



Review

Diabetes in Ethiopia: A systematic review of prevalence, risk factors, complications, and cost



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ABSTRACT

Aims: Diabetes is disproportionately increasing in low- and middle-income countries due partly to rapid urbanization, lifestyle changes, and limited resources. This is the first comprehensive review of prevalence, risk factors, complications and costs related to diabetes in Ethiopia.

Methods: We searched PubMed, MEDLINE, EMBASE, African MEDICUS, and IEEE Xplorer for studies on prevalence, risk factors, outcomes, treatments or cost of diabetes published in English from 1984 to 2019. Other sources such as Google Scholar were hand-searched for additional studies and we included 39 studies for our analysis.

Results: The review shows the prevalence of diabetes in Ethiopia ranged 2.0%–6.5% with the low 2% in smaller rural areas. Oral hypoglycemics and insulin were most common treatments. The most frequently reported diabetes-associated problems included retinopathy (2.7%–25%), neuropathy (4.8%–35.0%), depression (13.0%–61.0%), kidney diseases (18.2%–23.8%), hypertension (23.0%–54.82%), anemia (19.0%), and associated costs.

Conclusions: Diabetes and associated complications in Ethiopia are major causes of morbidity and mortality with consequential economic impact. Tailored strategies towards prevention and management of modifiable risk factors for diabetes are needed to reduce the burden. Resource reallocation for epidemiological surveillance, tailored prevention of modifiable risk factors and research are needed.

1. Introduction

Diabetes is a chronic metabolic condition manifested by elevated blood glucose levels when the pancreas produces little or no insulin (type 1 diabetes) or cells' resistance to insulin (type 2 diabetes) or both (Sierra, 2009). Type 2 diabetes accounts for over 90% of diagnosed cases globally and the remaining are other forms, including type 1 and gestational diabetes (Sierra, 2009), (International Diabetes Federation, 2013).

Diabetes is not fatal if managed effectively, but untreated hyperglycemia results in various multi-organ complications that cause acute and chronic morbidity and death (Beran and Yudkin, 2006). The

incidence of diabetes is alarmingly increasing with disproportionately higher rates in low- and middle-income countries (LMICs) toping others as the cause of hospital morbidity and mortality due partly to rapid lifestyle modification, urbanization, as well as increase in life expectancy (Mendenhall et al., 2014), (Aynalem and Zeleke, 2018). Often times, these estimations are from hospital data or with extrapolation from other similar settings, which impedes the development of tailored prevention strategies. There is less data about the magnitude of diabetes and underlying risk factors in the general populations. Another important aspect of diabetes is its economic impact due to long-term treatment and care needed for management of diabetes and its complications. The exorbitant expenses can take the household and national

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resources quickly, which could be a deterrent for poverty reduction initiatives (Jeet et al., 2018). While the situation might be similar with other resource limited settings, there is a need for a comprehensive review of what is known about diabetes in Ethiopia since the latest limited scope review is from 2012 (Nigatu, 2012). This study aims to provide a comprehensive review of available studies to estimate country-specific prevalence, risk factors, and complications, as well as incurred costs for treatment and management of diabetes in a resource-limited setting, particularly in Ethiopia where the absolute impact of diabetes would be high due to its large population, urbanization and lifestyle changes following the rapid economic development in the last two decades.

2. Methods

The PRISMA protocol with an extension for Scoping Reviews was used to perform this review (Hutton et al., 2015).

2.1. Search strategy

We used search terms, including ‘diabetes mellitus’ or ‘DM’, ‘diabetes complications’, ‘diabetes risk factors’, ‘diabetes treatment’, ‘diabetes outcomes’ and ‘financial burden of diabetes’ as well as the string ‘Ethiopia’ to search studies published in English between 1984 and 2019 on PubMed, MEDLINE, EMBASE, African MEDICUS, IEEE Xplorer, and other generic search engines (such as Google and Google Scholar). Additionally, we searched for non-indexed local journals such sites as from World Health Organization (WHO) and International Diabetes Federation (IDF), and unpublished electronic materials that focused on diabetes in Ethiopia through hand searches and personal communications with colleagues.

Inclusion criteria: The inclusion criteria used were: (i) articles published from 1984 to 2019; (ii) articles addressing one or more of the four areas of the review (prevalence of diabetes, risk factors, treatments and non-adherence for diabetes, diabetes outcomes and complications and cost of diabetes); (iii) articles published in the English language; and (iv) articles for which a full text were obtained for this review.

2.2. Selection and eligibility of studies

We screened the titles of the identified studies for eligibility and further screened the detail based on full text assessment. The search identified 289 studies from the electronic search engine of which 204 duplicates and 25 articles that were not relevant to the review excluded. Then 60 full-text articles were assessed for eligibility and further 21 full-text articles were excluded since inclusion criteria were not met. Finally, 39 studies were included in the final review (Fig. 1). Two reviewers extracted the data (MG and KB) and a third author (CJ) was consulted when disagreement occurred. The third reviewer hand searched for additional articles. The quality of the reviewed articles can be gleaned from the design of the study as well as the type of journal they were published on.

3. Results

3.1. Prevalence and distribution of diabetes in Ethiopia

The prevalence of diabetes in Ethiopia based on the identified studies is shown in Table 1. Ethiopia is among the top four countries in sub-Saharan Africa having the highest number of people with diabetes and hospital admissions due to diabetes (Abebe et al., 2016). However, diabetes still remains largely undiagnosed and untreated mainly in the rural settings (Abebe et al., 2014). According to the 2017 estimate by IDF, Ethiopia has 2.57 million (5.2%) adult people aged 20–79 years with diabetes, making it the largest diabetes population in sub-Saharan Africa. Of those, about 1.96 million of them (76%) do not even know

that they have diabetes (International Diabetes Federation, 2017).

3.2. Risk factors in Ethiopia

Risk factors for diabetes were not consistently reported across studies as well as that the risk factors were less classified for which type of diabetes and whether for incidence of diabetes or its sequelae. For example, a clinic-based study in Mekelle hospital, northern Ethiopia suggested that previous famine was a relevant predisposing factor for development of diabetes (Habtu et al., 1999), while another preceding study reported that under nutrition may probably be caused by the untreated diabetes per se (Lester, 1984). In the latter study, people with diabetes had indications of malnutrition, such as low mid-upper arm circumference, body mass index, body weight or lead body mass as well as disproportionate skeletal growth. Interestingly, a recent study conducted on patients with diabetes in the same hospital showed that clinical features, local prevalence of under nutrition, and glutamic acid decarboxylase (GAD) antibodies (GADA) and C-peptide heterogeneity showed a malnutrition-related form of diabetes (Gill et al., 2011). Authors, including Habtu and Fekadu reported that diabetes was strongly associated with low socioeconomic status, poor education, and other markers of poverty (Habtu et al., 1999), (Fekadu et al., 2010), (Alemu et al., 2009); however, these were survey studies and thus difficult to conclude causality.

Another study conducted in two zones of Ethiopia–Gondar and Jimma– using health surveillance data that included 2280 patients with diabetes showed that prevalence rates in both urban areas were five times higher than in the surrounding rural areas. Patients with insulin-requiring diabetes from rural and urban areas had a very low BMI and most were subsistence farmers or unemployed, which supports the findings that diabetes may be associated with under nutrition or higher poverty (Alemu et al., 2009). However, this may be artefactual; for example, it could be due to higher number of undiagnosed cases in rural areas because of low access to health facility and low self-awareness (Alemu et al., 2009), (Megerssa et al., 2013). The disease phenotype encountered in this area is very different from the classical type 1 diabetes seen in the Western world and most closely resembles previous descriptions of malnutrition-related diabetes, a category not recognized in the current WHO Diabetes Classification. There are discussions for re-opening the case for this condition (Alemu et al., 2009).

3.3. Standards of diagnosing and management of diabetes in Ethiopia

An overview of the guideline for diagnosing diabetes in Ethiopia is shown in Table 2, and the detailed standards can be found elsewhere (Ministry of Health Ethiopia, 2014). We only found a single study that studied the use and implementation of those standards in Ethiopia. This cross-sectional study was conducted at 21 health centers (primary healthcare level) and five regional hospitals (secondary healthcare level) in Addis Ababa and it showed that only 21% of patients with diabetes had access to regular blood glucose monitoring in the same health institution. It also shows that 51% of patients didn't have urine analysis, blood urea nitrogen, creatinine, and lipid profiles, and none received hemoglobin A1c test in 1–2 years of follow-up (Feleke and Enquesslassie, 2011). Consequently, nearly 75% of the patients were once admitted to hospitals due to uncontrolled diabetes. “Proper education” (not defined by authors) for diabetes was provided for 24% of the patients. This study asserted that a proxy indicator for the poor management and care could be the low (5%) proportion of patients who managed to undertake self-blood glucose monitoring at home; indeed, this could be due to inaccessibility of the point-of-care test tools. About 87% had regular follow up care at their respective health centers and hospitals (Feleke and Enquesslassie, 2011).

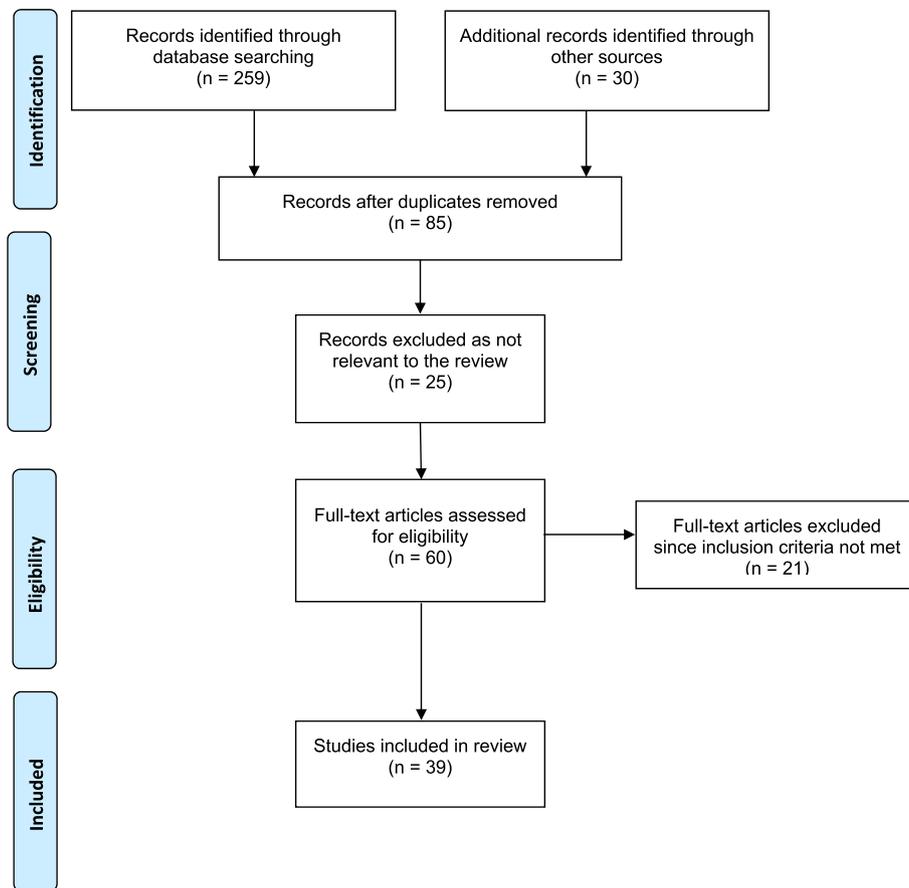


Fig. 1. Study selection.

3.4. Diabetes outcomes and prevalence of diabetes-related complications in Ethiopia

Diabetes is known to increase the risk of mortality and complications (Hall et al., 2011), (Nigatu, 2012), (Amare et al., 2013), (Burgess et al., 2014), (Haregu et al., 2012). Type 2 diabetes related complications have been becoming more prevalent in Ethiopia (Table 3) (Wabe et al., 2011). These complications included hypertension, neuropathy, renal diseases, lower extremity amputations, retinopathy, visual disturbances, and cataracts. Depression was also identified as one of the most common problems, especially in hospitalized patients (Agbir et al., 2010), (Tilahun et al., 2018). A cross-sectional study that was conducted in 2017 on 256 type 2 diabetes patients at university of Gondar comprehensive specialized hospital demonstrated that metabolic syndrome was a major health concern for patients with diabetes in Ethiopia

and they are at increased risk of developing complications such as cardiovascular disease (CVD) and premature mortality (Birarra and Gelayee, 2018). Another study in the same hospital showed vascular diseases were major complications with an incidence of 40.6 cases (95% CI: 33.2, 49.5) per 1000 person (Wolde et al., 2018). This evidence was supported by other studies. For example, a cross-sectional study in Jimma University Specialized Hospital in 2007 showed hypertension (46.5%), obesity (23.4%), and dyslipidemia (63.5%) as important complications observed (Tamiru and Alemseged, 2011). In the 2012 limited scope systematic review of epidemiology, complications and management of diabetes in Ethiopia, the authors reported that diabetic triopathy–retinopathy, neuropathy, nephropathy–are common among patients with diabetes in Ethiopia (Nigatu, 2012).

Table 1
Prevalence of diabetes.

Study	Site	Sample size	Population (age)	Mean (%)	Low (%)	High (%)	Remark
Lester, 1984	Yekatit 12 Hospital, Addis Ababa	849	All age patients with diabetes	79.1 T2D 20.1 T1D 0.6 Others			Includes T1D and T2D
Gizaw et al., 2015	Black Lion Hospital, Addis Ababa	8048	All patients	6.5	–	–	Of total, 72.0% T2D, 28.0% T1 D
Abebe et al., 2014	Town of Gondar and rural district in Dabat	2200	Residents ≥ 35 years	–	2.1	5.1	Higher prevalence in urban and lower in rural. Response rate 97.3%.
IDF, 2017	Country level	Adults	Population 20–79 years	5.2	2.2%	7.7%	Min and max are CI
Assefa et al., 2014	Ayder Referral Hospital, Mekelle	130	All age patients with diabetes	53.85% T1D 46.15% T2D	–	–	T1D and T2D

All areas were in Ethiopia.

T1D: Type 1 diabetes; T2D: Type 2 diabetes.

Table 2
Diagnostic Criteria for diagnosis of diabetes in Ethiopia.

Laboratory criteria	<ul style="list-style-type: none"> - Fasting plasma glucose (FPG) \geq 126 mg/dl - Hemoglobin A1C \geq 6.5% - Random plasma glucose of \geq 200 mg/dl in patients with classic symptoms of hyperglycemia or hyperglycemia crisis - 2 h plasma glucose of \geq 200 mg/dl during an oral glucose tolerance test
Clinical features	<ul style="list-style-type: none"> - No recognizable symptoms in many individuals particularly in type 2 diabetes - Large amounts of urine (polyuria) - Thirst and excessive drinking of water - Unexplained weight loss - Blurred vision - Recurrent skin infections - Recurrent itching of the vulva - Symptoms related to chronic complications (abnormal sensory/motor neurologic findings on extremities; foot abnormalities such as various deformities, ulcers, ischemia; visual impairment)

3.5. Treatments and treatment to non-adherence of diabetes in Ethiopia

Educational interventions targeted at reducing self-management concerns, improving dietary self-care behavior, and self-management confidence may help patients with type 1 and type 2 diabetes reduce glycemically abnormalities (Kebede and Pischke, 2019).

3.6. Treatment and management of diabetes

Treatment and care of diabetes is not mere management of hyperglycemia, but also prevention of complications, mainly reducing absolute risk for CVD that includes controlling hypertension, dyslipidemia, obesity, and decreasing smoking. More generally, the treatment and care comprise medical nutrition therapy, exercise, self-blood glucose monitoring, and screening for micro- and macro-vascular complications according to the guideline used in Ethiopia (Ministry of Health Ethiopia, 2014). Nonetheless, while we found no study that evaluated the overall quality of treatment in Ethiopia, some geographically limited studies have been made on this topic. For example, a study with a total of 252 patients with diabetes in West Ethiopia were included in another study, and of those, 150 (59.5%) had poor glycemically control (Dedefo et al., 2019). In public hospitals of Benishangul Gumuz, out of 383 patients responding, 45.7% had poor diabetes self-care practice (Chali et al., 2018). A recent study with 361 participants was conducted to assess the treatment pattern and the factors associated with blood pressure and fasting plasma glucose (FPG) control among patients with type 2 diabetes in the Federal Police Referral Hospital of Ethiopia. Of

the 361 participants who were checked about their current FPG level, only 142 (39.3%) had FPG < 130 mg/dl while 87 (24.1%) participants were found to control both BP and FPG levels (Shimels et al., 2018). Poor knowledge about diabetes was associated significantly with poor self-care practices (Dedefo et al., 2019). For both, persons with type 1 and type 2 diabetes, using diabetes apps for self-management was positively associated with self-care behavior (Kebede and Pischke, 2019). Among 419 patients with type 2 diabetes in Addis Ababa, 75.9% did not adhere to the recommended diet management and 83.5% did not adhere to self-monitoring of blood glucose level (Bonger et al., 2018). A total of 336 patients with diabetes were enrolled in Ayder comprehensive specialized hospital, Mekelle, Ethiopia. Out of the total, 61.9% of the study participants had poor glycemically control and the poor glycemically control was significantly higher in glucometer non-users (Mideksa et al., 2018). A cross-sectional study of 367 patients was conducted among patients with diabetes attending University of Gondar Hospital diabetes follow-up clinic. The proportion of poor glycemically control was 60.5% (61.4% type 1 diabetes and 59.8% type 2 diabetes) (Fasil et al., 2019). The study was conducted on patients with diabetes who have a follow-up at Jimma University Specialized Hospital diabetic clinic. Regarding the type of medications patients were using, 36.9% of them were taking insulin, 53.1% were taking oral glucose lowering agents and the remaining 10% were taking both insulin and oral medications (Ahmed et al., 2018).

Table 3
Prevalence of diabetes complications.

Reference	Site	Sample size	Study sample	Mean/Average (%)	Low (%)	High (%)	Remark
Gelaw et al., 2014	Clinic of Adama Referral Hospital	270	Adult PwD \geq 18 years	54.82% hyper-tension 32.96% visual impairment, 13.71% nephropathy 11.1% limb paralysis	-	-	
Lester, 1984	Yekatit 12 Hospital, Addis Ababa	849	All age PwD	7.0% retinopathy, 5.6% nephropathy, 9.4% neuropathy, 9.5% contracts	-	-	Diabetes includes both T1D and T2D
Assefa et al., 2014	Ayder Referral Hospital, Mekelle	130	All age PwD	40.5% DKA, 24.3% neuropathy, 16.2% hypo-glycemia, 8.1% nephropathy 5.4% cardio-vascular disease, 2.7% retinopathy, 2.7% sexual dysfunction	-	-	T1D and T2D
Abate et al., 2013	Fenote Selam Hospital	384	PwD aged \geq 7 years old	19.0% anemia	-	-	50.3% T1D 49.7% T2D
Nigatu, 2012	Ethiopia	Systematic review	PwD	35.0% neuropathy, 25.0% retinopathy, 15.0% nephropathy	-	-	-
Ahmed et al., 2018	Diabetic clinic, Jimma University Specialized Hospital	160	All ages PwD	22.5% DKA; 38.75% hypertension; 2.5% Asthma;	-	-	43.8% T1D 56.2% T2D
Fasil et al., 2019	University of Gondar Hospital	367	All ages PwD	17.7% Retinopathy; 7.9% neuropathy; 4.4% nephropathy	-	-	63.0% T1D 57.0% T2D

T1D; Type 1 diabetes; T2D; Type 2 diabetes; DKA; Diabetic ketoacidosis; GFR: Glomerular filtration rate.

3.7. Medications and non-adherence

Oral and insulin medication are the standard treatments for controlling glucose levels in persons with diabetes. Many persons with diabetes have other comorbid conditions such as elevated lipids and hypertension that require other medications for control. Where necessary, there would be additional treatments depending on the comorbidities of individual patients. Adherence to prescribed medication is crucial to reach metabolic control as non-adherence with blood glucose lowering or lipid lowering drug (such as statins) is associated with higher HbA1c and cholesterol, levels respectively (Wabe et al., 2011). Low adherence to prescribed diabetes medications is one of the major reasons for poor glycemic control in developing countries (Abebe et al., 2014). A recent cross-sectional study among 270 patients in Adama referral hospital in Ethiopia showed that 21.8% of the participants ascribed their non-adherence to forgetting to take their medications. Other factors include use of traditional and/or religious medicines (17.8%) and lack of finance (14.4%) (Ahmed et al., 2018), (Wabe et al., 2011). Another study in Gondar of Ethiopia reported over half of the patients did not adhere to the essential medications (Abebe et al., 2014). The main reasons for non-adhering was replacing with traditional medicines and dissatisfaction with health services (Abebe et al., 2014). Moreover, other evidence added that people did not adhere to prescribed medications due poor knowledge and self-awareness (Gelaw et al., 2014). Generally, patients with diabetes have poor control of serum glucose following poor adherence, which consequently leads to higher secondary complications and mortality (Wabe et al., 2011).

3.8. Relationship between anemia, infectious diseases and diabetes in Ethiopia

Diabetes is likely to increase the risk of anemia either due to certain oral diabetes drugs or due to not eating well, having conditions that interfere with absorption of nutrients or low immunity that could also be related to higher risk for infections (Hall et al., 2011), (Nigatu, 2012), (Amare et al., 2013), (Burgess et al., 2014), (Haregu et al., 2012). This section includes anemia, HIV and tuberculosis as the most common issues (other than the comorbidities that are traditionally linked with diabetes) identified in the review of the literature.

3.9. Anemia

Anemia is a global public health problem affecting both developing and developed countries from which nearly 1.3 billion individuals suffer (Alem et al., 2013). Anemia is mainly common in developing countries like Ethiopia. The anemic condition is worsened by the presence of other chronic diseases such as diabetes, tuberculosis, malaria and HIV, which affects health, quality of life and working capacity for many people across the world (Ababiya and Gabriel, 2014). A recent cross-sectional study about the association of anemia and renal function among patients with diabetes mellitus in Fenote Selam Hospital of Northwest Ethiopia showed significant association between anemia and glomerular filtration rate (GFR). Among 384 patients with diabetes included in the study, 19% were found anemic. Among which, 53 (13.8%), 48 (12.5%) and 283 (73.7%) of the patients with had estimated GFR < 60 ml/min/1.73 m, 60–90 ml/min/1.73 m, and 0.90 ml/min/1.73 m respectively (Abate et al., 2013). Women with diabetes had increased prevalence of anemia compared to men (Makadiya et al., 2014). Pregnant women, particularly in developing countries such as Ethiopia, suffer from anemia (Ababiya and Gabriel, 2014), (Alene and Dohe, 2014). Efforts should be dedicated to tackle this massive problem, for example, iron fortification of appropriate food items combined with iron supplements in specific population groups has proved to be efficient (Ababiya and Gabriel, 2014).

3.10. Tuberculosis

The rate of Tuberculosis (TB) in patients with diabetes is three times higher than people without diabetes (Amare et al., 2013), with paramount attenuation of immunity that favors the development of latent TB infection into an active form that occur in at least one third of people in the developing regions (Riza et al., 2014). A cross-sectional hospital-based study in Ethiopia showed the prevalence of diabetes was 8.5% among patients with pulmonary TB. The rate was higher in men, urban dwellers, and HIV co-infected persons (Getachew et al., 2013). Another cross sectional study conducted from 1989 to 1996 in Ethiopia showed the prevalence of TB in the population with diabetes was 5.8% (Feleke et al., 1999). Another recent study in Dessie referral hospital reported similar magnitude of TB (6.2%) (Amare et al., 2013). This study further showed that the prevalence of diabetes mellitus among active pulmonary TB cases was higher compared to people without active TB in Ethiopia. Most of the non-communicable disease tests were not available at primary health care level in Ethiopia (Haregu et al., 2012). Hence, launching a well-functioning chronic disease and TB control programs in countries like Ethiopia where the prevalence of HIV and TB epidemic is high would be important to avoid such preventable morbidity and mortality (Getachew et al., 2013).

3.11. HIV

According to WHO, there were approximately 36.9 million people living with HIV as of 2017 of which the majority (25.7 million) occurred in Africa, with 1.8 million people becoming newly infected globally (World Health Organization, 2018). According to the UNAIDS report, HIV prevalence in Ethiopian adults aged 15–49 years was estimated 1.5% in 2012 (UNAIDS, 2013). However, the influence of HIV infection on risk of diabetes is not clear and inconsistent in many studies. The study showed that the diabetes incidence in HIV-TB co-infected people was four times higher than HIV-negative TB patients (Getachew et al., 2013). However, the relationship between diabetes and HIV was heterogeneous. For example unlike the above one, another study showed a lower incidence of diabetes among people living with HIV (Haregu et al., 2012).

3.12. Mortality

Some of the reported causes of death in patients with diabetes included renal failure (the most common cause), chronic liver disease, hepatoma, cerebrovascular accidents, cardiac disease and ketoacidosis (Lester, 1984), (Gizaw et al., 2015), (Gelaw et al., 2014), (Feleke and Enquesselassie, 2011). A study was conducted by Gizaw and colleagues on diabetes mellitus in Addis Ababa, Ethiopia: admissions, complications and outcomes. This study reported that the overall inpatient mortality was found 89 deaths (21.0%), where 77 deaths occurred among patients with type 2 diabetes and the main complications for admission were diabetic foot ulcer and cardiovascular diseases (Gizaw et al., 2015). A systematic review was conducted on epidemiology of major non-communicable diseases in Ethiopia (Misganaw et al., 2014). This review reported that diabetes was top cause accounting for 5% of all mortality next to CVD and cancer. Another study assessed national mortality burden due to communicable, non-communicable, and other diseases in Ethiopia over 25 years from 1990 to 2015. Accordingly, diabetes was reported as one of the 11 top causes of mortality in Ethiopia (692.4 per 100,000 people; 95% uncertainty interval 415.0–1096.1) (Misganaw et al., 2017). However, diabetes could be an underlying cause of deaths leading to other complications. For example, this study showed that the top five causes of deaths were lower respiratory infections, 2987.2 (95% UI: 2165.5–4017.9), diarrheal diseases, 2502.3 (95% UI: 1410.4–4151.9), tuberculosis, 2405.2 (95% UI: 1676.8–3309.1), ischemic heart disease, 2380.3 (95% UI: 1446.5–3680.0), and HIV/AIDS, 1236.9 (95% UI: 861.1–1623.3) per

100,000 people. Diabetes could contribute to excess risk of disease directly or indirectly (Misganaw et al., 2017).

3.13. Cost of diabetes in Ethiopia

Diabetes is a chronic disorder that poses huge health and economic burden (Assefa et al., 2014). The International Diabetes Federation estimated the mean per person diabetes related expenditure in Ethiopia was around US\$ 25 in 2012 and USD\$ 29 in 2013, which is extremely lower compared to the global average of US\$ 1270 (International Diabetes Federation, 2013), but this is a very large expenditure relative to income in Ethiopia. A case-control study at Tikur Anbessa hospital in Ethiopia showed the direct cost of hospitalization among patients with diabetes (mean US\$ 154 in 2019 which is cost in 2007 inflated using Consumers Price Index) was significantly higher than for those without diabetes (mean US\$ 109 in 2019) and the substantial proportion of the total cost of admission is utilized for treating acute and long-term complications (Feleke and Enquesselassie, 2007). A recent study has been conducted on pharmaco-economic evaluation of anti-diabetic treatment at Ayder Referral Hospital in Ethiopia. This study found that cost of illness of diabetes per patient per year was US\$ 89 and insulin accounted most of the drug cost and total cost of illness of diabetes. It was also reported that diabetes with complications resulted in about US \$125 (1.65 times) higher cost of illness than that without complications (Assefa et al., 2014). No study was identified that evaluated the national cost of care among Ethiopian patients with diabetes (Assefa et al., 2014), (Feleke and Enquesselassie, 2007). Considering the lowest and highest prevalence of diabetes mellitus reported in Ethiopia, the expected number of patients with diabetes in Ethiopia lie between (diagnosed and undiagnosed) between 0.033* (latest Ethiopian population size) and 0.065* (latest Ethiopian population size). Diabetes imposes a large economic burden on the national health care system worldwide; thus more prevention efforts are needed to reduce this burden (Zhang et al., 2010).

4. Discussion

This is the first comprehensive review of diabetes in Ethiopia. Obtaining more valid and reliable data of diabetes in Ethiopia is very difficult (Megerssa et al., 2013), but the available studies showed the prevalence ranged from 3.3% to 6.5% but this was as low as 1.9% in some small rural areas (Alemayehu et al., 2018). This review found that there exists a large burden of complications, including retinopathy, neuropathy, depression, amputation of the lower limbs, kidney diseases, hypertension, and anemia. Worldwide, adherence rate for medications for diabetes control vary between 36% and 93% (Wabe et al., 2011), but the adherence rates were moderate to low in Ethiopia and the reasons for not taking medications were many. Obviously, the costs incurred due to the life-long treatment and care for diabetes, as well as management of the complications, were high for Ethiopia, a country with low national per capita income.

The burden of diabetes seems to have reached a point where the government of Ethiopia should commence population prevention strategies to prevent modifiable risk factors for this disease. Ethiopia is among the most populous countries in Africa (International Diabetes Federation, 2013); i.e., with 3.3–6.5% prevalence the absolute number of persons or patients with diabetes is large. The magnitude of the disease is expected to rise sharply due to a relative increase in income and adaptation of western lifestyles, especially in cities (Nigatu, 2012). It is not an exception in Ethiopia. 80% of the diabetes burden occurs generally in LMICs (International Diabetes Federation, 2013), given the resource in these areas is incommensurate with need makes the situation dire. Currently, Ethiopia has a scarcity of evidence regarding non-communicable disease and alternative treatment of diabetes (Nigatu, 2012). Thus, efforts to prevent and control should be emphasized. Prevention is way beyond any other strategies to control diabetes

because the treatment and care of patients with diabetes, as well as its complications, is unaffordable for many in low-income countries, such as Ethiopia (Nigatu, 2012), (Jaffiol, 2011). Worse, the magnitude of the disease and risk factors are not well documented (Abebe et al., 2014), (Abebe et al., 2013). For example, even in the economic and political capital city of the country, care is still below acceptable standard in spite of gradual improvement (Feleke and Enquesselassie, 2011). An essential part of the response to the public health problem is evidence (Nigatu, 2012). For informed planning for prevention and strategies, it is imperative to build systems and encourage researchers to produce population level data.

Diabetes does not cause death by itself but predisposes to several complications that cause morbidity and mortality (Cefalu et al., 2011). As such, the studies included in this review showed a number of complications that led patients to hospitalization, disability and deaths, including retinopathy, neuropathy, depression, lower limb amputations, kidney diseases, hypertension, and anemia as well as depression. While diabetes metabolic problems affect every organ of our body, the most predominant causes of death are cardiovascular and kidney diseases across all with diabetes (Wiedermann et al., 2002). Diabetes mellitus is a complex, chronic illness requiring continuous medical care with multifactorial risk reduction strategies beyond serum glycemic control. With well-controlled serum glucose level alone, there is less likely that many of the complications occur, particularly if diabetes is diagnosed and managed early (Stolar, 2010). However, this standard treatment and care for enhancing insulin production or replacement only would not be sufficient. Diabetes needs additional adjuvant treatments. The most important ones should include control of hypertension as well reduction of absolute CVD risk scores with healthy eating, physical activity, tobacco cessation, angiotensin-converting-enzyme inhibitors, and statins (Boussageon et al., 2017). Unfortunately, the studies included in this review were less explorative to show the level of use of such treatments and changes in lifestyle.

The current review showed that even the primary treatment–glycemic control–was not effective in many of the included studies. The main reasons were non-adherence to the standard treatments–rather replacing them with traditional medicines or quit taking–, low self-awareness, no or little access to health care facilities, unaffordability, and poor service where each of these factors needs tailored interventions at different levels. This suggests poor quality care for persons with diabetes in Ethiopia and the services are barely designed to provide continuity of services required to effectively identify, monitor, and help patients better manage diabetes. Ethiopia has an effective primary healthcare system (i.e., health extension program), which worked well in reducing infectious disease. This system could be adapted to help people with diabetes improve self-management of diabetes, monitor and control glycemic levels and reduce risks of complications. Self-management is the cornerstone of overall diabetes management and diabetes educators are an integral part of the diabetes management team (Wild et al., 2004). However, this may be out of reach for now due to low educational level and self-awareness. Tools such as mobile applications, or simply short text messages, could help to notify patients for medication time, provide core points of counseling, and potentially more (Kebede et al., 2019). The point-of-care testing technology could also be the future of non-communicable disease testing and monitoring although the costs may be expensive.

The findings in this review have to be interpreted in light of important limitations. Firstly, there was limited evidence to provide more reliable and valid estimates at national and regional level as well as according to patient characteristics, including by sex, ages, residence etc. There could also be studies that were not identified due to limited access or that most local studies in Ethiopia remained on shelf. Secondly, all studies did not clearly stratify the types of metabolic disease variant, either type 1 diabetes, type 2 diabetes, gestational or others that need distinct treatment and prevention. Indeed, there are only speculations, and less knowledge about the predisposing causes of

type 1 diabetes that make it difficult to establish tailored prevention. Additionally, gestational diabetes is temporary and often disappears after birth, but may again appear later in life. Thereby, most of the results and discussions focused on type 2 diabetes. Thirdly, most of the studies were surveys, by which it is not possible to tell about actual cause and effect. Fourth, while we used extensive search, there could still be missed out studies. Further, it was not possible to do further quality assessment of each study we included in the review beyond what can be gleaned from the study design used and the journal the study is published on.

Overall, this review showed considerable prevalence of diabetes and its complications. It also showed the risk factors that are associated with diabetes prevalence and outcomes in Ethiopia. For effective management and care of diabetes and its complications, ongoing care and self-management in patients with diabetes should be the central theme. Moreover, there should be resource relocation to epidemiological surveillance and tailored prevention of modifiable risk factors as well as ongoing research into improving management and care.

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Ethical approval

The study is approved by the institutional ethical review board of MUSC.

Conflicts of interest

The authors report no potential conflicts of interest relevant to this article.

Author contributions

MG proposed and developed the concept. MG and KGB designed the study and led the analysis of the data. MG, KB, CJ identified review papers and summarized the review. MG, KB and CJ had full access to the reviewed papers and take responsibility for the integrity and accuracy of the analyses. CJ reviewed available manuscripts and estimated Kappa. MG, KB, CJ, HGY, TW, MA contributed to the interpretation, drafting and critical editing of the manuscript. All authors approved the final manuscript. We thank the reviewers for useful feedback.

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