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RESEARCH ARTICLE

Therapeutic inertia: a retrospective examination of inpatient management for type 2 diabetes mellitus at a South African regional hospital during a singular hospitalisation

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Background: Therapeutic inertia (TI), the clinicians' hesitancy to either instigate or escalate therapeutic measures despite clinical evidence, has been identified as a significant hindrance in achieving ideal glycaemic management in type 2 diabetes mellitus (T2DM) patients globally, including in South Africa.
Objective: This research purposed to quantify the prevalence of TI in relation to long-term insulin initiation and intensification within inpatients during a single admission at a regional-level public hospital in South Africa.
Methods: A retrospective analysis of 300 consecutive inpatient admissions to Harry Gwala Regional Hospital from 28 May 2022 was conducted.
Results: From the 300 charts identified, 46 were deemed ineligible, leaving 254 for comprehensive assessment. TI was detected in 107 instances (42%), with 73 (68%) of these incidences pertinent to long-term insulin commencement or dosage adjustment during that admission. A younger demographic was the sole discernible protective factor against TI ($p = 0.035$).
Conclusions: The prevalence of TI among T2DM inpatients during a single admission within a KwaZulu Natal public institution is significant, mirroring figures from global studies. Most of this inertia is affiliated with insulin-based strategies, resonating with global patterns. Advanced investigations are imperative to pinpoint specific impediments and strategize countermeasures against TI in such an environment as well as in general.

Keywords: glycaemic management, insulin initiation, insulin intensification, retrospective analysis, therapeutic inertia (TI), type 2 diabetes mellitus (T2DM)

Introduction

Despite a plethora of compelling evidence and significant strides in the management of type 2 diabetes mellitus (T2DM), a substantial proportion of the affected population persistently fails to meet the requisite therapeutic benchmarks.[1,2] Therapeutic inertia (TI) – the phenomenon characterised by healthcare providers' reluctance to initiate or amplify therapy despite clinical indications – has emerged as a universal barrier in accomplishing optimal glycaemic control, which constitutes the mainstay of treatment.[3]

The primary objective of therapy is the amelioration of symptoms and the deceleration of the onset of both microvascular and macrovascular complications. The urgency of achieving these therapeutic benchmarks is substantiated by a multitude of expansive studies.[4–9] Given the inherently progressive nature of T2DM, a stepwise intensification of treatment over time becomes necessary to maintain adequate glycaemic control.[5] The phenomenon known as the "legacy effect", wherein early disease control leads to improved outcomes in the later stages of the disease, underscores the criticality of timely treatment escalation.[10]

Insulin continues to play a vital role in the management of T2DM, particularly in low- and middle-income countries (LMICs) where access to newer, costlier drugs is often limited. Despite its efficacy, insulin therapy presents numerous complexities that need to be thoroughly considered during initiation and intensification of treatment.

Global studies have highlighted the most significant inertia towards treatment intensification to be associated with insulin.[11,12] These findings predominantly pertain to the outpatient setting, reflecting the overall trend of diabetes management largely being conducted within outpatient facilities. There exists a dearth of studies spanning both inpatient and outpatient long-term care. Only a single small-scale study investigating TI exclusively in an inpatient population, during a single admission, has revealed similarly high rates of therapeutic inertia.[13]

Local data from South Africa align with international research, revealing a high proportion of individuals living with T2DM who fail to meet the therapeutic targets.[14,15] While local research in sub-Saharan Africa (SSA) hints at the influence of TI as a contributing factor, there is a lack of in-depth exploration on the subject.[16] Given the scarcity of both international and local data concerning TI in relation to long-term insulin initiation in inpatients, there is a clear opportunity for further research.

The explicit objective of this quantitative, retrospective chart review was to ascertain the prevalence of TI during a single admission, regarding insulin initiation and intensification as a

long-term treatment among inpatients with T2DM admitted to a regional-level public hospital in SSA.

Materials and methods

Ethical considerations

Ethical approval for this study was obtained from the Biomedical Research Ethics Committee (BREC/00003898/2022) of the University of KwaZulu-Natal. Permission to conduct the study at Harry Gwala Regional Hospital was received from the institution as well as the provincial Department of Health.

Setting

Inclusion criteria: Patients consecutively admitted to Harry Gwala Hospital's Department of Internal Medicine with a diagnosis of Type 2 diabetes mellitus (T2DM) were considered for the study. This encompassed both longstanding and newly diagnosed cases.

Exclusions were as follows: individuals aged below 18, gravid patients, admissions under psychiatric care, trauma-related admissions, and charts with insufficiencies or omissions.

Study objective: The aim was an examination of 300 clinical charts, equating to roughly 30% of T2DM admissions to the department within an annual period.

Data acquisition protocols: Data were extracted from patient charts using a standardised data capture instrument to record:

1. demographic details;
2. therapeutic protocols;
3. diabetic-induced complications;
4. concurrent medical conditions;
5. clinical diagnoses;
6. initial vital statistics upon admission;
7. documented glycaemic values;
8. laboratory evaluations;
9. treatment outcomes;
10. presence of therapeutic inertia,

Therapeutic inertia was defined in accordance with the SEMDSA 2017 guidelines.[17] Ward glucose monitoring charts, HbA1c on or prior to admission, and treatment modalities at the point of admission and discharge were juxtaposed for each patient and scrutinised for TI using the SEMDSA criteria, which included:

1. Indications for long-term insulin initiation pre/post-discharge:
   - HbA1c > 10% on or prior to admission.
   - Sustained glucose > 16.5 mmol/l prior to discharge as recorded on charts in ward.
   - Non-achievement of HbA1c targets (HbA1c < 7% unless otherwise delineated) on a dual oral hypoglycaemic agent regimen.
   - Presence of oral agent contraindications.
   - Onset of diabetic ketoacidosis (DKA).
2. Criteria for comprehensive therapeutic augmentation pre/post-discharge:
   - Non-achievement of HbA1c targets on current therapy (HbA1c < 7% unless otherwise stipulated).

Data analysis

Data were entered in MS Excel (Microsoft Corp, Redmond, WA, USA) and analysed in Stata version 17 (StataCorp LLC, College Station, TX, USA). Descriptive statistics such as frequencies and percentages were used to summarise categorical variables. Central tendency and dispersion of data were measured using means and standard deviations for normally distributed variables and medians and interquartile ranges for skewed variables. Continuous variable group means were compared using unpaired t-tests for normally distributed data, otherwise non-parametric (Mann–Whitney U) methods were used. A p-value of < 0.05 was regarded as statistically significant.

Results

Details of 300 charts were collected for consecutive admissions starting on 28 May 2022. Of these charts, 46 were excluded (individuals aged below 18, gravid patients, admissions under psychiatric care, trauma-related admissions, and charts with insufficiencies or omissions). Data were extracted for the remaining 254 charts and analysed.

Table 1 provides an overview of the demographic and clinical features of patients. The cohort comprised 69% females and 31% males. The average age of the patients was 65.7 years with a standard deviation (SD) of 11.7. A predominant 97.2% identified as African in ethnicity. Most patients (89%) had a preadmission history of diabetes mellitus. The average body mass index (BMI) was 34.5 kg/m^2. On or prior to admission, the mean HbA1c level stood at 9.0. Regarding their medication status, 38% were on oral treatments, 22% on insulin, and 10% on a combination of the two. In terms of outcomes, 84% of the patients were discharged, while 15% faced mortality in the hospital.

A high prevalence of comorbidities was noted in this cohort, particularly hypertension, kidney injury (which included both acute kidney injury and chronic kidney disease), dyslipidaemia, and heart failure (Figure 1). There was a high prevalence of diabetes-related complications (63% [159 cases]) noted (Figure 2).

Personalised HbA1c targets were documented in only six cases. Foot examination was recorded for seven cases and fundoscopy findings for 14 cases. In the cohort analysed, cardiovascular disease was the most prevalent admission diagnosis at 59%. Kidney injury (51%) and simple hyperglycaemia (41%) followed. Other significant diagnoses included anaemia (36%) and neurological conditions (33%). Community-acquired and hospital-acquired infections represented 28% and 12% respectively. The remaining conditions each constituted less than 13% of admissions (Table 2).

In terms of in-hospital treatment, 96% of patients were prescribed a sliding scale. Only 29% had their chronic treatment intensified while 23% had their chronic treatment de-intensified. The most common reason for treatment de-intensification was severe hypoglycaemia.

At discharge/transfer, 44% had no changes made to their medications. Diabetic medications were issued on discharge/transfer

Table 1: Demographics and clinical characteristics of patients

Factor	Number of patients (*n*)	%
Gender:		
• Male	79	31
• Female	174	69
Age (years ± SD):	65.7 (±11.7)	
Ethnicity:		
• African	247	97.2
• Other	7	2.8
History of preadmission DM:		
• Yes	226	89
• No	28	11
BMI kg/m^2(±SD)	34.5 (±11.5)	
BP (systolic/diastolic in mmHg) (± SD)	135.7/80 (±28.7/18.5)	
Mean HbA1c on admission (± SD)	9.0 (±2.8)	
Random glucose on admission (mmol/l)	12.5	
Antidiabetic medication on admission		
• Oral	97	38
• Insulin	56	22
• Oral + insulin	27	10
• Unknown/undocumented	31	12
• None	43	17
Outcome		
• Discharged	213	84
• Transferred	3	1
• Mortality in hospital	38	15

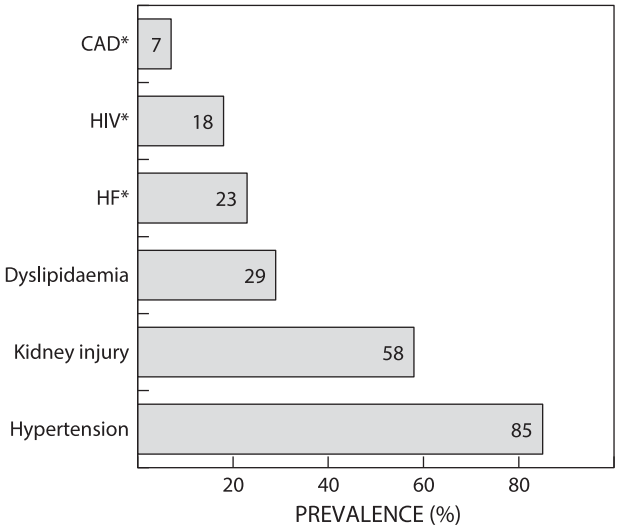

Figure 1: Prevalence of comorbidities in sample population. CAD: coronary artery disease, HF: heart failure, HIV: human immunodeficiency virus.

to the bulk (almost 70%) of patients. The remaining 30% had diabetic medications documented on discharge summaries but received no diabetic medications on discharge. Only 28 patients received lifestyle intervention on this admission. Of the patients who were discharged or transferred, 18 (7%) were not counselled concerning their chronic medications on discharge and only 7 (3%) had no follow-up plan.

There were 180 patients (71%) who had indications for treatment intensification. Of these, only 73 (41%) had their treatment intensified. The remaining 107 (42%) were identified as cases of TI. Of those cases, 27 (25%) had indications for insulin initiation and 46 (43%) had indications for insulin dose intensification. The remaining 34 cases (32%) had indications for additional oral agents or dose intensification of their current oral agents.

Stepwise logistic regression showed no statistically significant evidence that sex, ethnicity, HIV status, HIV stage, length of admission, follow-up, or outcome was associated with TI. Other variables including co-morbidities, diabetes-related complications, pre-admission T2DM, duration of T2DM, blood pressure, weight, height, blood glucose, and HbA1c were also not associated with TI. Younger age was the only variable that was associated with lower rates of therapeutic inertia ($p = 0.035$) (Table 3).

Discussion

There were high levels of TI documented in T2DM (42%), with most cases relating to long-term insulin intensification or initiation. These results are comparable to global studies, which show low levels of patients reaching glycaemic targets and a prevalence of TI that ranged from 18% to 50%.[1,2,18,19] The identified trend of TI being most profound at the stage of insulin initiation is echoed in this study with our group making up 25% of the prevalence of TI cases. However, in this study, most TI was related to long-term insulin dose intensification at 43% followed by TI to oral therapy at 32%.

Whether or not TI will contribute to poor glycaemic control in the long term remains to be determined in this population. With insulin initiation or dose titration, the risks of complications, readmissions, and even death need to be weighed up against potential benefit. There are conflicting international data regarding this topic, with studies documenting improved HbA1c 12 weeks post discharge with treatment intensification at transition of care.[20] Other studies have highlighted the adverse effect of treatment intensification during hospitalisation. These studies link treatment intensification, especially with insulin, to higher risks of death, emergency room visits, and readmissions after discharge.[21,22]

International data have shown that increasing age, duration of T2DM, use of oral agents, and increasing numbers of co-morbidities are associated with significant delays in treatment intensification. Higher HbA1c levels, higher BMI, and use of antiplatelet agents have been found to prompt earlier intensification of treatment. These findings have been replicated in both high- and middle-income countries.[23–27] In this cohort, younger age was the only protective factor identified. Obesity and higher HbA1c levels were not shown to be protective and the use of one or more oral agents was not associated with increased TI. The use of antiplatelet agents was not recorded in this study.

In our investigation, salient observations encompassed the omission of waist circumference recordings, a limited number of instances documenting both foot examinations and fundoscopic evaluations, and an infrequent specification of individualised HbA1c benchmarks. Waist circumference measurement in addition to BMI is advocated by local guidelines as it is an easy and reliable way to assess cardiometabolic risk and thus should be regularly documented.[17,28] In addition to this, both

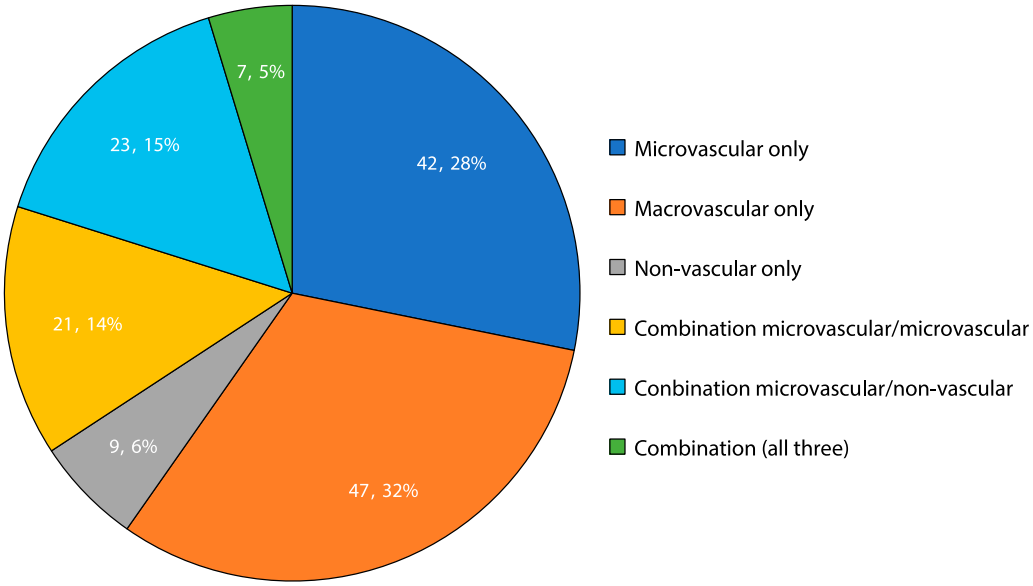

Figure 2: Diabetes-related complications (total number and percentages).

Table 2: Descriptive analysis of patient admission diagnosis

Diagnosis	Number	Percentage
Diabetic ketoacidosis (DKA)/hyperosmolar hyperglycaemic syndrome (HHS)	26	10
Simple hyperglycaemia	104	41
Hypoglycaemia	32	13
Cardiovascular disease	149	59
Acute kidney injury/chronic kidney disease	130	51
Infection (community-acquired)	73	28
Infection (hospital-acquired)	30	12
TB	6	2
Anaemia	91	36
Neurological	85	33
Gastrointestinal	29	11
Endocrine	7	3
Malignancy	7	3
Orthopaedic	7	3
Urology	6	2

Table 3: Logistic regression: characteristics associated with TI

Characteristic	OR	95% CI	*p*-value
(Intercept)	1.15	0.11, 11.4	> 0.9
Age	0.96	0.93, 1.00	0.035
Sex			
Female	–	–	
Male	1.80	0.78, 4.08	0.2

OR = odds ratio, CI = confidence interval.

international and local guidelines recommend screening for complications, including documenting foot examination, fundoscopy findings, and blood pressure readings among others, the benefit of which is early detection and intervention for those developing complications.[17,29] Thus, efforts should be made on these fronts to provide comprehensive diabetes care. Clinical attention to these findings could help improve diabetes care.

In general, the adoption of guideline-recommended strategies for in-hospital glycaemic control was commendable, with a vast 96% of the cohort receiving a prescription for short-acting insulin using a sliding scale, consistent glucose monitoring, and established procedures for hyperglycaemic crises.[17] It is heartening to note that the majority of patients were discharged with a well-defined diabetes post-care regimen, indicating that healthcare providers were cognisant of transition of care difficulties and the importance of long-term care. However, the non-issuance of anti-diabetic agents in more than 30% of cases on discharge warrants clinical attention. Prescription errors, including omission of medications such as in this study, have been highlighted as part of a worldwide problem. Data from the United Kingdom and the United States show that 1–2% of all patients admitted are harmed by medical error, the most common being errors of prescribing.[30–33] Rates of prescription errors in developing countries vary from 27% to 55% depending on definition, country, and method of study. This is significantly higher than in the developed world.[34,35] South African data show a prescription error rate in adults at a teaching hospital of 17.9%.[36] In comparison our study suggests errors within the range of those found in other LMICs; however, this was not a specific aim of this study. These findings warrant attention and identify one of the potential factors contributing to poor glycaemic control in a local population.

Outcomes in this cohort revealed a 15% mortality rate in hospital. This figure is in keeping with local data demonstrating a similar mortality rate for older patients admitted to medical wards at Groote Schuur Hospital in Cape Town, South Africa.[37]

Conclusion

This investigation ascertained that TI significantly contributes to the less-than-ideal management of T2DM within an inpatient population at regional hospital level on transition of care to ambulatory services. Prospective studies in this domain might encompass the outpatient milieu. Delving deeper could elucidate the underlying causes for the pronounced prevalence of TI and devise solutions tailored to our local context. Drawing from such insights, we could devise and implement innovative

strategies, analogous to the recent initiative by the American Diabetes Association: the "Overcoming Therapeutic Inertia" programme.[38]

Limitations

The deployment of fingerstick glucose and HbA1c measurements presented certain constraints. The glucometer operational in this context can register values solely within the range of 0.6–33.3 mmol/l, potentially leading to overestimations at lower thresholds and underestimations at elevated levels. Concurrently, the laboratory HbA1c assay in this environment caps at 16%, suggesting that the computed average values might be skewed towards underestimation.

Further limiting factors encompassed a modest patient cohort and an elevated documented incidence of concomitant medical conditions and sequelae. The reliance on HbA1c determinations in a demographic wherein inherent confounders such as anaemia, chronic renal insufficiency, or acute illness exist posed challenges. Such confounders might have given rise to perceived TI, with clinicians potentially deducing a skewed risk–benefit profile or questioning the reliability of results in distinct patient scenarios. The study attempted to mitigate this by using HbA1c on or prior to admission, rather than an HbA1c taken during the course of stay or close to discharge. Twenty-four-hour mean glucose values were unfortunately not routinely measure in this population.

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