Original Article

Exploring disparities: A comparative analysis of insulin-naïve, regular users, and inertia patients among type 2 diabetes mellitus outpatients in India

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Abstract

Introduction: Insulin utilization pattern varies greatly in type 2 diabetes mellitus (T2DM) patients. Clinical inertia in treatment intensification hinders glycemic control in T2DM management. This study investigated insulin prescription trends and various predictors among insulin naive, user, and insulin inertia (II) patients in T2DM. **Methodology:** A retrospective analysis of T2DM patient records from the diabetes clinic at a tertiary care center was conducted. Data on socio-demographics, anthropometry, disease characteristics, comorbidities, adherence, and medication prescribing patterns were collected. Analysis was done using tests of significance, odds ratio (OR), and multivariate logistic regression. **Results:** A total of 950 records were analyzed, with 17.3% of patients identified as insulin users (IU), 70.9% being insulin-naïve (IN), and 11.8% having II. IUs had significantly higher glycemic levels including HbA1c, fasting, postprandial, and random blood sugars compared to the other groups. Higher HbA1c levels were associated with significantly increased odds of insulin usage (OR: 3.46, confidence interval (CI): 1.94–6.16), while individuals taking sulfonylureas had lower odds of insulin usage (OR: 0.27, CI: 0.08–0.91). A significant association was also seen with the total number of oral antidiabetic drugs prescribed (four drugs; OR: 15.6, and five drugs; OR: 9.1). Other factors did not show a significant association. The regression model showed HbA1c level as low as 7.9% could indicate a future insulin requirement in 22% of patients. **Conclusion:** The study outlines differences in characteristics and parameters among T2DM patients who require or do not require insulin and highlights the challenges in insulin initiation in Indian T2DM patients. Findings on II underscore the need for timely treatment intensification.

Keywords: Barriers to insulin, glycemic control, insulin inertia, insulin initiation, T2DM management

Introduction

Type 2 diabetes mellitus (T2DM) remains a significant global health challenge, particularly in India, where its prevalence has reached epidemic proportions. Approximately 74 million adults are living with diabetes, representing a diabetes prevalence rate of 9.6% in the country International Diabetes Federation (IDF) Diabetes Atlas, 2021).[1] As one of the most common metabolic disorders affecting a vast population, T2DM poses a substantial burden on healthcare systems, necessitating continuous efforts to better understand its complexities and improve management strategies.

T2DM entails insulin secretion loss and resistance, leading to declining beta-cell function. Despite extensive use of oral

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Received: 16-01-2024 **Revised:** 08-04-2024
Accepted: 15-04-2024 **Published:** 18-10-2024

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_87_24

How to cite this article: Atal S, Bohra A, Kalra SS, Balakrishnan S, Joshi R. Exploring disparities: A comparative analysis of insulin-naïve, regular users, and inertia patients among type 2 diabetes mellitus outpatients in India. J Family Med Prim Care 2024;13:4244-51.

anti-diabetic drugs (OADs), many patients struggle for glycemic control,[2] often enduring inadequate control before treatment intensification. Median times for treatment initiation and intensification have been known to exceed up to seven years.[3] Clinical inertia stems from providers (50%), patients (30%), and system-level barriers (20%).[4]

In India, a study identified physician limitations and patient hesitations as barriers to insulin therapy initiation.[5] Initiatives like awareness campaigns and education can address these gaps. A survey of Indian healthcare professionals revealed a preference for multiple OADs over insulin therapy.[6] Differences in T2DM mechanisms and management emerge between young Indians and Europeans. The severe insulin-deficient diabetes (SIDD) subgroup, prevalent in Indians, exhibits insulin deficiency and hyperglycemia, while the mild obesity-related (MOD) subgroup is more common among Europeans. SIDD entails higher rates of complications like nephropathy and retinopathy.[7]

Patients with T2DM can thus be classified into distinct insulin treatment groups: insulin-naïve (IN) individuals who have not previously received insulin, insulin users (IUs) who are currently on some form of insulin therapy, and patients with insulin inertia (II), who experience a delay or resistance in starting insulin therapy despite persistent hyperglycemia and inadequate glycemic control on OADs.[8] It is important to understand the factors, demographic and clinical that predispose individuals to require insulin in T2DM, along with assessing the pattern of insulin use among such patients in tertiary care. While there are studies that have investigated IUs versus IN patients or evaluated the outcomes of insulin initiation, a comprehensive comparative investigation that includes patients with II is lacking in the existing literature. This analysis has been conducted to address this gap among these three distinct groups in the context of the Indian population.

Methodology

The study was carried out as a retrospective analysis utilizing patient records from the diabetes clinic at AIIMS Bhopal over the period from January 2019 to September 2022, for which permission was available from the Institutional Human Ethics Committee (No. IHEC-LOP/2021/IM0220R1).

The IU group included T2DM patients who were on at least one form of insulin therapy, and the IN group consisted of patients who were on OADs only. Patients with II were those with an HbA1c level greater than 9% or who were on three or more OADs. Socio-demographic data, disease characteristics, anthropometric measurements, comorbidities, adherence, and drug prescribing patterns were obtained for all the participants. In the demographics section of our diabetes study, self-reported genders were utilized to analyze and contextualize the health outcomes among diverse participant groups. Dietary, exercise, and medication adherence were recorded using validated, single, and self-reported questions.[9] A customized mobile app was used for data collection to ensure complete and secure data collection. The collected data was anonymized and linked to a unique hospital ID number for retrieval and authenticity. Patients were grouped as IU, IN, and II on the basis of the data from their last completed visit.

Descriptive statistics were employed to summarize the collected data. Statistical tests such as Chi-square tests, t-tests, and analysis of variance (ANOVA) along with post-hoc tests were used for comparisons, with the level of significance set at $P < 0.05$. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A step-wise multivariate logistic regression analysis was performed to examine the relationship between predictor variables and the occurrence of II. This approach resembles the step-forward method but also evaluates the removal of the least useful predictor during each addition, ensuring ongoing assessment for the removal of redundant predictors. The Nagelkerke R^2 value was used to assess the goodness-of-fit of the logistic regression model.

Results

Patient characteristics

A total of 950 records were analyzed in this study, and the patients were divided into three groups based on their insulin usage: IU, II, and IN patients. IUs accounted for 17.3% (n = 164) of the total participants, while the II group comprised 11.8% (n = 112) participants. The largest group, IN, consisted of 674 participants, representing 70.9% of the total sample size. There was a preponderance of males (60%) and the mean age of the participants was 53.96 ± 12.08 years. The group-wise comparison of demographics, measurements of anthropometric, glycemic, and non-glycemic parameters, lab values, and adherence are given in Table 1.

There was a significant difference in insulin usage based on gender with a preponderance seen in the male gender. The mean age did not significantly differ between the IU, II, and IN groups. There were no significant differences in systolic blood pressure (SBP) and diastolic blood pressure (DBP) among the three groups. IU had a significantly lower mean weight (65.95 ± 12.15 kg) compared to II individuals and IN individuals. IU had significantly higher mean fasting blood sugar (FBS), postprandial blood sugar (PPBS), random blood sugar (RBS), and HbA1c levels compared to II and IN groups ($P < 0.001$ for all). There were no significant differences in creatinine, total cholesterol, and triglyceride levels among the three groups. The analysis showed that there were no significant differences in medication and diet adherence between the three groups either. However, the difference in exercise adherence was found to be significant between the IU and IN groups.

The differences in the pattern of OADs and concomitant medications between the three groups were examined. There was a significant difference in the pattern of usage of OADs among the three groups ($P < 0.01$). IUs had a lower proportion

Table 1: Patient characteristics and clinical parameters

Characteristic/parameter	Insulin user mean (SD)/*n* (%)	Insulin inertia mean (SD)/*n* (%)	Insulin naive mean (SD)/*n* (%)	ANOVA *P*	Insulin user vs. insulin inertia *P*	Insulin user vs. insulin naive *P*
Females	67 (49.63%)	37 (41.57%)	201 (37.34%)	0.03	0.24	<0.01
Males	68 (50.37%)	52 (58.43%)	337 (62.66%)			
Age (yrs)	54.35 (12.32)	53.04 (11.28)	54.02 (12.17)	0.75	0.46	0.80
BMI (kg/m^2)	23.87 (4.46)	26.04 (4.04)	25.18 (4.66)	0.03	<0.01	0.06
Years lived with diabetes Mean±SD, median (IQR)	11.13±10.06, 10 (1.75–15.75)	9.77±7.35, 8.0 (4.5–12.5)	7.92±6.49, 6.0 (3.0–10.0)	<0.01	0.35	0.01
SBP (mm Hg)	139.1 (17.84)	140.4 (16.98)	138.06 (19.48)	0.54	0.6	0.6
DBP (mm Hg)	75.7 (10.04)	75.53 (11.49)	77.61 (10.57)	0.08	0.91	0.08
FBS (mg/dl)	161.51 (65.5)	149.65 (46.28)	142.2 (40.46)	0.01	0.27	<0.01
PPBS (mg/dl)	266.56 (79.4)	221.62 (82.19)	183.72 (70.35)	<0.001	0.1	<0.001
RBS (mg/dl)	232.57 (74.62)	192.95 (77.39)	188.58 (71.91)	<0.001	<0.01	<0.001
HbA1c (%)	8.92 (1.83)	8.43 (1.63)	7.29 (0.88)	<0.001	0.11	<0.001
Creatinine (mg/dl)	0.9 (0.39)	0.81 (0.16)	0.92 (0.24)	0.49	0.53	0.84
Total cholesterol (mg/dl)	168.2 (25.33)	117.1 (64.51)	146.85 (110.4)	0.6	0.12	0.67
Triglyceride (mg/dl)	111.2 (30.55)	121.86 (73.91)	145.54 (64.61)	0.42	0.77	0.26
Medication adherence	86.12%	86.67%	88.70%	0.43	0.88	0.22
Exercise adherence	32.52%	29.63%	19.89%	0.04	0.77	0.01
Diet adherence	20.16%	22.22%	13.04%	0.17	0.81	0.09
Comorbidities						
Hypertension	100 (60.98%)	61 (54.46%)	357 (52.97%)	0.09	0.34	0.03
Dyslipidemia	23 (14.02%)	13 (11.61%)	80 (11.87)	0.01	0.56	0.45
Coronary artery disease	1 (0.61%)	11 (9.82%)	0		0.05	
Stroke	1 (0.61%)	2 (1.79%)	0		0.741	
Hypothyroidism	11 (6.71%)	9 (8.04%)	35 (5.19%)	0.42	0.68	0.45
Complications						
Neuropathy	14 (8.54%)	5 (4.46%)	64 (9.49%)	0.44	0.89	0.32
Nephropathy	17 (10.37%)	8 (7.14%)	73 (10.83%)	0.42	0.36	0.88
Retinopathy	15 (9.15)	4 (3.57)	58 (8.61)	0.39	0.68	0.42

SD, standard deviation; BMI, body mass index; HbA1c, glycated hemoglobin; FBS, fasting blood sugar; PPBS, postprandial blood sugar; RBS, random blood sugar, SBP, systolic blood pressure; DBP, diastolic blood pressure

of sulfonylurea, dipeptidyl peptidase-4 (DPP-4) inhibitors, and thiazolidinedione usage compared to II individuals, while IN individuals had the lowest proportion. The total number of drugs prescribed also differed significantly among the three groups ($P < 0.001$). II individuals had a higher median number of drugs compared to IUs and IN individuals [Table 2].

The distribution of insulin regimens among the sample is as follows: intensive insulin 22 (13.41%), basal 46 (28.05%), pre-mixed insulin (PMI) 56 (34.15%), and nasal bolus 40 (24.39%). Additionally, the mean daily injections given to IUs were 1.24 ± 0.68 (median, inter-quantile range (IQR): 1, 1). Among the IUs, the mean total insulin dose per day was 33.8 ± 24.4 U. The mean daily dose of basal insulin (glargine) was 22.47 ± 12.6 U (n = 72), while that of bolus insulin was 42 ± 32 U (n = 46). The OAD usage among IUs showed that 46.5% of patients were on three OADs, while 29.3% and 17.2% were on two and one OADs, respectively, with the rest being on four or more OADs. Angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), gamma-aminobutyric acid (GABA), β-blocker, thyroxine (T4), tricyclic antidepressants (TCA), vit B12, and vit D3 showed no significant differences in usage among the three groups. IUs had a significantly higher proportion of prescription of aspirin, calcium channel blockers (CCBs), and statin compared to IN individuals ($P < 0.05$). However, the difference was not statistically significant when comparing IUs to II individuals.

Regression analysis

The step-wise logistic regression analysis was conducted to examine the relationship between probable predictor variables/factors and the occurrence of II as the outcome variable. All factors and variables found significant using t-tests were subjected to exploratory univariate logistic regression and those that were found significant again were subjected to step-wise multivariate regression analysis. Factors/variables that were entered were HbA1c, total OADs prescribed, metformin, DPP-4 inhibitors, sulfonylurea, sodium-glucose cotransporter-2 (SGLT2) inhibitors, and thiazolidinediones. We identified total OADs prescribed to have a statistically significant association with the likelihood of II while maintaining a good fit of the model. It included four and five OADs prescribed ($P < 0.05$). For a total of four and five OADs prescribed, individuals in this category had 15.6 and 9.1 times higher odds, respectively, of being in the II category. The Nagelkerke R^2 value was 0.67, indicating that the model explained 67% of the variation in the occurrence of insulin

Table 2: Therapy trends among the three groups of patients

Medication	Insulin user (*n*, %)	Insulin inertia (*n*, %)	Insulin naïve (*n*, %)	*P*	Insulin user v/s insulin inertia *P*	Insulin user v/s insulin naive *P*
OADs						
Metformin	108 (65.85%)	92 (82.14%)	435 (64.54%)	<0.01	0.003	0.75
DPP-4 inhibitors	82 (50.0%)	96 (85.71%)	204 (30.27%)	<0.001	<0.001	<0.001
Thiazolidinediones	47 (28.66%)	84 (75%)	82 (12.17%)	<.001	<0.001	<0.001
SGLT-2 inhibitors	32 (19.51%)	48 (42.86%)	21 (3.12%)	<0.001	<0.001	<0.001
Sulfonylureas	68 (41.46%)	99 (88.39%)	339 (50.3%)	<0.001	<0.001	0.04
Total OADs Median, IQR; mean±SD	2, 2; 2.05±1.33	4,2; 3.74±1.33	2,2; 1.60±1.12	<.001	<0.001	<0.001
Concomitant medications						
ACEIs	17 (10.37%)	8 (7.14%)	73 (10.83%)	0.49	0.36	0.86
ARBs	78 (47.56%)	41 (36.61%)	258 (38.28%)	0.07	0.07	0.03
CCBs	47 (28.66%)	21 (18.75%)	132 (19.58%)	0.03	0.06	0.01
Statins	62 (37.80%)	37 (33.04%)	176 (26.11%)	0.01	0.42	<0.01
Thiazide diuretics	15 (9.15%)	12 (10.71%)	72 (10.68%)	0.84	0.67	0.56
Loop diuretics	5 (3.05%)	0	6 (0.89%)	0.03	0.06	0.03
β-blocker	16 (9.76%)	14 (12.50%)	59 (8.75%)	0.44	0.47	0.69
Aspirin	61 (37.20%)	37 (33.04%)	159 (23.59%)	<0.001	0.48	<0.001
T4	5 (3.05%)	0	13 (1.93%)	0.29	0.17	0.49
Gabapentin	8 (4.88%)	5 (4.46%)	44 (6.53%)	0.56	0.87	0.43
TCA	3 (1.83%)	0	7 (1.04%)	0.34	0.15	0.40
Vit B12	3 (1.83%)	0	13 (1.93%)	0.34	0.15	0.19
Total concomitant medications median, IQR; mean±SD	2, 4; 1.99±1.99	1, 3; 1.64±1.84	1, 3; 1.55±1.79	0.02	0.14	<0.001

SD, standard deviation; IQR, inter-quantile range; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; T4, thyroxine; TCA, tricyclic antidepressants; OADs, oral anti-diabetic drugs

Table 3: Insulin user versus insulin inertia: multivariate step-wise logistic regression

Parameter	Odds ratio (OR)	95% confidence interval		*P*
		Lower bound	Upper bound	
(Intercept)	0.36	0.13	0.99	0.05
One OAD	0.75	0.17	3.36	0.7
Two OADs*	8.91×10^{-9}	0	∞	0.99
Three OADs*	8.91×10^{-9}	0	∞	0.99
Four OADs	15.6	4.25	57.24	<.001
Five OADs	9.1	2	41.45	<0.01
	Nagelkerke R^2	Sensitivity	0.85	0.67
	AUC	Specificity	0.87	0.91

*The odds ratio can take values between 0 and infinity for logistic regression coefficients. AUC, Area under curve

usage. The conditional estimates plot for four total OADs prescribed revealed a clear positive relationship with a narrow CI, indicating that in patients with II, prescribing four drugs was a common practice. OR of 8.91×10^{-9} suggests an almost negligible likelihood of individuals on two or three OADs being in the "II" category compared to the reference group, but the high *P* values (0.99) indicate a lack of statistical significance [Table 3 and Figure 1a-c].

We also conducted a logistic regression between IU and naïve groups. Similar steps were followed. To avoid collinearity, only HbA1c was selected for univariate analysis among FBS, PPBS, and RBS due to its superior goodness of fit.

HbA1c value and sulfonylureas prescription ($P < 0.05$) were found to have a statistically significant association with the odds of insulin usage (ORs of 3.46 and 0.27, respectively). The Nagelkerke R^2 value was 0.45, suggesting that the model explained 45% of the variation in the occurrence of insulin usage. The conditional estimates plot for HbA1c revealed a clear positive relationship, indicating that higher levels of HbA1c were associated with increased odds of insulin usage [Figure 1d]. The ORs for four and five OADs are very high, suggesting a strong preference for insulin usage over four or five OADs. However, the non-significant *P* values (0.99) imply that this relationship may not be statistically significant, indicating that factors beyond the number of OADs may be more important in determining insulin status in this population [Table 4].

HbA1c as a predictor of future insulin usage

To further find the level at which an increase in HbA1c could warrant future insulin usage, binary classification for specifying threshold was used. An HbA1c level as low as 7.9% could warrant a future insulin requirement in 22% of patients (95% credible interval). To confirm, HbA1c values were classified into subclasses using cutoffs of >8, >9.5, >11, >12.5, and >14, and step-wise multivariate logistic regression was performed. HbA1c >8% was associated with 6.62 greater odds of insulin usage ($P < 0.001$, CI: 3.66–11.96) and HbA1c >9.5% was associated with 5.52 times greater odds of insulin usage ($P < 0.001$, CI: 2.49–12.25) (sensitivity: 32%, specificity: 100%) [Figure 2].

Discussion

Diabetes presents a significant primary care challenge due to its widespread prevalence and chronic nature, necessitating comprehensive management approaches. Our study on insulin utilization patterns among T2DM patients in India underscores the importance of primary care physicians in addressing the complexities of diabetes management. The study aimed to investigate the characteristics among different groups of T2DM patients in terms of insulin usage, explore prescription trends, analyze the association between glycemic levels and insulin usage, and explore II. By investigating insulin prescription trends and barriers such as II, our study provides valuable insights for primary care practitioners, highlighting the need for tailored interventions to optimize treatment strategies and improve patient outcomes.

The characteristics of the participants showed that 11.8% exhibited II with a mean HbA1c of 8.4%. A study conducted in Scotland reported an HbA1c of 10.0% before initiating insulin therapy.[10] Another study indicated a worldwide HbA1c of 8.9%, with the UK specifically having a value of 9.9%.[11] We have used two criteria for II: either an HbA1c >9.0% or a prescription of OADs >3. The relatively lower HbA1c in such patients at our center could be suggestive of a trend toward the addition of more OADs before insulin usage to correct glycemic levels.

There is ambiguity in defining clinical inertia to insulin initiation with no well-adopted definition in the context.[12] Several international and national guidelines are available to guide physicians in the management of diabetes, providing stepwise treatment algorithms for type 2 diabetes. These guidelines include those from the American Diabetes Association (ADA),[13] the European Association for the Study of Diabetes (EASD),[13] the American Association of Clinical Endocrinologists (AACE),[14] the National Institute for Health and Care Excellence (NICE),[15] the IDF,[16] and the Indian National Consensus Group (INCG).[17] Traditionally, insulin therapy for type 2 diabetes is initiated when initial oral therapy, in double or triple combinations at maximum tolerated doses, fails to achieve optimal glycemic control. The NICE 2022 guidelines suggest considering triple therapy with metformin and another oral drug or starting insulin-based treatment for adults with T2DM if dual therapy with metformin and another oral drug fails to control HbA1c.[15] It recommends starting both neutral protamine Hagedorn (NPH) insulin and short-acting insulin, especially if the person's HbA1c is 75 mmol/mol (9.0%) or higher.[15] According to the Indian Council of Medical Research 2018 guidelines, indications for

Table 4: Insulin user v/s insulin naïve: Multivariate step-wise logistic regression

Parameter	Odds ratio (OR)	95% confidence interval		*P*
		Lower bound	Upper bound	
(Intercept)	7.25×10^{-5}	0	0.01	<0.001
HbA1c	3.46	1.94	6.16	<0.001
One OADs	0.29	0.06	1.32	0.17
Two OADs	1.19	0.25	5.7	0.84
Three OADs	1.24	0.21	7.22	0.82
Four OADs	5.23×10^{8}	2.20×10^{7}	1.24×10^{10}	0.99
Five OADs	4.45×10^{7}	3.21×10^{6}	6.15×10^{8}	1
Sulfonylurea prescribed	0.27	0.08	0.91	0.02
	Nagelkerke R^2	Sensitivity	0.72	0.45
	AUC	Specificity	0.85	0.85

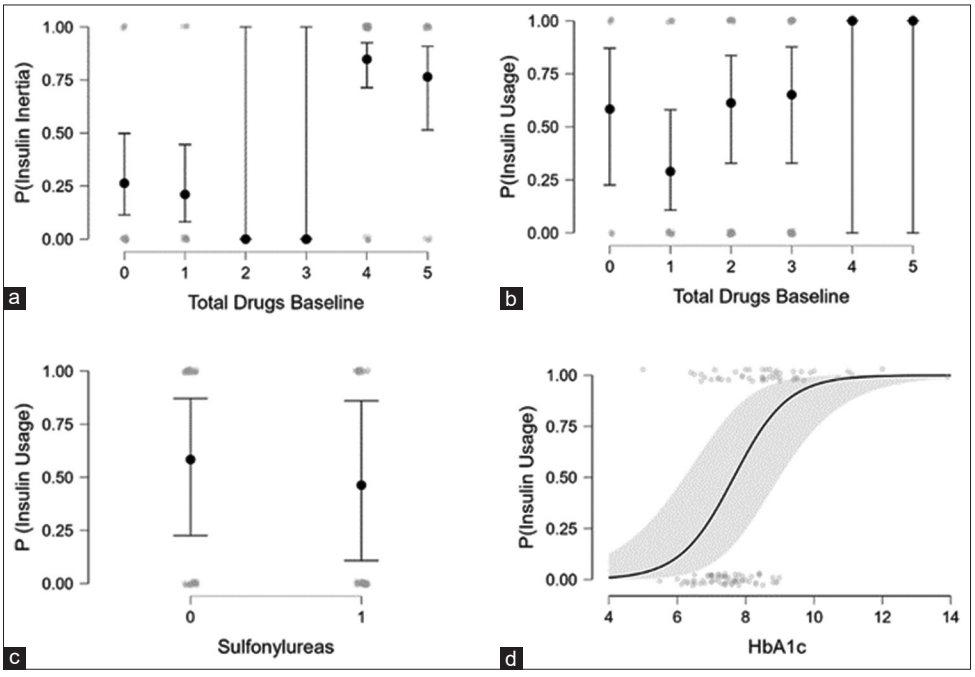

Figure 1: Conditional estimates plot: (a) total OADs prescribed (insulin inertia v/s user), (b) total OADs prescribed, (c) sulfonylurea, and (d) HbA1c (all insulin usage v/s naïve)

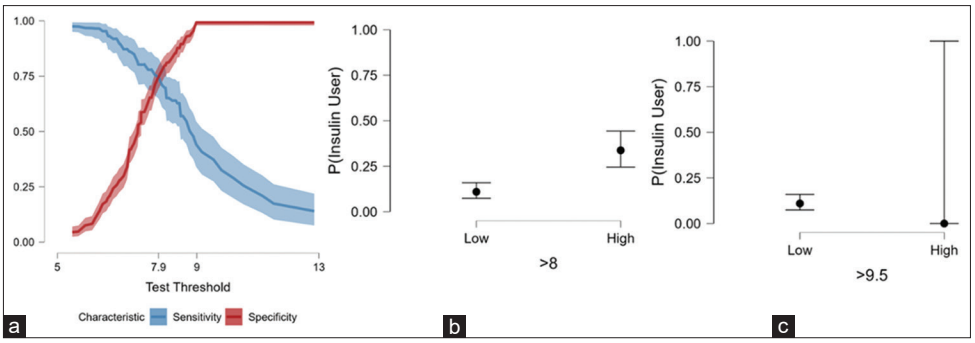

Figure 2: Insulin user v/s insulin naïve HbA1c: (a) HbA1c threshold v/s test characteristic (sensitivity, specificity); conditional estimates plots, (b) >8% HbA1c, and (c) HbA1c >9.5%

insulin use in T2DM include significant hyperglycemia with symptoms, high fasting plasma glucose or HbA1c levels (>9.0%), severe infections, and the presence of ketosis.[18] Overall, these guidelines emphasize the importance of considering triple therapy or insulin initiation for individuals who do not achieve glycemic control with oral medications, taking into account individualized factors and treatment goals. The amalgamation of these was used as a working definition for our study.

The ADA/EASD recommendation is to aim for a target HbA1c level of less than 53 mmol/mol (less than 7%) in most patients to reduce the risk of microvascular disease.[13] In selected patients who meet certain criteria (such as having a short duration of disease, a long life expectancy, and no significant cardiovascular disease), more stringent HbA1c targets between 42 and 48 mmol/mol (6–6.5%) may be considered, as long as they can be achieved without causing significant hypoglycemia or other adverse events. On the other hand, less strict HbA1c goals ranging from 58 to 64+ mmol/mol (7.5–8%+) are appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced complications, extensive comorbid conditions, or those who find it difficult to reach the target despite their best efforts according to the guidelines. IDF recommends initiating insulin therapy with either basal insulin or premixed insulin when first- and second-line therapies fail to achieve an HbA1c target of less than 7.0%.[16] On the other hand, INCG guidelines suggest starting insulin therapy with premixed insulin in newly diagnosed patients with fasting plasma glucose values over 150 mg/dL, postprandial glucose values over 200 mg/dL, and HbA1c over 8.5%.[17]

Regarding therapy trends, our study found significant differences in the usage of oral antidiabetic medications among the three groups. IUs had a lower proportion of usage of various classes of OADs other than metformin. This indicates a trend toward prescribing metformin and sulfonylurea and then switching to either insulin or DPP-4 inhibitors or thiazolidinediones. The Indian Council of Medical Research (ICMR) guidelines recommend sulfonylurea, DPP-4 inhibitors, or SGLT2 inhibitors as the first choice for dual therapy. However, as SGLT2 inhibitors were previously not available in generic form in the country, the cost could have impeded uptake.[18]

Among IUs, we observed that the majority were prescribed long-acting insulin, followed by pre-mixed insulin and short-acting insulin. Clinical evidence indicates several benefits of using basal insulin analogs, such as insulin detemir and insulin glargine, over intermediate-acting insulin like NPH. These benefits include better glycemic control, a reduced risk of hypoglycemia, and less weight gain. Basal insulin analogs have shown lower within-patient pharmacokinetic and pharmacodynamic variability, a relatively steady rate of absorption, and a flat action profile that lasts for 24 hours. Clinical experience suggests that a greater proportion of patients achieve HbA1c less than 7.0% when using once-daily basal insulin analogs. Additionally, the risk of overall hypoglycemia is reduced by 47%, and nocturnal hypoglycemia is reduced by 55% with basal analog insulin compared to basal human insulin. Both AACE/ACE and ADA/EASD guidelines recommend initiating insulin therapy with basal insulin. The general approach is to address fasting hyperglycemia with a single injection of basal insulin and then address postprandial hyperglycemia, if necessary, with other insulin options.[13,14]

We found that usage of aspirin and statins was significantly higher in IUs compared to IN individuals. This points toward the fact that insulin requirements are higher in patients with macrovascular complications and could indirectly point towards clinical inertia in initiation. The UK Prospective Diabetes Study (UKPDS) showed that early intensive diabetes management reduced the risk of microvascular complications and subsequent studies found reduced risks of myocardial infarction and death, while shorter-term trials with high-risk patients did not show clear benefits for macrovascular complications and mortality.[19] Delayed treatment intensification increases the risk of cardiovascular events.

Multivariate step-wise logistic regression analysis revealed that the total number of OADs prescribed, especially four or five drugs, was significantly associated with II, which is logically understandable. Predicament toward adding four or five drugs is attributed to inertia at both the patient's and physician's end. A one-unit increase in HbA1c was associated with 3.46 times higher odds of insulin usage. Similarly, individuals taking sulfonylureas had 0.27 times lower odds of insulin usage

compared to those not taking sulfonylureas. Lower usage of sulfonylurea in IU could be to prevent fasting hypoglycemia.

Several previous studies have identified reasons for this II. Patient-related factors such as drug side effects, difficulty in following treatment regimens, poor disease awareness, limited doctor-patient communication, and low education levels contribute to clinical inertia. Non-adherence to a proper diet, socioeconomic status, and the presence of acute or terminal illnesses pose additional barriers.[12] In the PANORAMA study conducted in France, patients' reluctance to intensify treatments led to over two-thirds of patients failing to reach their HbA1c goals.[20] Factors related to treatment complexity and poor efficacy, also contribute to clinical inertia. Barriers created by the healthcare system, such as poor coordination, inadequate support technologies, reimbursement issues, and bureaucratic difficulties, further hinder timely care. Implementing a person-centered care model and ensuring healthcare professionals stay updated can help address patient non-compliance and clinical inertia.[12]

Limitations

The retrospective cross-sectional design and single-center data collection may limit the generalizability of the findings. Further research is needed to validate the results in larger and more diverse populations. Additionally, exploring additional factors such as patient preferences, healthcare provider attitudes, and socioeconomic factors could provide a more comprehensive understanding of insulin therapy initiation barriers and patient acceptance. Our study does not address the chronological aspect of II.

Conclusion

This study provides valuable insights into differences in demographic and clinical characteristics, prescription trends among different groups of T2DM patients in relation to insulin use, and the critical issue of II. The findings suggest that addressing OAD polypharmacy, optimizing glycemic control, and considering individual patient and glycemic factors may help improve insulin initiation and management strategies. Further research is warranted to explore these factors in greater depth and to develop interventions aimed at overcoming barriers to insulin therapy initiation. Similar analyses at other Indian centers are needed to estimate the prevalence of II.

Acknowledgments

The Authors would like to thank Dr. Kenam Shah, Dr. Zeenat Fatima, Dr. Saurav Misra, and residents in the department of pharmacology for their assistance in data collection.

Ethics statement

Institutional Human Ethics Committee (IHEC) approval and waiver of consent were obtained as it is a minimal-risk study.

Human rights statement

- Name of institutional or national ethical committee on human experimentation: Institutional Human Ethics Committee (IHEC), AIIMS Bhopal, India (registration No. EC/NEW/INST/2020/1322).
- Date of approval: March 19, 2021 (amendment; original approval – June 12, 2019)
- Approval number: No. IHEC-LOP/2021/IM0220R1 (amendment; original approval No. IHEC-LOP/2019/IM0220)

Informed consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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