Burden of Diabetes and Prediabetes in Nepal: A Systematic Review and Meta-Analysis

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REVIEW

Burden of Diabetes and Prediabetes in Nepal: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Unhealthy behaviors, such as energy-dense food choices and a sedentary lifestyle, both of which are established risk factors for diabetes, are common and increasing among Nepalese adults. Previous studies have reported a wide variation in the prevalence of prediabetes and diabetes in Nepal, and thus a more reliable pooled estimate is needed. Furthermore, Nepal underwent federalization in 2015, and the province-specific prevalence, which is necessary for the de novo provincial government to formulate local health policies, is lacking. This study aims to provide a comprehensive summary of the current literature on various aspects of diabetes in Nepal, i.e., the prevalence of prediabetes and diabetes as well as of the awareness, treatment, and control of diabetes in Nepal.

Methods: This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched three electronic databases—PubMed, Scopus, and Web of Science—using a comprehensive search strategy to identify eligible studies published up to April 2, 2020. Data on prevalence estimates of prediabetes and diabetes were extracted and pooled in a meta-analysis using a random effect model. Subgroup analyses and meta-regression were conducted to assess heterogeneity across the studies. The quality of included studies was assessed using the New Castle-Ottawa scale.

Results: We included 14 eligible studies that comprised a total of 44,129 participants and 3517 diabetes cases. Half of the included studies had good quality. Overall, the prevalence of prediabetes and diabetes was 9.2% (95% CI 6.6–12.6%) and 8.5% (95% CI 6.9–10.4%), respectively. Among the participants with diabetes, only 52.7% (95% CI 41.7–63.4%) were aware of their diabetes status, and 45.3% (95%

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CI 31.6–59.8%) were taking antidiabetic medications. Nearly one-third of those under antidiabetic treatment (36.7%; 95% CI 21.3–53.3%) had their blood glucose under control. The prevalence of prediabetes and diabetes gradually increased with increasing age and was more prevalent among males and urban residents. There was a wide variation in diabetes prevalence across the provinces in Nepal, the lowest 2% in Province 6 to the highest 10% in Province 3 and Province 4.
Conclusions: The prevalence of prediabetes and diabetes was high in Nepal, while its awareness, treatment, and control were low. Our findings call for urgent nationwide public health action in Nepal.

Keywords: Diabetes; Meta-analysis; Nepal; Prevalence; Systematic review

Key Summary Points

Very little is known about the burden of diabetes and prediabetes, treatment and control across provinces of Nepal.

Current evidence, using systematic review and meta analyses of 14 studies comprising 44,129 participants and 3517 diabetes cases, suggests prediabetes prevalence of 9.2% and diabetes prevalence of 8.5%.

Only a half of patients with diabetes were aware of their diabetic status, and even fewer were taking antidiabetic medication. Only a third of those under therapy had their blood glucose under control.

This study further suggests that prevalence of prediabetes and diabetes increased with age and was most prevalent among males and urban residents. Prevalence of diabetes was fivefold higher in Province 3 and Province 4 compared to Province 6.

BACKGROUND

The burden of diabetes has posed insurmountable challenges in both low- and high-income countries [1]. In 2019, an estimated 463 million adults worldwide, aged 20–79 years, lived with diabetes, and the number is predicted to increase to 700 million by 2045 [2]. Moreover, nearly half of diabetes cases remain undiagnosed, leading to various complications such as neuropathy, nephropathy, retinopathy, cardiovascular disease, and stroke [3, 4]. Nearly 21% and 13% of the deaths from ischemic heart disease and stroke, respectively, were attributed to high blood glucose levels [5, 6]. Although two-thirds of people with diabetes are believed to reside in low- and middle-income countries (LMICs), the actual estimates of diabetes burden and deaths are still unknown because of limited data from LMICs [2].

South Asia, the most populous region in the world, is home to nearly two-thirds of all global diabetes cases. One-fifth of all adults in South Asia have diabetes, and the number has nearly doubled between 1990 and 2016 in countries like India [7, 8]. Diabetes literature in South Asia is predominantly from India, and little is known about the overall burden of diabetes in Nepal, a South Asian country between India and China, which has recently witnessed an epidemiologic transition and subsequent growing epidemic of chronic conditions [9]. In 2017, nearly 10,145 deaths were attributed to diabetes, which was also ranked as the 11th most common cause of disability-adjusted life years (DALYs) in Nepal (1226 DALYs per 10,000 population) [10]. Earlier studies from Nepal have reported a wide variation in diabetes prevalence, ranging from 0.8 to 19%. Thus, a more reliable pooled estimate is needed. A previous systematic review based on ten studies published between 2000 and 2014 reported a prediabetes and diabetes prevalence of 10.3% (95% CI 6.1–14.4%) and 8.4% (95% CI 6.2–10.5%), respectively [11]. Given that most of the included studies in the previous meta-analysis [11] had a small sample size and were limited by geography and that recently nationwide estimates have been

published [12, 13], an update to the previous meta-analysis is deemed important.

Early detection and proper management of diabetes can delay disease progression, including a significant reduction in the risk of diabetes-related complications [14]. It is noteworthy that in low-income settings like Nepal, individuals present themselves to a health provider only when symptoms are obvious; consequently, the actual burden of disease is highly underreported. Therefore, focusing only on prevalent diabetes may undermine the true burden and mislead preventive strategies. Hence, stakeholders should be cognizant of other aspects of diabetes, such as the hidden burden of prediabetes, as well as the awareness, treatment, and control of diabetes among the general population. Currently, our knowledge of the prevalence of prediabetes, as well as on the awareness, treatment, and control of diabetes, mostly come from small-sized studies limited to small geographies [15]. We have the opportunity to provide more reliable estimates by pooling the previous studies.

Moreover, and most importantly, Nepal underwent federalization in 2015 with significant restructuring of the nation's administrative units and handed the administrative authority to the local provincial governments. However, so far, province-specific estimates in the context of Nepal's new federal set up are lacking, which may hinder devising an appropriate strategy for curbing the diabetes epidemic in Nepal, specifically at the administrative or provincial level.

Hence, with an overarching aim of providing a comprehensive summary of the current literature on various aspects of diabetes in Nepal, this study, using a meta-analytical approach, will estimate the (1) pooled prevalence of prediabetes and diabetes nationwide, (2) pooled prevalence of prediabetes and diabetes by provinces, and (3) prevalence of awareness, treatment, and control of diabetes in Nepal.

METHODS

Data Sources and Search Strategy

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16]. Two authors (NS and SRM) searched three databases—PubMed, Scopus, and Web of Science—using a comprehensive search strategy to identify eligible studies published in the English language up to April 2, 2020. Search terms used were "diabetes," "prevalence," "blood glucose," "glucose intolerance," and "Nepal." Secondary searches that included screening the references of the included studies and the previous systematic review [11] resulted in the identification of an additional five eligible studies for full-text screening (Fig. 1). Study selection and eligibility criteria, data extraction and quality assessment, and data synthesis and analysis are described in detail in supplementary methods. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

RESULTS

Literature Search, Characteristics and Quality of Included Studies

The search strategy identified 662 citations. An additional five studies were identified from secondary searches. A total of 351 non-duplicate studies were retrieved and were assessed for the title and abstract screening (Fig. 1). Exclusion of irrelevant and non-original studies resulted in 19 studies for full-text screening. Five studies were excluded for the following reasons: self-reported diabetes and no data on diabetes prevalence by age groups. Finally, 14 studies [12, 15, 17–28] were included in this systematic review and meta-analysis.

The characteristics of the included studies are provided in Table 1. Briefly, the 14 studies together had a total of 44,129 participants and 3517 diabetes cases. We included only

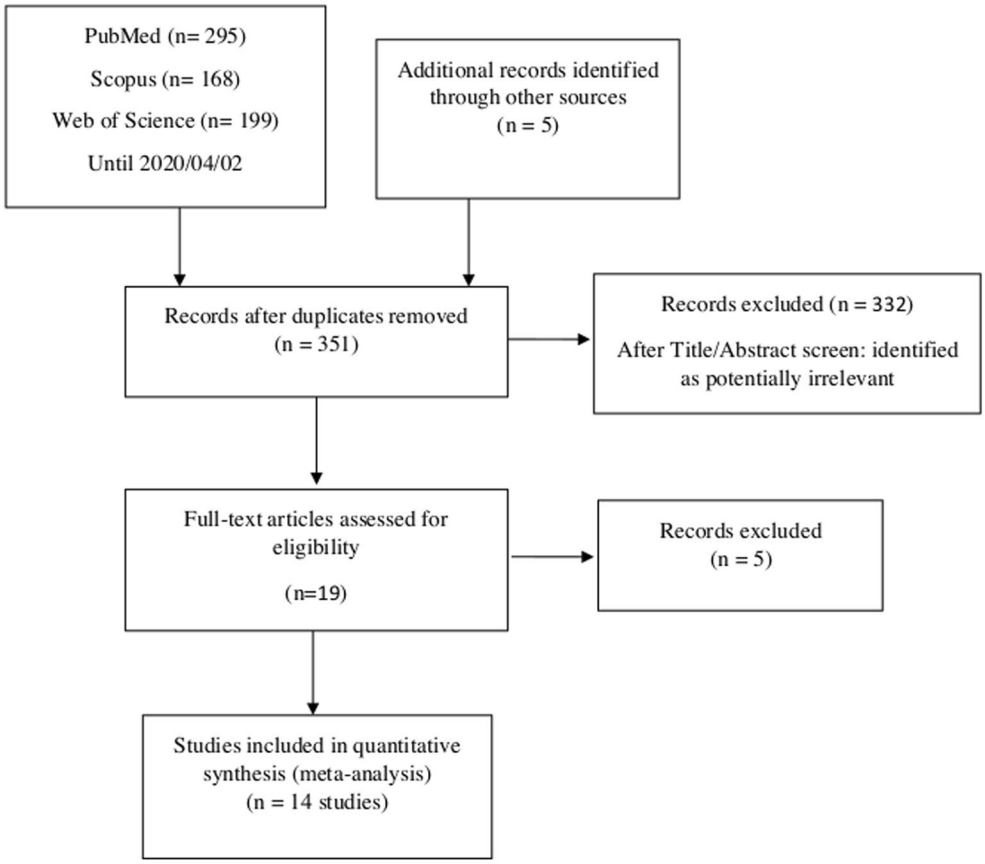

Fig. 1 PRISMA flow diagram for study selection for the systematic review and meta-analysis

participants aged ≥ 20 years old in the analysis. Similarly, prediabetes prevalence was reported in only ten studies with 22,658 participants and 3401 prediabetes cases. Except for one study [23], all included studies provided prevalence estimates for diabetes by gender, whereas four included studies [12, 17, 21, 26] provided similar estimates by urban/rural residence. Most of the included studies reported data from Province 1, Province 3, and Province 4. Only two nationwide studies reported data for all seven provinces of Nepal [12, 17].

Diabetes was defined in the included studies as previous physician-diagnosed diabetes, and/or taking antidiabetic medications, and/or a fasting blood glucose (FBG) of ≥ 126 mg/dl (7.0 mmol/l) or a 2-h oral glucose tolerance test (OGTT) blood glucose level of ≥ 200 mg/dl (11.1 mmol/l). Seven studies reported using FBG for diabetes diagnosis [15, 17, 19, 21, 24, 26, 27], five studies reported using both FBG and OGTT [12, 18, 20, 25, 28], one used FBG/urine [23], and one used the OGTT method [22]. These criteria for defining diabetes came from the World Health Organization (1985 and 1999) [29, 30] and the 1997 criteria from the American Diabetes Association (ADA) or its updates [31, 32]. Prediabetes was defined in the included studies as FBG level between 100 (5.6 mmol/l) and 125 mg/dL (< 7 mmol/l) or a 2-h OGTT blood glucose level between 140 (7.8 mmol/l) and 199 mg/dl (11 mmol/l).

The definition of diabetes awareness, treatment, and control was consistent between the included studies. Participants were considered to be aware of their diabetes status if a physician had previously told them that they had diabetes. Treatment of diabetes was defined as the current use of antidiabetic prescriptions. Control of diabetes was defined as a fasting blood

Table 1 Characteristics of included studies

Study	Survey year	Study city/province	Sample size (male/female)	Urban/rural areas	Age range	Prevalence		Diagnostic method
						Prediabetes	Diabetes	
Baral et al. 2000 [18]	1999	Dharan/Province 1	967 (487/480)	Urban	30–65	9.5	5.2	FBG/OGTT
Karki et al. 2000 [20]	1997–98	Dharan/Province 1	1840 (1040/800)	Urban	> 30	Not reported	6.3	FBG/OGTT
Singh and Bhattarai 2003 [26]	1999–2001	Kathmandu/Province 3	1841 (856/985)	Urban and rural	≥ 20	9.1	14.6	FBG
Sasaki et al. 2005 [22]	1990	Kathmandu/Province 3	592 (284/308)	Semi urban and rural	≥ 20	2.5	0.8	OGTT
Shrestha et al. 2006 [25]	2001–02	Kathmandu/Province 3	1012 (423/589)	Urban	≥ 40	11.5	19.0	FBG/OGTT
Ono et al. 2007 [27]	2006	Kathmandu/Province 3	740 (286/454)	Semi urban	> 20	19.2	9.5	FBG
Mehata et al. 2011 [21]	2005–06	Dharan/Province 1	2006 (1096/910)	Urban and rural	≥ 30	16.9	11.9	FBG
Sharma et al. 2011 [24]	2010	Province 1	14,009 (5327/8682)	Rural	≥ 20	Not reported	6.3	FBG
Sharma et al. 2013 [23]	2003–05	Dharan/Province 1	3218 (1542/1676)	Rural	≥ 20	Not reported	8.9	FBG/Urine
STEPS 2013 [17, 35]	2013	Nationwide	4143 (1336/2807)	Urban and rural	15–69	4.1	3.6	FBG
Gyawali et al. 2018 [11]	2016–17	Pokhara/Province 4	2310 (736/1574)	Semi urban	≥ 25	13.0	11.7	FBG
Dhungana et al. 2018 [19]	2014–15	Kathmandu/Province 3	345 (141/206)	Semi urban	18–70	11.1	10.5	FBG
Khanal et al. 2018 [28]	2014	Lamjung/Province 4	345 (154/191)	Semi urban	40–80	Not reported	15.7	FBG/OGTT
Selected NCDs 2019 [12, 13]	2017	Nationwide	11,253 (4313/6940)	Urban and rural	≥ 20	14.9	8.3	FBG/OGTT

FBG fasting blood glucose, *OGTT* oral glucose tolerance test

glucose level < 126 mg/dl among those under antidiabetic medication.

According to the New Castle-Ottawa scale, only half of the included studies were scored as good or very good quality (score 9–10) (Supplementary Table 1). Specifically, six studies scored lower in the selection bias domain [18, 20, 22, 24, 26, 27], and nine studies scored lower in the comparability bias domain [18–24, 26, 27] (Supplementary Table 1).

Prevalence of Prediabetes and Diabetes

The pooled prevalence of prediabetes and diabetes was found to be 9.2% (95% CI 6.6–12.6%) and 8.5% (95% CI 6.9–10.4%), respectively (Figs. 2, 3). However, there was substantial heterogeneity (I^2 = 97%) across the studies (Figs. 2, 3). The symmetrical funnel plot, as well as the non-significant Egger test, suggested no publication bias (p value 0.629) (Supplementary Fig. 1).

In the subgroup analysis by age, sex, and urban/rural residence, the prevalence of both prediabetes and diabetes gradually increased with increasing age (Supplementary Figs. 2 and 3) and was more prevalent among males and urban residents (Supplementary data). The high heterogeneity in the prevalence of prediabetes and diabetes, noted in the main analysis, existed even in the subgroup analysis by age (Supplementary Figs. 2 and 3) and gender (Supplementary data). Variation in the burden of prediabetes and diabetes was seen across provinces; prediabetes was most prevalent in Province 7 (19.0%; 95% CI 16.0–21.0%), whereas diabetes was more prevalent in Province 3 (10.0%; 95% CI 5.0–14.0%) and Province 4 (10.0%; 95% CI 6.0–14%) (Fig. 4 and Supplementary data).

In the meta-regression, the regression coefficient for the survey year, for both prediabetes and diabetes, was positive, but the finding was statistically non-significant (p = 0.067; Supplementary Figs. 4 and 5).

Awareness, Treatment, and Control of Diabetes

Among the participants with diabetes, around half of the participants were aware of their diabetes status (52.7%; 95% CI 41.7–63.4%). Less than half of the participants were taking antidiabetic medicines (45.3%; 95% CI 31.6–59.8%). Among those under antidiabetic medication, only around one third had their blood glucose controlled (36.7%; 95% CI 21.3–53.3%) (Supplementary Fig. 6).

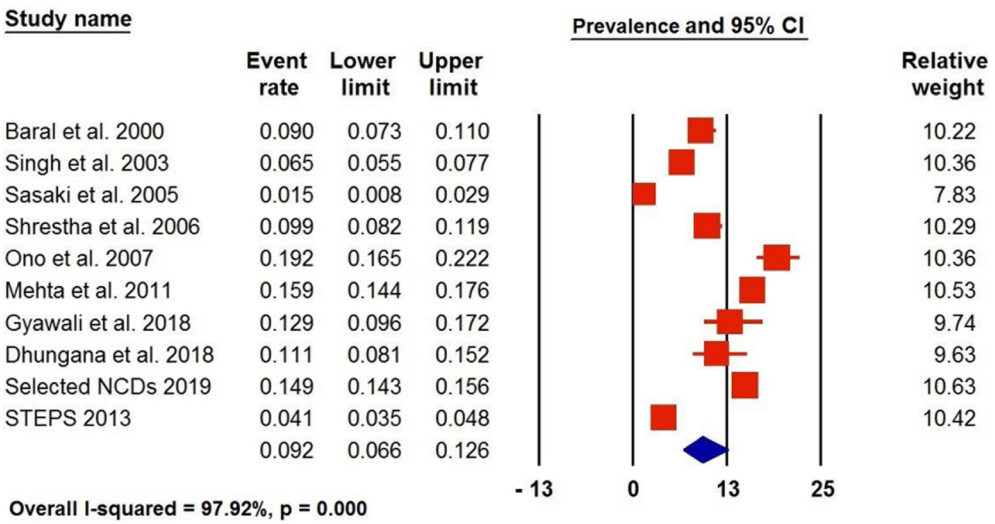

Fig. 2 Pooled prevalence of prediabetes among Nepalese adults (≥ 20 years)

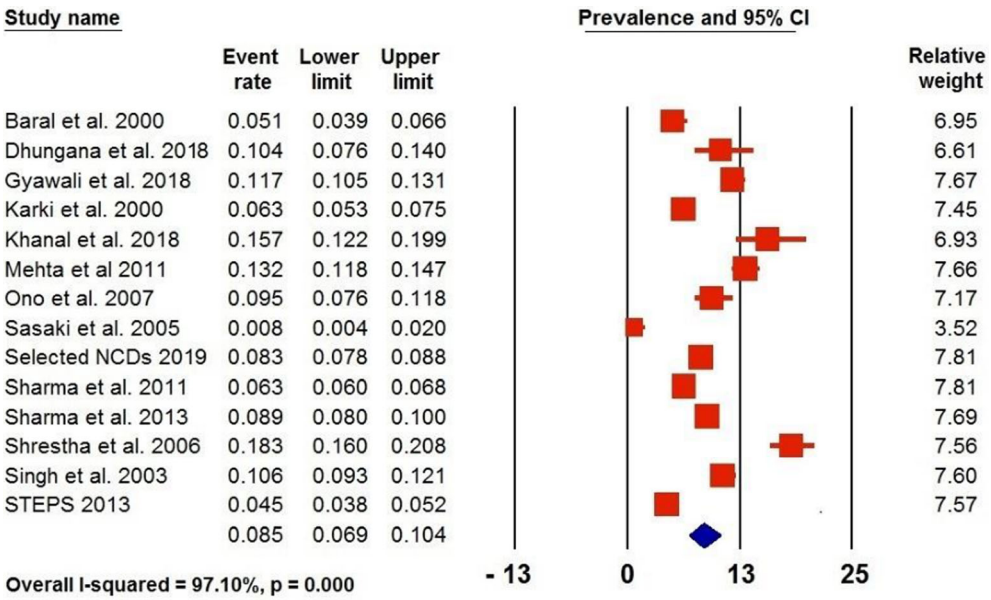

Fig. 3 Pooled prevalence of diabetes among Nepalese adults (≥ 20 years)

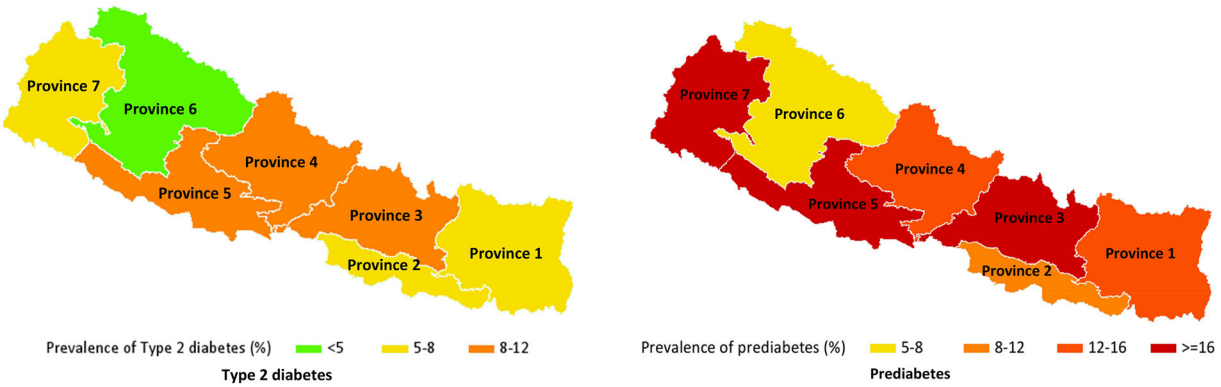

Fig. 4 Prevalence of prediabetes and diabetes disaggregated by Nepal's provinces (≥ 20 years)

DISCUSSION

This study comprehensively appraised the prevalence of prediabetes and diabetes among Nepalese adults. The pooled prevalence from the meta-analysis showed a high prevalence of prediabetes (9.2%) and diabetes (8.5%) but low awareness (52.7%) and treatment (45.3%) among diabetes patients and low diabetes control (36.7%) among those under antidiabetic treatment.

Our estimated prevalence for prediabetes was lower than in some of the previous studies from Nepal [12, 15, 21, 27] but comparable to others [18, 19, 25, 26]. Similarly, our estimated prevalence for diabetes was higher than in the earlier nationwide STEPS 2013 survey (3.6%) [17] but comparable to a recent nationwide survey on the prevalence of selected NCDs in Nepal (8.3%) [12]. A rapid surge in diabetes prevalence in recent years in Nepal is predicated based on the local social and cultural factors such as increasing urbanization and changes in food and lifestyle-related behaviors [33]. Increasing urbanization and urban-centric economic prosperity also incur rural to urban migration of population with changes in lifestyles [30]. The

rural population with high physical activities and low-calorie diets who have migrated to urban cities often change their diet to fast and junk food high in refined carbohydrates, sugar, and fats coupled with minimal physical activities [33]. In addition, the urban cities in Nepal neither have exercise-friendly spaces nor are the currently available spaces conducive to exercise because of commercial encroachment, high air pollution levels, and low awareness of benefits of exercise [30]. Paradoxically, the improving economy in Nepal seems to facilitate a more sedentary lifestyle, with a high intake of food (increase in affordability) with minimal energy expenditure [33]. Our findings corroborate the epidemiologic transition and increasing diabetes prevalence in the South Asian region [34]

Notably, cardio-metabolic and chronic diseases risk factors are high among the Nepalese population. The 2013 STEPS survey reported that only 0.4% of the Nepali population was completely free of the eight established risk factors for non-communicable diseases [35]. In another study, about 68% of the participants had at least one cardiometabolic risk factor [36]. These facts imply that in the absence of effective intervention strategies against diabetes, its burden may continue to rise among Nepalese. In fact, our coefficient from the meta-regression analysis suggested an increasing trend in diabetes prevalence from 1990 to 2017, although the finding was statistically non-significant, which could be due to a smaller number of studies (n = 14).

The findings related to the high prevalence of prediabetes and low prevalence of awareness, treatment, and control were concerning and may further explain the high burden of diabetes noted in this study. The prediabetes population is a crucial subgroup of interest because an estimated 5–10% of the prediabetes population progress into diabetes annually if no lifestyle intervention is initiated [37]. More than half of the participants with diabetes were unaware of their conditions or lacked treatment, which implies that they may not be benefiting from screening services or receiving regular care and/or may be unable to afford high treatment costs associated with diabetes. Although similar findings from Nepal are lacking, low awareness has been reported in global settings [38–41]. Previously, low awareness, treatment, and control of hypertension have been documented in a nationwide study among the Nepalese [42]. Given that timely diagnosis and prompt management of diabetes can prevent progression into diabetes complications, policymakers and stakeholders should be cognizant of such proxy indicators to prevent future epidemics.

We found a wide variation in diabetes prevalence across the provinces in Nepal, the lowest 2% in Province 6 to the highest 10% in Province 3 and Province 4. The province-wise differences in diabetes prevalence may also account for the high heterogeneity across the studies in our meta-analysis because the included studies that we pooled in the meta-analysis were conducted across different regions in Nepal. Diabetes is an important tracer of urbanization and is markedly shaped by environmental, social, political, and commercial determinants of health [30, 33, 43]. Province 3, the most developed province in Nepal with a human development index (HDI) of 0.560, had a nearly fivefold higher prevalence of diabetes compared to Province 6, the least developed province in Nepal with an HDI of 0.486 [44]. Provinces with greater rates of urbanization have also become a flashpoint for dietary transition with increased consumption of plant fat, sugar, and animal products [45]. The province-wise differences in diabetes burden may have policy implications at the local level. In the immediate term, provincial and municipal governments should take the initiative to increase awareness on lifestyle-related behaviors, including creating exercise-enabling environments such as allocation of public spaces, parks, and greeneries [30, 33]. Since the provincial set-up of Nepal is a recent phenomenon, information on health indicators at the provincial level is currently unavailable. Our study is the first of its kind to provide the burden of diabetes at the provincial level. Given that the provincial government is responsible for local governance, it may find the results helpful in understanding the local needs and identifying inequalities so that areas for public health actions can be prioritized.

Individual characteristics such as increasing age, male gender, and urban residence were associated with increased prevalence of diabetes in our study and are consistent with previous studies from Nepal [11, 17, 46] and across the globe [39, 40, 47, 48]. Urban areas saw a two-fold higher prevalence than rural areas. The urban-rural disparity in health outcomes is evident globally [49, 50] and also exists in Nepal [35]. Specifically, a sedentary lifestyle and access to high-calorie processed food and sugar-sweetened beverages are high in urban areas of Nepal, which increases the likelihood of diabetes among urban residents [35].

Limitations

This major limitation of this study is the high heterogeneity between the reported diabetes prevalence across the included studies. We could not perform additional subgroup analysis for the factors that may have contributed to heterogeneity across the included studies, such as the diagnostic method. We also could not perform a sensitivity analysis by removing studies that scored to be of poor quality or had a high risk of bias. Only two nationwide studies were available, and other included studies were mostly from Province 1 and 3. Additionally, there was a paucity of studies that reported on awareness, treatment, and control of diabetes from all over Nepal. Hence, it was not feasible to generate province-wise data for awareness, treatment, and control of diabetes. We did not include studies published in local journals that were not indexed in the selected databases and studies published in a non-English language. Nevertheless, we conducted comprehensive searches of three different databases to ensure that all relevant publications are included.

In line with the Sustainable Development Goals, the Multi-Sectoral Action Plan for Prevention and Control of NCDs by the government of Nepal aims to reduce NCDs, including diabetes, by one quarter by 2025 [51]. With a high burden of diabetes on the one hand and low awareness and treatment as well as poor availability of services for its prevention and management on the other [52], achieving such a goal may be challenging. Understanding the disease burden and identifying the high-risk populations and existing inequalities can help the provincial and federal government to prioritize resources and develop targeted interventions to meet such goals.

CONCLUSIONS

The prevalence of prediabetes and diabetes is high in Nepal, whereas its awareness, treatment, and control are low. Inequalities in the prevalence were seen at the provincial or the local government level and by individual characteristics. Further studies are needed to understand the underlying geographic drivers of the growing diabetes epidemic in Nepal. Given the scarcity of prevalence estimates at the provincial level, further studies in the provinces with limited data on the prevalence of prediabetes and diabetes, as well as nationwide studies with provincial-level information on awareness, treatment, and control of diabetes, are warranted. Our findings call for urgent nationwide public health actions such as screening people at risk of diabetes and prevention measures of the disease. Particularly mass screening aimed to identify the prediabetes cases and increasing awareness on diabetes management and lifestyle behaviors may be important. The findings can also inform local stakeholders and policymakers to prioritize areas for public health action and/or develop targeted interventions for the at-risk populations to curb the diabetes epidemic in Nepal.

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Disclosures. Nipun Shrestha, Shiva Raj Mishra, Saruna Ghimire, Bishal Gyawali, and Suresh Mehata have nothing to declare.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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