

Original Article

REASONS OF NON-COMPLIANCE TO METFORMIN AMONG TYPE 2 DIABETICS ATTENDING DIABETIC CLINIC IN LAHORE.

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ABSTRACT

Objective: To identify the factors associated with non-compliance to metformin therapy in patients with type 2 diabetes mellitus.

Method: This was a cross-sectional study, carried out at Jinnah-Allama Iqbal Institute of Diabetes and Endocrinology (JAIDE) Lahore from April 2018 to June 2018.

In this study newly diagnosed type 2 diabetic patients were given metformin for the duration of three months and their compliance was observed over that period. Metformin was given starting with low dose of 500mg once daily and then after two weeks was titrated to optimum dose of 500mg twice daily and maximum dose range of 1500-2000mg per day. Multiple factors contributed to patient's fall out including co-morbidities, shifting to alternative medicine and insulin and GIT intolerance. Blood sampling for A₁C estimation was done by A1C analyzer (TD4611A TAI Doc). Research data was collected by questionnaires and patients were called up for follow-up through telephonic communication.

Results: Out of 260 patients, 200 continued their trial smoothly on metformin while 23% (n=60) were dropped out of the study. GIT intolerance contributed to the major reasons of discontinuing the drug accounting for 35% (n=21) of the patients. Other reasons for non-compliance included change of therapy to insulin (12%) due to uncontrolled raised glucose levels and alternative medicine (5%) by their own decision, deranged LFTs (10%) and RFTs (7%), refusal to the therapy (7%) and various domestic issues (10%).

Conclusion: Though metformin is the first line drug for treating type 2 diabetes mellitus (T2DM) but GIT intolerance to metformin is one of the major reasons that some patients are unable to tolerate the drug at all.

Key Words: Metformin, Type 2 diabetes mellitus, Liver function test

INTRODUCTION:

Type 2 Diabetes mellitus (T2DM) is a group of metabolic disorders characterized by hyperglycemia with classic symptoms of polyuria, polydipsia, loss of weight, tiredness, and fatigue, propensity for infections.¹ There is rapidly rising prevalence of Diabete Mellitus worldwide and patients suffering from this disease are being expected to rise from 360 million in 2011 to as expected range of 550 million by the year 2030.

In various studies conducted by the Diabetic Association of Pakistan, 10% of the population ranging from 30 years or above are said to be suffering from T2DM. The estimated prevalence of T2DM in Pakistan is 6.7%.²

Hyperglycemia is investigated and diagnosed on the basis of blood sugar levels carried by; fasting or random blood sugar sampling, follow up OGTT and further glycated Hb (HbA_{1c}) is indicated \geq 6.5%.¹ Other tests are also carried out according to clinical assessment (due to complications) e.g; lipid profile, kidney function tests, urine albumin- creatinine ratio (ACR), ECG.¹

DM is a chronic disease and needs long term treatment which itself is a big challenge.³ The main objective for the management of DM is to control the blood sugar levels by;

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healthy lifestyles, strict diet modification and therapeutic treatment such as oral hypoglycemic agents including mono drug therapy/combination drug therapy and insulin.⁴

Metformin, an insulin-sensitizing agent is a first-line drug used for the treatment of type 2 diabetes mellitus (T2DM).⁵ The effects of metformin occur as a consequence of reduced hepatic glucose output primarily through inhibition of gluconeogenesis and to a lesser extent, due to glycogenolysis and increased insulin-stimulated glucose uptake in skeletal muscle and adipocytes. Metformin also increases insulin insensitivity.^{5,6}

The use of metformin is associated with side-effects of the gastrointestinal (GI) tract in 20 - 30% of patients. Common GI symptoms are nausea, vomiting, diarrhea, dyspepsia, bloating, metallic taste, cramp-like abdominal pain with changes in gut motility which sometimes becomes uncontrollable^{7, 8} and about 5% of diabetic patients prematurely discontinue the therapy due to these GI side effects.⁹

Despite its widespread use 35% of patients fail to reach initial target glycemic control with metformin.¹⁰ Reasons of failure may be differently related either to the therapy or the patient itself leading to the poor compliance to the pharmacological treatment.¹¹

The purpose of this study is to determine factors leading to non-compliance of metformin therapy and issues impeding the control of DM in Lahore, Pakistan so that quality based health-care services can be provided to the masses.

MATERIAL AND METHODS:

The sample size was calculated by WHO software based on S.K Lwanga and Lemeshow keeping the confidence (CI) level equal to 95% and the margin of error equal to 5%. Initially, a total of 260 patients with T2DM were included in the study.

Two hundred and sixty (260) patients with T2DM were enrolled in the study from Jinnah-Allama Iqbal Institute of Diabetes

and Endocrinology (JAIDE) Jinnah Hospital, Lahore. The study was conducted for a duration of three months from April 2018 to June 2018. Patients were selected by convenient sampling. Patients were diagnosed with T2DM according to the criteria of the American Diabetes Association has any one of the criteria; fasting (8 hr or longer fast) glucose ≥ 126 mg/dl (≥ 7.0 mmol/liter), two hours glucose ≥ 200 mg/dl (≥ 11.1 mmol/liter) during an oral glucose tolerance test (OGTT), non-fasting plasma glucose > 200 mg/dl or HbA_{1C} $\geq 6.5\%$.¹² Drug naïve patients were included in the present study with baseline A1C levels ranging between 7-9%. Out of 260, 200 patients continued their medication; however, 60 patients dropped out of the study.

Data was collected from these 60 patients using structured questionnaires comprising of age, sex, marital status, educational level, presence of other chronic diseases, the regularity of taking the medication, and follow-up.

Non-compliance was defined as missing more than one scheduled visit or discontinuation of medicine due to adverse effects or any other reason. Non-compliance was further assessed using the patients' self-report on how they had been taking their medication in the week preceding the interview and their regular attendance at the diabetic clinic. Further, patients were asked to recall if they had missed any doses of metformin on a day-to-day basis over a period of one week.¹³

GIT intolerance was defined as (questionnaire of side-effects filled by the doctor) the presence of at least one of the following gastro-intestinal symptoms: diarrhea, nausea, flatulence, abdominal pain, asthenia, and vomiting.

RESULTS:

In this study, 260 patients were enrolled initially .Out of which 200 were compliant and 60 were non compliant. These non-compliant patients were further observed for discontinuing the drug. The frequency

distribution of gender amongst compliant patients was 69% (n=138) females and 31% (n= 62) males (Fig 1). Whereas, in non-compliant patients 31% (n=19) were male and 69 % (n=41) were females (Fig 1). Male to female ratio was 1:3 and the median age was 59 years. Fig 2 shows that among non-compliant patients; 38% (n=23) were literate and 62% (n=37) were illiterate. Fig 3 shows the diverse reasons that made subjects to discontinue metformin. A considerable number of patients i.e, 35% (n=21) terminated the treatment because of GI adverse effects due to metformin. Patients who were shifted to insulin were second significant no i.e 12% (n=7). Deranged Liver Function Tests and Renal Function Tests comprise 10% (n=6) and 7% (n=4) of the patients respectively. Almost 8% (n=5) patients were shifted to alternative medicine while 7% (n=4) refused to participate. Domestic issues were also a great hindrance and almost 10% of patients refused treatment because of domestic issues while 3% of patients got pregnant and 8% (n=5) were non-adherent.

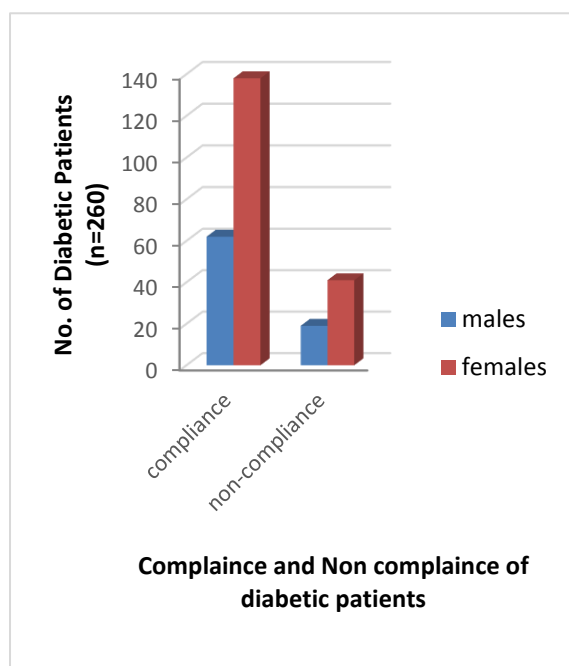


Figure 1: The gender distribution of the study population in compliance & non-compliance among T2DM patients (n=260)

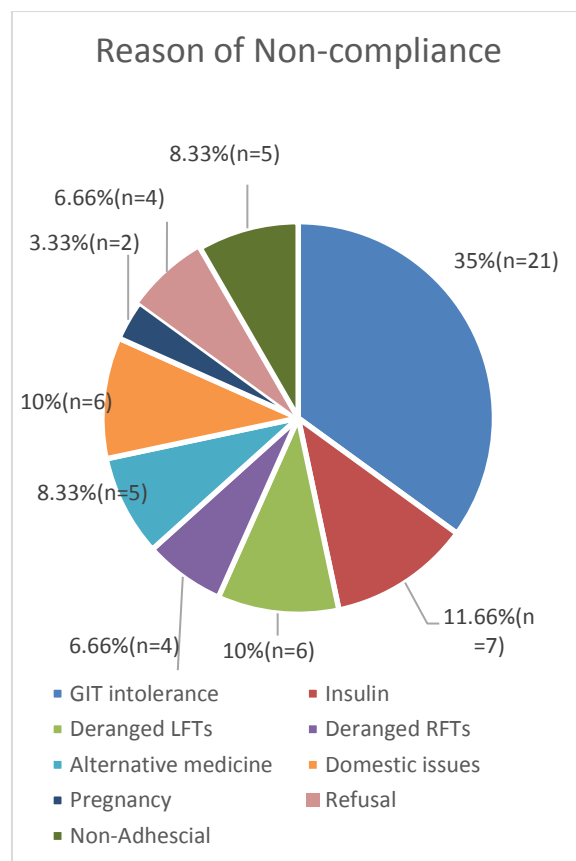


Figure 2: Pie chart showing reasons for non-compliance among the T2DM patients (n=60)

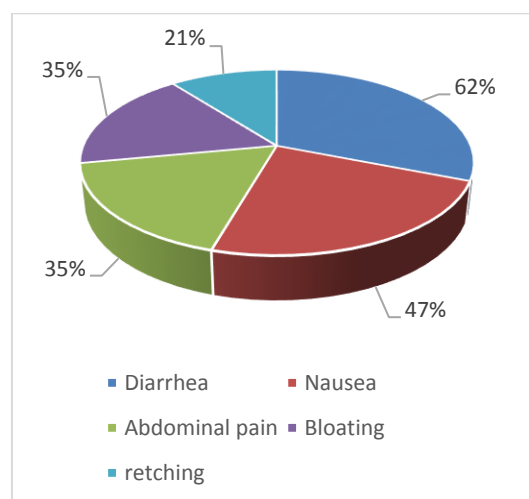


Figure 3: Frequency of GIT symptoms among 60 non-compliant T2DM patients (n=21)

DISCUSSION:

Type 2 diabetes mellitus (T2DM) is the most predominant form of diabetes¹⁴ and needs long term therapy for adequate

glycemic control and to reduce the incidence of complications.

However, compliance of patients tend to decrease with time being lower in patients on long term medication that severely compromises the effectiveness of treatment.¹⁵

Patient non-compliance is a serious issue and has been reported worldwide.¹⁶ It's not only limited to the failure to take medication but also in maintaining a healthy lifestyle, following a strict diet, going for proper follow-up visits including both regular tests and appointments with physicians.¹⁷

The usual first-line agent is considered metformin for the reduction of insulin resistance. It has proven benefits over other options of treatment, especially in overweight patients.¹⁴ Other benefits include neither significant weight gain nor hypoglycemia and an improved lipid profile.¹

According to some previous studies, there is considerable variation of metformin in maintaining adequate glycemic levels. Despite its extensive use, data shows that only 60-65% of patients successfully achieve the HbA1c target of less than 7% or adequate glycemic control with metformin.¹⁸ This might be due to the adverse effects of metformin that may make it less palatable for patients. The most common adverse effect is gastrointestinal upset, occurring in 10.4–19.3% of patients, usually in the first few weeks of therapy. Although it appears that few patients discontinue therapy early in the course of treatment, a significant portion of patients continue to experience these effect even at 6 months.¹⁹

Measuring the compliance of diabetic patients is a complex issue. In this study, we aimed to explore the factors contributing to non-compliance of diabetic patients to metformin therapy. Newly diagnosed 260 patients with T2DM were enrolled initially and they were followed up fortnightly. Out of which 200 diabetic patients followed all the requisites of treatment and achieved adequate glycemic control with HbA1c range of 7% to 9%

whereas remaining 60 patients failed to achieve adequate glycemic control and therefore labeled as non-compliant.

The major cause of non-compliance in most of the cases was early discontinuation of treatment due to GI adverse effects of metformin as the considerable number of patients i.e, 35% (n=21) terminated the treatment because of metformin. This observation was in accordance with previous studies in which patients were non-complaint to metformin treatment due to unwanted effects of metformin related to GIT upset.²⁰

About 12% (n=7) of patients were shifted to insulin because of uncontrolled fasting glucose levels which were measured after every two weeks contributed to one of the factors of non-compliance to metformin therapy as discussed in a previous study.²¹

Deranged LFTs in 10% (n=6) and RFTs in 7% (n=4) of diabetic patients were seen which led to a change in antidiabetic therapy. Same results were discussed in a previous study in which metformin was contraindicated in patients with deranged LFTs and RFTs.²²

The secret to success is adherence to the treatment plan advised by the physician but in our study, almost 8% (n=5) patients were shifted to alternative medicine such as Hikmat, spiritual healing (dum Darood), homeopathy owing to our socio-cultural factors further leading to complications of Diabetes Mellitus.²³ While 7% (n=4) straight away refused to participate in the treatment plan or follow the advice.

Domestic issues were also a great hindrance and almost accounted for 10% of patient non-compliance. Domestic issues included irregularity of follow-up due to financial issues, non-availability of transport followed by forgetfulness. Forgetfulness has been widely published as an important cause of irregularity of following up²⁴ further contributing to the non-compliance of the therapy in our study by up to 8% (n=5). These patients were called non-adherent to the treatment as they missed the prescribed doses may be due to lack of education and

good supervision. In addition to this 3% of the total number of patients got pregnant and stopped taking metformin.

In this study, we focused to understand the different reasons for non-compliance to metformin therapy through proper data collection so we can find proper solutions to eradicate the problems and educate the masses in detail about the disease to make the metformin therapy beneficial to the suffering patients.

CONCLUSION:

T2DM is a disease that requires long term therapy and a lot of patience for the compliance and success of the treatment. So we should try to avoid the factors discussed above leading to the non-compliance of the therapy by providing detailed and comprehensive patient education, support; whether it is financial or emotional and reassurance. Patients who are unable to visit clinics regularly should be provided transport facility or footstep visits by the administration. By solving these issues we can achieve control of presenting symptoms and complications and overcome noncompliance to metformin in T2DM.

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