Glycemic control amongst diabetic subjects on insulin therapy: Still off target!

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Introduction: Prevalence of diabetes is increasing worldwide. Good glycemic control is essential for prevention of complications of diabetes. Despite of availability of multiple medications, it is difficult to achieve good glycemic control. Insulin therapy is considered to be the best option available for attaining glycemic control. But, whether insulin therapy has achieved it is an important question to be addressed. **Objective:** To assess the glycemic control in subjects with diabetes on insulin therapy. **Materials and Methods**: A cross-sectional study was done at Karnataka Institute of Endocrinology and research, Bangalore, in 448 diabetic patients who were on insulin therapy as a part of their diabetic therapy. Data collected was analyzed using SPSS 22 version software. **Results**: Majority of the subjects were men (61.38%) and in the age group of > 60 years (44.9%). Many of the subjects on insulin therapy had duration of diabetes > 5 years, with 36.4% having duration of 10-20 years, while another 36% had duration of 5 -10 years. Premixed insulin (81.47%) was the most commonly used insulin regimen. 82.6% of the subjects were on conventional insulin and only 13.2% were on insulin analogues. Insulin syringe was the most commonly used delivery device, with 64.7% of subjects using it, while insulin pen was used by 33.5% subjects. Despite of insulin therapy, the glycemic control was poor and 81.4% had HbA1c >8%. Only 5.7% of the subjects had HbA1c <7%. 94.9% of the subjects reported that they were regular with their insulin therapy. Only 20.1% adjusted the insulin dose by self. **Conclusions**: The present study has found that despite being on insulin therapy, large percentage of subjects was unable to achieve good glycemic control.

Keywords: Diabetes Mellitus, Insulin

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Introduction

Type 2 diabetes mellitus is one of the most common chronic diseases worldwide. According to the current statistics, 425 million adults (1-in-11) have diabetes. Unfortunately, Diabetes is associated with high morbidity and mortality rate, having caused 4 million deaths in 2017 [1]. Due to the gradually increasing burden of diabetes, it has been recognized as one of the four priority non-communicable diseases targeted for action by the United Nations. It has been emphasised that early and aggressive management of diabetes is essential for risk reduction of diabetes related mortality and morbidity [2]. To achieve glycemic control, there are several classes of anti diabetic drugs available with different mechanism of action, efficacy and safety profile. Due to the slowly progressive beta-cell failure, most subjects with type 2 diabetes will require stepwise intensification of anti-diabetic therapy to maintain good glycemic control. Yet, only small percentage of subjects can maintain the goal with oral anti-diabetic drugs and over a period of time, large percentage of subjects will need addition of insulin therapy to attain an HbA1c level below 7% [3].

Being discovered in 1921, insulin is the oldest of the anti-diabetic medications available and hence has the most clinical experience. It is also the most effective agent in lowering blood glucose levels, when used in appropriate doses. In addition, unlike oral anti-diabetic drugs, there is no maximum dose of insulin beyond which therapeutic effect will not occur [4]. Despite of these advantages, it is observed that large percentage of subjects on insulin therapy have elevated HbA1c levels and experience years of uncontrolled hyperglycemia. This is attributable to several obstacles in implementing appropriate insulin therapy. Multiple patient and physician factors have been found to create barriers in achieving optimal glycemic control with insulin therapy. Concerns regarding injections, hypoglycaemia, weight gain and lifestyle restrictions are few reasons for delay in initiating and maintaining insulin therapy. Patient acceptance, willingness to comply with the therapy, use of appropriate regimen and dose titration also contribute to the treatment outcomes [5]. But, the data on glycemic control with insulin therapy is scarce. It is essential to analyse whether glycemic control with insulin therapy is achievable or not, so as to plan a strategy for optimising insulin therapy.

This study therefore aimed at assessing the glycemic control status in subjects with type 2 diabetes on insulin therapy, in the outpatient department of Karnataka Institute of Endocrinology and Research, Bangalore.

Objectives: To assess the level of glycemic control in subjects on insulin therapy.

Materials and Methods

Study design: A cross-sectional observational study was conducted in the outpatient department of Karnataka Institute of Endocrinology and research, Bangalore. 448 diabetic subjects who were on insulin therapy as a part of their diabetic therapy, of any age, and with diabetes of any duration were recruited for the study, between January to August 2015.

Inclusion criteria
01. Diabetic patients of any age and duration of diabetes.
02. On insulin therapy for at least 6 months duration.

Exclusion criteria
01. Subjects unwilling to participate in the study.
02. Pregnant women.

Ethical approval: The study was approved by the ethical committee of the hospital. The patients consent to participate in the study was taken, after the nature of the study was explained to them.

Data collection procedures: A questionnaire based interview of 448 diabetic patients who were self administering insulin as a part of their diabetic therapy was conducted. The questionnaire incorporated data on gender, age, occupation, educational status, duration of diabetes, duration of insulin use, type of insulin regimen, insulin delivery device used and drug compliance. Glycemic control was assessed by noting the current HbA1C.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square was used as the test of significance. Independent t test was used as the test of significance for quantitative data. Continuous data was represented as mean and standard deviation. P value <0.05 was considered as statistically significant.

Results

In the study, 95.5% of subjects were type 2 diabetics and 4.5% had type 1 diabetes. Mean age of the subjects in the study was 55±10.78 years. Mean age of type 1 diabetes subjects was 15.95±10.78 years and type 2 diabetes subjects was 56.82±11.66 years. Majority of subjects were in the age group of > 60 years (44.9%). 30.8% of the subjects were in the age group of 50-59 years. 10.7% subjects were in the age group of 40-49 years. 13.6% of the subjects were less than 39 years. 61.38% of the subjects were male and 38.62% of the subjects were females. 36.4% had duration of diabetes between 10 to 20 years; 25.7% had duration between 5 to 10 years, 15.2% had duration between 1 to 5 years, 12.3% had duration >20 years and 10.5% had duration <1 year. 34.8% of the subjects were using insulin for < 1 year, 33.9% between 1 to 5 years and 31.3% of subjects had duration of insulin use > 5 years. 14.1% of the subjects had education up to primary school, 27.5% had education up to high school, and 12.7% had studied up to pre-university / diploma, 23.7% were graduates and 22.1% were illiterate. 99.8% of subjects in the study were right handed and 17.9% of subjects had abnormal vision (Table 1). Regarding the type of insulin used, 8.04% of the subjects were using basal insulin, 8.48% were using bolus insulin, 81.47% were using premixed insulin and 6.03% were using basal-bolus insulin. 82.6% of the subjects were using conventional insulin, 13.2% were using analogue insulin and 4.2% were using combination of conventional and analogue insulin. With respect to the insulin device used, 64.7% of the subjects were using insulin syringe, 33.5% were using insulin pen and 1.8% were using both (Table 2).

Table-1: Baseline characteristics.

Characteristic		Frequency	Percent
Type of DM	Type 1	20	4.5
	Type 2	428	95.5
Age	< 39 years	61	13.6
	40 to 49 years	48	10.7
	50 to 59 years	138	30.8
	> 60 years	201	44.9
Mean age (Mean±SD)		55±14.36 years	
Mean age type 1 DM (n =20)		15.95±10.78 years	
Mean age type 2 DM (n =428)		56.82±11.66 years	
Gender	Male	275	61.38
	Female	173	38.62

Duration of diabetes	< 1 year	47	10.5
	1 to 5 year	68	15.2
	5 to 10 year	115	25.7
	10 to 20 year	163	36.4
	> 20 years	55	12.3
Education	Illiterate	99	22.1
	Primary school	63	14.1
	High school	123	27.5
	PUC and diploma	57	12.7
	Graduate and above	106	23.7

Table-2: Insulin regimen used.

Duration of insulin use	< 1 year	156		34.8	
	1 to 5 years	152		33.9	
	> 5 years	140		31.3	
Insulin regime used	Basal only	36		8.04	
	Bolus only	38		8.48	
	Pre mixed	365		81.47	
	Basal-bolus	27		6.03	
Type of insulin used	Conventional	370		82.6	
	Analogue	59		13.2	
	Conventional + analogue	19		4.2	
Insulin device used	Insulin syringe	298	64.7	40 IU	290	97.3
				100IU	8	2.7
	Insulin pen	150	33.5	Refillable	99	62.6
				Disposable	59	37.4

Table-3: Glycemic Levels in subjects on insulin therapy.

	Levels	Number	Percentage
HbA1c (n- 366)	< 7	21	5.7
	7 to 8	47	12.8
	> 8	298	81.4

Table-4: Practices among diabetic subjects with respect to insulin injection technique.

	Parameter	Yes		No		Total
		Count	%	Count	%	
1	Take insulin injections regularly	425	94.9	23	5.1	448
2	Adjust the dose of insulin by self	88	20.1	351	79.9	439

Mean HbA1c of subjects in the study was 9.91±1.97. Among type 1 diabetics, mean HbA1c was 10.85±2.76 and among type 2 diabetic mean HbA1c was 9.86±1.91. This difference in mean HbA1c between Type 1 and Type 2 DM subjects was statistically significant. 81.45% of the subjects had HbA1c>8, while 12.8% had HbA1c between 7-8. Only 5.7 % of the subjects had HbA1c<7 (Table 3). 94.9% were taking insulin regularly. Only 20.1% adjusted the insulin dose by self (Table 4).

Discussion

Diabetes is said to be uncontrolled when the blood glucose levels/glycosylated hemoglobin levels are not within the targets specified for that particular patient at a given time. HbA1c <7.0%, pre-prandial capillary plasma glucose of 80-130 mg/dl and peak postprandial capillary plasma glucose <180 mg/dl are considered as the glycemic targets for non-pregnant adults with diabetes by ADA recommendations [6]. Despite of the increasing therapeutic options for management of diabetes, inability to achieve good glycemic control remains the greatest challenge for the medical fraternity.

Several subsequently mentioned studies have documented high prevalence of uncontrolled diabetes. NHANES data from 1999-2002 showed that only 49.8% of the studied population had HbA1c <7%. On the basis of the survey, it was concluded that considerable proportion of U.S adults with diabetes did not achieve ADA recommendations [7].

The situation hasn't changed much over time. In a single-center, cross-sectional study of 452 type 2 diabetes subjects, conducted in Pakistan in 2003, prevalence of uncontrolled diabetes (HbA1c ≥ 8%) was found to be 38.9% [8]. A hospital-based cross-sectional survey in Ghana found that 86.4% of diabetics could not control their blood glucose level [9]. In a cross-sectional survey done in 2008–2010 among 12,077 Spanish individuals, about 71% had HbA1c <7%, 22% had blood pressure <130/80 mmHg, and 36% reached the LDL-cholesterol goal of <100 mg/dl.

Though the scenario appears better than other countries, the authors concluded that even in a country with universal healthcare coverage, glycemic control among aware diabetic individuals was poor and suggested a need for improvement in both clinical guidelines' implementation and patients' adherence [10]. Studies from India also show poor glycemic control amongst subjects with diabetes.

The Diab Care-Asia-India 1998 study (n = 2269) showed poor glycaemic control in over 50% of the study population. The mean HbA1c was 8.9±2.1% in this study [11]. More than a decade after this survey, DiabCare India 2011 study (n = 6168) also found that glycaemic control is sub-optimal in type 2 diabetes patients with a mean HbA1c of 8.9±2.1%.

It showed that only 19.7% of subjects with type 2 diabetes have good glycemic control in India [12]. A cross-sectional, retrospective analysis of 206 diabetic subjects in Mathura, Uttar Pradesh in 2018 showed a mean HbA1C of 9.1±11.6%. HbA1c level above 7% was found in 65% of cases. Age, duration of diabetes, drug utilization patterns and BMI were the significant factors impacting glycemic control [13].

Studies suggest that insulin therapy also has failed in achieving good glycemic control. In Diab Care India 2011 study, subjects on insulin, either alone or in combination constituted 41.8% of the study population [11]. In the Mathura study done in 2018, 23.8% of the subjects were on insulin therapy and 91.8% of these had poor glycemic control [13]. In another study of 423 type 2 diabetes subjects in Saudi Arabia, "poor glycemic control" defined by fasting blood glucose >130 mg/dL was seen in 74.9% of the subjects. Here, 78.3% of subjects on insulin therapy had poor diabetes control, while 73.2% subjects on oral drugs had poor glycemic control [14].

A Cross-sectional study of 5750 subjects with diabetes, in 14 centres in Brazil, mean HbA1c was 8.6±2.2%. HbA1c <7% was observed in only 26% of patients. Patients with HbA1c ≥8% were younger, non-whites, had longer diabetes duration, more sedentary, and treated more frequently with insulin than patients with HbA1c <8% [15]. In a cross-sectional study in 1111 adults with type 2 diabetes attending diabetes centres in Saudi Arabia, mean HbA1c was 8.5±1.9%.

About three-fourths of participants had inadequate glycaemic control (≥ 7%). Multivariable analysis showed that age ≤ 60 years, longer duration of diabetes, low household income, low intake of fruits and vegetable, low level of physical activity, high waist-hip ratio, low adherence to medication, and using injectable medications were independent risk factors for inadequate glycaemic control [16].

Among 480 subjects with self-reported diabetes in Phase I of INDIAB (2008 -2010), good glycemic control (HbA1c <7%) was observed only in 31.1% of urban and 30.8% of rural subjects. Younger age, duration of diabetes, insulin use, and high triglyceride levels were significantly associated with poor glycemic control. Insulin use was associated with poor glycemic control with odds ratio of 2.479 (95% CI, 1.012–6.072; P = 0.047) [17].

In the current study, mean was HbA1c was 9.91±1.97, which is almost 2 points above the ADA targets. Less than 6% had HbA1c <7, which denotes very poor performance with regards to diabetes control.

In the present study population, it was noted that premixed insulin was the most commonly used insulin regimen, conventional insulin was the commonest insulin used and insulin syringe was the commonest device used. It appears that use of multi-dose insulin regimen, insulin analogues, and pen devices could have helped in achieving better glycemic control.

Self titration of insulin dose was not done frequently by our subjects. This highlights the need for patients on insulin therapy to be educated on self titration of insulin dose, so as to achieve rapid glycemic control. In summary, use of better insulin regimens, frequent blood glucose monitoring and insulin dose modification might help better glycemic control.

There are few limitations of the present study. First, being a tertiary referral center, subjects with uncontrolled diabetes could be visiting this center, thus giving rise to selection bias. Second, since the study was cross-sectional, it doesn't provide information about temporal or causal association. It would have been interesting to analyse the causes for poor glycaemic control in these subjects including the disease factors, patient factors and treatment factors that led to inadequate control even with insulin therapy.

Conclusions

The present study has found that despite being on insulin therapy, large percentage of subjects had poor glycemic control. The study confirms the need for frequent counselling, re-evaluation and modification of factors responsible for persistent hyperglycemia. It ascertains the need to acknowledge that just initiating insulin therapy will not reduce hyperglycemia, but frequent monitoring and titration of insulin regimen is necessary for achieving optimal success with insulin therapy.

The study highlights the need to increase awareness among patients and healthcare providers regarding the importance of good glycemic control, so that decisions on treatment intensification can be taken and implemented at the appropriate time to protect patients from poor glycemic memory.

The study highlights that patients be empowered to effectively use insulin with the help of team-based aggressive glycemic management process and improve patient outcomes.

Contribution of the study to the existing knowledge

This study is one of the few studies performed to determine the glycemic control among insulin treated diabetic subjects. The main strength of the study is that it is a large survey. The study demonstrates that even with insulin therapy, large percentage of subjects have uncontrolled diabetes. It highlights that unless right insulin regimen and dose titration is used, insulin therapy will not lead to good glycemic control.

Author's contribution

Dr. Surekha Bhujanga Shetty: Concept, collection of study data, data compilation/ analysis and manuscript preparation.

Dr. Lalitha Ramachandrappa: Collection of study data, data compilation/ analysis and manuscript preparation.

Abbreviations

01. ADA: American Diabetes Association

02. HbA1c: Glycosylated Hemoglobin

03. IDF: International Diabetes Federation

04. NHANES: National Health and Nutrition Examination Survey

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