Quest Journals
Journal of Medical and Dental Science Research
Volume 8~ Issue 9 (2021) pp: 18-26
ISSN(Online) : 2394-076X ISSN (Print):2394-0751
www.questjournals.org

Research Paper

Average HBA1C at the time of insulin initiation in a particular patient group

Dr Mrinal Kanti Guha
Appollo clinic,26,Diamond Harbour Road,Kolkata

Purpose: *To describe the degree in insulin inception, portray its effect on glycemic control, and investigate factors impacting anticipated insulin commencement among Indian sort 2 diabetes mellitus (T2DM) patients.*
Methods: *A genuine world, review companion concentrate with territorial electronic wellbeing records from Kolkata, Eastern India was directed among T2DM patients. Grown-up patients inception uncontrolled with oral antidiabetic drugs (OADs; HbA1c ≥7%) and started on insulin treatment were incorporated. Time to insulin was portrayed. After inclination score coordinating, Wilcoxon rank-total test and chi-square test were utilized to analyze follow-up HbA1c (first HbA1c 3 months after insulin inception) between ideal (started insulin inside a half year after OAD disappointment) and deferred (started following a half year) insulin-commencement gatherings. Affectability investigation was likewise performed by direct and calculated relapse. Elements related with deferred insulin commencement were investigated utilizing calculated relapse.*
Results: *An aggregate of 940 patients were included, with mean ±SD age 66.3±11.9 years. In aggregate, 328 had HbA1c recorded 3 months after insulin inception. After affinity score coordinating (1:1 coordinating), 184 patients were included for additional examination. Middle subsequent HbA1c was lower in the ideal inception bunch than the postponed commencement bunch (7.25% versus 8.25%, P=0.009). Patients in the opportune commencement groups additionally had higher chances of accomplishing HbA1c<7% (OR=3.15, P=0.001). Results were affirmed by strategic relapse. Hypertension, coronary conduit illness, benchmark HbA1c, and clinic level at insulin inception were related with delays in insulin commencement.*
Conclusion: *Timely insulin inception after OAD disappointment is related with better glycemic control.*
Keywords: *type 2 diabetes mellitus, therapeutic inertia, delayed insulin initiation, glycemic control, HbA_{1c}*

Received 21 August, 2021; Revised: 03 September, 2021; Accepted 05 September, 2021 © The author(s) 2021. Published with open access at www.questjournals.org

I. INTRODUCTION

The overall commonness of diabetes mellitus (DM) is expanding, and the assessed trouble is relied upon to be 693 million cases continuously 2045.1 The predominance of DM was assessed to be 10.9% in Indian grown-ups in a 2013 public study, and about portion of treated patients (50.8%) had lacking glycemic control.2,3 DM is related with expanded dangers of retinopathy and nephropathy just as a two-to four overlay expanded danger of cardiovascular diseases. 4 The objective of glucose control for most DM patients is glycosylated hemoglobin (HbA1c) <7% (53 mmol/mol). Albeit oral antidiabetic drugs (OADs) are directed, because of illness movement and crumbling of pancreatic β-cell work, some sort 2 DM (T2DM) patients who can't handle blood glucose with OADs frequently require therapy escalation with insulin to keep up with target HbA1c levels.5 The American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), and India Diabetes Society (CDS) suggest therapy strengthening if target HbA1c has not been accomplished following 3 months. Notwithstanding, delays in therapy heightening with insulin are normal among patients with T2DM.6,7 Therapeutic idleness, characterized as the inability to start or increase treatment in an opportune way, is one of the principle explanations behind uncontrolled hyperglycemia in T2DM as per proof based clinical guidelines.8 Delays in insulin inception after OAD disappointment is normal in patients with T2DM, and this hesitance toward insulin commencement could be because of patient-, doctor , or medical services framework related factors.9

Deferrals in therapy strengthening can happen at all phases of T2DM therapy: from inception of oral treatment after disappointment of way of life adjustment with appropriate eating routine and normal exercise, utilization of OADs and insulin as mix treatment, or heightening of insulin. Past investigations conducted in different nations have exhibited the adverse consequence of postponements in therapy increase on glycemic

control,10 however there is a scarcity of information from India, despite the fact that T2DM has turning into a significant general wellbeing challenge in India. All things considered, the motivation behind this review study utilizing a local electronic clinical record information base in southeast India was to give certifiable proof of the degree of postponements in insulin commencement, the effect of deferrals in insulin inception on glycemic control after insulin commencement, and to investigate the potential components identified with delays in insulin inception among Indian patients with T2DM.

II. METHODS

Data Source

This investigation separated information from a territorial electronic wellbeing record data set in Kolkata, Eastern India. This provincial data set, contains major clinical data from different data frameworks . It remembers data for >2 billion clinical records having a place with 23 million patients from September 2001 to January 2018. The data set contains major clinical data frameworks, for example, emergency clinic data frameworks, lab data frameworks, electronic clinical records, and picture chronicling and correspondence systems. Information assortment, preparing, and the board was approved by the I.M.A. All information were organized, normalized, and oversaw in an integrands platform.11 The data set isn't unreservedly accessible, so survey and endorsement were acquired from India Electronics Corporation information.

Study Design and Patient Population

In this review partner study, patients with T2DM (as characterized by ICD10 or recently treated with OADs) matured ≥18 years who had been started on insulin treatment after disappointment of an OAD routine were recognized. In particular, patients were remembered for the examination in the event that they had at least one record of insulin solution, OAD solution before insulin inception and at least one record of preinitiation HbA1c ≥7%, and at least one record of post initiation HbA1c. Patients were rejected if insulin had been recommended just briefly after OAD inability to control blood glucose during medical procedure or patients who had gotten glucagon-like peptide-1 receptor agonist (GLP-1RA). This investigation was supported by the India Ethics Committee of Registering Clinical Trials (ChiECRCT-20,180,224). The investigation was planned and directed as per the ISPE Guidelines for Good Pharmacoepidemiology Practice. This observational investigation utilized information recently gathered, and didn't force any type of intercession. Accordingly, educated assent was not needed.

Definitions

The last OAD routine was characterized as the OADs utilized for treatment not long before insulin commencement. The list date was characterized as the date of OAD disappointment. In the event that preinitiation HbA1c levels were consistently ≥7%, the record date (OAD disappointment) was the date of first HbA1c perusing ≥7%. In the event that HbA1c levels were not generally ≥7%, the file date (OAD disappointment) was the date of first HbA1c ≥7% following the last HbA1c <7%. Preinitiation HbA1c, characterized as HbA1c in the 3 months after the principal remedy of the last OAD routine to insulin commencement, was utilized to distinguish the record date.

In our investigation, postponed insulin inception was characterized as absence of insulin commencement inside a half year after OAD disappointment. The time frame between the list date and insulin inception was viewed as the opportunity to insulin commencement. Patients were separated into two gatherings as per time to insulin commencement: ideal inception (≤6 months) and postponed commencement (>6 months). HbA1c estimated on the record date was viewed as pattern HbA1c. Follow-up HbA1c, characterized as first HbA1c estimated 3 months after insulin inception, was utilized for correlation between the postponed commencement and opportune inception gatherings.

Study Outcomes

The investigation result was the degree of deferrals in insulin commencement after OAD-routine disappointment in patients with uncontrolled DM. The quantity of patients started on insulin treatment inside 90 days, 3–6 months, and following a half year was assessed. Likewise, the effect of deferrals in insulin inception on glycemic control was evaluated. This was finished by looking at follow-up HbA1c levels, and follow-up HbA1c-target accomplishment (<7%) between the deferred inception bunch and opportune commencement bunch after inclination score coordinating (PSM). Besides, univariate and multivariate strategic/straight relapse models were utilized for affectability examinations to research the relationship between restorative dormancy and glycemic control. Elements related with delays in insulin commencement were additionally evaluated by multivariate calculated relapse.

Statistical Analysis

Spellbinding insights (implies, SD, medians, IQRs, recurrence, and rates) are utilized to report nonstop and straight out factors. PSM was performed to adjust the distinctions in frustrating factors between the deferred commencement and ideal inception gatherings. In view of writing audits and6,12 clinical and research insight, factors chose from gauge qualities for PSM were age-bunch, sex, last OAD routine, pattern HbA1c, hypertension, dyslipidemia, coronary course dis-straightforwardness, and clinic level at insulin inception. A 1:1 insatiable PSM calculation utilizing calipers of a particular width was conveyed to analyze patients between the postponed inception and convenient commencement gatherings. The best matches were characterized as sets with the most noteworthy digit match (0.0001) on PS. The coordinating with calculation continued successively to the following most elevated digit match. No more matches were made underneath the least permitted digit of 0.1.

After PSM, Wilcoxon rank-aggregate and chi-square tests were performed to analyze follow-up HbA1c levels and target-HbA1c achievement between the deferred and ideal commencement gatherings, separately. To additionally investigate the relationship between delays in insulin inception and glycemic control, straight and strategic relapse were utilized as affectability examinations, with delays in insulin commencement filling in as the free factor, consistent subsequent HbA1c levels or clear cut subsequent HbA1c (<7% or ≥7%) as the reliant variable, and similar factors utilized for coordinating in PSM as covariates. Box–Cox change was utilized to accomplish rough ordinariness of the appropriation of constant subsequent HbA1c levels to make them viable for straight regression.13 HbA1c <7% was given the reaction profile "1" and HbA1c ≥7% the reaction profile of "0".

The potential factors perhaps connected with delays in insulin inception — age-groups, sex, last OAD routine, standard HbA1c, hypertension, dyslipidemia, coronary vein illness, stroke, helpful division, and emergency clinic level — at insulin commencement were investigated utilizing the univariate and multivariate strategic relapse models, and ORs with 95% CIs were determined. Two-followed P<0.05 was considered genuinely huge. When directing strategic relapse, postponed commencement patients were given the reaction profile "1" and opportune inception patients the reaction profile "0". All factual investigations were con-ducted utilizing SAS adaptation 9.4 (SAS Institute, Cary, NC).

III. RESULTS

Baseline Characteristics

A sum of 940 patients were found qualified, of which 328 had HbA1c estimation accessible after insulin commencement (Figure 1). The mean ±SD age of the patients remembered for the examination was 66.3±11.9 years, and 51.5% were female. The greater part (82.9%) of patients had been treated with at least two OADs preceding insulin commencement. Mean ±SD pattern HbA1c was 9.4%±1.9%, with 49% of patients having a HbA1c ≥9% (Table 1). The 328 patients with accessible HbA1c estimations were exposed to PSM. After PSM coordinating, 184 patients (92 in each gathering) were incorporated for additional investigation.

Delays in Insulin Initiation in Indian Patients

Among 940 T2DM patients who had neglected to have blood glucose controlled on OAD treatment, 615 (65.4%), 64(6.8%), and 261 (27.8%) were started on insulin inside 90 days, 3–6 months, and following a half year, separately, which demonstrated that in excess of a fourth of patients experienced postponements in insulin commencement (>6 months) in this investigation.

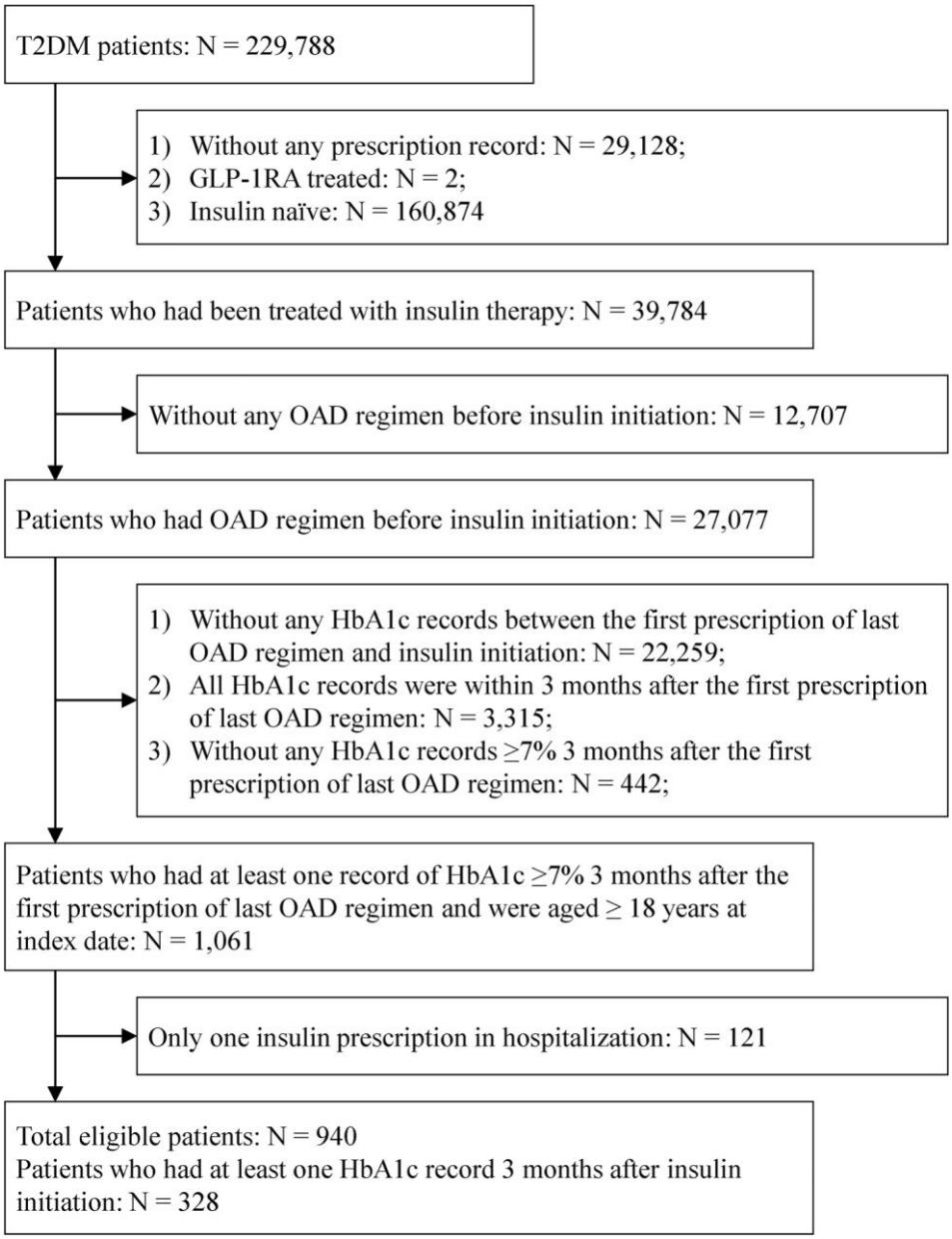

Figure 1 Screening of eligible patients.

Abbreviations: GLP1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycosylated hemoglobin; OAD, oral antidiabetic drug.

Impact of Delays in Insulin Initiation onGlycemic Control

The effect of deferrals in insulin inception in both the postponed and convenient commencement groups was surveyed by considering glycemic control after insulin inception. The 328 patients who had HbA1c records accessible for 90 days after insulin inception were qualified for PSM. All benchmark and clinical attributes were even after PSM (Supplementary Table 1). After PSM, 184 patients were utilized for correlation between the postponed and ideal inception gatherings, with 92 patients in each gathering. Among 184 PSM patients, Wilcoxon rank-total test uncovered middle HbA1c levels to be fundamentally lower in the ideal inception bunch than the deferred commencement bunch (7.25% versus 8.25%, P=0.009), proposing the useful effect of early commencement of insulin treatment (Table 2). In aggregate, 38% of patients in the convenient commencement bunch accomplished the treatment objective of HbA1c <7% after 3

	Patients (n=940)
Demographics	
Age (years)[#]	
Mean ± SD	66.3±11.9
Median (IQR)	66 (58–75)
Age-group (years)	
<65	401 (42.66%)
≥65	539 (57.34%)
Sex	
Male	456 (48.51%)
Female	484 (51.49%)
Last OAD regimen	
One OAD	161 (17.13%)
Two OADs	322 (34.26%)
Three or more OADs	457 (48.62%)
Medical insurance status	
With	710 (96.47%)
Without	26 (3.53%)
Missing	204
Therapeutic department at insulin initiation	
Endocrinology	472 (50.27%)
Others	467 (49.73%)
Missing	1
Hospital level at insulin initiation	
Secondary	226 (24.04%)
Tertiary	714 (75.96%)
Clinical characteristics	
Baseline HbA_{1c} level (%)[#]	
n	940
Mean ± SD	9.37 ± 1.94
Median (IQR)	8.90 (7.80–10.55)
Baseline HbA_{1c} group	
7≤ and <8	278 (29.57%)
8≤ and <9	201 (21.38%)
≥9	461 (49.04%)
Comorbidities	
Hypertension	627 (66.70%)
Dyslipidemia	627 (66.70%)
Hyperuricemia	13 (1.38%)
Coronary artery disease	205 (21.81%)
Demographics	
Atherosclerosis Stroke	58 (6.17%) 125 (13.30%)

Complications	
Diabetic foot	4 (0.43%)
Retinopathy	1 (0.11%)
Neuropathy	11 (1.17%)

Notes: #Age and baseline HbA_{1c} levels were abnormally distributed. Data were presented as n (%) unless otherwise indicated.

Abbreviations: HbA_{1c}, glycosylated hemoglobin; OAD, oral antidiabetic drug.

long stretches of insulin treatment, while the comparing figure of patients accomplishing the treatment objective in the postponed commencement bunch was just 16% (P=0.001) after PSM (Table 3). The affectability investigations were led among 328 patients utilizing direct and calculated relapse models to additionally portray the relationship between delays in insulin commencement and glycemic control and to adapt to confounders. Postponements in insulin inception filled in as the autonomous variable, and ceaseless (straight) or all out follow-up HbA1c levels (calculated) filled in as the reliant variable. Since the appropriation of nonstop HbA1c levels were slanted, a Box–Cox change was performed before incorporation as a reliant variable in direct relapse. Further, to preclude the impact of frustrating variables, like age, sex, last OAD routine, standard HbA1c, hypertension, dyslipidemia, and coronary course infection, at benchmark and medical clinic level at insulin commencement, these components were changed in the relapse model. Multivariate direct relapse showed that there was no genuinely huge contrast in Box–Cox changed mean subsequent HbA1c levels between the gatherings (P=0.193, Supplementary Table 2). Multivariate strategic relapse uncovered the ideal commencement bunch had higher chances of accomplishing the treatment objective (OR 2.52, 95% CI 1.26–5.04; P=0.009) than the postponed inception bunch (Supplementary Table 3).

Factors Associated with Delays in Insulin Initiation

A calculated relapse model was likewise used to investigate potential elements related with delays in insulin commencement. Multivariate calculated relapse investigation uncovered that presence of one OAD routine (OR 1.59, 95% CI 1.04– - 2.41; P=0.03) or a twofold OADs routine (OR 1.44, 95%

Table 2 Wilcoxon Rank-Sum Test of Median Follow-Up HbA_{1c} Levels (%) Before and After PSM

Group	**Before PSM**				**After PSM**			
	n	**Median(IQR)**	**Statistics**	***P*-value**	**n**	**Median(IQR)**	**Statistics**	***P*-value**
Timely initiation	234	8.00 (7.00, 9.20)	0.68	0.495	92	7.25 (6.60, 8.75)	−2.60	0.009*
Delayed initiation	94	8.25 (7.20, 8.90)			92	8.25 (7.15, 8.85)		

Note: *$P<0.05$.

Abbreviations: HbA_{1c}, glycosylated hemoglobin; PSM, propensity-score matching.

Table 3 Chi-Square Test of Follow-Up HbA_{1c}-Goal Attainment (<7%) Before and After PSM

	Before PSM				**After PSM**			
	Timely initiation	**Delayed initiation**	**OR (95% CI)**	***P*-value**	**Timely initiation**	**Delayed initiation**	**OR (95% CI)**	***P*-value**
<7%	58 (24.79%)	15 (15.96%)	1.74 (0.93–3.25)	0.082	35 (38.04%)	15 (16.30%)	3.15 (1.57–6.32)	0.001*
≥7%	176 (75.21%)	79 (84.04%)			57 (61.96%)	77 (83.70%)		

Note: *$P<0.05$.

Abbreviations: HbA_{1c}, glycosylated hemoglobin; PSM, propensity-score matching.

CI 1.03–2.03; *P*=0.034) prior to insulin initiation, HbA_{1c} level 7%–8% (OR 3.09, 95% CI 2.16–4.41; *P*<0.001) or
8%–9% (OR 2.47, 95% CI 1.66–3.67; *P*<0.001), tertiary-class hospital (OR 1.95, 95% CI 1.29–2.94; *P*=0.001), presence of hypertension (OR 1.69, 95% CI 1.17–2.45; *P*=0.005), and coronary artery disease (OR1.60, 95% CI 1.10–2.34; *P*= 0.015) were associated with a higher possibility of experiencing delays in insulin initiation (Supplementary Table 4).

IV. DISCUSSION

In this investigation, delays in insulin inception (characterized as absence of insulin commencement inside a half year after OAD disappointment) were seen in 27.8% of patients with T2DM. Since there is no standard limit term for characterizing delays in therapy increase among patients with OAD-treatment disappointment, various examinations have announced various edges. In our examination, insulin was the lone therapy escalation routine dissected. Yu et al showed 57.5% of patients with poor glycemic control getting monotherapy with metformin were strengthened by add-on treatment, including insulin.14 Previously led studies have announced huge deferrals in insulin inception after OAD failure.15–17 Rubino et al showed assessed delays in insulin commencement of 1.8 years in 25% and 4.9 years in half of T2DM patients after OAD failure.16 Trends in postponed insulin inception and escalation have been noticed around the world also. In the Western Pacific locale, around 66% of T2DM patients had HbA1c >9% at commencement of insulin, in spite of 74% having been treated with at least two OADs,18 though in Middle East and north African areas, 67.6% had HbA1c >9% at insulin inception, notwithstanding 68.3% of them having been treated with at least two OADs.19 The dissimilarity in the distributed writing may be because of various definitions utilized for delays in increase and furthermore the strengthening regimens utilized. Our investigation discoveries prove the extent of deferrals in insulin treatment in true medical care settings in current clinical practice in India.

In our examination, a HbA1c level of 7% (53 mmol/mol) or higher was viewed as the benchmark for patient choice. Nonetheless, different examinations have considered HbA1c levels of ≥6.5 or 8%.20,21 Moreover, our investigation considered therapy increase as expansion of insulin alone after OAD disappointment. Interestingly, different examinations have considered expansion of one more OAD after metformin to heighten the therapy regimen20 or expansion of a third OAD or injectable medication to the past OAD regimen.21 Also, in our investigation there were numerous insulin experienced patients without HbA1c ≥7% before insulin inception (prohibited), which showed that Indian medical care suppliers may strengthen therapy by alluding to fasting or postprandial blood–glucose levels other than HbA1c. Accordingly, future examination might consider these as beneficial markers to HbA1c when passing judgment on OAD-routine inability to control blood glucose.

The fundamental examinations uncovered that after PSM, middle subsequent HbA1c was lower and the level of patients accomplishing the HbA1c focus of <7% was higher in the convenient inception bunch than the postponed commencement bunch. The aftereffect of HbA1c-objective achievement was affirmed by affectability multivariate calculated relapse, however the consequence of normal subsequent HbA1c was distinctive between the Wilcoxon rank-total test and affectability straight relapse (Box–Cox change). The explanation is that the Wilcoxon rank-aggregate test tests the distinction in middle subsequent HbA1c level, while straight relapse tests the distinction in mean Box–Cox changed subsequent HbA1c level. Additionally, in view of the slanted dissemination of follow-up HbA1c levels, medians would be a more hearty pointer of focal propensity and a superior decision to portray normal subsequent HbA1c. Our discoveries are in accordance with other studies.6,12 utilized a half year as the edge to characterize delays in insulin commencement, and announced that HbA1c dropped from 9.4% to 7.9% in patients who had insulin inception inside a half year of OAD-treatment disappointment, while, the comparing change in HbA1c was from 9.0% to 8.2%. The mean change in HbA1c was likewise fundamentally more prominent in the convenient inception bunch (−0.33%, 95% CI −0.41% to −0.25%) inside 1 year of follow-up, which is in accordance with our present examination. Different investigations have additionally shown huge deferrals in therapy heightening to be related with poor glycemic levels and expanded occurrence of vascular complications.16,22,23

Early inception of insulin is helpful in recuperation and protection of β-cell work, accomplishing tight glycemic control, modifying sickness movement, and forestalling cardiovascular risk.24,25 This was featured by Goodall et al, who thought about the clinical outcomes of postponed insulin commencement versus convenient commencement. This examination announced expanded future (around 0.61 years), quality-changed life assumption (0.34 years), and furthermore critical decreases in DM-related intricacies among ideal insulin–started T2DM patients.15 Another investigation exhibiting certifiable clinical and monetary out-comes among early versus postponed insulin commencement detailed that 32% of patients that had insulin started early showed huge decreases in HbA1c, reasoning that early insulin inception might be savvy in con-savaging hyperglycemia contrasted with deferred initiation.25

This investigation additionally investigated potential components affecting deferrals in insulin

inception. A low HbA1c level at the file date was one of the components related with higher chances of encountering delays in insulin commencement. Further, HbA1c >9% was the most grounded impacting factor for insulin commencement. Our discoveries are practically identical with other comparative studies.10,21,26 Additionally, patients getting at least one OAD regimens in our investigation were related with higher chances of encountering deferred inception of insulin. This may be on the grounds that doctors are bound to build the portion or add one more OAD to strengthen treatment in Indian patients treated with a couple of OADs with poor glycemic control. Notwithstanding, patients getting at least three OADs with poor glycemic control were bound to be escalated with insulin. Comparative discoveries have been seen in different examinations with patients getting at least two OADs at the hour of insulin commencement with HbA1c ≥9%.18,19

In our study, the presence of comorbidities, such as coronary artery diseases and hypertension, was associated with higher odds of delays in insulin initiation. This could be because patient visits are time-constrained, and the physician and patient may have prioritized to treata comorbidity, which might have led to delays in treatmentintensification.[28] All these comorbidities have been reported in previous studies to be linked to a likelihood of delays in intensification of therapy.[27,29-31] Furthermore, in our study health-care providers in tertiary-care hospitals were less likely to ensure timely initiation of insulin than in secondary hospitals. This could be because patients visittertiary hospitals mostly when their glucose level is high or they have been unable to be controlled in lower-tier hospitals. This suggests that the clinical situation of patients in tertiary-care hospitals may be different. However, previous studies have shown that health-care providers in tertiary- are hospitals tend to intensify treatment with insulin after OAD failure, because of better knowledge of DM management, updated recommendation guidelines, and less concern about hypoglycemic events.[30,31] Furthermore, studies suggest that specialists are more likely to use insulin therapies[32] and that they tend to initiate insulin treatment sooner than primary-care physicians.[33] This probably reflects a referral bias, with specialists managing the most advanced and complex patients and hence those with the worst glycemic control. However, in this study we had no relevant data to assess differences in delays in insulin initiation between specialists and primary-care physicians.

The cause of delays in insulin initiation is complex. Itis challenging for both health-care providers and patients to overcome. On the part of the patient, consequences of hypoglycemia, inconvenience of self-injection and monitoring blood glucose, concerns of weight gain, or the unacceptability of insulin injection could lead to rejection and nonadherence to treatment with insulin. Bailey et al suggested that a consideration of clinical and organizational context is necessary to reinforce timely administration of insulin, especially with respect to time constraints for diagnosis and management of comorbidities, health- care costs, and appreciation of patient concerns.

One of the strengths of this study is that the database considered covers multiple and different levels of hospitals within the city, which allowed for better capturing of medical information and patient visits. In this study, PSM was used and was well balanced to correlate with the timing of insulin initiation and HbA_{1c} outcomes. Univariate and multivariate logistic/linear regression models were additionally used to test the robustness of the PSM results.

V. CONCLUSION

This retrospective cohort analysis showed that more thana quarter (27.8%) of patients with T2DM had delayed initiation of insulin. Delays in effective insulin getting started were involved with poor glycemic control. More adroit examinations are needed to research the long haul bene-attacks of convenient insulin commencement and to set up explanations behind delays in insulin inception. This thus will help medical services suppliers bring issues to light of opportune commencement of insulin treatment among patients lethargic to OADs.

REFERENCES

[1]. International Diabetes Federation, 8 edition, IDF diabetes atlas, fact sheet South East Asia, 2017. Available: http://diabetesatlas.org/resources/2017-atlas.html [Accessed 1 Aug 2018].

[2]. Marín-Peñalver JJ, Martín-Timón I, Sevillano-Collantes C, Del Cañizo-Gómez FJ. Update on the treatment of type 2 diabetes mellitus. *World J Diabetes*. 2016;7(17):354–395. doi:10.4239/wjd. v7.i17.354

[3]. Fu AZ, Sheehan JJ. Change in HbA1c associated with treatment intensification among patients with type 2 diabetes and poor glycemiccontrol. *Curr Med Res Opin*. 2017;33(5):853–858. doi:10.1080/ 03007995.2017.1292231

[4]. Society CD.Chinese guideline for the prevention and treatment of type 2 diabetes mellitus (2017 edition). *Chin J Diabetes Mellitus*. 2018;10(1):4–67.

[5]. Kumar SP, Sandhya AM A study on the glycemic, lipid and blood pressure control among the type 2 diabetes patients of North Kerala, India. Indian Heart J2018;**70**:482–5.doi:10.1016/j.ihj.2017.10.007

[6]. Khunti K, Gomes MB, Pocock S, et al. Therapeutic inertia in the treatment of hyperglycaemia in patients with type 2 diabetes:a systematic review. *Diabetes Obes Metab*. 2018;20(2):427–437. doi:10.1111/dom.13088

[7]. Khunti K, Millar-Jones D. Clinical inertia to insulin initiation and intensification in the UK: a focused literature review. *Prim Care Diabetes*. 2017;11(1):3–12. doi:10.1016/j.pcd.2016.09.003

[8]. Aschner P New IDF clinical practice recommendations for managing type 2 diabetes in primary care. Diabetes Res Clin Pract2017;**132**:169–70.doi:10.1016/j.diabres.2017.09.002

[9]. Jabbar A, Abdallah K, Hassoun A, et al. Patterns and trends in insulin initiation and intensification among patients with type 2 diabetes mellitus in the Middle East and North Africa region. *Diabetes Res Clin Pract*. 2019;149:18–26. doi:10.1016/j.diabres.2019.01.017

[10]. Romanelli RJ, Chung S, Pu J, Nimbal V, Zhao B, Palaniappan L. Comparative effectiveness of early versus delayed metformin in the treatment of type 2 diabetes. *Diabetes Res Clin Pract*. 2015;108(1):170–178. doi:10.1016/j.diabres.2014.12.019

[11]. Mata-Cases M, Franch-Nadal J, Real J, et al. Therapeutic inertia in patients treated with two or more antidiabetics in primary care: factors predicting intensification of treatment. *Diabetes Obes Metab*. 2018;20(1):103–112. doi:10.1111/dom.13045

[12]. Khunti K, Wolden ML, Thorsted BL, Andersen M, Davies MJ. Clinical inertia in people with type 2 diabetes: a retrospective cohort study of more than 80,000 people. *Diabetes Care*. 2013;36 (11):3411–3417. doi:10.2337/dc13-0331

[13]. Calvert MJ, McManus RJ, Freemantle N. Management of type 2 diabetes with multiple oral hypoglycaemic agents or insulin in primary care: retrospective cohort study. *Br J Gen Pract*. 2007;57 (539):455–460.

[14]. Mashitisho MLI, Mashitisho BG. Early insulin therapy in patients with type 2 diabetes mellitus. *J Endocrinol Metabol Diabetes S Af*. 2016;21(1):13–15. doi:10.1080/16089677.2016.1160539

[15]. Bhattacharya R, Zhou S, Wei W, Ajmera M, Sambamoorthi U. A real-world study of the effect of timing of insulin initiation on outcomes in older medicare beneficiaries with type 2 diabetes mellitus. *J Am Geriatr Soc*. 2015;63(5):893–901. doi:10.1111/jgs.13388

[16]. Khunti S, Davies MJ, Khunti K. Clinical inertia in the management of type 2 diabetes mellitus: a focused literature review. *Br J Diabetes*. 2015;15(2):65–69. doi:10.15277/bjdvd.20 15.019

[17]. Higgins V, Piercy J, Roughley A, et al. Trends in medication use in patients with type 2 diabetes mellitus: a long-term view of real-world treatment between 2000 and 2015. *Diabetes Metab Syndr Obes*. 2016;9:371–380. doi:10.2147/DMSO.S120101

[18]. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: an algorithm for glycemic control. *Endocr Pract.* 2009;15(6):540-559.

[19]. Wallia A, Molitch ME. Insulin therapy for type 2 diabetes mellitus. *JAMA.* 2014; 311(22):2315-2325.

[20]. nternational Diabetes Federation. IDF Diabetes Atlas 9th edition 2019. Available at: www.diabetesatlas.org (accessed 22 April 2020).

[21]. Sharma SK, Mudgal SK, Thakur K, Gaur R. How to calculate sample size for observational and experimental nursing research studies? Natl J Physiol Pharm Pharmacol. 2020;10:1–8

[22]. Mayberry LS, Osborn CY. Family support, medication adherence, and glycemic control among adults with type 2 diabetes. Diabetes Care. 2012;35:1239–45.

[23]. Kalra S, Ghosal S, Shah P. Consensus on bridges for barriers to insulin therapy. J Assoc Physicians India. 2017;65(3 Suppl.):23–30

[24]. Kloner RA, Nesto RW Glucose-insulin-potassium for acute myocardial infarction: Continuing controversy over cardioprotection. Circulation 2008;117:2523-33

[25]. Ivers NM, Jiang M, Alloo J, Singer A, Ngui D, Casey CG, *et al*. Diabetes Canada 2018 clinical practice guidelines: Key messages for family physicians caring for patients living with type 2 diabetes. Can Fam Physician 2019;65:14-24.

[26]. Bebakar WMW, Chow CC, Kadir KA. On behalf of the BIAsp-3021 study group. Adding biphasic insulin aspart 30 once or twice daily is more efficacious than optimizing oral antidiabetic treatment in patients with type 2 diabetes. Diabetes Obes Metab 2007;9:724-32.

[27]. Christiansen JS, Vaz J, Metelko et al. Twice daily biphasic insulin aspart improves postprandial glycemic control more effectively than twice daily NPH insulin, with low risk of hypoglycaemia, in patients with type 2 diabetes. Diabetes Obes Metab 2003;5:446-54

[28]. Boehm B, Home P, Behrend C et al. Premixed insulin aspart 30 vs. premixed human insulin 30/70 twice daily: a randomized trial in type 1 and type 2 diabetic patients. Diabet Med 2002;19:393

[29]. Raskin P, Allen E, Hollander P, et al. for the INITIATE Study Group. Initiating insulin therapy in type 2 diabetes: a comparison of biphasic and basal insulin analogs. Diabetes Care 2005;28:260-5.