Original Article

Current Glycemic Status and Diabetes Related Complications Among Type 2 Diabetes Patients in India: Data from the A_1chieve Study

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Abstract

Background : According to the ICMR – INDIAB study, there are 62.4 million people living with diabetes in India. Type 2 diabetes (T2DM) is a progressive disease and hampers the quality of life of the patients due to micro and macrovascular complications. There are few studies on the status of glycemic control in the country. Such data would be useful to allocate health resources and plan measures for instituting better control of diabetes.

Methods : The A_1chieve study was an observational study of patients 66,726 with T2DM who were initiated, on or switched to, insulin analogues, alone or in combination with oral glucose lowering drugs at the discretion of their physician in accordance with local, routine clinical practice. This study reports on the participants in India from the A1chieve study.

Results: Baseline data of A_1chieve study in 20,554 Indian T2DM patients showed that the mean HbA_{1c} was 9.2%. Diabetes control was worse in those with longer duration of diabetes (9.9 ± 5.5 years). Use of insulin was clearly suboptimal showing evidence of clinical inertia. The prevalence of both macrovascular and microvascular complications was high due to poor glycemic control. The prevalence of neuropathy was the most common complication followed by cardiovascular (23.6%), renal (21.1%) and eye (16.6%) complications. The prevalence of foot ulcer was 5.1%. Many patients had multiple complications.

Conclusion : Glycemic control in India is poor and this has resulted in a high prevalence of complications. This emphasizes the fact that effective control of T2DM is urgently needed to prevent or reduce the risk of developing the complications of diabetes in Indian T2DM patients.

Introduction

Diabetes mellitus is one of the most common chronic diseases across the world and number of diabetic patients is on rise. In 2011 there were 366 million people with diabetes globally, and this is expected to rise to 552 million by 2030.[1] Most people with diabetes live in low- and middle-income countries like India, and these countries will also see the greatest increase over the next 19 years.[1] The recently published ICMR-INDIAB national study reported that there are 62.4 million people with type 2 diabetes (T2DM) and 77 million people with pre-diabetes in India.[2] These numbers are projected to increase to 101 million by the year 2030.[1]

The complications related to diabetes pose a significant health care burden and a deterrent to overall quality of life. The Chennai Urban Population Study (CUPS) and Chennai Urban Rural Epidemiology Study (CURES) are one of the few population based studies on complications of diabetes in India and show that there is a huge burden due to diabetes related complications in India. The prevalence of diabetic retinopathy (DR) was 17.6%, microalbuminuria in 26.9% neuropathy was 26.1%, coronary artery disease (CAD) was 21.4% and peripheral vascular disease (PVD) was 6.3%.[3-7] This translates to millions of people on India with each of the complications of diabetes and many with multiple complications. The cost of treatment for diabetic complications adds to the health care costs.[8] India thus faces a huge health care burden due to high prevalence of Type 2 diabetes and its complications.

It has been shown unequivocally that good glycemic control helps to prevent diabetic complications.[9,10] Assessment of the current glycemic status and the burden of diabetes related complications are therefore important in order to allocate community and health resources in any country. While there is lot of data in western countries, such data are limited from developing countries like India.

A_1chieve study was an observational study of people with type 2 diabetes using insulin analogs in a real life clinics in India and such studies are extremely useful as they give a true picture of what is happening in the real world. We present the baseline data of Indian patients participated in the A_1chieve study which gives us the extent of diabetes related complication and glycemic status of T2DM in India.

Methods

Study design

The A_1chieve® was a 24-week; international, prospective, multicentre, non-interventional, observational study of people with T2DM who were initiated on or switched to insulin analogs alone or in combination with oral hypoglycemic agents (OHA). The study design has been described earlier in this supplement and also been published earlier.[11] Here we are discussing the glycemic status and diabetes related complications in Indian cohort of the A_1chieve® study.

Participants

A total of 66,726 people were included in the A1chieve study

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across the world, out of which total 20,554 participants (30.8%) were from India, the largest from any single country. Any current and prior medications were allowed for patient inclusion other than the insulin analogues being evaluated. These participants received treatment with Insulin analogs and the treatment was at the discretion of their physician in accordance with local, routine clinical practice.

The baseline data recorded was the demographic parameters, medical history including detailed history of diabetes and its complications with management. The laboratory parameters recorded were HbA_1c, fasting & postprandial sugar levels and lipid profile.

Prior approval was taken by ethics committee for the protocol, clinical report forms (CRF) and informed consent documents (ICD). The study excluded women who were pregnant or had an intention of getting pregnant during the study period. Patients could withdraw at any time and use of the study insulins could be terminated at any time at the discretion of the physician, following clinical evaluation; patients who withdrew from the study were not replaced. For the participants who had withdrawn from the study, data was collected till their last visit. The participating investigators were trained on the protocol, safety reporting and CRF completion for the study.

Assessment and outcome measures

The primary objective of this study was to evaluate the clinical safety of the insulin analogues by the incidence of serious adverse drug reactions (SADRs), including major hypoglycemic events. The baseline data also gave the current glycemic status in Indian cohort.

Statistics

Analysis of all variables, including safety and efficacy outcomes, was performed using any participant entered into the study who had the data relevant to that analysis. A detailed note on the statistics used in analysis of results has been published earlier and also described earlier in the supplement. [8]

Table 1 : Overview of Baseline Characteristics

	Total	No therapy	OHA alone	Insulin ± OHA
n	20554	1314	15509	3731
Percent of total	-	0.6	75.8	18.2
Sex M / F (%)	62.8 / 37.2	56.9 / 43.1	62.7 / 37.3	65.5 / 34.5
Age (years)	51.8 ± 10.1	54.6 ± 12.6	50.8 ± 9.5	55.3 ± 10.5
Weight (kg)	68.9 ± 10.5	63.4 ± 8.4	69.1 ± 10.2	69.9 ± 12.1
BMI (kg/m^2)	26.3 ± 3.7	28.4 ± 4.9	26.1 ± 3.4	26.5 ± 4.3
Diabetes duration (yrs)	5.7 ± 3.8	2.2 ± 4.8	5.7 ± 3.8	9.9 ± 5.5
HbA1c (%)	9.2 ± 1.4	9.3 ± 1.3	9.2 ± 1.3	9.2 ± 1.5

Data represented as Number, Percent, Mean ± SD

Results

Participants

Out of the total 20,554 patients enrolled from India, 1,314 did not receive any medication for diabetes, 15,509 were receiving OHA and 3,731 were taking insulin with or without OHA. Thus total 16,823 patients were insulin naïve i.e. no prior insulin therapy and 3731 were insulin "experienced" i.e. received insulin prior to this study. The baseline characteristics of these patients are presented in Table 1.

The male to female ratio was 1.7:1 in the patients recruited for this study. Average age of the patients enrolled in the study was 51.8 ± 10.1 years. The patient with less duration of diabetes (5.7 ± 3.8 years) and age 50.8 ± 9.5 years received OHA only. Many of the patients who were having long standing diabetes (9.9 ± 5.5 years) were on insulin with or without OHA. This indicates the stepwise approach to therapy is being followed by the practitioners across the country i.e., initiating therapy with lifestyle modification followed by OHA & then insulin. More than 75% patients were on OHA alone and only 18% patients had prior treatment with insulin reflecting the clinical inertia in initiating insulin therapy in type 2 diabetes.

The mean HbA_{1c} of 9.2% in this cohort indicates the poor glycemic control in our country. This was often due to delay in initiating therapy with insulin. The mean fasting plasma glucose levels were 194 ± 54 mg/dl [10.8 ± 3 mmol/l] in insulin naïve patients while the "insulin experienced" patients recorded a mean FPG of 196 ± 54 mg/dl [10.9 ± 3 mmol/l]. The mean postprandial sugar levels at the baseline were 288 ± 66 mg/dl [16.1 ± 3.7 mmol/l], 289 ± 66 mg/dl [16.1 ± 3.7 mmol/l], 275 ± 72 mg/dl [15.3 ± 4 mmol/l], in all, insulin naïve & insulin "experienced" patients respectively. The baseline parameters were comparable to global data which was published by Home *et al*[11]

The prevalence of complications is described in Table 2. High prevalence of complications related to Type 2 diabetes was seen in the patients with long standing diabetes (9.9 ± 5.5 years) most of whom were on Insulin with or without OHA. Overall prevalence of both macrovascular and microvascular complications was high due to poor glycemic control. Neuropathy (24.6%) was the most common complication seen in these patients followed by cardiovascular (23.6%) renal (21.1%) and eye complications (16.6%). Many patients had multiple complications.

Discussion

T2DM is a progressive disease. Increasing insulin resistance and impaired pancreatic beta cell function are the main pathophysiologic defects in T2DM.[12,13] The beta cell failure is progressive in nature and many T2DM patients cannot maintain their glycemic goal with lifestyle therapy or with OHA.[14,15] The stepwise approach in type 2 diabetes management gives rise to "Clinical inertia" and accumulates glycemic burden to the patients with years of dianbetes.[16-18] The poor glycemic control

Table 2 : Prevalence of Macro- and Micro-Vascular Complications at Baseline

Complications	Total n = 19346	No therapy n = 1227	OHA alone n = 14430	Insulin ± OHA n = 3689
Cardiovascular (%)	23.6	2.2	22.0	37.0
Neuropathy (%)	24.6	4.4	21.3	44.4
Renal (%)	21.1	2.1	19.3	34.5
Eye (%)	16.6	2.3	14.4	30.0
Foot ulcer (%)	5.1	0.8	4.9	7.5

Data represented as Percent

due to delay in initiation of insulin is highlighted in various studies like INITIATE[19] and IMPROVE.[20]

Recently presented preliminary results from the Diabcare India 2011 study also showed mean HbA_1c of 8.97 ± 2.2% where data of more than six thousand diabetic patients from India was analyzed indicating the poor glycemic control in India.[21] The results of A_1chieve study substantiate the observations of previous studies with mean HbA_1c of 9.2 ± 1.4 at the baseline. It is a clear indication that the "clinical inertia" is still playing a major role in maintaining the glycemic burden to Indian diabetic patients. Moreover, whatever may be the therapy, the HbA_{1c} levels were way beyond the recommended targets. This indicates that there is definitely delay in initiating effective treatment, a further reflection of "clinical inertia" on the part of physicians in India.

India contributed to almost one third of the 66,726 patients that participated in the A1chieve study across the world. Many patients were receiving OHA alone despite poor diabetes control. This indicated the resistance to initiate insulin to the patient. The prevalence of complications was unacceptably high reflecting the poor glycemic control causing damage which leads to various microvascular and macrovascular complications of diabetes.

"Clinical inertia" is defined as failure to intensify treatment of a patient who is not at their HbA_{1c} goal. Berlowitz *et al*.[22] demonstrated that HbA_{1c}-related clinical inertia is widespread. As discussed earlier, various studies have shown that clinical inertia is prevalent across the world and this study shows India is no exception to this.

Though we have well-defined management goals, effective therapies and clinical practice guidelines, there is often a failure to take appropriate action despite recognition of the problem. This is a common problem in management of patients with asymptomatic chronic illnesses like T2DM. Use of "soft" reasons to avoid intensification of therapy and lack of education, training and practice organization aimed at achieving therapeutic goals are the common reasons for clinical inertia.

Diabetic patients are generally started with lifestyle modification and OHA monotherapy followed by combination of various OHA for years. This stepwise approach often leads to accumulation of glycemic burden. Initiation of insulin is delayed until absolutely necessary as most patients are initiated on insulin only after multiple OHA have failed. Insulin therapy is initiated only when the HbA_{1c} levels has deteriorated to over 9% as seen in the present study as well. Doctors often delay insulin therapy worrying that the daily injections, modification of lifestyle due to insulin and dependence on insulin for life. Therefore patients often feel that insulin therapy indicates the last stage of diabetes. There is a need to change this mindset among doctors and thus among patients.

The ICMR – INDIAB study shows that India has 62.4 million people[2] with diabetes but awareness levels are also low. The CURES reported that nearly 25% of the Chennai population was even unaware of a condition called diabetes.[23] Clinical inertia in achieving glycemic targets in such patients is expected to be even more due to the low rates of awareness of diabetes and its complications resulting in poor glycemic control as seen in the present study. Moreover other factors like poverty, lack of accessibility to healthcare services and inadequate follow-up are additional factors in developing countries like India.

The A_1chieve study baseline data thus emphasizes the need for effective treatment in the type 2 diabetes. Extensive educational programs emphasizing the importance of effective control and optimum treatment of diabetes for both healthcare providers as well as the patients might help to improve this scenario in India. If this is not done urgently, millions of people in India would be at risk of developing the dreaded complications of diabetes which could seriously affect the health not only of the individuals but of the community as a whole.

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