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RESEARCH ARTICLE

Prevalence of metabolic dysfunctionassociated fatty liver disease and its association with glycemic control in persons with type 2 diabetes in Africa: A systematic review and meta-analysis

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Abstract

Metabolic dysfunction-associated fatty liver disease (MAFLD) and type 2 diabetes (T2D) are interconnected metabolic disorders with significant health implications. However, a comprehensive understanding of the extent of their co-occurrence in Africa is lacking. The aim of this review was to determine the prevalence of MAFLD and its association with glycemic control (HbA1c) in persons with T2D in Africa. A systematic search was conducted on PubMed, Medline, Embase, Scopus, Global Health, and Web of Science from their inception to December 6, 2023. Data on MAFLD prevalence and correlation coefficients regarding its association with glycemic control were pooled through random effect meta-analyses. Potential sources of heterogeneity were investigated using subgroup analysis and metaregression. A total of 10 studies were included in the meta-analysis of MAFLD prevalence, while 2 were incorporated in the analysis of the association between MAFLD and glycemic control. The pooled prevalence of MAFLD in persons with T2D was 48.1% (95% CI: 36.1-60.3). The subgroup analysis revealed regional variations in MAFLD prevalence, with rates of 44.7% (95% CI: 28.7–62.0) in sub-Saharan Africa and 55.3% (95% CI: 36.2–73.0) in Northern Africa. Additionally, we observed an increasing trend in MAFLD prevalence, recording 55.1% (95% CI: 43.6–66.1) in the recent five years. There was a weak positive correlation between MAFLD and HbA1c (r = 0.33, 95% CI: 0.18–0.47). The findings of this study highlight a high prevalence of MAFLD in persons with T2D in Africa, with a suggested link between MAFLD and suboptimal glycemic control. Therefore, healthcare providers should prioritize the screening and management of MAFLD in individuals with T2D to enhance their metabolic health.

Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD), formerly referred to as nonalcoholic fatty liver disease (NAFLD), has emerged as a significant public health concern, with a global prevalence of 32.4% [1]. MAFLD is the commonest form of liver disease and it constitutes the majority of liver-related morbidity and mortality cases globally [2,3]. The defining features of MAFLD include hepatic steatosis, coupled with the presence of either T2DM, overweight/obesity, or evidence of metabolic dysregulation [4,5].

T2D is a major risk factor for MAFLD and a predictor of poor liver-related health outcomes among people living with MAFLD [6,7]. In a previous meta-analysis, researchers found a 55.5% prevalence of MAFLD among individuals with T2D worldwide (compared with the 32.4% in the general population) [7]. Notably, studies indicate that while most individuals with MAFLD do not experience progressive disease, those with concurrent T2D face a twofold risk of developing advanced liver disease including cirrhosis and advanced fibrosis [8]. Moreover, MAFLD has been linked to an elevated risk of cardiovascular disease, compounding the existing burden in individuals with diabetes [9]. Recent study has reported that among persons at risk for MAFLD, persons with T2D pose nearly a three-fold risk of chronic kidney disease [6]. Even more disconcerting, studies have demonstrated that among individuals with MAFLD, those with T2D are at a higher risk of liver-related mortality compared with those without T2D [10–12].

Research has established a bidirectional relationship between T2D and MAFLD, with insulin resistance (IR) emerging as a pivotal mechanism [13]. Notably, studies have demonstrated that IR in persons with T2D can foster hepatic fat accumulation by facilitating heightened delivery of free fatty acids (FFAs) and stimulating hepatic lipogenesis [13,14]. Conversely, MAFLD has been found to exacerbate IR in the liver, thereby worsening glycemic control and increasing the risk of T2D and its progression [13,14]. In addition to IR, other factors such as genetic predisposition, inflammatory pathways, and the gut-fat-liver axis have been implicated in the link between these conditions [13,15].

Given the intricate relationship between T2D and MAFLD, along with its implications for health, clinical practice guidelines recommend screening individuals with diabetes for MAFLD and advanced liver fibrosis [16,17]. However, evidence supporting this recommendation in Africa is currently limited. The estimated prevalence of MAFLD among individuals with T2D in Africa stands at 30.4%, a figure derived from a synthesis of only four studies [7]. This represents a modest fraction of the total 88 studies considered globally as of September 2018, highlighting substantial gap in our understanding of this crucial health connection in the African context [7]. Africa is experiencing a rapid epidemiological transition, marked by changes in lifestyle, diet, and an increase in the prevalence of metabolic diseases [18]. As of 2021, the continent had 24 million adults grappling with diabetes, with projections indicating a 134% surge in these cases by 2045 [19]. Concerningly, the burden of MAFLD is expected to rise in tandem with these changes. This underscores the urgent need for comprehensive research initiatives in the African context to address this health challenge and inform tailored strategies for prevention and management.

The scarcity of data on the epidemiology of MAFLD and T2D in Africa may be a critical limitation in devising region-specific preventive and management strategies. Understanding the prevalence of MAFLD in this demography is crucial, as it can influence healthcare policies, resource allocation, and early intervention efforts. Therefore, this study aimed to determine the prevalence of MAFLD (primary outcome) and its association with glycemic control (HbA1c) in persons with T2D in Africa (secondary outcome).

Methods

Prior to this study, an extensive search of electronic medical databases was done to ensure no pre-existing systematic review on this study had been conducted. Following this, a protocol for the review was developed and duly registered on PROSPERO (CRD42023491271). The review process adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (S1 Checklist) [20].

Search strategy

A three-step approach was used to identify all relevant studies for this review. Initial search was conducted on PubMed, Medline, Embase, Scopus, Global Health, and Web of Science from their inception to December 6, 2023. These were then supplemented with additional search on Africa-specific databases including African Index Medicus (AIM), and African Journals Online (AJOL). Furthermore, we meticulously examined the reference lists of pertinent studies to ensure a thorough exploration of the available literature. The search strategy for this review was built on the terms "non-alcoholic fatty liver" or "metabolic dysfunction-associated fatty liver", "type 2 diabetes", and "Africa". Controlled vocabulary and keywords to the search terms were used, with the Boolean operators 'OR' and 'AND' applied appropriately. No limits were applied to the search. The full details of the search strategy are provided in (S1 Text).

Inclusion and exclusion criteria

The inclusion criteria for this review were: 1) observational study design; 2) persons with T2D; 3) studies conducted in an African country; 4) MAFLD prevalence was provided or calculable with enough data provided; 5) involved adult participants aged 18 years or older; and 6) studies published in English language.

Studies were excluded if we were unable to ascertain how MAFLD was diagnosed (e.g., imaging modalities, hepatic steatosis index, liver-spleen attenuation index, fatty liver index, or liver biopsy). However, studies were included irrespective of the absence or presence of secondary liver disease etiologies (such as excessive alcohol consumption) in the T2D participants. This was to enable us to capture studies conducted both before and after the shift from the term NAFLD to MAFLD.

Study selection and quality assessment

The articles retrieved from our search were imported into Endnote 20 to remove duplicate records. The remaining articles were then uploaded to Rayyan (https://www.rayyan.ai/) for title, abstract, and full-text screening. Relevant information from each study were extracted using a preconceived and standardized data extraction matrix in Microsoft excel. The information retrieved included first author's name, publication year, country, study design, sample characteristics (sample size, gender distribution, average age of participants, years lived with T2D, average HbA1c, body mass index), and data on MAFLD including the number of T2D participants with the disease and diagnostic tool used. The study selection and extraction of data were executed by two independent reviewers (EE and SA), with any disagreements resolved through discussion with a third reviewer (PAD).

A quality-weighing approach was used to assess the methodological limitations of the included studies. We used the Joanna Briggs Institute (JBI) checklist for prevalence studies [21]. This tool addresses 9 critical questions with response options, "Yes", "No", "Unclear" and "Not applicable". We determined that studies that had 7–9, 5–6, and less than 5 "Yes" were having low, moderate, and high risk of bias respectively.

Data analysis

A logit transformation of the prevalence data on MAFLD was performed as recommended by Warton and Hui [22], with the 95% confidence interval (CI) calculated using the Clopper-Pearson interval. A DerSimonian-Laird's random-effect model meta-analysis was used to pool the prevalence of MAFLD. As a secondary outcome, we pooled the correlation coefficients (r)across studies to estimate the association between MAFLD and HbA1c. The strengths of the pooled correlation coefficients were interpreted as weak, moderate, and strong associations for r < 0.4 (or > -0.4), between 0.4 and 0.7 (or -0.4 to -0.7), and > 0.7 (or < -0.7), respectively [23,24]. We assessed heterogeneity between studies using the I² statistic, with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively [25]. Subgroup analysis and meta-regression were conducted to identify potential sources of heterogeneity. The variables considered included African regions (sub-Saharan vs Northern), diagnostic modalities for MAFLD (ultrasound vs index-based tests), and year of publication (< 2019 vs > 2019). The 2019-year cutoff was chosen to ensure an equal distribution of studies (n = 5) in each subgroup, thereby mitigating potential selection bias related to the imbalance of data points in each group. To assess the impact of each individual study on the overall results, a leave-one-out sensitivity analysis was conducted by systematically omitting one study at a time. The presence of publication bias was evaluated using Egger's regression-based test [26] and Begg's rank correlation test [27], with p < 0.05 indicating significant publication bias.

Results

A total of 659 references were identified from our search, consisting of 652 records from major databases (PubMed, Medline, Embase, Scopus, Global Health, and Web of Science) and seven from other supplemental searches on AJOL, AIM, and reference lists of relevant articles. Having removed duplicate and non-relevant records, 10 articles were ultimately included in this review (**Fig 1**) [20].

Characteristics of included studies

Full details of the characteristics of the included studies are presented in Table 1. This review consisted of nine cross-sectional and one case control studies published between 2011 and 2023. The studies were conducted in 6 different Africa countries, with majority coming from Nigeria (n = 3) [28–30], followed by Ethiopia (n = 2) [31,32], Morocco (n = 2) [33,34], and one each from Egypt [35], Ghana [36], and Sudan [37]. A total of 1667 T2D participants were involved, with the sample size ranging from 80 to 281 across studies. Nine studies provided the gender proportion of the participants, with females constituting 61.1%. The participants had a mean age above 50 years and have lived with diabetes for periods ranging from 4 to 10 years. Majority of them were overweight and obese (BMI > 25 kg/m²) and had poor glycemic control (HbA1c > 7%). Diagnosis of MAFLD was based mostly on ultrasonography, with just a few using Fatty Liver Index and Hepatic Steatosis Index.

Quality assessment of included studies

Full detail of the quality assessment is shown in (S1 Table). The quality score across studies ranged from 8 to 3, with a mean score of 6.1. Majority (n = 6) of the studies were of low risk of bias, having a score above 7 [29–32,34,36]. In contrast, four studies fell below a cut-off score of 5, indicating a higher risk of bias [28,33,35,37]. Methodological flaws were identified in various areas, including a lack of clarity regarding participant response rates, appropriateness of the sample frame, sampling methodology, adequacy of sample size, and the statistical analysis

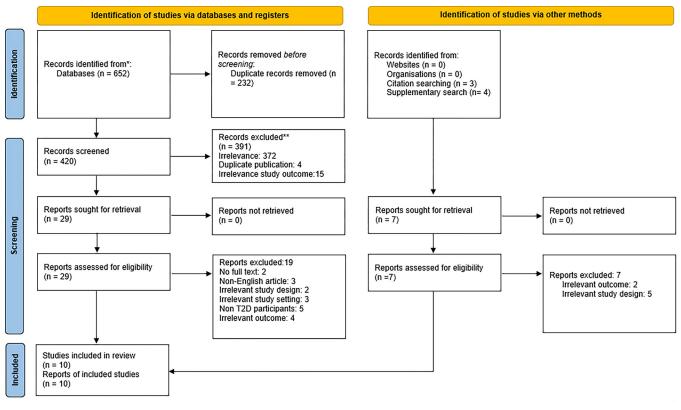


Fig 1. PRISMA flow chart summarizing the article selection process.

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Table 1. Characteristics of included studies.

First author (Year)	Country	Design	Sample size	Female %	Mean age	Mean diabetes duration	Mean HbA1c	Mean BMI	Diagnostic tool of MAFLD	MAFLD prevalence	HbA1c correlation
Zawdie (2018) [<u>31]</u>	Ethiopia	Cross- sectional	96	53.1	NR	NR	NR	23	Ultrasound	73	NR
Olusanya (2016) [29]	Nigeria	Case control	168	64.9	53.2	NR	NR	28.47	Ultrasound	16.7	NR
Afolabi (2018) [<u>30]</u>	Nigeria	Cross- sectional	80	62.5	60.9	NR	8.5	25.9	Ultrasound	68.8	r = 0.270 p = 0.015
Abebe (2022) [<u>32</u>]	Ethiopia	Cross- sectional	101	39.6	NR	4	8	25.82	Fatty Liver Index	58.4	r = 0.35 p = 0.008
Wiafe (2023) [<u>36</u>]	Ghana	Cross- sectional	218	78.0	NR	NR	NR	NR	Ultrasound	51.4	NR
Assarra (2022) [<u>34]</u>	Morocco	Cross- sectional	180	NR	60	9.2	10.4	NR	Ultrasound	45.6	NR
El-Ashmawy (2019) [<u>35]</u>	Egypt	Cross- sectional	270	46.7	52.6	7.4	NR	NR	Ultrasound	73.3	NR
Almobarak (2015) [37]	Sudan	Cross- sectional	167	53.3	NR	NR	NR	NR	Ultrasound	50.3	NR
Fennoun (2020) [<u>33]</u>	Morocco	Cross- sectional	281	76.9	54.15	10.5	10.23	29.53	Hepatic Steatosis Index	45.2	NR
Onyekwere (2011) [<u>28]</u>	Nigeria	Cross- sectional	106	55	57.2	7.4	NR	31	Ultrasound	9.5	NR

Abbreviations: BMI-body mass index, MAFLD-non-alcoholic fatty liver disease, NR-not reported.

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Study	Cases	Total	Prevalence (%)	95% CI	Weight	Events per 100 observations	
Zawdie (2018)	70	96	72.9	[62.9; 81.5]	9.8%	_ 	
Olusanya (2016)	28	168		[11.4; 23.2]	9.9%		
Afolabi (2018)	55	80	68.8	[57.4; 78.7]	9.7%		
Abebe (2022)	59	101	58.4	[48.2; 68.1]	10.0%		
Wiafe (2023)	112	218	51.4	[44.5; 58.2]	10.3%		
Assarrar (2022)	82	180	45.6	[38.1; 53.1]	10.3%		
El-Ashmawy (2019)	198	270	73.3	[67.6; 78.5]	10.3%		
Almobarak (2015)	84	167	50.3	[42.5; 58.1]	10.2%		
Fennoun (2020)	127	281	45.2	[39.3; 51.2]	10.4%		
Onyekwere (2011)	11	106	10.4	[5.3; 17.8]	9.1%		
Random effects model		1667	48.1	[36.1; 60.3]	100.0%		
Heterogeneity: $l^2 = 95\%$, $\tau^2 = 0.5992$, $p < 0.01$ 0 20 40 60 80 100 Prevalence (%)							0

Fig 2. Forest plot for MAFLD prevalence in persons with T2D.

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employed. While the included studies presented prevalence rates and clearly specified the number (n) of T2D patients with MAFLD, none of them provided the confidence interval for the estimates.

Prevalence of MAFLD

The prevalence of MAFLD ranged from 10.4% (95% CI: 36.1–60.3) in Nigeria [28] to 73.3% (95% CI: 67.6–78.5) in Egypt [35]. The pooled prevalence of MAFLD was 48.1% (95% CI: 36.1–60.3). There was a significantly high heterogeneity among the studies ($I^2 = 95\%$, p < 0.01) as shown in Fig 2.

Sensitivity analysis

A leave-one-out sensitivity analysis was conducted to assess the impact of each individual study on the overall results. The result showed that no single study had a significant influence on the pooled prevalence of MAFLD (S1 Fig).

Subgroup and meta-regression analysis

As shown in S2 Fig, the subgroup analysis by region revealed a 44.7% (95% CI: 28.7–62.0) prevalence in sub-Saharan Africa and a 55.3% (95% CI: 36.2–73.0) prevalence in Northern Africa. The prevalence of MAFLD according to year of study publication recorded 40.5% (95% CI: 18.6–67.0) in articles published before 2019 and 55.1% (95% CI: 43.6–66.1) for those published from 2019 till date. Based on diagnostic modalities, the prevalence of MAFLD for ultrasound and index-based tests was 47.0% (95% CI: 31.8–62.8) and 51.2% (95% CI: 38.4–63.8) respectively. The test of subgroup difference (X^2) in MAFLD prevalence did not show a significant variation. The result of the meta-regression revealed that the region, year of study publication, and diagnostic modalities did not significantly influence the overall prevalence of MAFLD among persons with T2D in Africa (Table 2).

Table 2. Subgroup and meta-regression.

Subgroup	Studies	Prevalence (95% CI)	<i>I</i> ² (%)	P value	X ² value	P value	Coefficient	P value
Africa region					0.63	0.43	-0.4211	0.47
Sub-Saharan	7	44.7 (28.7-62.0)	96	< 0.01				
North	3	55.3 (36.2-73.0)	96	< 0.01				
Publication year					0.95	0.33	-0.5794	0.26
< 2019	5	40.5 (18.6-67.0)	97	< 0.01				
<u>≥</u> 2019	5	55.1 (43.6-66.1)	93	< 0.01				
Diagnostic modality				< 0.01	0.16	0.69	-0.1850	0.79
Ultrasound	8	47.0 (31.8-62.8)	96	< 0.01				
Index-based	2	51.2 (38.4-63.8)	81	0.02				

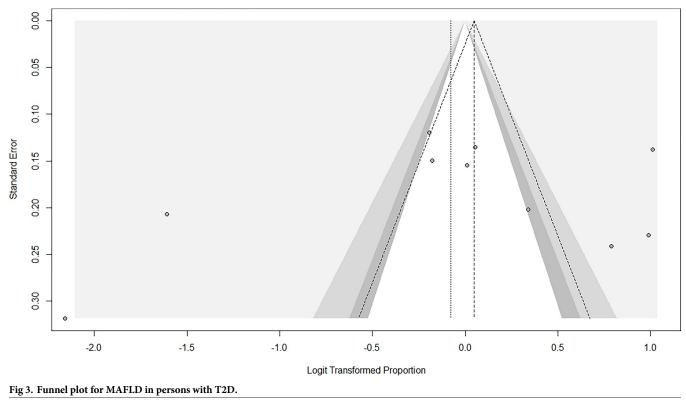
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Publication bias

The funnel plot for studies that assessed the prevalence of MAFLD among persons with T2D showed no asymmetry, indicating that no publication bias was present (Fig 3). This was statistically confirmed with Egger's regression-based test (p = 0.475) and Begg's rank correlation test (p = 0.929).

Association between MAFLD and glycemic control

Two articles assessed the association between MAFLD and HbA1c, with both identifying a significant positive correlation between these variables [30,32]. The correlation coefficient recorded 0.27 in Afolabi et al.'s study [30] and 0.35 in Abebe et al.'s study [32]. As shown in



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Author(s) and Year	Sample SizeCo	prrelation Coefficient (r)	F	Fisher's z _r [95% Cl]		
Afolabi (2018)	80	0.27		0.28 [0.05, 0.50]		
Abebe (2022)	101	0.35	· 	0.37 [0.17, 0.56]		
RE Model (Q = 0.34, df	= 1, p = 0.56; l ² =	0.0%)		0.33 [0.18, 0.47]		
	[1	1]		
	-3	-1.39	0	1.39		
	Fis	her's z Transformed Cor	relation Coefficient			

Fig 4. Forest plot for the association between MAFLD and glycemic control.

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Fig 4, the result of the meta-analysis indicates a weak positive correlation between MAFLD and HbA1c (r = 0.33, 95% CI: 0.18–0.47).

Discussion

Previous global meta-analysis has identified the prevalence of MAFLD among persons with T2D in Africa to be 30.4% [7]. However, this estimate was derived from only four studies in a subgroup analysis, raising concerns about its representativeness across diverse populations and healthcare contexts in Africa. Our systematic review and meta-analysis, focusing on the African continent, addresses this gap and provides novel insights into the prevalence of MAFLD and its association with glycemic control among individuals with T2D.

Our meta-analysis, incorporating data from ten studies, revealed a substantial 48.1% prevalence of MAFLD among individuals with T2D in Africa. This prevalence was notably high in both Northern and sub-Saharan Africa, indicating that MAFLD poses a significant burden that transcends geographical barriers within the region. Interestingly, our findings surpass the prevalence of MAFLD in the general population in the same region, which was determined to be 28.2% [38]. This high prevalence is concerning and supports the American Diabetes Association's recommendations for screening, early detection and treatment of MAFLD in persons with T2D [16].

In comparison to global and regional estimates in other continents, our findings suggest a lower prevalence of MAFLD among individuals with T2D in Africa. For instance, Younossi et al. reported a 55.5% prevalence of MAFLD among individuals with T2D globally, with rates exceeding 50% across Asia, Europe, and Latin America [7]. However, with the increasing adoption of Westernized lifestyle (a factor known to perpetuate MAFLD and T2D) in Africa [39], it is likely that future studies will observe an increasing trend in the prevalence rate. Notably, our subgroup analysis revealed a noticeable increase in the prevalence rate of MAFLD among persons with T2D in Africa, recording 55.1% in studies published after 2019. This indicates a changing landscape and underscores the need for continuous monitoring and intervention strategies to address the rising burden of MAFLD among individuals with T2D in the African continent.

HbA1c serves as a strong predictor of complications associated with diabetes, as well as diabetes-related deaths. Persons with T2D and exhibiting elevated HbA1c levels face an increased risk of developing both macrovascular and microvascular complications [40,41]. Consequently, treatment objectives for T2D frequently emphasize the importance of maintaining optimal HbA1c levels [42]. A previous study has demonstrated that improvement in glycemic control in persons with T2D was associated with improvement in MAFLD [43]. Thus, our finding that MAFLD is positively associated with HbA1c underscores the interconnected nature of these conditions and highlights the need for targeted interventions.

Although the underlying mechanism of the association between MAFLD and glycemic control is not fully understood, studies have delineated plausible pathways by which improvements in glycemic control might improve the course of MAFLD. In individuals with diabetes and MAFLD, de novo lipogenesis (DNL) significantly contributes to hepatic triglyceride accumulation. Improved glycemic control can restrict the availability of glucose as a substrate for hepatic DNL [43]. Additionally, glucose plays a role in activating stellate cells, which is pivotal in the fibrotic response of MAFLD [44]. Therefore, optimizing glycemic control has the potential to modulate the fibrotic response to lipid and inflammatory factors, key drivers of advanced MAFLD.

The findings of this study present significant implications for healthcare practice and public health policy in Africa. It is imperative for healthcare providers to adopt an integrated approach encompassing dietary interventions, physical activity promotion, weight management strategies, and pharmacological modalities targeting enhanced glycemic control and liver health. Moreover, clinicians must recognize the interconnected nature of T2D and MAFLD and integrate screening protocols into routine diabetes care, particularly among those with poorly controlled T2D. By addressing both T2D and MAFLD in tandem, healthcare providers can mitigate the risk of disease progression and associated complications, ultimately improving the quality of care for affected individuals.

Strength and limitation

The major strength of our study was the inclusion of relatively higher number of studies, providing a more comprehensive assessment of the prevalence of MAFLD among individuals with T2D in Africa. However, the findings may not be fully generalizable to all populations in Africa as the included studies were from only six countries and excluded non-English articles. Moreover, our result on the association between MAFLD and glycemic control was gleaned from only two studies. Furthermore, the meta-analysis on the MAFLD prevalence exhibited a high level of heterogeneity which remained unexplained even after examining some of the potential moderators. It is worth noting that the studies incorporated in this review excluded participants with secondary liver etiologies (such excessive alcohol consumption) which does not capture the entire spectrum of MAFLD.

Recommendations for future research

Future research on T2D and MAFLD in Africa should prioritize several key areas to advance our understanding and improve clinical care in persons with these conditions. Firstly, future studies should aim to include a diverse representation of populations across different regions within Africa to ensure the generalizability of findings. Additionally, longitudinal studies are needed to unravel the underlying mechanisms linking T2D and MAFLD in the African context. Such research is critical for translating findings into actionable recommendations for both clinical practice and public health policy. Given the evolving paradigm shift from NAFLD to MAFLD, research endeavors in Africa must adapt to encompass these changes to comprehensively grasp the spectrum of MAFLD and its impact on health in the African population.

Conclusions

This review identified a high prevalence of MAFLD among persons with T2D which is likely to transcend across the geographical areas of Africa. MAFLD was positively associated with

glycemic control. Our findings highlight the importance of adopting a comprehensive approach to diabetes care in Africa, one that includes regular screening and intervention for MAFLD.

Supporting information

S1 Checklist. PRISMA 2009 checklist. (DOCX)

S1 Fig. Forest plot of sensitivity analysis. (DOCX)

S2 Fig. Forest plots of subgroup analysis. (DOCX)

S1 Table. Quality assessment of included studies. (DOCX)

S1 Text. Search strategy. (DOCX)

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