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# PROFILING OF CLINICAL DYNAMICS OF TYPE 2 DIABETES MELLITUS IN PATIENTS: A PERSPECTIVE REVIEW

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**Abstract**

Type 2 diabetes mellitus (T2DM), also known as Non-Insulin Dependent Diabetes Mellitus (NIDDM) is one of the common metabolic disorders in the world. T2DM accounts for around 90% of all cases of diabetes mellitus, afflicting millions worldwide. It is a significant global health burden with a steadily increasing prevalence. In T2DM, the response to insulin is diminished, and this is defined as insulin resistance. Risk factors for T2DM are diverse. Some are modifiable, and others are not. Modifiable risk factors include overweight/obesity, lack of exercise or physical inactivity, poor nutrition, etc. Non-modifiable risk factors include age, ethnicity/race, family history, history of gestational diabetes mellitus, etc. The starting points and mainstays of treatment for T2DM are diet and lifestyle modifications such as increased physical activity and stoppage of smoking. In addition to the diet and lifestyle modifications, drugs are also used in the management of T2DM. This study aimed to profile the clinical dynamics of type 2 diabetes mellitus in patients. Current literatures from different databases including MEDLINE, PubMed, EMBASE, CINAHL, Google Scholar, etc. on the topic were searched online and reviewed.

***Keywords:*** Clinical dynamics, Type 2 diabetes mellitus, Perspective review, Glycated hemoglobin, Fasting plasma glucose, Impaired fasting glycemia, Oral glucose tolerance test, Impaired glucose tolerance.



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## Introduction

Diabetes mellitus is a condition defined as a constellation of diseases of metabolic origin. Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors [32]. It is characterized by hyperglycemia which results from defects in the secretion of insulin, the effect of insulin on glucose in the bloodstream or both of them [1]. Depending on the etiology of DM, factors contributing to hyperglycemia include impaired insulin secretion, decreased glucose utilization, and increased glucose production [20]. On the long run, the effects of hyperglycemia on different organs of the body as a result of uncontrolled diabetes mellitus are associated with prolonged damage, malfunction, and collapse of function of different organ systems in the body which mostly include the visual, urinary, nervous, cardiovascular and hematological systems [1]. This perspective review aimed to summarize the current understanding of the clinical dynamics of T2DM with respect to epidemiology, risk factors, etiology, pathogenesis, clinical features, diagnosis, treatment, complications (both acute and chronic) and prognosis.

## Method

Current literatures from different databases including MEDLINE, PubMed, EMBASE, CINAHL, Google Scholar, etc. on the topic were searched online and reviewed.

## Discussion

The International Diabetes Federation (IDF) Diabetes Atlas (2021) reported that 10.5% of the adult population of the world (20-79 years) has diabetes mellitus, with almost half unaware that they are living with the condition. By 2045, IDF projections show that 1 in 8 adults, approximately 783 million, will be living with diabetes mellitus, an astonishing increase of 46%. Approximately 537 million adults (20-79 years) are living with diabetes mellitus. 3 in 4 adults with diabetes mellitus live in low- and middle-income countries [42]. In 2021, the International Diabetes Federation (IDF) estimated that sub-Saharan Africa had almost 24 million adults aged 20-79 years who were living with diabetes mellitus with a regional prevalence of 4.5%. However, 54.0% of the people living with diabetes mellitus in the region are undiagnosed. The burden of DM is huge in developing countries as a result of inequitable distribution of medical facilities for early diagnosis and reasonable blood glucose level determination [61].

According to WHO Global Report on Diabetes Mellitus, the global prevalence of diabetes mellitus (aged-standardized) has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population [79]. This reflects the increasing prevalence of type 2 diabetes mellitus risk factors, particularly obesity. In people with T2DM, 90% are overweight or obese. DM prevalence has risen faster in low- and middle-income countries than in high-income countries [13]. The highest prevalence rates are currently in the Eastern Mediterranean and Middle East with North and South America close behind. There is however considerable variation between IDF regions and within each region. For example, in the Western Pacific, the tiny island of Nauru has a comparative prevalence in 2007of 30.7%, whilst nearby Tonga has less than half that rate at12.9%, the Philippines 7.6% and China 4.1%. In Europe, comparative prevalence rates vary from 1.6% in Iceland to 7.9% in Germany, Austria and Switzerland. The UK prevalence rate is 2.9% (age adjusted) and 4.0% (absolute), increasing to 3.5% and 4.6% respectively by 2025 [6].

In absolute numbers, 537 million adults (20-79 years) are living with diabetes mellitus globally - 1 in 10. This number is predicted to rise to 643 million by 2030 and 783 million by 2045 [43]. Alarmingly, it is believed that there are almost as many as such numbers with undiagnosed diabetes mellitus. Age-adjusted prevalence is set to rise from 9.3 to 10.9% in 2045 worldwide. The numbers of those with impaired glucose tolerance are equally startling with a prevalence of 7.5% in 2019, projected to rise to 8.6% in 2045 [43]. The relative proportions of type 1 to type 2 vary from 15%: 85% for Western populations to 5%: 95% in developing countries. A key demographic change to the rising prevalence of diabetes mellitus worldwide is an increasing proportion of people >65years of age [42].

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder afflicting millions worldwide. It is a significant global health concern with a steadily increasing prevalence [55]. The global incidence of diabetes mellitus is on the increase, more markedly in developing nations. It is no longer a condition that predominates in wealthy countries like it used to be in the past [80]. In the 21st century, it is one common disease condition coming to light as a disease of public health concern worldwide [22]. More than 3 in 4 adults in low and middle income nations live with diabetes [22], in Africa, 1 in every 22 adults are living with diabetes consisting of 24 million individuals of the African population [22]. This number is projected to increase to 55 million (by 129%) by the year 2045 [22].

Literature search showed that there are few data available on the prevalence of T2DM in Africa as a whole. Studies examining data trends within Africa point to evidence of a dramatic increase in prevalence, in both rural and urban settings, and affecting both gender equally [53, 55]. Poverty, social inequality, and limited access to quality healthcare have exasperated the diabetes mellitus epidemic in Africa. Through the middle of the 1980s, diabetes mellitus was considered rare in sub-Saharan Africa, with reported prevalence rates in several countries reportedly less than 1% [48]. Africa has since experienced a six-fold increase in DM cases, rising from 4 million cases in 1980 to 25 million cases in 2014.

In sub-Saharan Africa, swift transformations in socio-demographic, cultural and economic factors propel the increasing prevalence and risk factors of diabetes and other non-communicable diseases [5]. Various hereditary, metabolic, lifestyle and some other human factors play a role in the pathogenesis of type 2 diabetes mellitus [32]. A lack of exercise is believed to cause 7% of cases of type 2 diabetes mellitus [32]. Smokers are 30-40% more likely to develop type 2 diabetes mellitus than non-smokers [32]. Other human factors such as increasing age, female gender, certain medications and disease conditions also play a minor role [32].

Risk factors for type 2 diabetes mellitus are diverse. Some are modifiable, and others are not. Modifiable risk factors include overweight/obesity (increased body mass index - BMI) [57], lack of exercise or physical inactivity [6, 8], poor nutrition, smoking, and alcohol use, among others appear to be the primary culprits [32, 62]. Non-modifiable risk factors for type 2 diabetes mellitus include age [10], ethnicity/race [15], family history (genetic predisposition) [6], history of gestational diabetes, and low birth weight [32].

Unlike type 1 diabetes mellitus [16], type 2 diabetes mellitus usually develops as a result of interactions of metabolic and genetic factors. History of diabetes mellitus in the family, gestational diabetes mellitus in any previous pregnancies and ethnicity interact with advanced age, obesity and overweight, poor diet, sedentary lifestyle and smoking to raise the risk of diabetes mellitus in individuals [80]. In type 2 diabetes mellitus, the strongest risk factor both in terms of greatest relative risk and clear evidence is being overweight and this is mostly as a result of unhealthy diet and sedentary lifestyle [19]. It is estimated that physical inactivity together with being overweight caused a large percentage of the global burden of diabetes mellitus [19]. Even though, it may vary from population to population, there is also an increased risk of type 2 diabetes mellitus in people with an increased body mass index or waist circumference [68], for instance patients from south-east Asia developed diabetes mellitus at a much lower body mass index when compared to people of European descent [58].

Furthermore, several unhealthy nutritional practices have been described to cause excessive weight gain, hence increasing the risk of type 2 diabetes mellitus. These include excessive consumption of saturated fatty acids, insufficient dietary fiber intake and excessive consumption of fat in diet [80]. Sweetened beverages produced with enormous amount of free sugars worsen the risk of obesity when consumed in excessive quantities, and this risk is particularly high in children [64, 82] with recent researches suggesting an association of excessive intake of sugar-sweetened beverages with increase in the risk of type 2 diabetes mellitus [41, 47, 51, 65]. Dietary intake in early childhood increases the risk of type 2 diabetes mellitus in later stages of life. The factors that seem to increase this risk include poor development of the fetus, infants weighing less

than 2500g at birth and infants weighing more than 4000g at birth [80]. Smoking increases the risk of developing type 2 diabetes mellitus and this risk is highest in heavy smokers [77] with the risk increased for about 10 years after smoking is stopped [50, 80].

Diabetes development comprises various processes of pathogenesis which extend from destruction of β-cells in the islets of Langerhans of the pancreas by autoimmune processes leading to deficiency of insulin to abnormal functions that cause cells to become resistant to the action of insulin [1]. Impaired secretion of insulin and defective insulin function are often coexistent in patients with diabetes mellitus making it unclear which feature primarily contributes to hyperglycemia [1]. T2DM is an insulin-resistance condition with associated beta-cell dysfunction. Initially, there is a compensatory increase in insulin secretion, which maintains glucose levels in the normal range. As the disease progresses, beta cells change, and insulin secretion is unable to maintain glucose homeostasis, producing hyperglycemia. Most of the patients with T2DM are obese or have a higher body fat percentage, distributed predominantly in the abdominal region [28, 31, 32]. This adipose tissue itself promotes insulin resistance through various inflammatory mechanisms, including increased free fatty acids (FFAs) release and adipokine dysregulation. Lack of physical activity, prior to GDM in those with hypertension or dyslipidemia also increases the risk of developing T2DM [23, 31, 32, 35, 39, 69].

Insulin resistance is a characteristic metabolic defect in the great majority of patients with type 2 diabetes mellitus, and this defect can be demonstrated in the pre-diabetic state many years prior to the development of hyperglycemia [66]. As a consequence of insulin resistance, the β cell produces increased amounts of insulin, and if sufficient, the compensatory hyperinsulinemia maintains glucose levels within the normal range. Both longitudinal and cross-sectional studies have demonstrated that the earliest detectable abnormality in NIDDM is a disturbance in the body's ability to respond to insulin [32] because the pancreas is able to appropriately augment its secretion of insulin to offset the insulin resistance, glucose tolerance remains normal. However, with time, the beta-cell fails to maintain its high rate of insulin secretion and the relative insulinopenia (i.e. relative to the degree of insulin resistance) leads to the development of impaired glucose tolerance and eventually overt diabetes mellitus. The cause of pancreatic "exhaustion" remains unknown but may be related to the effect of glucose toxicity in a genetically predisposed beta-cell [11]. In those individuals disposed to develop diabetes mellitus, β cell function eventually declines, and relative insulin insufficiency occurs. Thus, insulin resistance combined with β cell failure leads to the decompensated hyperglycemic diabetic state [67].

Type 2 diabetes mellitus is a heterogeneous, polygenic disorder [27], and the responsible genes have been identified in selected subtypes of the disease. T2DM is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure [26, 30]. This leads to a decrease in glucose transport into the liver, muscle cells, and fat cells. There is an increase in the breakdown of fats with hyperglycemia. The involvement of impaired alpha-cell function has recently been recognized in the pathophysiology of type 2 DM [35, 55].

Polydipsia, polyuria and weight loss that may be accompanied by polyphagia and blurred vision are common symptoms of pronounced hyperglycemia. Patients with diabetes mellitus most commonly present with increased thirst, increased urination, lack of energy and fatigue, bacterial and fungal infections, and delayed wound healing. Type 2 DM may present in one of 4 ways: Classical symptoms, Incidental diagnosis, Acute complications notably hyperglycemic hyperosmolar state, and Chronic complications. Classical symptoms of T2DM that may be seen at diagnosis are polydipsia, polyuria, polyphagia, fungal infections (especially genital candidiasis), etc. Type 2 DM may be an incidental finding - incidental diagnosis [9].

Diabetes mellitus can be diagnosed either by glycated hemoglobin ($HbA_1C$) criterion or plasma glucose concentration (fasting or 2-hour postprandial plasma glucose). Patients with $HbA_1C$ greater than 6.5% (48mmol/L) are diagnosed as having DM. $HbA_1C$ test gives an average of blood glucose control over the last 3 months [70]. Fasting plasma glucose (FPG) levels of more than 126mg/dL (7.0mmol/L) is consistent with the diagnosis. The two-hour Oral Glucose Tolerance Test (OGTT) is a test in which plasma glucose is measured before and 2 hours after the ingestion of 75g of glucose. DM is diagnosed if the plasma glucose (PG) level in the 2-hour sample is more than 200mg/dL (11.1mmol/L).

The World Health Organisation (WHO) and the American Diabetes Association (ADA) use a fasting plasma glucose (FPG) of 7.0mmol/L or higher to define diabetes mellitus. This originates from epidemiological studies in the 1990s which appeared to show that the risk of microvascular complications (e.g. retinopathy) increases sharply at a FPG threshold of 7.0mmol/L [81]. The relationship between plasma glucose and microangiopathy is likely to be continuous, thus a FPG of 7.0mmol/L is an arbitrary cut-off for defining diabetes which may be lowered in the future [44]. FPG, 2-h PG after 75g OGTT, and $HbA_1C$ are equally appropriate for diagnostic testing. It should be noted that the tests do not necessarily detect diabetes mellitus in the same individuals. The concordance between the FPG and 2-h PG tests is imperfect. The overlap depends on the ethnic and geographical population, and on other characteristics such as age and body mass index [2, 61].

Numerous studies have confirmed that compared with FPG and $HbA_1C$ cut-off points, the 2-h PG value diagnoses more people with diabetes mellitus. Glycated hemoglobin ($HbA_1C$) has been accepted as the most reliable and accurate test for establishing the diagnosis as well as for evaluating glycemic control in diabetic patients. When using $HbA_1C$ to diagnose diabetes mellitus, it is important to recognize that $HbA_1C$ is an indirect measure of average blood glucose levels and to take other factors into consideration that may impact hemoglobin glycation independently of glycemia such as age, ethnicity/race, and anemia/hemoglobinopathies [63].

Monitoring progress in diabetes mellitus prevention and control is very important to strengthening appropriate surveillance mechanisms by conducting periodic population-level surveys that include measurement of risk factors and blood glucose [78]. For all cases of diabetes mellitus, the cornerstone of therapy is a combination of lifestyle modifications (diet and exercise) and pharmacotherapy (when applicable). A diet low in saturated fat, refined carbohydrates, high fructose corn syrup, and high in fiber and monounsaturated fats needs to be encouraged. Aerobic exercise for duration of 90 to 150 minutes per week is also beneficial. The major target in T2DM patients, who are obese, is weight loss [14, 45].

For patients with type 1 DM, a regime of basal-bolus insulin is the mainstay of therapy. Also, insulin pump therapy is a reasonable choice. In patients with type 2 DM whereby adequate glycemia cannot be achieved, metformin is the first-line therapy. Following metformin, many other therapies such as oral sulfonylureas, dipeptidyl peptidase-4 (DPP-4) inhibitors, Glucagon-like peptide-1 (GLP-I) receptor agonists [25], Sodium-glucose linked transporter-2 (SGLT2) inhibitors [26, 29, 37, 74, 75], thiazolidinediones e.g. pioglitazone, especially if the patient has fatty liver disease, alpha-glucosidase inhibitors e.g. acarbose; and insulin, are available.

The starting points and mainstays of treatment for type 2 diabetes mellitus are diet and lifestyle modifications such as increasing exercise and stopping smoking. The major aims are to reduce the weight of obese patients and improve glycemic control, but also to reduce risk factors for cardiovascular disease (CVD), such as hyperlipidemia [28, 31] and hypertension [36, 39], which account for 70–80% of deaths in type 2 diabetes mellitus [6]. In addition to the diet and lifestyle modifications, drugs are also used in the management of T2DM. These drugs include biguanides (sensitizers) e.g. metformin; sulfonylureas (secretagogues) e.g. glimepiride, glibenclamide; thiazolidinediones e.g. pioglitazone and the newer classes of drugs. These are summarized in Table 1 below.

**Table 1: Glucose-lowering medications**

| Class (example) | $HbA_1C$ reduction | Weight effect | Adverse effects | CVS benefit | Renal benefit |
|---|---|---|---|---|---|
| Biguanides (e.g. metformin) | 0.8–1.0% | Neutral | Lactic acidosis, GI | Yes | N/A |
| Sulfonylureas (e.g. glimepiride, etc) | 0.8–2.0% | ↑ | Hypoglycemia | N/A | N/A |
| Thiazolidinediones (e.g. pioglitazone) | 0.6–1.5% | ↑ | Edema, fractures (rare), bladder cancer (rare) | Yes | N/A |
| DPP-4 inhibitor (e.g. vildagliptin) | 0.40% | Neutral | Pancreatitis (rare) | No | No |
| SGLT-2 inhibitor (e.g. dapagliflozin) | 0.4–0.8% | ↓ | Genitourinary infections | Yes | Yes |
| GLP-1 receptor Agonist (e.g. liraglutide) | 0.5–1.8% | ↓ | GI | Yes | Yes |

*Source: Oxford Handbook of Endocrinology and Diabetes. 4th Edition, Oxford University Press, 2022* [56]

Current guidelines regarding glucose-lowering medications states that diet and exercise are sufficient to achieve adequate glycemic control in <10% of type 2 DM patients. When control worsens, an oral hypoglycemic agent is generally introduced. Metformin is the recommended initial glucose-lowering medication for most patients with T2DM. If the individualized $HbA_1C$ target is not reached with metformin alone, then a 2nd line glucose-lowering agent should be added [56]. Factors to consider when choosing which agent should be used include drug efficacy, costs, side effects, patient preference, and comorbidities.

Current NICE guidelines (published in 2015) recommend the addition of a DPP-4 inhibitor, or sulfonylurea, or pioglitazone as 2nd line therapy. In contrast, the ADA/European Association for the Study of Diabetes (EASD) consensus statement (published in 2018) recommended that medications with proven benefits in CVD, heart failure, and renal protection should be prioritized for at-risk patients. This is based on recently published cardiovascular outcome trials (CVOTs) which have demonstrated that specific SGLT-2 inhibitors and GLP-1 receptor agonists substantially improve cardiovascular outcomes, heart failure, and slow down the progression of renal disease [23, 25, 26, 29, 30, 46, 56, 74, 75, 76].

Less commonly used glucose-lowering agents are other less encountered glucose-lowering agents such as α-glucosidase inhibitors (e.g. acarbose) and prandial insulin secretagogues (e.g. rapeglinide, nateglinide) [56]. The majority of people with T2DM will require insulin injections at some point in their lives. Various insulin formulations are available, which differ in terms of onset and duration of action and the risk of hypoglycemia. Insulin is highly efficacious and can be used to achieve almost any glycemic target if not limited by hypoglycemia. The main disadvantages of insulin, compared with other glucose-lowering therapies, are hypoglycemia, weight gain, and the need for glucose monitoring. Successful use of insulin therapy is highly dependent on appropriate patient selection, provision of adequate patient training and support, and frequent review and dose titration to safe glucose targets [52].

Persistent hyperglycemia in uncontrolled diabetes mellitus can cause several complications, both acute and chronic. Diabetes mellitus is one of the leading causes of cardiovascular disease (CVD), blindness, kidney failure [38, 71, 72], and amputation of lower limbs. Acute complications include hypoglycemia and

diabetic ketoacidosis for type 1 DM; and hypoglycemia, hyperglycemic hyperosmolar state and hyperglycemic lactic acidotic coma for type 2 DM. Chronic microvascular complications are nephropathy [30, 33, 34], neuropathy, and retinopathy, whereas chronic macrovascular complications are coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease (CVD). It is estimated that every year, 1.4 to 4.7% of middle-aged people with diabetes mellitus have a CVD event [4].

Chronic hyperglycemia in synergy with the other metabolic aberrations in patients with diabetes mellitus can cause damage to various organ systems, leading to the development of disabling and life-threatening health complications, most prominent of which are microvascular (retinopathy, nephropathy, and neuropathy) [24, 30] and macrovascular complications leading to a 2-fold to 4-fold increased risk of cardiovascular diseases [20, 40, 73]. Poor growth and increased susceptibility to some infections may follow chronic uncontrolled hyperglycemia. Diabetic ketoacidosis or non-ketotic hyperosmolar syndrome are two acute consequences of uncontrolled diabetes that may be life threatening [1]. An abundance of microvascular and macrovascular complications present as a sequel to untreated diabetes. These complications can affect many bodily systems [5]. Moreover, diabetes mellitus bears close association with some other diseases such as hypercholesterolemia and hypertension that affect cardiovascular health. Their interactions may also increase the risk of unfavourable outcomes in people suffering from diabetes mellitus [5].

It is important to recognize that all diabetic patients are at risk of complications and type 2 DM may present with complications. Acute complications of type 2 DM include hyperglycemic hyperosmolar state (HHS), also known as hyperosmolar non-ketotic state (HONKS) which is an acute, severe disorder primarily seen in T2DM. It is associated with absolute or relative insulin deficiency, volume depletion, and acid–base abnormalities with potentially serious complications if not promptly diagnosed and carefully treated [9]. In addition, a debilitating condition (prior stroke or dementia) or social situation that compromises water intake usually contributes to the development of the disorder [49]. The other less encountered acute complication for T2DM is lactic acidotic coma.

Most of the morbidity and mortality associated with type 2 DM is attributable to the chronic complications. Due to its complications, DM causes an enormous national burden with respect to morbidity. Diabetes-related chronic complications can be divided into vascular and non-vascular complications and are similar for type 1 and type 2 DM. The vascular complications of DM are further subdivided into microvascular (retinopathy, neuropathy, nephropathy), and macrovascular complications (coronary artery disease (CAD), peripheral arterial disease (PAD), cerebrovascular disease (CVD)). Microvascular complications are diabetes specific, whereas macrovascular complications have additional pathophysiologic features that are shared with the general population. Non-vascular complications include infections, skin changes, hearing loss, and increased risk of dementia and impaired cognitive function [9].

Diabetic retinopathy is the leading cause of blindness in adults aged 20 through 74 years [17] and diabetic kidney disease accounts for 40% of all new cases of end-stage renal disease [60].Diabetes is the leading cause of non-traumatic lower extremity amputation [59]. Heart disease and strokes occur 2 to 4 times more frequently in adults with diabetes than in those who are healthy [30, 40]. Diabetic retinopathy [9], diabetic nephropathy [24, 38, 54, 72], diabetic neuropathy [66], coronary artery disease [21], diabetic foot [9] are some common chronic complications of DM.

The management of diabetes and related complications is seriously hindered by substandard care [7]. To essentially prevent, manage and control diabetes mellitus, it is imperative to understand the different aspects of the disease [18]. Yet, numerous studies have persistently shown poor understanding of diabetes mellitus among the population at large [18]. The standard of health care is increasingly being measured by patient-focused medical care assessment [3]. Many qualitative and quantitative methods are available for this patient-based assessment of care; nonetheless, patient satisfaction questionnaires are more commonly used [3].

The DCCT phase demonstrated that improvement of glycemic control reduced non-proliferative and proliferative retinopathy (47% reduction), albuminuria (39% reduction), clinical nephropathy (54% reduction), and neuropathy (60% reduction). Improved glycemic control also slowed the progression of early diabetic complications [12]. In clinical practice, intervention techniques for diabetic macrovascular disease are often disappointing because of the severity and widespread nature of the atherosclerotic vascular disease. The early diagnosis of type 2 DM is therefore very important [63].

Recent guidelines have stressed the importance of strict glucose, blood pressure and lipid control in type 2 diabetic subjects [63]. This morbidity and premature mortality is putting increased pressure on health care resources [8]. The UK Prospective Diabetes Study (UKPDS) has shown that in type 2 DM subjects, good blood glucose control [66] and tight blood pressure control [67] can prevent complications or delay their progression. The early detection of retinopathy, nephropathy and neuropathy can lead to a reduction in the incidence of blindness, kidney failure and amputation due to diabetes mellitus.

Recent studies have challenged the long-held belief that T2DM is a permanent and chronically progressive condition. Significant weight loss can normalize blood glucose levels and lead to remission of T2DM. Remission rates are highest in people with a short duration of T2DM, before the development of irreversible damage to the pancreatic β-cells. Almost 50% of participants on a very low-calorie diet (~800kcal/day for 3–5 months) in the Diabetes Remission Clinical Trial (DiRECT) attained diabetes remission after 1 year. Importantly, this trial demonstrated that diabetes remission is a practical target in 1° care. Even higher diabetes remission rates are seen after bariatric surgery. An individual who has achieved diabetes remission, regardless of the method used, will need ongoing support to prevent weight gain and thereby minimize the risk

of relapse of T2DM. It is unknown what effect diabetes remission has on the development or progression of diabetes-related complications, and so it is important that these individuals are recalled for annual review, including retinal screening [56].

## Conclusion

There is a pressing need to improve access to accurate information with regards to type 2 diabetes mellitus and the quality of management of type 2 diabetes mellitus, particularly in low- and middle-income countries through well-designed and maintained diabetes mellitus registries. Such data are essential for a better understanding of the disease burden and moreover, for ensuring a better planning and provision of appropriate medical care for patients with type 2 diabetes mellitus.

## Prospects for further research

Prospects for further research include to review reasons for poor glycemic control in type 2 diabetes mellitus patients with low socio-economic status, and to review the available effective treatment options for type 2 diabetes mellitus in comorbid states.

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## Conflict of Interest

The authors guarantee responsibility for everything published in this manuscript, as well as the absence of a conflict of interest and the absence of their financial interest in performing this research and writing this manuscript.

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## Authors Contribution

All authors contributed in different aspects of the research.

## References

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010; 33(Suppl 1): S62–S69. DOI: 10.2337/dc10-S062.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes care*. 2014; 37(1): S81-90.
3. Ajayi IO, Olumide EA, Oyediran O. Patient satisfaction with the services provided at a general outpatients' clinic, Ibadan, Oyo State, Nigeria. *African Journal of Medicine & Medical Science*. 2005; 34(2): 133–140.
4. Akalu Y, Birhan A. Peripheral Arterial Disease and Its Associated Factors among Type 2 Diabetes Mellitus Patients at Debre Tabor General Hospital, Northwest Ethiopia. *J Diabetes Res*. 2020; 2020: 9419413.
5. Atun R, Davies JI, Gale EA, Bärnighausen T, Beran D, Kengne AP, *et al*. Diabetes in sub-saharan Africa: From clinical care to health policy. *The Lancet Diabetes & Endocrinology*. 2017; 5(8): 622–667.
6. Bilous R, Donnelly R, Idris I. *Handbook of Diabetes Mellitus*. 5th Edition. John Wiley & Sons Ltd. 2021.
7. Birabwa C, Bwambale MF, Waiswa P, Mayega RW. Quality and barriers of outpatient diabetes care in rural health facilities in Uganda – a mixed methods study. *BMC Health Services Research*. 2019; 19: 706. DOI: 10.1186/s12913-019-4535-x.
8. Borch-Johnsen K. Costs and profits of prevention. In: Hitman, GA, (ed.), *Type 2 Diabetes: Prediction and Prevention*. Chichester: J Wiley. 1999.
9. Campbell IW. Epidemiology and Clinical Presentation of Type 2 Diabetes. *International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Value in Health*. 2000; 3(l1): S3-S6. DOI: 10.1046/J.1524-4733.2000.36014.X.
10. Centers for Disease Control and Prevention. National Diabetes Fact Sheet: General Information and National Estimates on Diabetes in the United States. *US Department of Health and Human Services, Centers for Disease Control and Prevention.* 2005. .Available online: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2005.pdf
11. DeFronzo RA, Bonadonna RC, Ferrannini E. Pathogenesis of NIDDM. A balanced overview. *Diabetes Care*. 1992; 15(3): 318-368. DOI: 10.2337/diacare.15.3.318.
12. Diabetes Control and Complications Trial (DCCT): Results of Feasibility Study. *Diabetes Care*. 1987; 10(1): 1-19.
13. Diawara A, Coulibaly DM, Hussain TYA, et al. Type 2 diabetes prevalence, awareness, and risk factors in rural Mali: a cross-sectional study. *Sci Rep*. 2023; 13: 3718. DOI: 10.1038/s41598-023-29743-1.
14. Eckstein ML, Williams DM, O'Neil LK, Hayes J, Stephens JW, Bracken RM. Physical exercise and non-insulin glucose-lowering therapies in the management of Type 2 diabetes mellitus: a clinical review. *Diabet Med*. 2019; 36(3): 349-358.
15. Egede LE, Dagogo-Jack S. Epidemiology of type 2 diabetes: focus on ethnic minorities. *Med Clin North Am*. 2005; 89: 949– 975.
16. Ekechi HO, Ikwuka AO, Udeh FC, Epete MA, Uche VU. Hepatorenal Protective Functions of Coconut Water in Alloxan-Induced Type 1 Diabetes Mellitus. *World Journal of Current Medical and Pharmaceutical Research*. 2023; 5(4): 114-122. DOI: 10.37022/wjcmpr.v5i4.276.
17. Ferris FL, Davis MD, Aiello LM. Treatment of diabetic retinopathy. *New England Journal of Med*. 1999; 341: 667-678.
18. Foma MA, Saidu Y, Omoleke SA, Jafali J. Awareness of diabetes mellitus among diabetic patients in the Gambia: A strong case for health education and promotion. *BMC Public Health*. 2013; 13: 1124. DOI: 10.1186/1471-2458-13-1124.
19. Global Burden of Diseases. Risk Factors Collaborators. Global, regional, and national comparative risk assessment

of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015; 386(10010): 2287–2323.

20. Goyal R, Singhal M, Jialal I. Type 2 Diabetes. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing. 2023. Available online: www.pubmed.ncbi.nlm.nih.gov/30020625/
21. Haffner SM, Lehto S, Ronnemaa T, et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in non-diabetic subjects with and without prior myocardial infarction. *N Engl J Med.* 1998; 339: 229–234.
22. IDF. Diabetes facts & figures. *International Diabetes Federation*. 2021; Available online: https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html
23. Ikwuka AO. Clinical dynamics in patients with diabetes mellitus type 2 and concomitant essential hypertensive disease treated with dapagliflozin. *Journal of the 22nd International Medical Congress of Students and Young Scientists*. 2018; p. 32.
24. Ikwuka AO. Clinical dynamics of nephropathy in patients with diabetes mellitus type 2 and concomitant essential hypertensive disease. *Clinical Medicine*. 2019; 19(2): s39. DOI: 10.7861/clinmedicine.19-2-s39.
25. Ikwuka AO. Clinical effectiveness of GLP-1 RAs in patients with metabolic syndrome diseases. *Endocrine Practice*. 2019; 25(1): 104-105. DOI: 10.1016/S1530-891X(20)46611-X.
26. Ikwuka AO. Clinical effectiveness of SGLT-2 inhibitors in patients with diabetes mellitus type 2 and essential hypertensive disease. *Endocrine Practice*. 2018; 24(1): 74. DOI: 10.1016/S1530-891X(20)47129-0.
27. Ikwuka AO. *Dr. Aloy's Core Essential Series (DACES) Medical Genetics*. 1st Edition. Science and Education Publishing, USA. 2023; p. 9. ISBN: 978-1-958293-02-7.
28. Ikwuka AO. Dyslipidemia risk severity in patients with diabetes mellitus type 2 and essential hypertension. *Journal of the 21st International Medical Congress of Students and Young Scientists*. 2017; p. 59.
29. Ikwuka AO. Effectiveness of dapagliflozin in patients with diabetes mellitus type 2 and essential hypertension. *Book of abstracts of the 7th International Students' Scientific Conference of Young Medical Researchers*. 2017; p. 102. Available online: http://www.stn.umed.wroc.pl/files/lm/Accepted_papers.16113.pdf
30. Ikwuka AO. Features of kidney damage in patients with arterial hypertension and type 2 diabetes mellitus and optimization of treatment. *Specialized Academic Council IFNMU*. 2018; Available online: http://www.ifnmu.edu.ua/images/zagalna_informacia/spec_vcheni_radi/2017-2019/%D0%9420.601.01/Ikvuka/Avtoreferat.pdf
31. Ikwuka AO. Influence of dyslipidemia in patients with diabetes mellitus type 2 and essential hypertension. *The Pharma Innovation Journal*. 2017; 6(3): 101-103. Available online: http://www.thepharmajournal.com/archives/?year=2017&vol=6&issue=3&part=B
32. Ikwuka AO. Risk factors for the pathogenesis of diabetes mellitus type 2. *Materials of 84th Scientific and Practical Conference of Students and Young Scientists with Internatrajrajional Participation "Innovations in medicine"*. 2015; p. 19. Available online: http://www.ifnmu.edu.ua/images/snt/files/konferenciya/Tezu_2015.pdf
33. Ikwuka AO, Haman IO. Features of kidney damage in patients with diabetes mellitus type 2 and essential hypertension. *Journal of 86th Scientific and Practical Conference of Students and Young Scientists with International Participation "Innovations in medicine"*. 2017; p. 144. Available online: http://www.ifnmu.edu.ua/images/snt/86-konf-tezi%20(1).pdf
34. Ikwuka AO, Virstyuk NG, Luchko OR. Features of the functional state of kidneys in patients with diabetes mellitus type 2 and essential arterial hypertension. *Materials of scientific-practical conference with international participation "Babenkivski reading"*. 2017; p. 48.
35. Ikwuka AO, Paliy Yu. Structural changes of the left ventricular myocardium in patients with essential arterial hypertension and diabetes mellitus type 2. *Abstracts of the 87th Scientific Conference of Students and Young Scientists with International Participation "Innovations in medicine"*. 2018; p. 25-26. Available online: https://www.ifnmu.edu.ua/images/snt/zaproshennia_eng.pdf
36. Ikwuka AO, Virstyuk NG. Pattern of cardiac remodelling of the left ventricle in patients with essential hypertensive disease and concomitant type 2 diabetes mellitus. *Clinical Medicine*. 2019; 19(3): s92. DOI: 10.7861/clinmedicine.19-3-s92.
37. Ikwuka AO, Virstyuk NG. Influence of SGLT2 inhibitor and A2RB (AT1) on fibrogenesis and heart failure in patients with essential hypertensive disease combined with diabetes mellitus type 2. *E-Poster No. 143 of the 44th &45th Annual General and Scientific Meeting of the West African College of Physicians (WACP), 1 - 3 November, 2021*. 2021; DOI: 10.13140/RG.2.2.26912.87047.
38. Ikwuka AO, Virstyuk N. Prognostic markers of nephropathy in patients with dual metabolic syndrome diseases (essential hypertensive disease and concomitant type 2 diabetes mellitus). *Endocrine Practice*. 2022; 28(5): S65-S66. DOI: 10.1016/j.eprac.2022.03.164.
39. Ikwuka AO, Virstyuk N. Patterns and Influence of Cardio-Metabolic Insufficiency in Patients with Essential Hypertensive Disease and Concomitant Type 2 Diabetes Mellitus. *Endocrine Practice*. 2023; 29(5): S32-S33. DOI: 10.1016/j.eprac.2023.03.076.
40. Ikwuka AO, Virstyuk NG, Luchko OR, Kobitovych I. Heterogeneity Of Renal Pathogenicity On The Background Of Asymptomatic Hyperuricemia In Patients With Dual Metabolic Syndrome Diseases (Essential Hypertensive Disease and Type 2 Diabetes Mellitus). *British Journal of*

*Medical and Health Research*. 2023; 10(2): 1-9. DOI: 10.5281/zenodo.7690636.

41. Imamura F, O'Connor L, Ye Z, Mursu J, Hayashino Y, Bhupathiraju SN, Forouhi NG. Consumption of sugar-sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. *British Medical Journal*. 2015; 351: h3576.
42. International Diabetes Federation (IDF). *About diabetes: Facts & figures*. 2023. Available online: www.idf.org/about-diabtes/diabetes-facts-figures/
43. International Diabetes Federation (IDF). *IDF Diabetes Atlas*. 10th Edition. 2021.
44. International Expert Committee. International Expert Committee report on the role of the $HbA_1C$ assay in the diagnosis of diabetes. *Diabetes Care*. 2009; 32(7): 1327-1334.
45. Lai LL, Wan Yusoff WNI, Vethakkan SR, Nik Mustapha NR, Mahadeva S, Chan WK. Screening for non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus using transient elastography. *J Gastroenterol Hepatol*. 2019; 34(8): 1396-1403.
46. Lean MEJ, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *Lancet*. 2017; 391: 541–551.
47. Ley SH, Hamdy O, Mohan V, Hu FB. Prevention and management of type 2 diabetes: dietary components and nutritional strategies. *Lancet*. 2014; 383(9933): 1999–2007.
48. Levitt NS. Diabetes in Africa: Epidemiology, management and healthcare challenges. *Heart.* 2008; 94(11): 1376–1382. DOI: 10.1136/ hrt.2008.147306.
49. Loscalzo J, Kasper DL, Longo DL, Fauci AS, Hauser SL. *Harrison's Principles of Internal Medicine*. 21st Edition. Mc Graw Hill. 2022.
50. Luo J, Rossouw J, Tong E, Giovino GA, Lee CC, Chen C, Ockene JK, Qi L, Margolis KL. Smoking and diabetes: does the increased risk ever go away? *American Journal of Epidemiology*. 2013; 178(6): 937–945.
51. Malik VS, Popkin BM, Bray GA, Després J-P, Willett WC, Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. *Diabetes Care*. 2010; 33: 2477–2483.
52. Marso SP, McGuire DK, Zinman B, et al. Efficacy and Safety of Degludec versus Glargine in Type 2 Diabetes. *New England Journal of Medicine*. 2017; 377(8): 723–732. DOI: 10.1056/ NEJMoa1615692.
53. Mbanya JC. The burden of type 2 diabetes mellitus in the African diaspora. Available online: www.medscape.com/viewarticle/560718_2
54. Olefsky JM, Kruszynska YT. Non-insulin dependent diabetes: etiology, pathogenesis and natural history. In: DeGroot LJ, Jameson JL, Burger H, et al, eds. *DeGroot's Textbook of Endocrinology*. 4th ed. Philadelphia, Pa: WB Saunders Co. 2022.
55. Olokoba AB, Obateru OA, Olokoba LB. Type 2 Diabetes Mellitus: A Review of Current Trends. *Oman Medical Journal.* 2012; 27(4): 269–273.
56. Owen K, Turner H, Wass J. *Oxford Handbook of Endocrinology and Diabetes*. 4th Edition. Oxford University Press. 2022.
57. Pan DA, Lillioja S, Kriketos AD, Milner MR, Baur LA, Bogardus C, et al. Skeletal muscle triglyceride levels are inversely related to insulin action. *Diabetes*. 1997; 46(6): 983-988. DOI: 10.2337/diab.46.6.983.
58. Ramachandran A, Ma RC, Snehalatha C. Diabetes in Asia. *Lancet*. 2010; 375(9712): 408–418.
59. Reiber GE, Boyko EJ, Smith DG. Lower extremity foot ulcers and amputations in diabetes. In: Harris MI, Cowie CC, Reiber G, Boyko E, Stern M, Bennett P, eds. *Diabetes in America*. 2nd ed. Washington, DC: US Government Printing Office. 1995; p. 409-428.
60. Ritz E, Orth SR. Nephropathy in patients with type 2 diabetes mellitus. *N Engl J Med*. 1999; 341(15): 1127-1133. DOI: 10.1056/NEJM199910073411506.
61. Rodriguez-Gutierrez R, Mancillas-Adame LG, Rodríguez-Tamez G, Diaz Gonzalez-Colmenero A, Solis-Pacheco RC, Elizondo-Plazas AS, et al. Hypertriglyceridemia and Its Association with HbA1c Test: A Prospective *In Vivo* Controlled Study. *International Journal of Endocrinology*. 2019; Article ID: 4784313. DOI: 10.1155/2019/4784313.
62. Schulz LO, Bennett PH, Ravussin E, Kidd JR, Kidd KK, Esparza J, Valencia ME. Effects of traditional and western environment on prevalence of type 2 diabetes in Pima Indians in Mexico and the U.S. *Diabetes Care*. 2006; 29(8): 1866–1871. DOI: 10.2337/dc06-0138.
63. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights*. 2016; 11: 95-104. DOI:10.4137/BMI.S38440.
64. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta analyses of randomised controlled trials and cohort studies. *British Medical Journal*. 2013; 346: e7492.
65. The InterAct Consortium. Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct. *Diabetologia*. 2013; 56: 1520–30.
66. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998; 352(9131): 837–53.
67. UK Prospective Diabetes Study (UKPDS) Group. Tight blood pressure control and risk of macrovascular disease and microvascular complications in type 2 diabetes (UKPDS 38). *Br Med J*. 1998; 317(7160): 703–13.
68. Vazquez G, Duval S, Jacobs DR Jr, Silventoinen K. Comparison of body mass index, waist circumference and waist/hip ratio in predicting incident diabetes: a meta-analysis. *Epidemiologic Reviews*. 2007; 29: 115–28.
69. Virstyuk NG, Ikwuka AO, Haman IO, Adebomi MS. Diabetes mellitus type 2, arterial hypertension and dyslipidemia. *Materials of 2nd International Scientific and Practical*

*Conference "Therapeutic readings: modern aspects of diagnosis and treatment of diseases of internal organs"*. 2016; p. 46-47.

70. Virstyuk NG, Ikwuka AO. Diagnostic and prognostic markers of the diabetes mellitus type 2 course in connection with essential arterial hypertension taking into account the kidney function. *Precarpathian Journal Pulse* (ISSN: 2304-7437). 2017; 8(44): 53-62.
71. Virstyuk NG, Ikwuka AO. Features of asymptomatic hyperuricemia in patients with diabetes mellitus type 2 and concomitant essential arterial hypertension. *Clinical and Experimental Pathology*. 2018; 1(63): 22-26. DOI: 10.24061/1727-4338.XVII.1.63.2018.5.
72. Virstyuk NG, Ikwuka AO. Nephropathic characteristics in patients with diabetes mellitus type 2 and essential hypertensive disease. *Art of Medicine*. 2019; 1(5): 44-47. DOI: 10.21802/artm.2019.1.9.44.
73. Virstyuk NG, Ikwuka AO. Asymptomatic hyperuricemia and functional state of the kidneys in patients with essential arterial hypertension and concomitant diabetes mellitus type 2. *European Journal of Clinical Medicine*. 2021; 2(3): 100-104. DOI: 10.24018/clinicmed.2021.2.3.65.
74. Virstyuk NG, Ikwuka AO, Didushko OM. Effect of dapagliflozin on the level of uric acid during asymptomatic hyperuricemia in patients with diabetes mellitus type 2 and concomitant arterial hypertension. *Art of Medicine*. 2018; 1(5): 21-26. Available online: https://art-of-medicine.ifnmu.edu.ua/index.php/aom/article/view/179/150
75. Virstyuk NH, Ikwuka AO. Dapagliflozin influence on the clinical course of diabetes mellitus type 2 and essential hypertension in patients. *Recent Advances in Environmental Science from the Euro-Mediterranean and Surrounding Regions*. Springer International Publishing AG. 2018; p. 2007-2008. DOI: 10.1007/978-3-319-70548-4_582.
76. Virstyuk NH, Ikwuka AO, Losyuk LV, KobrynskaOYa, Markiv HD. Dapagliflozin utility in patients with diabetes mellitus type 2 and essential hypertensive disease. *Actual Problems of Modern Medicine*. 2017; 4(60) 1: 76-79. Available online: http://www.umsa.edu.ua/journal2stat4_2017_eng.html
77. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *Journal of the American Medical Association*. 2007; 298(22): 2654–2664.
78. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. *Report of a WHO/IDF consultation*. 2006. Available online: http://apps.who.int/iris/bitstream/10665/43588/1/9241594934_eng.pdf
79. World Health Organization. *Global Diabetes Report*. 2016. Available online: https://idf.org/our-network/regions-members/africa/members/10-gambia.html
80. World Health Organization. *Global report on diabetes*. 2016; Available online: https://www.who.int/publications/i/item/9789241565257
81. World Health Organization. Use of glycated hemoglobin (HbA1c) in diagnosis of diabetes mellitus. *Abbreviated report of a WHO consultation*. 2011. Available online: www.who.int/diabetes/publications/report-hba1c_2011.pdf
82. World Health Organization. *WHO Guideline: sugars intake in adults and children*. 2015; Available online: https://www.who.int/publications-detail-redirect/9789241549028