

# Insulin Analogues (Insulin Detemir and Insulin Aspart) Versus Traditional Human Insulins (NPH Insulin Regular Human Insulin) in Basal Bolus Therapy for Patients with Type-I Diabetes Mellitus

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## ABSTRACT

**Objective:** To compare the effect of Insulin analogues (Insulin Detemir and Insulin Aspart) versus Traditional Human Insulins (NPH Insulin Regular Human Insulin) in basal bolus therapy for patients with Type-I Diabetes Mellitus.

**Study Design:** Comparative cross-sectional study.

**Place and Duration of Study:** Department of Medicine, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Jun 2021 to Jun 2022.

**Methodology:** The sample population comprised of 125 type I diabetes mellitus patients which were diagnosed in our department and managed. Patients were divided into two Groups via lottery method. Group A received the Insulin analogues (Insulin Detemir and Insulin Aspart) while Group B received the Human Insulins (NPH Insulin Regular Human Insulin). Glycosylated hemoglobin, weight gain, hypoglycemic episodes and compliance were compared in both Groups at the end of three months.

**Results:** Out of 125 patients of Type-I diabetes mellitus included in the study, 85(68%) were male while 40(32%) were female. Mean age of the patients was  $14.93 \pm 3.75$  years. 62(49.6%) patients were managed with insulin analogue while 63(50.4%) were managed with human insulin. Statistical analysis revealed that glycemic control ( $p$ -value-0.001) was better in patients who took insulin analogues. Hypoglycemic episodes were also significantly less ( $p$ -value-0.002) in patients who took insulin analogues.

**Conclusion:** Insulin analogues (Insulin Detemir and Insulin Aspart) emerged as better treatment option for patients of Type-I diabetes Mellitus when compared to Traditional Human Insulins (NPH Insulin Regular Human Insulin) in our study participants.

**Keywords:** Diabetic Control, Human Insulin, Insulin analog, Type-I DM.

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## INTRODUCTION

Diabetes mellitus is one of those metabolic illnesses which has been increasing at an alarming rate in all parts of the world in last few decades.<sup>1,2</sup> This disease does not confine to one organ but almost the organ system of the human body gets involved and damage with time especially in patients with poor control of disease.<sup>3</sup> Control of blood sugars can be achieved by multiple management options and similarly monitoring of glycemic control and complications is also achieved by multidisciplinary approach.<sup>4</sup>

Oral hypoglycemic agents and insulin are usual modes of treatment in patients suffering from diabetes

but options usually narrow down in patients who are being managed for Type-I diabetes.<sup>5</sup> Rapid involvement has been seen in last two decades in management of this disease with the help of various types of Insulin. Duration of onset and action are usually the differentiating points in various types when it comes to pharmacokinetic profile.<sup>6</sup>

A lot of work has been done in recent past when it comes to compare various forms of insulin in management of patients suffering from Diabetes mellitus. Hermensan *et al.*, published a study comparing insulin analogues and human insulin and concluded that insulin detemir/insulin aspart was better option as compared to NPH insulin/regular human insulin in management of Type-1 DM.<sup>7</sup> Margaritidis *et al.*, in 2021 compared human Insulin and Insulin Aspart for efficacy and safety. Their team after studying ample number of patients concluded

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that both forms were effective and safe and no statistically significant difference was observed between the two forms.<sup>8</sup> A study conducted in 2017 compared Insulin analogues and human insulin in patients of Type-I DM who were prone to develop hypoglycemia. They revealed that treatment with insulin analogue reduces the occurrence of nocturnal hypoglycemia and provided better glycemic control as compared to Human Insulin.<sup>9</sup>

As most of the population of our country is from younger age Group and Type-I diabetes also diagnosed in younger patients which sometime present with complications or with diabetic coma. A local study analyzed data with regards to switch of patient from one form to other form of insulin.<sup>10</sup> Limited local studies had targeted younger population with type-I diabetes Mellitus in order to compare efficacy and safety of different forms of insulin. We therefore conducted this study with the rationale to compare the effect of Insulin analogues (Insulin Detemir and Insulin Aspart) versus Traditional Human Insulins (NPH Insulin Regular Human Insulin) in basal bolus therapy for patients with Type-I Diabetes Mellitus.

## METHODOLOGY

This comparative cross-sectional study was conducted at Medicine department of Pak Emirates Military Hospital, Rawalpindi Pakistan, between June 2021 to June 2022. Non-probability consecutive sampling technique was used to gather the sample for the study. Sample size was calculated by using the WHO sample size calculator by using population prevalence of efficacy and patient satisfaction for insulin analogue in Type I diabetes patients as 87%<sup>11</sup> and keeping margin of error as 10%.

**Inclusion Criteria:** Sample was drawn from the Type I diabetic patients between the age of 11 and 20 years diagnosed and managed at medicine department of our tertiary care hospital.

**Exclusion Criteria:** Patients with type II diabetes or those already diagnosed with Type-I diabetes and brought with diabetic coma or complications were excluded. Patients with unclear diagnosis or suspicion of any endocrine tumor were not made part of the study. Those patients who were allergic to any type of insulin were also not included. Minors whose parents or primary caregivers did not consent were also not recruited in our study.

Patients and their parents or primary care givers (in case of minors) were given description of study

after getting IREB approval via letter no A/28/175(2). Patients of Type I DM (diagnosed as per set criteria)<sup>11</sup> were divided into two equal Groups via lottery method. Group A received the Insulin analogues (Insulin Detemir and Insulin Aspart) while Group B received the Human Insulins (NPH Insulin Regular Human Insulin). All the patients were followed up regularly for three months to record data for this study. Glycosylated hemoglobin, weight gain, hypoglycemic episodes and compliance were compared in both Groups at the end of three months.

HbA1c was done by technique of high performance liquid chromatography in all the study participants at base line and at the end of three months. Reduction in HbA1c of 2% or more was considered as significant reduction at the end of three months.<sup>12</sup> Both forms of insulin were given in standard doses set by treating physician as per requirement on the basis of clinical and laboratory parameters set for patients of Type-I diabetes mellitus.<sup>13</sup> More than one episodes of hypoglycemia in three months as considered significant. Discontinuation of insulin treatment by the patients during the course of treatment in these three months was considered as noncompliance. Weight gain of 3% or more from baseline was considered as significant weight gain.<sup>14</sup>

All statistical analysis was performed using Statistics Package for Social Sciences version 24.0. Frequency and percentage was calculated for the gender of the patients participating in the study and all the dependent variables. Mean and standard deviation was calculated for age of the patients. Chi-square test was used to look for difference in glycosylated hemoglobin, weight gain, hypoglycemic episodes and compliance in both Groups at the end of three months. The *p*-values were considered significant if less than or equal to 0.05.

## RESULTS

Out of 125 patients of Type-I diabetes mellitus included in the study, 85(68%) were male while 40(32%) were female. Table-I summarized the basic demographic and clinical characteristic of Type-I DM patients included in our study. Mean age of the patients was 14.93±3.75 years. 62(49.6%) patients were managed with insulin analogue while 63(50.4%) were managed with human insulin. Out of total patients, 30(24%) were underweight, 55(44%) had normal BMI while 40(32%) were obese or overweight. When non-compliance was studied, 85(68%) had no non-

compliance while 40(22%) had non-compliance. Table-II revealed the results of statistical analysis. It is shown that glycemic control ( $p$ -value-0.001) was better in patients who took insulin analogues. Hypoglycemic episodes were also significantly less ( $p$ -value-0.002) in patients who took insulin analogues. Weight gain ( $p$ -value-0.890) and non-compliance ( $p$ -value-0.796) was not statistically different in both the study Groups.

**Table-I: Characteristics of Study Participants (n=125)**

| Study parameters                                                            | Values              |
|-----------------------------------------------------------------------------|---------------------|
| Age (years)                                                                 |                     |
| Mean±SD                                                                     | 14.93±3.75 years    |
| Range (min-max)                                                             | 11 years - 20 years |
| Gender                                                                      |                     |
| Male                                                                        | 85(68.0%)           |
| Female                                                                      | 40(32.0%)           |
| Body Mass Index at Baseline                                                 |                     |
| Underweight                                                                 | 30(24.0%)           |
| Normal                                                                      | 55(44.0%)           |
| Obese and over weight                                                       | 40(32.0%)           |
| Type of insulin                                                             |                     |
| Human Insulin                                                               | 63(50.4%)           |
| Insulin Analogue                                                            | 62(49.6%)           |
| Significant reduction of Glycosylated Hemoglobin at the end of Three Months |                     |
| No                                                                          | 29(23.2%)           |
| Yes                                                                         | 96(76.8%)           |
| Non Complaint with in Three Months                                          |                     |
| No                                                                          | 85(68.0%)           |
| Yes                                                                         | 40(22.0%)           |

**Table-II: Comparison of various variables between patients managed with Insulin Aspart and Human Insulin (n=125)**

| Factors                        | Insulin Analogues, n=62 | Human Insulin, n=63 | p-value |
|--------------------------------|-------------------------|---------------------|---------|
| Significant reduction in HBA1c |                         |                     |         |
| No                             | 07(11.3%)               | 52(82.5%)           | 0.001   |
| Yes                            | 55(88.7%)               | 11(17.5%)           |         |
| Significant weight gain        |                         |                     |         |
| No                             | 44(70.9%)               | 44(69.8%)           | 0.890   |
| Yes                            | 18(29.1%)               | 19(30.2%)           |         |
| Non-Compliant                  |                         |                     |         |
| No                             | 46(74.2%)               | 48(76.2%)           | 0.796   |
| Yes                            | 16(25.8%)               | 15(23.8%)           |         |
| >1 hypoglycemic episodes       |                         |                     |         |
| No                             | 57(91.9%)               | 45(71.4%)           | 0.002   |
| Yes                            | 05(8.1%)                | 18(28.6%)           |         |

## DISCUSSION

Insulin analogue emerged as better option in achieving glycemic control in our study participants as compared to Human Insulin. Type-I diabetes is usually a clinical challenge for treating teams. Pediatricians, endocrinologists and metabolic diseases experts manage this together in settings with ample resources. In Pakistan usually medical specialist bear the burden of this complex disorder. As insulin is usual mode of treatment in these patients so treating teams usually have to decide regarding type of insulin

to be used. In this study, we compared the effect of Insulin analogues (Insulin Detemir and Insulin Aspart) versus Traditional Human Insulins (NPH Insulin Regular Human Insulin) in basal bolus therapy for patients with Type-I Diabetes Mellitus.

Laranjeira *et al.*, in 2018 published an overview of systematic reviews and meta-analysis of RCTs and came up with the conclusion that insulin analogues are better in preventing hypoglycemic episodes in patients suffering from Type-I DM.<sup>15</sup> Our study had similar findings and most of the Type-I DM patients included in the study had better glycaemic control and lesser hypoglycaemic episodes who were managed with Insulin analogues as compared to those managed with Human Insulin. Melo *et al.*, in 2019 published systematic review and meta-analysis comparing short-acting insulin analogues versus regular human insulin in patients with Type-I diabetes mellitus.<sup>16</sup> Insulin analogues turned out to be better in their study as compared to Human insulin. Our results concluded that Insulin analogues (Insulin Detemir and Insulin Aspart) emerged as better treatment option for patients of Type-I diabetes Mellitus when compared to Traditional Human Insulins (NPH Insulin Regular Human Insulin) in our study participants. Martin *et al.*,<sup>17</sup> in 2021 published a systematic review and network meta-analysis with an objective to assess safety and efficacy of various forms of Insulin for management of Type-I DM. They concluded that second-generation basal insulins showed similar glycaemic control as first generation did, with better safety profile in patients with Type-I DM. Our results supported their findings and Insulin analogues turned out to be better when compared with Human Insulin. A study published in Japan assessed same parameter in a different way and tried to look for difference in difference glycemic control parameters after shifting patients from Human Insulin to Insulin Analogues.<sup>18</sup> The author found that Insulin analogues were better option in this regard and advocated their use. We did not switch from one type to another but in parallel comparison, at the end of three months we found Insulin analogues to be better for glycemic control in patients suffering from Type-I DM.

## LIMITATION OF STUDY

Main limitation of this study remains lack of long term follow up. As Type-I DM is a life long illness therefore longitudinal cohort studies are required to ascertain longer term risks and benefits of both forms of Insulins in these patients. Multiple factors may interfere with independent variables studied in this analysis therefore strict control of

confounding factors in future studies may also be beneficial in generating generalizable results.

## CONCLUSION

Insulin analogues (Insulin Detemir and Insulin Aspart) emerged as better treatment option for patients of Type-I diabetes Mellitus when compared to Traditional Human Insulins (NPH Insulin Regular Human Insulin) in our study participants.

**Conflict of Interest:** None.

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## Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MHZ & MAM: Data acquisition, data analysis, critical review, approval of the final version to be published.

BA & RT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MHQ & SA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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