

# DOES THE TYPE OF INSULIN REGIMEN MATTERS TO AFFECT ADHERENCE AND GLYCEMIC PROFILE IN DIABETIC PATIENTS?

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## ABSTRACT

**Objective:** To determine level of adherence to different insulin regimens, its effect on glycemic profile and to find out reasons leading to non adherence.

**Methodology:** This cross sectional study was conducted at the Department of Endocrinology, Hayatabad Medical Complex, Peshawar, from February 2016 to December 2016. Two hundred patients; 148 on basal bolus and 52 on pre-mix insulin regimen were assessed. Adherence status was determined using Morisky medication adherence scale (MMAS=0). Fasting and random glucose levels were also recorded. After stratification into different groups, chi square test was applied while mean fasting glucose levels were compared using independent samples t test.

**Results:** Overall adherence to insulin treatment was only 26.5%. Only 10% patients were highly adherent to treatment (MMAS=0). Only 33% patients had their fasting sugar in reasonable range (<140mg/dl). Among 148 patients on basal bolus regimen, only 15.5% were adherent to treatment while adherence to pre-mix insulin was 57.7%. Fasting sugar levels were much better in pre-mix group vs. basal bolus group (p value <0.05). Non-affordability was the main constraint responsible for non-adherence (54%).

**Conclusion:** Adherence to insulin treatment than insulin type was more important in improving diabetes care. Premix insulin was a reasonable alternative to achieve glycemic control as the cost of drug remains main reason for non adherence.

**Key Words:** Diabetes mellitus, Insulin, Adherence

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## INTRODUCTION

Diabetes mellitus (DM) is a life long illness either from insulin deficiency or resistance resulting in metabolic disturbances leading to different macro and micro vascular complications<sup>1</sup>. Insulin is the only treatment option in patients having type 1 DM and is also used for patients suffering from type 2 DM when oral hypoglycemic drugs are not working<sup>1</sup>. Initiating insulin therapy and then keeping the patient adherent to it is one of the most effective method of treating diabetes mellitus and preventing its complications<sup>2</sup>.

Despite starting patients on insulin, there still is increased mortality and morbidity in diabetic patients than in non-diabetic patients. One of the reasons for this is the non-adherence to insulin<sup>1</sup>. Patient's adherence to insulin is very critical for optimizing the glycemic control and thus preventing complications of diabetes mellitus. Non-adherence may be due to lack of patient's education and counseling by the healthcare provider,

patient's related factors<sup>3</sup>, the type of insulin being used and the economical factors. On behalf of physicians, the most important step is the proper counseling regarding the use and efficacy of using insulin and its different regimens according to patients' needs, affordability and convenience to use. It has been seen that proper counseling by the physicians results in good glycemic control and decreased rate of development of diabetes related complications<sup>4</sup>. Non-adherence to insulin is common in patients even after proper counseling. Multiple patient's related factors are involved which result in patients non-adherence and decreased compliance to insulin therapy which can be in the form of either missing the dose or not taking the proper dose<sup>5</sup>. This even involves the different genders with adherence to the treatment being different in different genders<sup>6</sup>. Other few patients related factors are increasing age, travelling, fear of injection and insulin related side effects and embarrassment of injecting insulin in the public. Compliance may also be an issue because of different

types of insulin, number of injections per day, their type of delivery device and cost of medication<sup>7</sup>.

Proper management of diabetes mellitus results in good metabolic profile. This further decreases the risk of cardiovascular events<sup>8</sup> and other complications. There is also a very significant economic benefit of treating DM. This benefit comes mostly in the form of decreased hospitalization of patients for optimization of glycemic control and much less complications of diabetes mellitus<sup>9</sup>; which may be either acute in the form of hypoglycemia and diabetic ketoacidosis or chronic in the form of repeated infections, cardiovascular and cerebrovascular events, nephropathy and eyes related issues. All these effects due to non-adherence to insulin has worse economical impact on the patients as well as the health care system.

Identifying and addressing all the factors causing this non-adherence to insulin in our region can result in good compliance to DM treatment. This will result in improved outcomes in the form of good glycemic control, better metabolic profile of the patients and decreased rate of development of diabetes mellitus related problems. This will have a major effect on the patient's economic well being as well as decreased burden on the hospitals for treating such patients. This will also help in shifting the paradigm of DM management from doing secondary prevention (treating strokes, acute coronary syndrome and repeated infections etc.) to the primary prevention of the diabetes related complications.

In the current study, adherence to two different insulin regimens; basal bolus and premix insulin was assessed and its effect on mean fasting glucose was determined. Both insulin regimens have their own pros and cons; basal bolus is more physiological and gives some degree of freedom to patients in diet but requires multiple injections per day and is more costly. Premix insulin is more economical and requires twice daily dosing but puts a lot of restrictions on patients in terms of diet. The aim of study was to determine reasonable insulin regimen which should have good impact on glycemic profile and to which patients remain adherent in a resource limited country like Pakistan where most of the people can't afford optimum treatment.

## METHODOLOGY

The study was reviewed and approved by the local ethical review committee. It was a descriptive cross sectional study conducted at Department of Endocrinology, Hayatabad Medical Complex (HMC), Peshawar from February 2016 to December 2016. As a tertiary care hospital HMC provides health services to a large section of population of Khyber Pakhtunkhwa (KPK) as well as bordering Afghanistan and Tribal areas. All patients with either type 1 or type 2 DM of any age and

either gender were included in the study. Patients were enrolled both from the outdoor clinics (OPDs) and Endocrinology wards. These patients were already taking either basal bolus insulin or premix insulin therapy for the last 3 months at least. All patients taking single daily injection of basal insulin, modified basal bolus (regular plus premix), patients admitted with acute complications of DM like diabetic ketoacidosis or hyperosmolar coma and those who were on insulin for less than three months were excluded from the study. Similarly patients with gestational diabetes, in whom insulin therapies are later on stopped after delivery, were also not included in the study. After obtaining informed consent, simple random sampling of patients was done. Fasting glucose levels were checked on follow up after a week. A total of 200 cases were selected for the study. As an incentive, patient were offered counselling and guidance regarding their glycemic control.

Demographic details like age, gender, locality, level of education and contact details were recorded. Our patients either didn't consent to disclosure of their monthly income or were unaware of their monthly income so the monthly income was not included in our proforma. Random and fasting glucose levels were done with finger prick test on our glucometer (accu check), details about the type of insulin therapy, duration of insulin therapy, availability of glucometer and frequency of blood glucose monitoring at home were recorded in a proforma. Adherence to insulin therapy was assessed by personal interview using Morisky medication adherence scale (MMAS-4)<sup>10</sup> using the patients mother tongue to further increase the strength of our study. It is an item questionnaire which has been used in assessment of drug compliance of chronic illnesses. This 4 items scale is scored 0 to 4 where 0 refers to high adherence and 4 refers to highly non-adherence. Adherence was further classified into low, medium and high on the basis of MMAS-4 score; 0= high adherence, 1-2= medium adherence and 3-4= low adherence.

## RESULTS

A total of 200 patients were enrolled in the study. The demographic and clinical features are shown in Table 1. Mean age of the patients was  $47.04 \pm 16.65$  years and mean duration of illness was  $12 \pm 4.5$  years.

Regarding the monitoring of blood glucose 33.5% of patients reported only monthly or less frequently, 52% were checking their blood glucose levels weekly while only 14.5% patients were checking their blood sugar daily. None of the patients reported multiple checking of blood glucose levels during the day, most of the patients didn't have an HbA1c levels at presentation, most of the patients (60%) didn't have a glucometer available at home.

Overall adherence to insulin treatment was only 26.5%. Only 10% patients were highly adherent to insulin therapy (MMAS-0), 16.5% showed medium adherence (MMAS-1,2) while 73.5% showed low level of adherence (MMAS-3,4) to treatment. Mean fasting sugar levels were  $226 \pm 93$  mg/dl in adherent group vs.  $254 \pm 95$  mg/dl in non-adherent group. Only 33% patients had their fasting sugar in reasonable range ( $<140$ mg/dl). Similarly, mean random glucose levels were  $316 \pm 90$

mg/dl in adherent vs.  $359 \pm 95$  mg/dl in non-adherent group. Level of adherence among different population is shown in Table 3. Patients on premix insulin were much more compliant to treatment (57.7%) vs. basal bolus (15.5%), Table 3. Non-affordability was the major factor (54%) responsible for non-adherence, other factors responsible for non-adherence are summarized in Table 4.

**Table 1: Demographics (n=200)**

Variables		Frequency	Percentage
Gender	Males	85	42.5%
	Females	115	57.5%
Locality	Rural	152	76%
	Urban	48	24%
DM Type	DM1	18	09%
	DM2	182	91%
Literacy	Educated	58	29%
	Uneducated	142	71%
Insulin Regimen	Premix	52	26%
	Basal bolus	148	74%
Adherence	Yes	53	26.5%
	No	147	73.5%

**Table 2: Level of adherence among different populations**

Population	Adherence	P Value
Urban	43/152 (28.3%)	0.308
Rural	10/48 (20.8%)	
Educated	12/58 (20.7%)	0.234
Uneducated	41/142 (28.9%)	

**Table 3: Regimen wise distribution of adherence and glycemic profile**

Variables	Premix	Basal Bolus	P Value
Adherence	57.7%	15.5%	0.00
Mean FBS	$206 \pm 73$	$260 \pm 98$	0.008

**Table 4: Factors leading to non-adherence**

Factors	Percentage
Non-affordability	54%
Injection Fear/Phobias	13.5%
Lack of Family Support	9%
Side Effects	8.5%
Lack of Proper Counselling	7%
Negative Beliefs	3.5%
Forgetting the Dose	2.5%
Miscellaneous	2%

## DISCUSSION

Adherence to treatment is the corner stone of DM which is unfortunately a difficult management issue in a chronic disease like DM where treatment has to be throughout the life. Complications of DM are directly related to the uncontrolled glycemic profile over the long run<sup>11</sup>. In our study, most of the patients were non-adherent to treatment despite the presence of marked osmotic symptoms. Non-adherence status in our patients was much higher (74%) than reported by Peyrot et al (33%)<sup>12</sup>. It can be explained on the basis of so many reasons in our patients namely lack of knowledge about the disease and its complications, lack of proper counselling, economical factors, support from the family, fear of injection, side effects, negative beliefs regarding insulin etc. Most of our patients belonged to the rural areas and majority of them were illiterate. There wasn't any statistically significant effect of literacy or rural locality of living on insulin adherence. Imtiaz et al found a negative impact of illiteracy on drug compliance<sup>13</sup>. Educated patients have usually clear concepts about prevention of diabetes and compliance with drugs; however, surprisingly a study conducted in the UK has shown that patients with lower levels of education have a good compliance, which may be due to the fact that the patients with lower literacy rates have a greater trust in their physicians<sup>14</sup>.

Highly significant difference in adherence status between basal bolus and premix insulin was noted (p value <0.05). Multiple factors can be responsible for this difference in our patients. Multiple injections per day in basal bolus vs. premix may be one reason leading to injection phobias and fear from injections as reported by Shahid et al<sup>15</sup> and lack of family support and lack of confidence to inject insulin themselves as reported in a study from Iran<sup>16</sup>. Similarly basal insulin is much more costly in comparison with premix insulin, also requiring frequent monitoring which our patients couldn't afford. Almost 54% patients reported the cost to be the major constraint for adherence.

Despite the fact that free insulin for diabetes program is currently run by government; mechanism for giving free insulin to DM patients is so complicated that they usually don't get free insulin. Also most of the times only premix insulin is available for free. This was also reported by Riaz et al<sup>17</sup> that most of the patients in Lahore depend upon the government hospital to get free insulin. Despite many advances and improvements in insulin therapy many myths still surround adherence to it; these attitudes and beliefs have been explored in studies around the world<sup>18</sup>. Dilek et al<sup>19</sup> found in their cohort that negative beliefs about insulin therapy rather than injection fear was the reason for poor adherence. Our patients have the common fear of getting used to

medication and that the insulin might damage their organs or that insulin therapy is started in the last stages of diabetes. In our study, risk of dependency was the main concern of our patients besides other factors, another misbelief was to stop or decrease insulin therapy when sugar was controlled thinking that the disease was cured. Few patients with abdominal injections thought that it will cause fluid accumulation in their abdomen. These wrong misconceptions and perceptions of the patients can be corrected by proper doctor patient communication. This communication is lacking in the heavy rush of our OPDs. Gul et al<sup>20</sup> found that 50% with diabetes never received any education about diabetes or the patient counseling lasted about a maximum of 5 minutes. Mean fasting and random glucose levels of patients on premix insulin regimen were much better (p value 0.008) than those on basal bolus regimen because patients were more compliant to premix insulin vs. basal bolus. It signifies that adherence to insulin therapy has a direct impact on glycemic profile.

## CONCLUSION

Glycemic profile and mean sugar levels of patients were directly related to the adherence status to insulin regimen. Non affordability was the major reason leading to non-adherence and subsequently affecting control of DM.

## RECOMMENDATIONS

Basal bolus regimen of insulin is more physiological and ideal insulin regimen but is more expensive and requires extensive monitoring during the day. Also it requires calculating carbohydrate content of the meal and adjusting the dose of boluses according to it. Because of these, basal bolus regimen is less practical in a resource limited country like Pakistan where most of the patients can't afford it. Premix insulin may be a cheaper alternative which is much more cost effective and much easier to adhere with.

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#### CONTRIBUTORS

GH conceived the idea, planned the study and drafted the manuscript. MS, KU, MMS and HS helped acquisition of data, did statistical analysis and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.