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Patient's Health Effects of Switching from Innovator to Biosimilar Insulin: A Pilot Study

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ABSTRACT

Background: Biosimilar insulins offer a cost-effective alternative to originator (biological) insulin products, but real-world comparative data on adherence, barriers to treatment, economic burden, and long-term outcomes remain limited. This cross-sectional study evaluated differences in treatment adherence, self-reported barriers, economic burden, and glycaemic outcomes between patients with diabetes using originator versus biosimilar insulin therapy. **Methods:** This cross-sectional study enrolled n=104 (100%) patients with diabetes mellitus on stable insulin therapy (innovator 39 (37.5%), and biosimilar 65 (62.5%) insulin) from 4 clinical sites in Maharashtra and patient pool. Data collection included demographic and clinical characteristics, self-reported adherence (missed doses and reasons for nonadherence), barriers to insulin administration, difficulties during insulin use, factors improving adherence, economic burden (monthly out-of-pocket expenses), and glycaemic parameters (HbA1c, FBS, PPBS) at start of therapy (SoT) and last day of data collection (LDOD). Quality of life was assessed using the Revised Diabetes Quality of Life Questionnaire (RV-DQOL13). Independent t-tests and chi-square tests were done for statistical analysis. **Results:** The biosimilar insulin group demonstrated significantly lower economic burden (₹2,416.92 ± 694.58 vs. ₹3,979.49 ± 1,087.05; mean difference ₹1,562.56, 95% CI: ₹1,216.28–₹1,908.85; $p < 0.0001$, Cohen's $d = 1.75$). Cost-related barriers to insulin administration were dramatically lower in the biosimilar group (1 (1.5%) vs. 17 (43.6%); $\chi^2 = 30.116$, $p < 0.0001$). Quality of life was significantly better in all three RV-DQOL13 domains for biosimilar users: satisfaction (mean=9.72 ± 2.61 (sd) vs. mean=11.97 ± 2.74 (sd), $p < 0.0001$, $d = 0.85$), impact (mean=7.46 ± 1.71 (sd) vs. mean=8.59 ± 1.67 (sd), $p = 0.001$, $d = 0.67$), and worry (mean=5.45 ± 1.16 (sd) vs. mean=6.03 ± 1.42 (sd), $p = 0.026$, $d = 0.45$). No significant differences were observed in glycaemic control at LDOD between groups (HbA1c: mean=7.88 ± 1.92(sd) vs. mean=8.08 ± 2.42(sd), $p = 0.642$; FBS: mean=152.16 ± 41.78 mg/dL vs. mean=168.58 ± 44.87 mg/dL, $p = 0.110$; PPBS: mean=174.56 ± 55.93 mg/dL vs. mean=187.67 ± 52.79 mg/dL, $p = 0.317$). **Conclusions:** Adoption of biosimilar insulin was associated with substantially lower economic burden, fewer cost-related barriers to treatment, and better quality of life compared with innovator insulin, while maintaining comparable glycaemic control. These findings support biosimilar insulin as an effective and economically advantageous alternative for diabetes management, with potential to improve treatment access and adherence in resource-limited settings.

Keywords*: type 2 diabetes, type 1 diabetes, biosimilar insulin, innovator insulin, insulin adherence, economic burden, quality of life, barriers to insulin therapy, India.*

INTRODUCTION

Globally, 'diabetes mellitus' has emerged as a major public health challenge with approximately 537 million adults estimated to be living with diabetes (2021), and India contributing approximately 74 million of these cases.[1-2] Insulin therapy is essential for achieving optimal glycaemic control in individuals with type 1 diabetes (T1DM) and in a substantial proportion of patients with type 2 diabetes (T2DM) who fail to achieve glycaemic targets with oral antidiabetic agents.[3] Despite the established benefits of intensive insulin therapy in preventing long-term complications,[4-6] persistent adherence to insulin regimens remains suboptimal.[7] Previous studies have identified multiple barriers to insulin adherence, including fear of injections, hypoglycaemia risk, weight gain, interference with daily activities, embarrassment, and the complexity of insulin administration.[8-10] In low- and middle-income countries, the cost of insulin presents an additional formidable barrier, often leading to rationing of doses, missed injections, and suboptimal glycaemic control.[11] The expiration of patents for several innovator (biological) insulin products has led to the development of biosimilar insulins—highly similar versions approved through abbreviated regulatory pathways. Biosimilar insulins typically cost 20%-30% less than innovator products, potentially improving medication access and adherence.[12] Randomized controlled trials have demonstrated comparable glycaemic control and safety profiles between biosimilar and innovator insulins.[13-14] However, real-world evidence from low- and middle-income countries examining the comparative effectiveness of biosimilar insulins on patient-reported outcomes, adherence behaviours, economic burden, and quality of life remains limited. Patient-reported outcomes (PROs), including diabetes-related distress, barriers to insulin treatment, and quality of life, are increasingly recognized as important measures of diabetes care quality.[15] These outcomes may be particularly relevant in low-resource settings where cost-related barriers significantly impact treatment adherence. Understanding whether biosimilar insulins can reduce economic barriers while maintaining clinical efficacy is essential for guiding health policy decisions in developing countries. This cross-sectional study aimed to compare treatment adherence patterns, self-reported barriers, economic burden, quality of life, and glycaemic outcomes between patients with diabetes using innovator versus biosimilar insulin therapy in a real-world Indian clinical setting.

METHODS

Study Design and Setting - This cross-sectional study was conducted at a 4 clinical site in Maharashtra and patient pool. The study protocol was reviewed and approved by the ethics committee and the study performed in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice. It was ensured that all participants for the study provided their informed consent prior to participation.

Study location and period – The study was conducted in Mumbai - Pune (India) region and patient data recorded during January to March 2026.

Participants **-** Participants were recruited from a 4 clinical site in Maharashtra and patient pool. The key inclusion criteria for the study were: diagnosis of diabetes mellitus (T1DM or T2DM); stable insulin therapy (either innovator/biological insulin or biosimilar insulin) for at least 3 months; age ≥18 years; and ability to complete the study questionnaire. Main exclusion criteria were: pregnancy; severe cognitive impairment; current participation in an interventional clinical trial; and use of both innovator and biosimilar insulin concurrently or within the past 3 months. Participants were categorized into two different groups based on the type of insulin therapy prescribed: innovator (biological) insulin group (n = 39) and biosimilar insulin group (n = 65). Accordingly, total n=104 participants (insulin therapy) with comprehensive datapoints were included for the final statistical analysis.

Justification for Sample Size: The study was of cross-sectional nature with no 'a priori' sample size estimation determined, thus a post-hoc power analysis using observed effect sizes for the two key outcomes were employed, such as - economic burden (representing monthly out-of-pocket expenses); and quality-of-life (RV-DQOL13: satisfaction) [22] domains. The data analysis was done successfully using the G*Power software (v.3.1.9.7; Universität Düsseldorf, Germany) containing following parameters: two-tailed independent t-test, $\alpha = 0.05$, and the actual sample sizes ($n_1 = 39$ for innovator insulin, $n_2 = 65$ for biosimilar insulin).

Data Collection - Data were collected using a structured questionnaire and medical record abstraction. The following information was obtained: *Demographic and Clinical Characteristics* - Age, gender, education level, type of diabetes mellitus (T1DM/T2DM), duration of diabetes, diabetes control status (controlled/uncontrolled based on clinical assessment), presence of chronic diseases (hypertension, thyroid disorders, hyperlipidaemia, chronic kidney disease); *Adherence Assessment* - Self-reported prevalence of missed insulin doses (yes/no), number of missed doses per week, reasons for nonadherence (assessed across 12 domains including "away from home," "forget," "cost of medication is high," "feeling embarrassed," etc.); *Barriers to Insulin Administration* - Self-reported barriers assessed across six domains (hypoglycaemia, weight gain, fear of needles, self-injection, complex administration route, cost of medication); *Difficulties During Insulin Use* - Assessed across nine domains including preparation of injection, insulin storage requirements, variable timings of administration, adjusting insulin doses, and cost of medication; *Factors Improving Adherence* -Assessed across six domains including minimizing number of injections, convenient time regimen, confidence in taking medication in public, belief in efficacy of treatment, social support, and cost of medication; *Economic Burden* -Monthly out-of-pocket expenditure on insulin therapy (in Indian Rupees, ₹); *Quality of Life* - Assessed using the Revised Diabetes Quality of Life Questionnaire (RV-DQOL13) [22], which includes three domains: satisfaction domain, impact domain, and worry domain. Lower domain scores indicate better quality of life; and, *Laboratory Parameters* - Fasting blood sugar (FBS), Glycated haemoglobin (HbA1c), and post-prandial blood sugar (PPBS) were recorded at start of therapy (SoT) and at the last day of data collection (LDOD). Duration of therapy (months) was recorded for each parameter.

Statistical Analysis - Statistical analyses were performing using MS-Excel. Demographic and clinical variables were analysed and summarized using Descriptive statistics, Categorical variables using frequencies and percentages, and continuous variables using mean ± standard deviation (SD). Associations between insulin therapy groups (innovator vs. biosimilar) and categorical variables were assessed using the chi-square test of association. Differences in continuous variables between the two independent groups were analysed using the unpaired (independent samples) t-test. Cohen's d was calculated to measure effect sizes, with d ≥ 0.50 considered large, 0.20-0.50 moderate, and <0.20 small.[16] All of the statistical tests, these were two-tailed, with p-value < 0.05 considered as statistically significant. Analyses were conducted using available case data; missing values were excluded from respective analyses without imputation.

RESULTS

Participant Characteristics - A total of n=104 (100%) participants were recruited where 39 (37.5%) was among the innovator insulin group and 65 (62.5%) in the biosimilar insulin group. Baseline demographic characteristics are presented in Table 1. The majority of participants were male 64 (61.5%), with a higher proportion of males in the biosimilar group 44 (67.7%) vs. innovator 20 (51.3%), compared to females 40 (38.5%) in biosimilar 21 (32.3%) vs. innovator 19 (48.7%); p= 0.096). Education levels were comparable between groups (p = 0.430). Mean age was similar between groups (innovator: 55.56 ± 12.99 years; biosimilar: 56.57 ± 10.57 years; p = 0.668). Height was significantly different (innovator: 164.13 ± 7.59 cm; biosimilar: 167.82 ± 6.55 cm; p = 0.010), but BMI was comparable (25.37 ± 3.08 vs. 25.30 ± 3.74 kg/m²; p = 0.924).

Table 1: Demographics of study participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	*χ2*	*p'*	*df*
Gender								
Male	64	20	51.3%	44	67.7%	2.773	0.096	1
Female	40	19	48.7%	21	32.3%			
Education Level								
Illiterate—No Formal Education	30	8	20.5%	22	33.8%	4.889	0.430	5
Primary School	13	5	12.8%	8	12.3%			
Secondary School	13	7	17.9%	6	9.2%			
High School	17	6	15.4%	11	16.9%			
Graduate	29	13	33.3%	16	24.6%			
Postgraduate	2	0	0.0%	2	3.1%			

Note - Chi-square test: p' value < 0.05 (statistically significant)

Diabetes Mellitus Type and Duration – The diabetes mellitus type proportion in case of Biosimilar group was significant with T2DM patients 59 (90.8%) vs. innovator 28 (71.8%), p = 0.011), while the innovator group had higher number of T1DM patients 11 (28.2%) vs. biosimilar 6 (9.2%). In terms of the duration, the difference was significant between groups (p= 0.033), with higher proportion of biological group with more than 10 years in 33 (48.7%) vs. 14 (21.5%).

Table 2: Type and duration of Diabetes Mellitus in participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	*χ2*	*p'*	*df*
Type of Diabetes Mellitus								
T1DM	17	11	28.2%	6	9.2%	6.418	0.011	1
T2DM	87	28	71.8%	59	90.8%			
Duration of Diabetes Mellitus								
<2 Years	2	1	2.6%	1	1.5%	8.762	0.033	3
2-5 Years	23	6	15.4%	17	26.2%			
6-10 Years	46	13	33.3%	33	50.8%			
>10 Years	33	19	48.7%	14	21.5%			

Diabetes control								
Uncontrolled	23	18	46.2%	5	7.7%	20.934	<0.0001	1
Controlled	81	21	53.8%	60	92.3%			

Follow-up Facilities and Pattern - The majority of participants in both groups received care from private hospitals/clinics (innovator: 31 (79.5%); biosimilar: 57 (89.1%), with no significant difference in follow-up facilities between groups (p = 0.262) (Table 3). The pattern of follow-up for diabetes care in the past year showed no significant difference (p = 0.140), with most participants missing 1-2 appointments (innovator: 50 (47.4%); biosimilar: 32 (50.0%) (Table 4).

Table 3: Follow-up Facilities in participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	$\chi 2$	*p'*	*df*
Follow-up Facilities								
No Routine Follow up	4	3	7.7%	1	1.6%	3.992	0.262	3
Primary Healthcare	7	4	10.3%	3	4.7%			
Int Med/Endocrine Govt Hosp	4	1	2.6%	3	4.7%			
Private Hospitals/Clinics	88	31	79.5%	57	89.1%			

Table 4: Pattern of Follow-up for Diabetes Care in Last Year of study participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	$\chi 2$	*p'*	*df*
Pattern of Follow-up for Diabetes Care in Last Year								
Never Missed Follow-Up	15	6	15.8%	9	14.1%	5.484	0.140	3
Missed 1–2 Appointments	50	18	47.4%	32	50.0%			
Missed > 2 Appointments	34	11	28.9%	23	35.9%			
No Follow-up/Appointment Last Year	3	3	7.9%	0	0.0%			

Presence of Chronic Diseases - The prevalence of chronic diseases was similar between groups (i.e. 24 (61.5%) for innovator, 44 (67.7%) in biosimilars; ==0.523) (Table 5). However, hypertension was most significantly common with the biosimilar group 31 (47.7%) vs. innovator 9 (23.1%); p = 0.012), followed by Hyperlipidaemia in biosimilar 16 (24.6%) vs. innovator 9 (23.1%); p=0.859), when compared with other chronic diseases such as thyroid disorders, CKD, and other chronic kidney ailments.

Table 5: Presence of Chronic Diseases in participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	$\chi 2$	*p'*	*df*
Presence of Chronic Diseases								
Yes	68	24	61.5%	44	67.7%	0.408	0.523	1
No	15	15	38.5%	21	32.3%			
Hypertension	40	9	23.1%	31	47.7%	6.240	0.012	4
Thyroid disorders	13	4	10.3%	9	13.8%	0.287	0.592	
Hyperlipidaemia	25	9	23.1%	16	24.6%	0.032	0.859	
CKD	5	4	10.3%	1	1.5%	4.048	0.044	
Other Chronic Kidney	1	0	0.0%	1	1.5%	0.606	0.436	

Prevalence of Missed Insulin Doses - As shown in Table 6, the proportion of participants reporting missed insulin doses was high in both groups (innovator: 31 (79.5%); biosimilar: 51 (78.5%); p = 0.901). The number of doses missed per week was also comparable between groups, with highest misses for 1-2 doses per week among biosimilars 28 (43.1%) vs. innovator 19 (48.7%); p = 0.404).

Table 6: Prevalence of missed insulin doses among patients

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	$\chi 2$	*p'*	*df*
Prevalence of missed insulin doses among patients								
Do you forget to take insulin?	82	31	79.5%	51	78.5%	0.015	0.901	1

How many doses do you miss in a week?								
NA	22	8	20.5%	14	21.5%	4.018	0.404	4
1-2 doses	47	19	48.7%	28	43.1%			
3-4 doses	25	8	20.5%	17	26.2%			
5-6 doses	6	1	2.6%	5	7.7%			
Greater than 6 doses	4	3	7.7%	1	1.5%			

Self-Reported Reasons for Nonadherence - Table 7 presents the self-reported reasons for nonadherence with insulin doses. Significant differences were observed between groups for several reasons:

"Away from home" was more frequently reported in the biosimilar group 38 (58.5%) vs. innovator 15 (38.5%), p = 0.048);

"Forget" was more common in the biosimilar group 39 (60.0%) vs. innovator 15 (38.5%), p = 0.033);

"Ran out of medication" was more common in the innovator group 11 (28.2%) vs. biosimilar 5 (7.7%), p = 0.005);

"Cost of medication is high" was dramatically more common in the innovator group 10 (25.6%) vs. 1 (1.5%), p < 0.0001);

Table 7: Self-reported reasons for nonadherence with insulin doses in participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	*χ2*	*p'*	*df*
Reasons for Missing Insulin								
Away from home	53	15	38.5%	38	58.5%	3.901	0.048	11
I cannot adhere to dietary regimen	8	3	7.7%	5	7.7%	0.000	1.000	
Feeling embarrassed to take it in public	25	10	25.6%	15	23.1%	0.088	0.767	
The time to take it is not appropriate	10	4	10.3%	6	9.2%	0.030	0.864	
Forget	54	15	38.5%	39	60.0%	4.530	0.033	
Took only when blood sugar is high	0	0	0.0%	0	0.0%	0.000	0.000	
Time consuming	2	1	2.6%	1	1.5%	0.136	0.712	
Regimen is complex	1	0	0.0%	1	1.5%	0.606	0.436	
Fear of injection pain	8	3	7.7%	5	7.7%	0.000	1.000	
Ran out of medication	16	11	28.2%	5	7.7%	7.879	0.005	
Took only when felt sick	1	0	0.0%	1	1.5%	0.606	0.436	
Cost of medication is high	11	10	25.6%	1	1.5%	14.971	<0.0001	

Self-Reported Barriers During Insulin Administration - Self-reported barriers as experienced by these patients while insulin administration was recorded (Table 8). It was found that Hypoglycaemia was the most significant barrier between the groups, with biosimilar 34 (52.3%) vs. 21 (53.8%) in innovators; p=0.879). In the case of cost of medication parameter, it emerged to be the most significant difference between groups, with innovator 17 (43.6%) reporting that high costs of access to insulin products were a barrier; however, only 1 (1.5%) of the biosimilar group ($\chi^2 = 30.116$, $p < 0.0001$) found it to be a challenge.

Table 8: Self-Reported Barriers Experienced by the Patients during Insulin Administration in participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	*χ2*	*p'*	*df*
Self-Reported Barriers								
Hypoglycaemia	55	21	53.8%	34	52.3%	0.023	0.879	5
Weight gain	39	12	30.8%	27	41.5%	1.206	0.272	
Fear of needles	34	8	20.5%	26	40.0%	4.207	0.040	
Self-injection	35	12	30.8%	23	35.4%	0.233	0.630	
Complex administration route	17	5	12.8%	12	18.5%	0.567	0.451	
Cost of Medication	18	17	43.6%	1	1.5%	30.116	<0.0001	

***Difficulties During Insulin Use* -** Table 9 presents difficulties encountered during insulin use. Significant differences between biosimilars vs. innovator groups, most prominent being were:
Adjusting insulin doses –26 (55.4%) vs. 12 (30.8%); p=0.015;

Insulin prescribed at bedtime – 25 (38.5%) vs. 12 (30.8%); p=0.428; while
Cost of medication was more common in the innovator group 13 (33.3%) vs. 3 (4.6%), p < 0.0001).

Table 9: Difficulties among Diabetic Patients during Insulin Use in participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	*χ2*	*p'*	*df*
Difficulties among Diabetic Patients during Insulin Use								
Preparation of injection	13	0	0.0%	13	20.0%	8.914	0.003	8
Insulin prescribed at bedtime	37	12	30.8%	25	38.5%	0.629	0.428	
Keeping insulin at cold temperature	33	11	28.2%	22	33.8%	0.358	0.550	
Variable timings of insulin administration	35	16	41.0%	19	29.2%	1.519	0.218	
Adjusting insulin doses	48	12	30.8%	36	55.4%	5.943	0.015	
Using more than 1 type of insulin	16	7	17.9%	9	13.8%	0.315	0.575	
Following instruction of health professionals	6	4	10.3%	2	3.1%	2.311	0.128	
Insulin prescribed with meals every day	8	3	7.7%	5	7.7%	0.000	1.000	
Cost of Medication	16	13	33.3%	3	4.6%	15.442	<0.0001	

Factors Improving Adherence - Table 10 shows factors that participants reported would improve adherence to insulin injections. The biosimilar group consistently reported higher utilization of adherence-enhancing strategies:
Minimize number of injections – biosimilars 44 (67.7%) vs. innovators 18 (46.2%), p = 0.030;
Convenient time regimen – 35 (53.8%) vs. 10 (25.6%), p = 0.005;
Confidence in taking medication in public - 27 (79.4%) vs. 9 (50.0%), p = 0.029;
Cost of medication (lower cost as enabling factor) – innovator 20 (51.3%) vs. biosimilar 2 (3.1%), p < 0.0001 [Note: This refers to the biosimilar group having lower cost concerns]

Table 10: Factors Improving Adherence to Insulin Injections in participant

		Biological Insulin (n=39)		Biosimilar Insulin (n=65)		Chi-square test		
	N	*No.*	*%*	*No.*	*%*	*χ2*	*p'*	*df*
Factors Improving Adherence to Insulin Injections								
Minimize number of injections	62	18	46.2%	44	67.7%	4.697	0.030	5
Convenient time regimen	45	10	25.6%	35	53.8%	7.900	0.005	
Confidence in taking medication in public	36	9	50.0%	27	79.4%	4.779	0.029	
Belief in efficacy of the treatment	32	8	20.5%	24	36.9%	3.081	0.079	
Social support	22	11	28.2%	11	16.9%	1.860	0.173	
Cost of Medication	22	20	51.3%	2	3.1%	33.959	<0.0001	

Economic Burden (Table 11) - The biosimilar insulin group demonstrated substantially lower economic burden compared with the innovator group (mean=₹2,416.92 ± (sd) 694.58 vs. mean=₹3,979.49 ± (sd) 1,087.05). The mean difference of ₹1,562.56 was highly significant (95% CI: lower (₹1,216.28) to upper (₹1,908.85); t = 8.950, p < 0.0001), with a very large effect size (Cohen's d = 1.75).

Quality of Life (Table 11) – The quality of life assessed using the RV-DQOL13 questionnaire [22], was significantly better in the biosimilar group across all three domains:

Satisfaction domain total score (lower scores = better): mean=9.72 ± 2.61 (sd) vs. mean=11.97 ± 2.74 (sd) (mean difference 2.25, 95% CI: 1.18–3.32; t = 4.183, p < 0.0001; Cohen's d = 0.85)

Impact domain total score (lower scores = better): mean=7.46 ± 1.71 (sd) vs. mean=8.59 ± 1.67 (sd) (mean difference 1.13, 95% CI: 0.45–1.81; t = 3.294, p = 0.001; Cohen's d = 0.67)

Worry domain total score (lower scores = better): mean=5.45 ± 1.16 (sd) vs. mean=6.03 ± 1.42 (sd) (mean difference 0.58, 95% CI: 0.07–1.09; t = 2.263, p = 0.026; Cohen's d = 0.45)

Table 11: Demography, Economic burden, and QOL total score of participants in Insulin

Group Statistics	Biological Insulin (n=39)	Biosimilar Insulin (n=65)	Difference		95% C.I of the Difference		Unpaired t test	
	Mean (SD.)	*Mean (SD.)*	*Mean*	*SEM*	*Lower*	*Upper*	*t'*	*p'*

Demography								
Age	55.56 (12.99)	56.57 (10.57)	-1.01	2.34	-5.64	3.63	-0.430	0.668
Height (cm)	164.13 (7.59)	167.82 (6.55)	-3.69	1.41	-6.48	-0.89	-2.618	0.010
Weight (kg)	68.74 (12.29)	71.54 (12.53)	-2.79	2.52	-7.79	2.20	-1.109	0.270
BMI (kg/m²)	25.37 (3.08)	25.30 (3.74)	0.07	0.71	-1.34	1.48	0.096	0.924
Economic burden	3979.49 (1087.05)	2416.92 (694.58)	1562.56	174.58	1216.28	1908.85	8.950	0.000
Quality of life								
Satisfaction Total Score	11.97 (2.74)	9.72 (2.61)	2.25	0.54	1.18	3.32	4.183	0.000
Impact domain Total Score	8.59 (1.67)	7.46 (1.71)	1.13	0.34	0.45	1.81	3.294	0.001
Worry domain Total Score	6.03 (1.42)	5.45 (1.16)	0.58	0.26	0.07	1.09	2.263	0.026

N: Count; SD: Standard deviation; SE: Standard error: Mean Diff. (95% CI): Difference between group means with 95% Confidence Interval; Unpaired t-test: Statistical test used to compare means between two independent groups; t': t statistic value obtained from the unpaired t-test; p: p < 0.05 considered statistically significant.

Laboratory Parameters and Glycaemic Outcomes - Table 12 presents the comparative analysis of glycaemic parameters between groups.

At the *start of therapy (SoT),* no significant differences were observed between groups for any parameter:
HbA1c: 10.38 ± 2.14% (innovator) vs. 9.77 ± 1.67% (biosimilar) (p = 0.105)
FBS: 247.69 ± 66.78 mg/dL vs. 233.73 ± 56.84 mg/dL (p = 0.350)
PPBS: 284.25 ± 78.20 mg/dL vs. 279.59 ± 71.44 mg/dL (p = 0.799)

At the *last day of data collection (LDOD),* glycaemic control remained comparable between groups:
HbA1c: 8.08 ± 2.42% (innovator) vs. 7.88 ± 1.92% (biosimilar) (p = 0.642; Cohen's d = 0.09)
FBS: 168.58 ± 44.87 mg/dL vs. 152.16 ± 41.78 mg/dL (p = 0.110; Cohen's d = 0.38)
PPBS: 187.67 ± 52.79 mg/dL vs. 174.56 ± 55.93 mg/dL (p = 0.317; Cohen's d = 0.24)
All effect sizes for between-group differences in glycaemic outcomes at LDOD were small (Cohen's d < 0.4). The duration of therapy was comparable between groups for all parameters (p > 0.05).

Table 12: Laboratory Parameters in Participants

Group Statistics		Biological Insulin (n=39)	Biosimilar Insulin (n=65)	Difference		95% C.I of the Difference		Unpaired t test	
	N	Mean (SD.)	Mean (SD.)	Mean	SEM	Lower	Upper	t'	p'
HbA1c (SoT)	39	10.38 (2.14)	9.77 (1.67)	0.62	0.38	-0.13	1.36	1.634	0.105
	65	9.77 (1.67)							
HbA1c (LDOD)	39	8.08 (2.42)	7.88 (1.92)	0.20	0.43	-0.65	1.05	0.466	0.642
	65	7.88 (1.92)							
Total Duration for HbA1c (Months)	39	4.97 (1.20)	4.78 (1.42)	0.19	0.27	-0.35	0.73	0.698	0.487
	65	4.78 (1.42)							
FBS (SoT)	29	247.69 (66.78)	233.73 (56.84)	13.96	14.83	-15.64	43.56	0.941	0.350
	41	233.73 (56.84)							
FBS (LDOD)	3	168.58	152.16	16.4	10.1	-3.82	36.66	1.61	0.11

	1	(44.87)	(41.78)	2	5			7	0
	43	152.16 (41.78)							
Total Duration for FBS (Months)	29	4.97 (1.18)	4.60 (1.33)	0.37	0.31	-0.24	0.98	1.209	0.231
	42	4.60 (1.33)							
PPBS (SoT)	28	284.25 (78.20)	279.59 (71.44)	4.66	18.20	-31.66	40.99	0.256	0.799
	41	279.59 (71.44)							
PPBS (LDOD)	30	187.67 (52.79)	174.56 (55.93)	13.11	13.00	-12.82	39.04	1.008	0.317
	43	174.56 (55.93)							
Total Duration PPBS (Months)	29	4.97 (1.18)	4.56 (1.32)	0.40	0.31	-0.21	1.02	1.316	0.192
	41	4.56 (1.32)							

Summary of Effect Sizes - Table 13 summarizes the effect sizes (Cohen's d) for key outcome measures comparing biosimilar vs. innovator insulin groups:

Table 13. Effect Sizes (Cohen's d) for key outcome measures

Outcome Measure	Cohen's d	Interpretation
Economic burden (lower in biosimilar)	1.75	Very large
QOL - Satisfaction (lower/better in biosimilar)	0.85	Large
QOL - Impact (lower/better in biosimilar)	0.67	Large
QOL - Worry (lower/better in biosimilar)	0.45	Moderate
HbA1c at LDOD (biosimilar slightly lower)	0.09	Small (negligible)
FBS at LDOD (biosimilar lower)	0.38	Small
PPBS at LDOD (biosimilar lower)	0.24	Small

The effect sizes using Cohen’s d measure indicated that economic burden was lower in biosimilar with very large effects (d=1.75); QOL for satisfaction and impact were lower/better in biosimilar groups (d=0.85 and 0.67 respectively); and, very small (negligible) effects observed for HbA1c/FBS/PPBS at LDOD indicating lower values for biosimilar groups.

DISCUSSION

This cross-sectional study compared treatment adherence patterns, barriers to insulin therapy, economic burden, quality of life, and glycaemic outcomes between patients with diabetes using innovator versus biosimilar insulin in a real-world Indian clinical setting. Our findings reveal that biosimilar insulin adoption was associated with substantially lower economic burden, fewer cost-related barriers to treatment, and significantly better quality of life across all measured domains, while maintaining comparable glycaemic control to innovator insulin.

Critical Barrier: Economic Burden - The most profound finding of our study was the dramatic difference observed between groups for the economic burden aspect. Biosimilar insulin patients normally incurred lower out-of-pocket expenses on monthly basis, compared with innovator insulin users (₹2,416.92 vs. ₹3,979.49, $p < 0.0001$, Cohen's d = 1.75). Ultimately, such differences translated into patient-reported critical barriers: 17 (43.6%) of innovator insulin users identified cost as the biggest barrier to insulin administration, while only 1 (1.5%) of biosimilar users experienced it to be a challenge ($p < 0.0001$). Also, the "cost of medication is high" was cited as the prime reason for their nonadherence by 10 (25.6% innovator group) compared with 1 (1.5% biosimilar group) with significance levels ($p < 0.0001$). The study findings well align with previous research demonstrating insulin cost as a major barrier to optimal diabetes management, especially found in low- and middle-income nations.[11,17-18] In India, it is found that the out-of-pocket health expenditures on an average account for 62% (approximate) of total healthcare spending,[19] and medication expenses could compel patients to ration insulin or skip few doses, inherently leading to suboptimal glycaemic control with increases in risk of complications.[18] If biosimilar insulin adoption could lead to potential cost savings then these could improve both access and adherence to treatment for the larger populace.

Improvements to Quality of Life - Significantly better quality of life was reported among biosimilar groups across all three domains (RV-DQOL13), and large effect sizes were observed for satisfaction (d = 0.85) and impact (d = 0.67) domains, suggesting clinically meaningful differences. Reduced financial stress has a critical role as economic burden is understood to negatively impact the psychological well-being for chronic disease management. Despite higher rates of difficulties (e.g., preparation of injection, adjusting insulin doses, etc.) in the biosimilar group, the overall quality of life however remained superior, suggesting reduced cost benefits outweighed such challenges. It is noteworthy that biosimilar users reported higher rates of strategies that could improve adherence, including minimizing number of injections (biosimilars 44 (67.7%) vs. innovators 18 (46.2%), p = 0.030) and convenient time regimens (35 (53.8%) vs. 10 (25.6%), p = 0.005). These differences may reflect better patient education or more proactive management approaches within the healthcare system caring for biosimilar users, or they may indicate that reduced financial barriers enabled patients to adopt more effective management strategies.

Comparable Glycaemic Control - Despite the substantial differences in economic burden and quality of life, glycaemic control at the last day of data collection was comparable between groups. Both groups showed clinically meaningful improvements from baseline: mean HbA1c decreased from 10.38 (SOT) to 8.08 (LDOD) in the innovator group and from 9.77 to 7.88 mean in the biosimilar group. The absence of significant differences in HbA1c, FBS, or PPBS at LDOD, combined with uniformly small effect sizes (d < 0.4 for all comparisons), strongly supports the therapeutic equivalence of biosimilar insulin in real-world clinical practice. These findings are consistent with previous randomized controlled trials demonstrating comparable glycaemic efficacy between biosimilar and innovator insulins.[12-14] However, our study extends these findings by demonstrating that this equivalence holds in a resource-limited setting where adherence may be compromised by cost barriers. Notably, the biosimilar group achieved slightly better glycaemic outcomes on all three parameters at LDOD, though these differences were not statistically significant.

Adherence Patterns - We observed high rates of missed insulin doses in both groups (i.e. 31 (79.5%) in innovator vs. 51 (78.5%) biosimilars), with no significant difference in overall missed dose prevalence or the number of doses missed per week. This finding is concerning and consistent with previous literature documenting suboptimal insulin adherence globally.[7,20] The comparable adherence rates between groups suggest that while cost is a significant barrier, other factors influence adherence regardless of insulin type. Interestingly, the pattern of reasons for nonadherence differed between groups. Biosimilar users were more likely to miss doses due to being "away from home" with 38 (58.5%) vs. innovator 15 (38.5%), and "forgetfulness" 39 (60.0%) vs. 15 (38.5%), while innovator users were more likely to report "ran out of medication" 11 (28.2%) vs. 5 (7.7%); and "cost of medication is high" 10 (25.6%) vs. 1 (1.5%). In such cases, differences indicated that cost-related barriers could dominate innovator group, while behavioural or practical barriers predominated the biosimilar group. These clinical implications arising from such distinction highlight that interventions for biosimilar users could shift focus on portable insulin storage solutions and memory aids, while innovator users may more benefit from possible financial assistance initiatives.

Difficulties and Barriers - Higher prevalence for "fear of needles" among the biosimilar group 26 (40.0%) vs. 8 (20.5%), p = 0.040) and "adjusting insulin doses" 36 (55.4%) vs. 12 (30.8%), p = 0.015) calls for critical attention with higher proportions of T1DM patients from the innovator group 11 (28.2%) vs. 6 (9.2%) populations reflecting higher differences. T1DM patients typically receive more intensive diabetes education and may develop greater confidence in dose adjustment over time. Alternatively, these differences might indicate that biosimilar users require additional training in injection techniques and insulin dose adjustment.

Strengths and Comparison with earlier studies – Our study follows the methodological framework established by Hermanns *et al.* (2015), who evaluated the PaQ insulin delivery device's impact on patient-reported outcomes using the BIT, ITAS, and PAID questionnaires.[21] Like that study, we used validated instruments (RV-DQOL13) [22] and reported effect sizes to contextualize the clinical significance of our findings. However, while Hermanns *et al.* focused on a device-based intervention in a controlled pilot study (n = 18 completers), [21] our study compares two pharmacologic treatments in a larger real-world cross-sectional sample (n=104). Our finding of large effect sizes for economic burden (d=1.75) and quality of life domains (d=0.45-0.85) exceeds the moderate-to-large effects reported in the PaQ study (d=0.70 for BIT total score),[21] suggesting that the cost differential between biosimilar and innovator insulin may have more substantial clinical impact than device-based interventions.

Limitations - This study too has few imperative limitations. First, the cross-sectional design excludes causal inference and may not establish whether the observed differences are directly attributable to insulin type or reflect other confounding factors. Second, the non-randomized assignment to treatment groups introduces potential selection bias: T2DM patients were significantly overrepresented in the biosimilar group, and baseline characteristics differed between groups. Third, assessments for adherence and barriers using self-reported basis normally could be subject to recall and social desirability bias. Fourth, the study has not assessed any biosimilar immunogenicity cases or long-term complication rates. Fifth, the study also did not collect certain personal information on socioeconomic status, which may have confounded relationship effects among insulin type and outcomes.

Future Directions – Future studies should consider prospective, larger, and controlled trials with longer follow-up (longitudinal) to confirm these findings, and implement assessment outcomes for treatment persistence, diabetic complications, insulin antibody formation, and healthcare utilization across various healthcare settings. Few studies could integrate inductive methods (qualitative research) to explore provider and patient perspectives on such biosimilar adoption. These would be beneficial and inform strategists in the domain on quality implementation ease barriers to enhance biosimilar uptake.

CONCLUSIONS

The comparative biological vs. biosimilar insulin treatment cross-sectional study clearly demonstrated that adoption of biosimilar insulin was associated significantly with lowered economic burden, cost-related barriers to treatment, and meaningful health outcomes in terms of better quality of life across all the measured domains. It is also necessary that glycaemic control comparable to innovator insulin is fairly maintained. Very large effect sizes for economic burden reduction (Cohen's d = 1.75) and large effect sizes for quality-of-life improvements (d = 0.45-0.85) indicate that biosimilar adoption provides clinically meaningful benefits beyond therapeutic equivalence. These findings from the study highly support biosimilar insulin as an effective, economically beneficial, and patient-preferred alternative for such diabetes management (insulin therapy). Policymakers from low- or middle-income countries may consider encouraging biosimilar insulin adoption as a viable strategy to enhance treatment access, mitigate financial barriers, and augment quality of life among insulin-treated patients with diabetes without compromising the glycaemic outcomes.

Abbreviations

BMI=Body Mass Index; CKD=Chronic Kidney Disease; CI=Confidence Interval; FBS=Fasting Blood Sugar; HbA1c=Glycated Haemoglobin; LDOD=Last Day of Data Collection; PPBS=Post-Prandial Blood Sugar; PRO=Patient-Reported Outcome; QALY=Quality-Adjusted Life Year; QOL=Quality of Life; RV-DQOL13= Revised Diabetes Quality of Life Questionnaire (13-item) [22]; SD=Standard Deviation; SEM=Standard Error of the Mean; SoT=Start of Therapy; T1DM=Type 1 Diabetes Mellitus; and, T2DM=Type 2 Diabetes Mellitus.

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