Brief overview of diabete mellitus

Gudisa Bereda*

ABSTRACT

Introduction: Diabetes mellitus is a metabolic disorder characterized by hyperglycaemia in which glucose is underutilized due to defects in insulin secretion, insulin action, or both. The common risk factors for occurrence of complications were gender, long duration with diabetes, poor and inadequate glycemic control, negative attitude towards diabetes, poor treatment adherence, and poor knowledge about the disease and its management.
Glucocorticoids reduce hepatic and peripheral tissue sensitivity to insulin through post-receptor mechanisms.

Objective: To encapsulate the definitions, classifications, prevalence, risk factors, diagnostics procedure, goal of management, lifestyle modifications, treatment, and complications of diabetic mellitus.

Methodology: The authors used 88 different published articles for the accomplishment of this review article. Google search engine was used for accessing published articles from databases like Google Scholar, Research Gate, PubMed, NCBI, NDSS, PMID, PMCID, Cochrane Database and Clindamed international library.

Findings: A role for excess glucagon cannot be underestimated; indeed, type 2 diabetes is an islet paracrinopathy in which the reciprocal relationship between the glucagon-secreting alpha cell and the insulin-secreting beta cell is lost, leading to hyperglucagonemia and hence the consequent hyperglycemia. Protease inhibitors may bind to as yet uncharacterized target proteins that regulate lipid metabolism, leading to elevated circulating fatty acids that could interfere with insulin signaling or enter the fatty acid cycle and compete with glucose cycle intermediates. Biguanides which reduce gluconeogenesis in the liver include metformin. The burden of diabetes is even higher in developing countries and in Ethiopia; systematic review result showed that prevalence of diabetes mellitus is between 2% and 6.5%.

Conclusion: Diabetes is chronic disease occurred due to increased blood glucose level because of the body cannot produce at all or secrets in sufficient insulin hormone or not use it effectively. The common risk factors for occurrence of complications were gender, long duration with diabetes, poor and inadequate glycemic control, negative attitude towards diabetes, poor treatment adherence, and poor knowledge about the disease and its management.

Abbreviations

ADA: American Diabetes Association; DKA: Diabetic Ketoacidosis; DM: Diabetes Mellitus; T2DM: Type-2 Diabetes Mellitus; T1DM: Type 1 Diabetes; HIV: Human Immunodeficiency Virus; HbA1c: Glycosylated Hemoglobin; HTN: Hypertension; HHS: Hyperosmolar Hyperglycemic State; IDF: International Diabetes Federation; IDFA: International Diabetes Federation Atlas; OGTT: Oral Glucose Tolerance Test; NCDs: Non Communicable Diseases; UDM: Undiagnosed Diabetes Mellitus; WHO: World Health Organization.

Department of Pharmacy, Negelle Health Science College, Guji, Ethiopia
**Author for correspondence: E-mail: gudisabareda95@gmail.com*

KEYWORDS

- diabetes mellitus
- insulin
- hemoglobin

Introduction

Diabetes is chronic disease occurred due to increased blood glucose level because of the body cannot produce at all or secrets in sufficient insulin hormone or not use it effectively. Hence, the nonexistence of insulin or the cell is not sensitive to use insulin leads to increased blood glucose level which is the hallmark of diabetes [1]. Diabetes mellitus (DM) affects more than 422 million people around the world. By the year 2040, the number of people with diabetes is expected to rise to 642 million, most of who are going to reside in low- or middle-income countries [2]. Diabetes is a growing public health problem affecting people worldwide, with a rapidly increasing prevalence in both developing and developed countries [3].

Definitions of Diabetes Mellitus

Diabetes mellitus is a serious, chronic metabolic disorders that characterized by high sugar level either when the pancreas does not produce enough insulin, or when the body cannot effectively use insulin. Type 2 Diabetes Mellitus (T2DM) accounts about 90% of all diagnosed cases of diabetes among adults [4]. Type-2 Diabetes Mellitus (T2DM) is the most common form of diabetes sometimes called age-onset or adult-onset diabetes. It is a milder form of diabetes because of its slow onset (sometimes developing over the years) and because it usually can be controlled with diet and oral medications. The consequences of uncontrolled and untreated T2DM, however, are just as serious as those of Type I. The causes of Diabetes Mellitus are unclear. However, there seem to be hereditary (genetic factors) and environmental factors involved [5]. Type 2 diabetes constitutes about 85–95% of all diabetes in high-income countries with a higher percentage in low- and middle-income countries due to rapid socio-cultural changes, ageing populations, increasing urbanization, reduced physical activity and unhealthy lifestyle and behavioral patterns [6, 7].

Classifications of Diabetes Mellitus

According to the current classification there are two major types: type 1 diabetes (T1DM) and type 2 diabetes (T2DM). The distinction between the two types has historically been based on age at onset, degree of loss of β cell function, degree of insulin resistance, presence of diabetes-associated autoantibodies, and requirement for insulin treatment for survival. However, none of these characteristics unequivocally distinguishes one type of diabetes from the other, nor accounts for the entire spectrum of diabetes phenotypes [8].

Type 1 diabetes is characterized by the rate of β-cell destruction is rapid in some individuals and slow in others. The rapidly progressive form of T1DM is commonly observed in children but may also occur in adults. Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Others may have modest hyperglycaemia that can rapidly change to severe hyperglycaemia and/or ketoacidosis in the presence of infection or other stress. Still others, particularly adults, may retain residual β-cell function sufficient to prevent ketoacidosis for many years. At the time of classical clinical presentation with T1DM, there is little or no insulin secretion as manifested by low or undetectable levels of C-peptide in blood or urine [9-11]. Type 2 diabetes is characterized by a combination of peripheral insulin resistance and inadequate insulin secretion by pancreatic beta cells. Insulin resistance, which has been attributed to elevated levels of free fatty acids and proinflammatory cytokines in plasma, leads to decreased glucose transport into muscle cells, elevated hepatic glucose production, and increased breakdown of fat. A role for excess glucagon cannot be underestimated; indeed, type 2 diabetes is an islet paracrinopathy in which the reciprocal relationship between the glucagon-secreting alpha cell and the insulin-secreting beta cell is lost, leading to hyperglucagonemia and hence the consequent hyperglycemia. For type 2 diabetes mellitus to occur, both insulin resistance and inadequate insulin secretion must exist. For example, all overweight individuals have insulin resistance, but diabetes develops only in those who cannot increase insulin secretion sufficiently to compensate for their insulin resistance. Their insulin concentrations may be high, yet inappropriately low for the level of glycemia [12, 13].

Drug Induced Diabetes

The diabetogenic properties of drugs are important for two main reasons. First, polypharmacy is an unfortunate but common necessity in managing patients with diabetes; clear understanding of the potential hyperglycemic effects of drugs is therefore helpful in anticipating and avoiding deterioration in glycemic control.

Secondly, A role for excess glucagon cannot be underestimated; indeed, type 2 diabetes is an islet paracrinopathy in which the reciprocal relationship between the glucagon-secreting alpha cell and the insulin-secreting beta cell is lost, leading to hyperglucagonemia and hence the consequent hyperglycemia [14-16].

Antihypertensive and Cardiovascular Agents

■ Thiazide diuretics

The severity of glucose intolerance is strongly correlated with the degree of hypokalemia ; the impairment of insulin secretion is secondary to potassium depletion, which appears to inhibit the cleavage of proinsulin to insulin and is reversible on restoring normokalemia. [17-19]. Calcium - channel blockers: Verapamil inhibits the second phase of glucose - stimulated insulin release by blocking the uptake of calcium into the cytosol of β - cells; it also inhibits sulfonylurea and glucagon- induced insulin secretion [20,21]. β - Adrenoceptor antagonists: Long - term studies suggest that β adrenoceptor antagonists induce insulin resistance, possibly partly through weight gain [22].

■ HIV protease inhibitors

Striking syndrome of peripheral lipodystrophy, hyperlipidemia and insulin resistance has also been described in patients receiving HIV protease inhibitors, especially long term. The mechanism is not fully understood; Carr et al . Propose that protease inhibitors may bind to as yet uncharacterized target proteins that regulate lipid metabolism, leading to elevated circulating fatty acids that could interfere with insulin signaling or enter the fatty acid cycle and compete with glucose cycle intermediates[23,24].

■ β2-Adrenoceptor agonists

β2- Adrenoceptor agonists stimulate insulin secretion, but this effect is overwhelmed by increased hepatic glucose output, and the usual net effect is hyperglycemia[25].

■ Oral contraceptive pills and estrogen replacement therapy

As with glucocorticoids, post - receptor insulin resistance appears to be responsible; in vivo studies have demonstrated a decrease in insulin sensitivity in women without diabetes taking certain contraceptive pills, and a number of implantable hormonal contraceptives have been linked to alterations in carbohydrate metabolism, including impaired glucose tolerance and increased insulin resistance [26-29].

■ Glucocorticoids

Glucocorticoids reduce hepatic and peripheral tissue sensitivity to insulin through post- receptor mechanisms [30].

■ Drugs used in psychiatric disorders

Antipsychotic a gents Hyperglycemia occurs occasionally with conventional antipsychotic drugs, but the use of the newer atypical antipsychotics, especially clozapine and olanzapine, have been widely reported to be associated with the development of de novo diabetes mellitus and exacerbation of pre - existing diabetes [31-33].

Prevalence of Diabetes Mellitus

Worldwide the magnitude of diabetes in 2019 was estimated as 9.3% (463 million individuals), rising to 10.2% (578 million individuals) by 2030 and 10.9% (700 million individuals) by 2045. Diabetes is a challenge for millions of people in both developed and developing countries. Evidence in Ethiopia showed that an estimated 3.8% of the population had DM [34,35]. The global prevalence of diabetes in adults has been increasing, according to the 2017 International Diabetes Federation Atlas (IDFA) report; there are 451 million people with diabetes worldwide. These figures were expected to rise to 693 million by 2045. Nearly half of all people living with diabetes (49.7%) were estimated to be undiagnosed. In addition, approximately 5 million deaths worldwide were attributable to diabetes in the 20–99 year age range [36,37]. All countries, irrespective of their economic developmental, epidemiological and demographical variability, are facing an increasing burden of non-communicable diseases including diabetes mellitus. Diabetes mellitus with other NCDs are responsible for an increasing burden of diseases in developing countries. In Sub-Saharan Africa, NCDs are predicted to exceed infectious diseases by the year 2030. It has been projected that the number of people with diabetes will increase to 300 million by 2025 and 366 million by 2030 from 171 million in 2000 [38,39]. The prevalence of diabetes mellitus (DM) is 8.8% globally and 7.1% in Africa region among the adult population. It has been gradually increasing for the past three decades and is growing most rapidly in low and middle-

income countries [40, 41]. The prevalence of diabetes will increase in future in all countries, mostly to developing countries. This is due to modernization, economic well being, and a westernized lifestyle; the burden of diabetes and its complications increases significantly in Africa[42, 43]. In 2013, globally there were ~382 million people living with diabetes, with a global prevalence of 8.3%. According to the international diabetes federation (IDF), in 2015 ~415 million people were affected and, by 2040, this number could reach 642 million. Diabetes has historically had a higher burden in high-income countries, but the disease is growing rapidly in developing countries, accounting for ~80% of all global diabetic cases [44-46]. Hence, diabetes mellitus (DM) is likely to become one of the most prevalent and economically important diseases of the 21st century largely owing to an increasing incidence of type 2 diabetes mellitus (T2DM) in the developed nations and many of the developing nations [47]. Around 80% of people with diabetes and about five million diabetes-related deaths were reported in low income and middle-income countries. In Africa, DM affected 21.5 million (5.1%) people in 2014 and is expected to rise to 41.5 million by 2035, with an increase of 93%. Moreover, about 13.4 million (62.3%) of peoples with the DM do not know they had been affected by the disease in 2014.2,11 Ethiopia is one of the top five countries with the highest number of people affected by DM in Sub Saharan Africa.12 According to the 2014 IDFA report, the number of adults aged 20–79 years living with DM was 2.135 million (4.8%) and the total diabetes associated death was 34,262 in the country. In addition, Ethiopia has three-quarters (75.1%) of persons with undiagnosed diabetes mellitus (UDM), which accounts for about 1,603,100 people in the 2014 estimates [48-50]. The World Health Organization (WHO) estimated the number of cases of diabetics in Ethiopia to be 800,000 in 2000 and projected that it would increase to 1.8 million by the year 2030 [51]. In Ethiopia, the prevalence of diabetes admission has increased from 1.9% in 1970 to 9.5% in 1999 of all medical admissions most importantly uncontrolled blood glucose due to non-compliance to antidiabetic medications [52, 53]. The World Health Organization (WHO) projected that 300 and 700 million people will suffer from diabetes by 2025 and 2045, respectively. The burden of diabetes is even higher in developing countries and in Ethiopia; systematic review result showed that prevalence of DM is between 2% and 6.5% [54, 55].

Risk Factors for Occurrence Complications of Diabetes Mellitus

The common risk factors for occurrence of complications were gender, long duration with diabetes, poor and inadequate glycemic control, negative attitude towards diabetes, poor treatment adherence, and poor knowledge about the disease and its management [56-62]. The major risk factors in the development of T2DM are family history, obesity, race/ethnicity, age increment (>/=40 year), previous identified impaired fasting glucose or impaired glucose tolerance hypertension (HTN), hyperlipidemia and history of gestational DM [63]. Diabetes is a chronic condition caused by a relative or an absolute lack of insulin. Its hallmark clinical characteristics are symptomatic glucose intolerance resulting in hyperglycemia and alterations in lipid and protein metabolism [64].

Diagnostics of Diabetes Mellitus

Four diagnostic tests for diabetes are currently recommended, including measurement of fasting plasma glucose; 2-hour (2-h) post-load plasma glucose after a 75 g oral glucose tolerance test (OGTT); HbA1c; and random blood glucose in the presence of signs and symptoms of diabetes. People with fasting plasma glucose values of ≥ 7.0 mmol/L (126 mg/dl), 2-h post-load plasma glucose ≥ 11.1 mmol/L (200 mg/dl), HbA1c ≥ 6.5% (48 mmol/mol); or a random blood glucose ≥ 11.1 mmol/L (200 mg/ dl) in the presence of signs and symptoms are considered to have diabetes. If elevated values are detected in asymptomatic people, repeat testing, preferably with the same test, is recommended as soon as practicable on a subsequent day to confirm the diagnosis [65, 66].

Goals of Diabetes Mellitus

Diabetes management aims to delay the onset of disease complications, and to hinder its progression, mostly by improving glycemic control and controlling the risk of cardiovascular disease [67, 68]. To prevent diabetic complications including organ damage and micro vascular complications the blood glucose level should be maintained at an optimum level because poor glycemic control leads to diabetic ketoacidosis, cognitive impairment, immune

dysfunction and hospitals admissions due to May complications [69]. Diabetes management involves strictly maintaining a person's blood glucose level close to the normal range. There is a strong relationship between an elevated blood glucose level and the risk of complications and mortality in people with diabetes [70, 71]. The American Diabetes Association (ADA) has designated HbA1c level of <7% as a goal of optimal blood glucose control and the American Association of Clinical Endocrinologist has further recommended HbA1c level of < 6.5% [72]. Achieving optimal glycemic level may not be an easy task. It depends on the type of treatment received patients' adherence and comorbidities [73, 74].

Lifestyle Modification In The Prevention of Type I Diabetes Mellitus

Moreover, WHO has recognized the importance of dietary control in diabetes mellitus and has given its recommendation regarding the distribution of nutrients in diabetic patients. Carbohydrates 45%, Total fat 35%, Mono-unsaturated fatty acids 20%, Poly-unsaturated fatty acids <8%, Saturated and trans-fatty acids <7%, Protein 15%-20%, and Cholesterol <20 mg/day [75].

Diabetes Mellitus Drugs Therapy

The four major groups of antidiabetic agents are: Biguanides which reduce gluconeogenesis in the liver include metformin, Insulin secretagogues which stimulate the pancreas to secrete insulin such as sulfonylureas, Insulin sensitizers which improve sensitivity of peripheral tissues to insulin such as thiazolidinediones and Insulin analogues which provide insulin exogenously [76]. In the absence of contraindication metformin is the first and most widely used pharmacological treatment. It lowers blood sugar levels and help to reduce cardiovascular risk without increased risk of hypoglycaemia and weight gain [77, 78].

Diabetes Mellitus Complications

Diabetes Mellitus (DM) is a metabolic disorder characterized by hyperglycaemia in which glucose is underutilized due to defects in insulin secretion, insulin action, or both. As of 2014, an estimated 387 million people had DM worldwide [79]. It has various long-term complications which negatively impact the individuals' quality of life and potentially their life spans, causing deleterious effects for both individuals and societies. Diabetes complications are categorized as microvascular (nephropathy, neuropathy, and retinopathy) or macrovascular (cardiovascular and cerebrovascular disease) [80, 81]. The most common chronic complications were erectile dysfunction (64%), visual disturbance (33.8%), and cardiovascular disorders (30.1%), though hypertension alone was (68%), neuropathy (29.5%), and nephropathy (15.7%). Likewise acute complications had similar trend which ranges 30.5% among which diabetic ketoacidosis (DKA) was 71%, followed by hypoglycemia (19.4%) but hyperosmolar hyperglycemic state (HHS) was insignificant [82-84]. Diabetes-related complications are the major cause of premature deaths and disability in the world, which is 2–4 times more prevalent in patients with DM than in the general population [85]. It is a leading cause of blindness, end stage renal disease and stroke. These complications are two to five times more common among diabetic patients [86]. Diabetes may result in a wide range of physiological as well as psychological problems including sexual disorder. The lower sexual functions or dysfunctions termed as loss of libido may be observed in both females and males as a consequence of DM. In addition, severe vision loss, acute renal diseases which may require dialysis or kidney transplant, myocardial infarction otherwise known as heart attack, cerebrovascular diseases like stroke, and hypertension are markedly observed. Due to the intensity of the adverse effects of diabetes, it is important to find out the determinants to address the issue in order to contribute to improving country health situation [87-88].

Discussion and Conclusion

A role for excess glucagon cannot be underestimated; indeed, type 2 diabetes is an islet paracrinopathy in which the reciprocal relationship between the glucagon-secreting alpha cell and the insulin-secreting beta cell is lost, leading to hyperglucagonemia and hence the consequent hyperglycemia. Protease inhibitors may bind to as yet uncharacterized target proteins that regulate lipid metabolism, leading to elevated circulating fatty acids that could interfere with insulin signaling or enter the fatty acid cycle and compete with glucose cycle intermediates. Biguanides which reduce gluconeogenesis in the liver include metformin. The burden of diabetes is even higher in developing countries and in Ethiopia; systematic

review result showed that prevalence of diabetes mellitus is between 2% and 6.5%. Diabetes is chronic disease occurred due to increased blood glucose level because of the body cannot produce at all or secrets in sufficient insulin hormone or not use it effectively. The common risk factors for occurrence of complications were gender, long duration with diabetes, poor and inadequate glycemic control, negative attitude towards diabetes, poor treatment adherence, and poor knowledge about the disease and its management.

Acknowledgments

The authors acknowledged Endnote-8, Google scholar, Medscape and PubMed

Data Availability

The data used in this study can be obtained on written request to the corresponding author.

Funding

None

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