Evaluation of the Therapeutic Approach and Outcome of Type 2 Diabetes Mellitus Management Strategies in Cameroon

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Authors’ contributions

This work was carried out in collaboration among all authors. Authors CNF, LMCS and TEF designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author NVN and Author DM managed the analyses of the study. Author TEF managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is a metabolic syndrome that is characterized by chronic hyperglycaemia, and can lead to chronic long-term complications. The prevalence of diabetes mellitus in Cameroon has been reported at 5.9% in 2017. Studies conducted in 2011, showed that only 41% of patients had a good glycaemic control which was, HbA1c < 6.5. The aim of this study was therefore to evaluate the treatment intensification with time in T2DM patients in the Yaoundé diabetic Centre in Cameroon.

Methods: The study was a cross-sectional analytical study. In a group of T2DM patients followed up at the National Obesity Centre (NOC) with poorly controlled blood sugar (HbA1c ≥ 7%). The treatment intensification and outcome were evaluated between the periods January 2016 to April 2019.
The majority of DM is a metabolic disorder characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both [1-3]. There are mainly four types of DM: type 1 diabetes mellitus (T1DM) is immune-mediated and requires daily administration of insulin; type 2 diabetes mellitus (T2DM) is characterized by inadequate production of insulin and inability of the body to respond fully to insulin (insulin resistance). The gestational diabetes is glucose intolerance in hyperglycaemia of variable severity with onset or first recognition during pregnancy [4], and complicates 2-4% of all pregnancies. Weight gain and presence of placenta hormones increases insulin resistance [5].

Other specific types of diabetes include a wide variety of relatively unknown conditions, primarily specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use [3-5]. The International Diabetes Federation (IDF) estimates that in 2017, 425 million people worldwide, representing 8.8% of adults between 20-79 years had diabetes. The prevalence is predicted to increase to 629 million by 2045 if these trends continue. This is especially a concern in the Sub-Saharan Africa (SSA) which had a prevalence of 15.5 million people in 2017. Meanwhile, Cameroon registered a prevalence of 5.9% in 2017 and caused about 15,757 diabetes related deaths that year [2,6]. Thus, diabetes is an important public health problem.

The majority of DM is T2DM which accounts for 90-95% of all the types. Associated to T2DM are long-term complications represented by cardiovascular diseases, cerebrovascular accidents, end-stage renal disease, retinopathy and neuropathies which are responsible for the major causes of morbidity, disability and premature death [1,4]. Also, huge economic burdens are associated to diabetes affecting the families and nations [3,7]. More so, Africa has the highest proportion of undiagnosed diabetes with over two-thirds (69.2%) of people with diabetes unaware they have the disease [2].

The non-pharmacologic therapy (diet, exercise and weight loss) remains a critical component in the treatment of diabetes. However, pharmacologic therapy is often necessary to achieve optimal glycaemic control. Various classes of anti-diabetic agents target the different pathophysiologic factors contributing to diabetes: reduces insulin resistance [8] - Biguanides (Metformin), Thiazolidinedione; stimulates insulin release [8,9], Sulfonylurea, Meglitinides; slows the digestive/absorptive process [10-11], Alpha-Glucosidase Inhibitors; improves glucose-dependent insulin secretion [12]. Glucagon Like Peptide-1 (GLP-1) Agonists, Dipeptidyl Peptidase-4 (DPP-4) Inhibitors; blocks reabsorption of glucose in the kidneys [3,12-14]. Sodium-Glucose Transporter-2 (SGLT-2) Inhibitors, enhances glucose-stimulated release of the GLP-1 [15]. Bile acid sequestrants (Colestevalam); increases insulin sensitivity - Dopamine-2 Agonists (Bromocriptine); slows gastric emptying - Amylin Analogues (Pramlintide) and facilitate glucose entry into the cell - Insulin [6,16-18].

According to the IDF [2], healthy lifestyle is the first approach to T2DM management with an
initiation of an oral medication when lifestyle modifications fail to achieve targets. The numerous anti-diabetic agents translates into more therapeutic options and complex decision-making [7]. These drugs can either be used alone or in combination. Metformin is the most commonly used initial treatment worldwide and subsequent treatment changes are based on failure to achieve target HbA1c after a three months period [8–10,19]. With the failure of a maximal tolerated metformin dose to achieve HbA1c target over 3 months, treatment is intensified with a second orally administered agent (Sulfonylurea, DPP-4 inhibitors) or basal insulin. While initiation of insulin is not delayed in patients not achieving glycaemic goals [9,20].

Despite the wide range of available medications and their benefits, studies have indicated that recommended glycaemic goals are achieved by less than 50% of patients [21]. About 29% of the patients have a good glycaemic control that is, HbA1C (<6.5%) in Africa and only 41% in Central Africa [22-23]. In Cameroon glycaemic control is poor with one in four known diabetic patients in a population-based survey having an optimal fasting blood glucose level [24]. As a result, hyperglycaemia and long-term complications are rising leading to increased morbidity and premature mortality, as well as increased costs to health services.

Several reasons may account for this poor glycaemic control and include poor adherence to treatment and lifestyle modifications [14,25], poor blood glucose monitoring [15,26], failure to keep appointments [5,27] but more likely could reflect the contributions from the failure of clinicians to intensify therapy appropriately in individuals who are likely to benefit from such intensification - therapeutic inertia [17–19]. A recent study in the US revealed that the median time to treatment intensification among those in whom metformin monotherapy failed exceeded one year while the median time to treatment intensification was 14 months overall [20,28] although the ADA/EASD consensus recommendation is three months [5, 29].

Thus, from the facts from aforementioned studies, a majority of patients are not attaining the objectives set for the management of T2DM and a good prescription or therapeutic decision could lead to early optimal glycaemic control and thus reduce the risk of complications. This study sorts to evaluate treatment intensification over time in T2DM patients in Cameroon. With treatment intensification defined as an addition of an OAD or insulin to already existing drug(s) after an observation of a poor HbA1c level [30]. To evaluate the notion of therapeutic inertia in type 2 diabetes patients and its impact on blood glucose targets.

2. MATERIALS AND METHODS

2.1 Study Site

The study was carried out in the national obesity Centre (NOC) in the endocrinology and metabolic diseases service of the Yaoundé central hospital and happens to be a major teaching hospital in Yaoundé. NOC is a service specialized in endocrinology and a center for research projects aimed at sensitizing the public on diabetes and contributing to the development of national policies for the prevention, diagnosis and management of diabetes. It has a clinical research unit, a biochemistry laboratory, a unit for diet and nutrition and a unit for the free management of type 1 diabetes children.

2.2 Type of Study

This was a hospital-based cross-sectional analytic study carried out for a period of 7 months running from November 2017 to May 2018, with a period of recruitment of four months (January to April, 2018).

2.3 Study Population

Target population: It consisted of patients diagnosed for type 2 diabetes already. They were patients recruited during external consultations, doing follow up at the NOC and through calls, for those patients who participated in a previous study at this center.

2.4 Eligibility Criteria

The inclusion included type 2 diabetes patients, an HbA1c ≥ 7% between January 2016 and October 2017 with at least a follow-up time frame of six months from poor glycaemia. The patient must signed informed consent.

Those not included in the study were patients with doubts about the type of diabetes, newly diagnosed diabetes patients, patients with a follow-up time in the clinic less than 6 months and patients who were inconsistent at the clinic (less than two visits in the last 12 month).
2.5 Sampling

At the reception in the hospital, all the medical records of outpatients, as well as the register of H3A were screened to seek for eligible patients.

2.6 Therapeutic Inertia

This study evaluated therapeutic inertia and its impact on blood glucose targets through the consultation of patients’ medical booklets at the hospital, but also the H3A register. The participants were screened amongst patients with T2DM who came for monthly consultations at the NOC while others were called using a database of a free HbA1c study done at this centre between March 2016 and March 2017 (H3A program). From this database, those with HbA1c ≥7% were called and invited. The study was explained to the patients with the use of an information sheet consent was obtained. A face-to-face interviewer questionnaire was used to collect data while information not given by the patient was completed from the medical booklet. Since there were no electronic records to obtain accurate medication histories of patients, only patient’s medical booklets were used.

Patients who had not done a second HbA1c test, were educated on its usefulness and referred to a clinician for the test to be prescribed. The presence of this control HbA1c result called for a second appointment so that it could be noted. The questionnaire was available in the English and French language. In line with current views, therapeutic inertia was defined as the failure to intensify therapy (an addition in the number of drug classes) when indicated. It should be kept in mind that ADA guidelines state that HbA1c should be <7.0%. By comparing the classes of anti-diabetic agents used at the start before the measured elevated HbA1c (index treatment) used for this study with those prescribed later or not, we established whether pharmacotherapy had been intensified; the researcher had to answer ‘yes’ or ‘no’ to questions about the action taken during each of the patients visit regarding anti-diabetic treatment after a poor baseline HbA1c ≥7%; (1) anti-diabetic treatment has been maintained; (2) a new oral anti-diabetic treatment has been added (either metformin, sulphonylurea, glitazone, glinide, alpha-glucosidase inhibitor, dipeptidyl peptidase-4 inhibitor, or a combination of oral anti-diabetics); (3) insulin has been added; (4) the dose of some of the anti-diabetic agents has been increased; (5) drug classes have been switched.

Time to treatment intensification was calculated by subtracting the first date an elevated HbA1c was presented to the clinician from the first date of treatment intensification. From this calculation, they were grouped into immediate intensification (same day), delayed intensification and never intensified.

2.7 Judgment Criteria

The time until treatment intensification had two subsets of patients:

- Proportion of patients that received treatment intensification which was either immediate or delayed, giving proportions that received intensification in less than or equal to 3 months, in 6 months, in 12 months and in greater than a year.
- Proportion of patients who never had their treatment intensified (till end of study) - (therapeutic inertia).

2.8 Data Analysis

All data collected were entered and statistical analysis performed using Epi info Version 3.5.4 software and results compiled with Microsoft Excel 2013. Chi II-test for categorical variables were used to compare groups (treatment intensified and therapeutic inertia) on various variables. The significant level was at 5%, giving a statistical significance at p-value < 0.05. Kaplan-Meier analysis was performed for time until intensification to evaluate the probability for treatment to be intensified based on glycated haemoglobin levels (at <8 and ≥8%), with the use of statistical package for social sciences (SPSS) version 20.0. Data were presented as mean and standard deviation (SD), frequency, percentage or ranges.

2.9 Ethical Considerations

Ethical clearance to carry out this study was obtained from the Institutional Research Ethics Committee of the Faculty of Medicine and Biomedical sciences of the University of Yaoundé I and the Center Regional Ethics Committee for Human Health Research. The authorisation to carry out the study at the Yaoundé Central Hospital was obtained from the Director of the hospital. The rights of patients and workers in these hospitals were duly respected throughout this research in which participation was voluntary.
Nine hundred and fifteen patients’ records were screened. One hundred and seventy two met up inclusion criteria. Sixty two were excluded; 28 patients had less than 2 visits for last 12 months and 15 patients had lost a section of their follow-up records, while 16 declined to participate. Thus, 111 patients participated. Fig. 1 shows the consort flow diagram of the study.

3. RESULTS

3.1 Baseline Characteristics of the Population

3.1.1 Socio-demographic characteristics

Fig. 1 shows the age and sex distribution for all participants. The population had 31 males (27.9%) and 80 females (72.1%). The ages ranged from 37 to 78 years with a mean age of 59 ± 10 years.

The majority of the population was from the West (43%) and was married (52/111). The distribution for socio-demographic characteristic is presented on Table 1.

3.2 Medical History

3.2.1 Diabetes duration

More than half of the participants had a diabetes duration of ≥ 5 years. Fig. 2 demonstrates the ranges in duration of diabetes.

3.2.2 Treatment of the population

Twenty-six participants were on Metformin monotherapy, higher than other monotherapy and representing the second highest treatment category in the population. Most, 32 (28.8%) of the participants were on oral anti-diabetic (OAD) bitherapy, with Metformin and Sulfonylurea combination making up the greater therapy in the population. Insulin only was the therapeutic option for 22 participants. Table 2 gives the distribution by therapeutic option of study participants.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>General population N=111</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region</td>
<td></td>
</tr>
<tr>
<td>Centre</td>
<td>45 (40.5)</td>
</tr>
<tr>
<td>Far North</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>Littoral</td>
<td>5 (4.5)</td>
</tr>
<tr>
<td>North West</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>West</td>
<td>48 (43.2)</td>
</tr>
<tr>
<td>South</td>
<td>7 (6.3)</td>
</tr>
<tr>
<td>South West</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>52 (47)</td>
</tr>
<tr>
<td>Single</td>
<td>12 (11)</td>
</tr>
<tr>
<td>Divorced</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Widowed</td>
<td>41 (36)</td>
</tr>
<tr>
<td>Separated</td>
<td>1 (1)</td>
</tr>
<tr>
<td>F Co-habiting</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Profession</td>
<td></td>
</tr>
<tr>
<td>Civil servant</td>
<td>11 (9.9)</td>
</tr>
<tr>
<td>Private sector</td>
<td>13 (11.7)</td>
</tr>
<tr>
<td>Informal sector</td>
<td>20 (18.0)</td>
</tr>
<tr>
<td>Retired</td>
<td>23 (20.7)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>44 (39.6)</td>
</tr>
</tbody>
</table>

Table 1. Socio-demographic characteristics of the population

Fig. 1. Age and gender of the population

Excluded [N=62]
- < 2 visits for last 12 months [N=28]
- Treatment initiation [N=3]
- Missing records [N=15]
- No consent [N=16]
**Fig. 2.** Diabetes duration range of study population

**Table 2.** Therapy of study participants

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Frequency (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OAD Monotherapy</td>
<td>27</td>
<td>24.3</td>
</tr>
<tr>
<td>Metformin</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Sulfonylurea (SU)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>OAD Bitherapy</td>
<td>32</td>
<td>28.8</td>
</tr>
<tr>
<td>Metformin/SU</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Metformin/DPP4i</td>
<td>3</td>
<td>2.7</td>
</tr>
<tr>
<td>OAD Tritherapy</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Metformin/SU/DPP4i</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Insulin only</td>
<td>22</td>
<td>19.8</td>
</tr>
<tr>
<td>Insulin/OAD mixture</td>
<td>27</td>
<td>24.3</td>
</tr>
<tr>
<td>Insulin/Metformin</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Insulin/SU</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Insulin/Metformin/SU</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Insulin/Metformin/DPP4i</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>111</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

**Fig. 3.** Number of non-diabetic medication of the study participants
Sixty-two percent of the participants were on more than 2 other non-diabetic medications in addition to their anti-diabetic medication. Fig. 3 shows the distribution for the number of non-diabetic medication of the participants.

### 3.2.3 Complications/co-morbidities

Seventy-nine percent of the study population had at least a diabetic complication or a co-morbidity. Sixty percent were hypertensive and 26% had diabetic neuropathy. Table 3 gives the dispersion for the other diseases present.

### 3.2.4 Glycaemic equilibrium

Patients on treatment are expected to reach targets of HbA1c < 7% faster. However, the population HbA1c ranged from 7 to 16% with a mean level of 9.3 ± 2.0%. Seventy-two percent of the population had a poor blood glucose control (HbA1c ≥ 8%), with a mean capillary blood glucose of 200 ± 108 mg/dl. Fig. 4 gives the various percentages of participants according to cut-offs at <8%, <9%, <10% and ≥10%.

### 3.2.5 Intensification of treatment in participants

The participants had a mean follow-up time of 16 [11-21] months from baseline with a mean of 4 ± 2 visits within past 12 months. Forty of them had their treatment intensified, 5 cases were immediate, but delayed in 35 patients ≤3 (20), 3-6 (7), 6-12 (3), >12 (5) months. Seventy-one participants had no intensification. The mean HbA1c for the intensified group was 9.7 ± 2.0% against therapeutic inertia group, 9.0 ± 1.9%.

### Table 3. Distribution for complications and co-morbidities in the population

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>Population N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic retinopathy</td>
<td>16 (14)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>29 (26)</td>
</tr>
<tr>
<td>CVD</td>
<td>4 (4)</td>
</tr>
<tr>
<td>PVD</td>
<td>4 (4)</td>
</tr>
<tr>
<td>HT</td>
<td>67 (60)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>28 (25)</td>
</tr>
</tbody>
</table>

Among participants who had at least a medication added (40), 25 (62.5%) had an addition of medication within 3 months from baseline result. No significant associations were seen to characterize this group. The distribution for the proportion of patients with time to treatment intensification is shown on Fig. 5 below.

### 3.2.6 Impact of intervention

The second HbA1c after the baseline was used to evaluate the evolution of blood sugar control in the 2 groups of participants. Twenty-nine of 40 of the intensified group had a second HbA1c test result and 54 for the non-intensified group. The HbA1c reduced in the global population, but more reduction was seen in the non-intensified group, 7.0 ± 1.6% against 8.0 ± 2.0%. Table 4 shows the difference in HbA1c before and after intensification of treatment.

![Fig. 4. Distribution of participants by HbA1c range](image-url)
Fig. 5. Proportion of patients intensified over time

Table 4. Comparison of baseline and re-evaluated HbA1c (%)

<table>
<thead>
<tr>
<th>Group of participants</th>
<th>Baseline</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (N=111)</td>
<td>9.3±2.0</td>
<td>7.4±1.7</td>
</tr>
<tr>
<td>Intensified (N=40)</td>
<td>9.7±2.0</td>
<td>8.0±1.6</td>
</tr>
<tr>
<td>Non-intensified (N=71)</td>
<td>9.0±1.9</td>
<td>7.0±1.6</td>
</tr>
</tbody>
</table>

Table 5. Socio-demographic and medical history variables with the Odds ratios

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (CI 95%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt; 40 years)</td>
<td>0.10 [0.01-0.89]</td>
<td>0.04</td>
</tr>
<tr>
<td>Duration of diabetes (&gt;5 years)</td>
<td>0.32 [0.13-0.79]</td>
<td>0.01</td>
</tr>
<tr>
<td>Number of non-diabetic medications (&gt;2)</td>
<td>0.37 [0.16-0.85]</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 6. Baseline treatment and association to treatment intensification

<table>
<thead>
<tr>
<th>Treatment type</th>
<th>OR (CI 95%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>8.67 [2.49-30.28]</td>
<td>0.000</td>
</tr>
<tr>
<td>Bitherapy</td>
<td>0.20 [0.07-0.54]</td>
<td>0.002</td>
</tr>
<tr>
<td>Metformin/SU</td>
<td>0.14 [0.04-0.48]</td>
<td>0.002</td>
</tr>
<tr>
<td>Metformin/Insulin</td>
<td>0.09 [0.02-0.46]</td>
<td>0.000</td>
</tr>
</tbody>
</table>

3.3 Factors Associated to Treatment Intensification

Several variables were analyzed for an influence on the decision to intensify patient's treatment. In a multivariable logistic regression model that accounted for age, gender, index treatment type (monotherapy, bitherapy, Insulin only, Metformin dosage ≥ 2000 mg, Metformin/Sulfonylurea combination, Metformin/insulin combination), duration of diabetes >5 years, number of other non-diabetic medications >2, the association to treatment intensification was stronger with patients age, index treatment (monotherapy, bitherapy, Metformin/Sulfonylurea combination, Metformin/insulin combination), duration of diabetes and number of other non-diabetic medications. Table 5 shows the socio-demographic and medical history variables with the Odds ratios that influenced intensification. Older volunteers were less likely to have their treatment intensified with an Odds ratio (OR) of 0.10 95% CI [0.01 - 0.89], p-value <0.05. Participants with a duration of diabetes greater...
than 5 years were also less likely to receive intensification (p-value <0.05).

Those on monotherapy were 8 times more likely to receive intensification, than the other treatment types (p-value <0.05). Table 6 shows the distribution of baseline treatment and its influence on treatment intensification.

### 3.3.1 Kaplan Meier distribution curve

Stratification by initial HbA1c 7–7.9% and ≥ 8%. The x-axis is presented in days, and the y-axis is presented as the cumulative probability of not experiencing an intervention. The influence of baseline HbA1c on inertia could not be seen clearly through analysis, so the Kaplan Meier curve was drawn to bring out this factor. The green line represents baseline hba1c ≥ 8% and shows a lower probability for those in this group to stay without treatment intensified from about 180 days (6 months) compared to those at HbA1c levels < 8% (blue line) with a high probability to stay free from intensification.

### 4. DISCUSSION

This hospital-based cross-sectional analytical study was carried out with the main objective to evaluate the notion of therapeutic inertia in type 2 diabetes patients and its impact on blood glucose targets at the Yaoundé Central Hospital. The study consisted of a group of 111 T2DM volunteers, with a mean age of 59 ± 10 years, and diagnosed for diabetes since an average of 9 ± 7 years, with 2/3 of the participants on bitherapy and insulin therapy. For a period of about 16 months, treatment intensification was done only in 40 (36%) participants, and monotherapy was the only factor with strong positive association to treatment intensification. Forty-five percent of participants had HbA1c <7% at re-evaluation.

An antidiabetic treatment was added in 36% of the patients. Therefore, therapeutic inertia was present in 64% of the patients. This result was comparable to the one reported by Sidorenkov et al. [22,31]: for the same HbA1c goal with 1975 patients above target, not returning to control and not on maximum treatment, only 759 (38%) received a treatment intensification (addition of 1 drug or dose). Yet, these results were high compared to other studies; by Paul et al. [32] who had treatment intensified (addition of a second OAD or insulin to the first OAD) in 46% of the patients and thus, a therapeutic inertia indication of 54% at the same HbA1c goals [33-34]; while Tunceli et al. [35] had 4336 (56%) with a treatment change, and 60% representing an addition of a new class of antidiabetic agent, but recorded inertia in 35% of patients.

![Fig. 6. Kaplan-Meier curves for measuring time until intervention](image-url)
Secondly, among those who received intensification, the proportion of patients with time to treatment intensification < 6 months was 80%, which is better than that reported by Paul et al [36,32] with a proportion of 26%. This study also had a median time to treatment intensification of 1 month, far less than all studies [median time of 14 months in the United State despite Metformin monotherapy failure [36,37]; and median time of > 7.1, > 6.1 or 6.0 years, for patients taking one, two or three OADs respectively [38,39]. However, these results are not directly comparable, as the studies were differently designed.

Thirdly, 45% of the participants reached treatment targets, with both groups reaching targets. This is comparable to a study done in South Africa by Govender et al [12,40]. However, the non-intensified group according to the results seemingly showed a better outcome (46% above targets) than the intensified group (72% above targets), that is, a mean HbA1c of 7.0 ± 1.6% against HbA1c of 8.0 ± 1.6%. Compared to a study mentioned above, 32 and 46% of patients receiving early treatment intensification within 6 and 12 months of diagnosis continued to have poor glycaemic control over 2 years post diagnosis [HbA1c >7.5%], while though 54% of the patients never had treatment intensification their average HbA1c level remained above 6.5%, but below 7%, during 2 years post diagnosis. However, another study by Yu et al. [29,32] demonstrated a better HbA1c outcome for early intensification (< 6 months) with mean HbA1c of 7.9% against therapeutic inertia [late (≥6 months) or never intensified], with HbA1c of 8.2%.

The observation of TI could have several reasons. First, the perception of intensification, which includes a dosage increase (of insulin or the same medication), and was shown to represent the greatest intervention according to the results. Among the total number of visits for the participants, a new drug was added in 40.2% of cases (45 prescriptions), and doses increased in 59.8% of cases (67 prescriptions) against 227 visits with Hba1c ≥7%. Secondly, this could be influenced by adherence. Two-third of the population’s treatment consisted of bitherapy, Insulin monotherapy (the therapeutic option for 19.8 % of the patients) and insulin mixture (24.3%). Unlike other studies [41-44], the participants showed an early initiation of Insulin, probably due to specialty care [19,45]. This tells the state and number of patients that could not attain glycaemic goals on Metformin alone. Patients on such treatment might be perceived as taking maximum treatment and patients’ care focused on improving adherence (especially for those with poor observance).

Thirdly, it could be due inertia - proper, where clinicians overestimate the care provided; use “soft” reasons to avoid intensification of therapy; or due to lack of training, and lack of motivation to aim at achieving therapeutic goals earlier.

The outcome was observed to be better in the TI group probably due to aforementioned reasons, but also, perhaps better medication knowledge and improved self-monitoring by the patients. The re-evaluation of HbA1c was also observed at different time intervals from visit 1, it was not within the recommended time of 3 months, which could give a clearer picture for all patients at the same time-point with respect to intensification or not.

Lastly, this study demonstrated strong associations with monotherapy, age, duration of diabetes and other medications to treatment intensification. Older patients were less likely to have a treatment increase. Results regarding age from other studies seem conflicting. While Tunceli et al. [35], Fu et al. [36,46], all demonstrated a significant association between younger age and treatment increase, Mata-cases et al. demonstrated that age was the same for both the intensified and non-intensified groups. This perhaps because older patients often have more comorbidities and thus prone to polypharmacy, which could hinder treatment intensification. This factor may be verified by the significance in the association of the number of non-diabetic medication >2, to intensification (OR of 0.37, CI 95% (0.16 - 0.85), P-value = 0.018). This was comparable to the results of the study by Ajmera et al. [6,47] on the time to treatment intensification among elderly patients; with polypharmacy being the only significant barrier to treatment intensification in this group [48,49]. In same like, a duration of diabetes greater than 5 years significantly hindered treatment intensification. This may be because patients with T2DM are often highly motivated near the time of diagnosis, so an early intensification could be done to improve glycaemic control soonest to prevent diabetes complications, but also not allow for time to pass and perhaps lose the patient to follow-up.

Participants on monotherapy were 8 times more likely to receive an intensification. Monotherapy
is a treatment option in most newly diagnosed patients and ADA recommends a second-line therapy when a monotherapy management fails. Meanwhile, bitherapy was a significant barrier to treatment intensification, notably combinations of Metformin to a Sulfonylurea and Metformin to insulin [OR at 0.14, CI 95% (0.04-0.48), p-value = 0.0015 and OR at 0.09, CI 95% (0.02-0.46), p-value = 0.0034] respectively. According to the mechanisms of action of these two combinations (Metformin which improves peripheral glucose uptake and use; insulin stimulates glucose uptake from the systemic circulation and suppresses hepatic gluconeogenesis, regulating glucose homeostasis, while Sulfonylureas stimulate insulin secretion by beta cells in the pancreas) and the pathophysiology of T2DM, the clinician may be prone to think such chronic regimen could give the patient maximum control [50].

At the end of this study, it was observed that it had the following limitations: the definition of TI was rigorous and a more rigorous level of HbA1c cut-off would be more appropriate and even if it were raised to chronic cut-off points such as >8%, very few participants would be found. Lastly, the time during for the study was short to measure the impact of other interventions which could contribute to patient care and the influence of therapeutic inertia on the development of complications related to T2DM.

5. CONCLUSION

At the end of this study to investigate the therapeutic approach and outcome in type 2 diabetes mellitus management, the following conclusion was arrived at:

Therapeutic inertia affected two third of the population. Monotherapy was significantly associated to treatment intensification. A good proportion of patients with an indication of treatment intensification had it within three months from index elevated HbA1c. Both the intensified and non-intensified treatment groups had patients reaching treatment targets. Treatment intensification reduced the number of patients with poor glucose control.

CONSENT

As per international standard or university standard, patient’s written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Ethical clearance to carry out this study was obtained from the Institutional Research Ethics Committee of the Faculty of Medicine and Biomedical sciences of the University of Yaoundé I and the Center Regional Ethics Committee for Human Health Research The authorization to carry out the study at the Yaoundé Central Hospital was obtained from the Director of the hospital

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


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