their respective advantages and disadvantages, the present study aims to achieve glycaemic control of type II diabetic patients with persistent hyperglycemia on adding Insulin based regimen to patients on OHAs alone.

### MATERIALS AND METHOD

The present study is observational study in which we enrolled 50 patients presented in OPD/ Emergency with persistent dysglycemia were admitted in department of Medicine for evaluation and management of persistent hyperglycemia and hypoglycaemia at J K Hospital during the session 2023-2024. A comprehensive history and battery of investigations were used to collect and analyse the patient data.

### RESULTS

A total of 50 patients with persistent hyperglycemia were enrolled in the study. Patient age range from 30 years to 85 years were subsequently analyzed in the present study. Among the 50 patients who were included in the study, 21 (42%) were male and rest 29 (48%) were females showing higher number of female patients. The peak incidence of diabetic patients with hyperglycemia was from fourth to sixth decade. Patients who developed diabetes at an earlier age presented with early dysglycemia and hyperglycemia.

Among diabetics 36% of the cases were from urban and rest 64% were

from rural background. The higher number of patients from rural area had persistent hyperglycemia, which may be attributed to lack of medical facilities, economic and educational barrier.

In the study it was observed that total of 42% of patients presented with five to ten years of duration of illness, followed by more than ten years duration. Dysglycemia was significantly high in these patients as compared to patients of less than 5 years duration diabetes and patients with longer duration > 10 years presented with severe degree of hyperglycemia. While the duration of regular management of diabetes was relatively late from onset of diabetes in years.

HbA1c levels Control correlated with degree and extent of hyperglycemia, patients with HbA1c of <7% (good control), none of the patient had good control, whereas patients with HbA1c >7- 8.5 were only 8%, which shows inadequate control. While 92% of patients were poorly controlled diabetics. (Tab.1)

All of the patients showed compliance to Medical Nutritional Therapy and Life Style Modification and Medications.

In study we found that Oral Hypoglycemic drugs OHA was the most common preferred therapy, seen in 66% of patients with Biguanide, Sulphonylurease, SGLT2i, DPPV4i were preferred oral drugs in various combinations. This showed more reliance of patient as well as prescribers on oral therapy and polytherapy in various combinations as 60% of patients were on multiple drugs. Only 6% of patients were on insulin therapy and another 28% on both oral drugs and injectable insulin therapy. This signifies the taboo, lack of education and hesitation in accepting Insulin as regular therapy as only 4% of patients were on basal bolus regimen. The Mixtard Insulin was preferred in 30/70 combination, as economical and less number of doses required.

**Table No: 1 : Diabetes and Management Variables**

Duration of Diabetes	<5 years	5-10 years	>10 years
Number of patients	15	21	14
Degree of hyperglycemia : HbA1c	Well controlled	Inadequately controlled	Poorly controlled
	<7 %	7 - 8.5 %	> 8.5
Number of patients	0	4	46
Type of Medications	OHA	OHA + Insulin	Insulin

Number of patients	33	14	3
Type of OHA	Single	Dual	Multiple
Number of patients	8	19	30
Type of Insulin Regimen	Basal Insulin	Mixtard Insulin (30/70)	Basal bolus
Number of patients	5	10	2
Duration of regular Therapy (Compliance)	< 1 year	1– 5 years	>5 years
Number of patients	21	17	12
Insulin Mode of Delivery	Pen	Syringe	Not specified
Number of patients	5	12	None

In our study patients had poor glycaemic control with persistent hyperglycemia despite ongoing treatment and management, which is reflected by high HbA1c level. This signifies lacunae in diabetic management and requires improvisation through patient education,

**Table No: 2: Diabetic Management Revision and Treatment Implementation**

Insulin Therapy Acceptance	Male	Female	Total patients Acceptance	Total Patients Declined Insulin	OHAs	Admission RBS 250 – High	After Insulin initiation and OHAs modification RBS 100 -180
Total Patients No : 50	18	25	43	7			
Type of Insulin	Male	Female	Total				
Basal Regimen	5	6	11		Yes		Yes
Basal & Bolus Regimen	3	2	5				
Premixed Insulins Total	10	17	27				Yes
Mixtard Insulin (30/70)	8	9	17				
Mixtard Insulin (50/50)	2	8	10				
OHAs	Yes	Yes	Yes	Yes		Yes	Yes
MNT	yes	Yes	Yes	Yes			
LSM	Yes	Yes	Yes	Yes			

The most acceptable Insulin in our study were premixed insulins with 62.80 % patients : Mixtard Insulin in 30/70 and 50/50 combinations. Of which 39.53% of patients were on Mixtard 30/70 and rest 23.25 % on Mixtard Insulin 50/50 had better glycemic control. Total of 39.53% of female were Mixtard Insulin was also higher percentage than 23.25 % of male patients.(Tab.2)

Among OHAs all the patients who were treated had suboptimal dosing and combinations.

Along with initiation of insulin therapy we initiated Metformin in full doses and it was seen that this combination had the better glycemic control and acceptance. It is attributed to both due to economical factors and easy acceptance by the patients. Other drugs used commonly were Sitagliptin and Linagliptin. For the patients who declined Insulin therapy Metformin, Voglibose, Empagliflozin and Sulphonylureases ,non sulphonylureases insulin secretogauges, alfa glucosidase Inhibitors were mainstay of treatment.

In our study it was observed the patients were not fully aware of insulin injection technique , timings and sites , for which we educated the patients and caregivers. In the same way the patients were not aware of timing of oral drug intake. Patients were educated to increase awareness and compliance of treatment with importance of both Life Style Modification and Medical Nutrition Therapy.

On admission the Random Blood Glucose ranged from 250 mg/dl to Hi, which after management controlled to target levels by regular Blood glucose monitoring.

**DISCUSSION**

T2DM is characterized by a progressive loss of b-cell function and glycemic control. Suboptimal glycemic control often results in microvascular and macrovascular complications<sup>8</sup>, which warrant the identification of effective and simple treatment regimens with high-level glycemic control and good patient compliance and convenience. The most recent ADA consensus statement<sup>9</sup> encourages early use of insulin, whereas, commonly used agents such as gliptins and

counselling, increasing awareness for the benefits of insulin therapy with or without OHAs.

In our study, we prescribed Basal insulins (Glargine), Premixed or Mixtard Insulin (30/70, 50/50) were prescribed and for Bolus Insulin, Short acting Insulins were preferred over rapid acting insulin which is attributed to economic reasons. OHAs were used adjuvant to Primary Insulin therapy, Metformin, Pioglitazone, Glimepride and other sulphonylurease and nonsulphonylurease, Sitagliptin, Linagliptin and other DPPV4i, Empagliflozin and other SGLT2i, and Voglibose. One or more of these drugs were used in optimum combinations with insulin for better glycemic control.

Total Insulin acceptance was 86%, of which 85.70% were males and 86.20% were female with roughly equal acceptance and 14 % totally declined and refused for any form of injectable therapy. Hence were put on multiple OHAs.

Basal insulin with OHAs was initiated in 25.58% patients who accepted Insulin Injectable therapy and showed better acceptance and glycemic control than previously followed only OHA treatment. Insulin and OHAs dose titrated as per blood glucose levels.

Only 11.63% of patients showed acceptance to basal bolus regimen, it is attributed to both higher number of injection doses and economic burden.

sodiumglucose cotransporter-2 (SGLT2) inhibitors are considered second tier. However, these guidelines faced criticisms such as insulin treatment is associated with hypoglycemia, weight gain, and low treatment satisfaction and compliance.

In light of this dilemma, this study reports the glycemic control, cardiovascular risk factors, weight gain and rate of hypoglycaemia by educating patient to increase awareness and compliance.

Although most patients prefer OHAs over insulin, the addition of insulin to oral regimens is a well-established approach that is effective for many patients<sup>7</sup>. Treatment modalities such as extended reliance on OHAs result in hyperglycemia for long periods, which contributes to microvascular complications and beta-cell destruction that in turn accelerates treatment failure. Wallia and Molitch (2014) reported that insulin-based regimens are effective and safe as a short-term treatment option to gain rapid glycemic control.<sup>10</sup>

Therefore, in the present study ,Patients were educated to increase awareness and compliance of treatment with importance of both Life Style Modification and Medical Nutrition Therapy.

**CONCLUSION**

Our study showed that diabetic patients presented with variable duration of diabetes with delayed treatment and management leading to persistent hyperglycaemia. This is due to high insulin resistance and insulin deficiency, which is prevalent in south Asian phenotype requiring multiple drug therapy. Hence we came to conclusion that the patients of Indian subcontinent may require insulin, preferably a basal insulin along with oral hypoglycaemic drugs from early stages diagnosis for better glycaemic control and preservation of residual pancreatic function. This will be helpful in attaining better glycemic control and overall improvement. Patient's education to increase awareness, acceptance of insulin as regular modality of treatment along with oral therapy and compliance to diabetic management is integral for better glycemic control and health.

Further studies are required to assess the extent of insulin resistance

and insulin deficiency in Indian subcontinent and to address the optimal initial therapy with insulin and type of insulin regimen and add on oral hypoglycemic agents.

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