BMC Public Health

RESEARCH

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The prevalence of Hemophilia A in males in Africa: evidence from a systematic review and meta-analysis

Mitiku Bonsa Debela[1*], Kebebe Bekele[1] and Demisu Zenbaba[1]

Abstract

Background Hemophilia A (HA) is an X-linked recessive bleeding disorder characterized by reduced or absent coagulation factor (F) VIII activity. The empirical evidence on the prevalence of HA in Africa has reported inconsistent findings and seems to present such a wide range of prevalence that it is hard to swiftly ascertain its average extent. Hence, this review aimed to pool the results of primary studies reporting the prevalence of HA into a single estimate in the region.

Methods We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Articles published in EMBASE, PubMed, Web of Science, SCOPUS, Science Direct, and Cochrane Library databases were searched. Observational studies revealing the prevalence of HA in Africa between 2010 and 2023 were incorporated. We assessed the quality of each study using the Newcastle-Ottawa quality assessment tool. The prevalence of HA was estimated as the cases (the sample size) per 100,000 population multiplied by 1000. To produce the pooled estimate, Der Simonian random-effects models were computed with Metaprop on the STATA command. The studies' heterogeneity was assessed using the I-squared (I^2) value test and the Galbraith plot. A funnel plot was conducted to evaluate publication bias.

Results Of the 337 studies accessed, we included 15 that fulfilled the eligibility criteria. The random-effect model meta-analysis demonstrated the overall pooled prevalence of HA was 6.82 cases per 100,000 persons (95% confidence interval: 5.16, 8.48) with heterogeneity ($I^2 = 0.00\%$, $p < 0.001$).

Conclusions This systematic review and meta-analysis revealed that HA is an alarming problem that may pose a future threat to public health in Africa. Given the detrimental effects of the disease on health and the complications involved, we recommended that African regions increase patient access to factor VIII medication, improve carrier detection rates, and take the initiative toward the development and access to gene therapy.

Keywords Epidemiology, Hemophilia, Meta-analysis, Prevalence, Systematic review, Africa

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Introduction

Background to the study

Hemophilia A (HA) is an X-linked recessive bleeding disorder characterized by reduced or absent coagulation factor (F) VIII activity [1–3]. Hemophilia is classified into HA (Factor VIII Deficiency), HB (Factor IX Deficiency), and HC (Factor XI Deficiency). HA and B are rare X-linked bleeding disorders caused by mutations in the genes encoding coagulation factor VIII (FVIII) and factor IX (FIX). **HA is associated with diverse mutations of the factor VIII gene and a variety of phenotypes that affect primarily males** [4, 5]. Care for people with hemophilia is still challenging, particularly in settings with little resources where treating hemophilia may not be given the same priority as other illnesses that are more significant for public health [6].

Study has shown that there are around 400,000 hemophiliacs worldwide, and only 25% of them receive the necessary care [7]. In addition, 10,276 hemophiliac individuals from 40 countries were registered in 2022. Severe hemophilia affected over half (49%) of the patients; 99% of the patients were male, 85% had HA, and 67% were from low- to middle-income countries [8].

Furthermore, based on the World Federation of Hemophilia's 2018 global survey, 1,075 individuals in Malaysia were assessed to have hemophilia, with 900 (83.7%) and 172 (16%) instances of hemophilia A and B, respectively, spanning the age range of 19–44 [9]. In addition, the findings from Iran showed that from 2007 to 2016, the prevalence of hemophilia in males grew from 7.2 cases per 100,000 to 15.9 cases per 100,000. Comparably, from 8.4 cases per 100,000 live births in 2007 to 16.3 cases 100,000 live births in 2016, hemophilia had become more common. Of all the hemophilia, 63.4% were severe [10].

Other findings showed that missense mutations are the most prevalent genetic risk factors for HA, particularly in mild to moderate instances. However, they also pose the least probability of developing an inhibitor. Conversely, the most frequent mutation linked to severe HA is intron 22 inversion [11]. Another study documented that acquired hemophilia A (AHA) is caused by the presence of autoantibodies or a defect in coagulation factor VIII directed against factor VIII (FVIII), resulting in spontaneous bleeding. AHA is associated with a high risk of mortality from bleeding, treatment complications, and the presence of underlying diseases [12, 13].

In the context of Africa, hemophilia's burden is a considerable public health issue. Added to that, the magnitude of the disease still remains underdiagnosed in many African countries, despite great advancements in the developed world's hemophilia care, leading to a high degree of impairment and medico-social ramifications [14, 15]. The empirical evidence on the prevalence of HA in Africa has reported inconsistent findings and seems to present such a wide range of prevalence that it is hard to swiftly ascertain its average extent. For instance, the proportion of people diagnosed with HA ranges from 1.8 cases per 100,000 persons to 5.4 cases per 100,000 persons in Morocco [16], 2.2 cases per 100,000 persons [17] to 9.6 cases per 100,000 persons in Ethiopia [18], and 2. 1 cases per 100,000 persons to 8.2 cases per 100,000 persons in South Africa [19].

Besides, the authors acknowledge that there is paucity of information about the regional pooled estimate of HA, despite the fact that significant primary research has reported the burdens of HA. The knowledge of the regional overall pooled prevalence of the disease would be relevant for patients, health care facilities, regional governments, the World Federation of Hemophilia, policymakers, academicians, and other stakeholders. Knowing the burdens of the disease will enhance evidence-based, quality health care. Hence, the purpose of this systematic review and meta-analysis was to present the combined prevalence of HA in Africa.

Materials and methods

Study setting and period

We conducted this systematic review and meta-analysis in Africa. The data extraction and analysis period was from April 1, 2024, through May 5, 2024.

The current population of Africa is 1,486,743,172, based on the latest United Nations estimates. The population density in Africa is 49 per km2 (128 people per mi2). The total land area is 29,648,481 km2 (11,447,338 sq. mi). The United Nations projects that by 2050, Africa's population will reach close to 2.5 billion. As of 2023, Nigeria was Africa's most populous country, with over 223,804,632 million people, followed by Ethiopia with 126,527,060 million people [20].

Most African countries have integrated universal health coverage (UHC) as a goal in their national health strategies. Yet, progress in translating these commitments into expanded domestic resources for health, effective development assistance, and ultimately, equitable and quality health services and increased financial protection has been slow [21]. The global commitment towards UHC seems substantial at the moment. However, actual progress towards UHC has been slow in some regions, particularly in Africa where the coverage of essential health services is low in many settings [22].

Searching strategies

We used the databases of PROSPERO, the Joanna Briggs Institute (JBI), and the Cochrane Library to search for papers. It was verified whether there were any active review projects pertaining to the topic of the present review. To ensure scientific accuracy and establish a systematic approach, a pre-planned search strategy

was employed during the development of this review. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocol (PRISMA) to assess primary studies from EMBASE, PubMed, Web of Science, SCOPUS, Science Direct, Cochrane Library databases, Google Scholar (search engine), and African journals online. We also examined and included gray literature such as surveillance reports, academic dissertations, and when these fulfilled our inclusion criteria.

For this review, relevant articles was identified using the following mesh terms: PubMed search strategy: (Hemophilia A"[Mesh] OR "Hemophilia A"[Mesh] OR "bleeding disorder] OR "Hemophilia A with Vascular Abnormality" [Supplementary Concept] OR "Hemophilia A"[Mesh] OR "Blood Coagulation Disorders"[Mesh] (("Hemophilia A/epidemiology"[Mesh] OR "Hemophilia A/etiology"[Mesh]))"Hemophilia A/risk factors"[Mesh])) "Hemophilia A/determinant"[Mesh])) "Hemophilia A/associated factors"[Mesh])) AND ("Africa"[Mesh] OR "Africa South of the Sahara"[Mesh] OR "South Africa"[Mesh] OR "Africa, Western"[Mesh] OR "Africa, Southern"[Mesh] OR "Africa, Northern"[Mesh] OR "Africa, Eastern"[Mesh] OR "Africa, Central"[Mesh] OR "Namibia"[Mesh] OR "Mozambique"[Mesh]).

The key terms were used in combination using Boolean operators like "OR" or "AND." The review was restricted to full texts, open access articles, and English-language publications. This search involved articles that were published from April 5, 2024, to May 5, 2024. Besides, during the advanced PubMed search, it used all fields and mesh words. The first reviewer performed the initial search and completed it on May 5, 2024. The review then scanned the literature for updates. The review then scanned the literature for updates.

Eligibility of the study

In this review, we used CoCoPop (Condition, Context, and Population) mnemonic for prevalence to determine inclusion and exclusion eligibility criteria.

Inclusion criteria

We included studies adhering to the following eligibility criteria: (a) Study designs: observational studies (cross-sectional); (b) condition (outcomes of interest): studies reported prevalence of HA; (c) context (settings): studies conducted on the African continent; (d) population: studies reported HA in males; (e) Publication status: published and unpublished articles; (f) Time frame: articles published from January 1, 2010, up to May 5, 2024; (g) Language of published articles: articles written in English.

Exclusion criteria

After contacting the principal investigator via email at least twice, we excluded those primary articles that were not fully accessed during the search procedure. Studies that failed to report outcomes of interest (HA) were discarded after their whole texts were examined. Additionally, studies with pre-set criteria of poor quality were also excluded. The articles that fulfilled the inclusion criteria were the only ones included in the full-text review.

Quality assessment and data extraction

We removed the duplicate papers using Endnote (version X8). Relevant studies were identified using a priori defined inclusion criteria relating to the patient, population, setting and outcome of interest (HA). New Castle Ottawa Scale (NOS) [23], modified for cross-sectional study was used to assess the quality of studies included in this review [24]. Studies with a score ≥ 8 were considered high quality; those with a score between 4 and 7 were considered moderate quality; and those with a score ≤ 3 were considered low-quality studies. The two authors (KB and DZ) independently assessed the quality of the included articles. We resolved a disagreement through discussion among those reviewers. If not, to address contradictions, the third reviewer was involved by taking the two authors' mean scores. The data was extracted using a structured data extraction spreadsheet (Microsoft Excel). All the abstracts included during the title and abstract reviews go to full-text review, and the necessary data was extracted. Data was defined and extracted by MBD and double-checked by second reviewers. The authors were notified if the data for selecting papers was incomplete or ambiguous. Two writers (KB and DZ) independently extracted all the required data. The outcome of interest data extraction format consists of the first author's name, publication year, study location, the analysis design, sample size, number of participants with the outcome (case), and response rate.

Outcome of measurement and statistical analysis

We obtained the PROSPERO registration number (CRD42024531191) for this systematic review and meta-analysis. We considered studies reporting the prevalence of HA as an outcome of interest. This was further estimated as the cases (the sample size) per 100,000 population multiplied by 1000. The data was analyzed using STATA 17 version software. The pooled prevalence of HA was computed with Metaprop on STATA command [25] and presented in a forest plot with a corresponding 95% confidence interval. Der Simonian and Laird random-effects models, effect size (ES) was computed. We checked publication bias by funnel plotting. To identify and visualize the presence of heterogeneity, we used the Galbraith plot and the I-squared (I^2) statistics. I^2 less than 50% were used to declare significant or considerable heterogeneity. The effect size and the standard error (SE) of the logarithm of prevalence were computed.

Results

Selection and identification of studies

A total of 337 primary studies were accessed from Embase ($n=34$), Web of Science ($n=31$), SCOPUS ($n=19$), Cochrane Library ($n=10$), African journals online ($n=21$), Science Direct ($n=9$), PubMed ($n=29$), Goggle Scholar ($n=107$), and manual search ($n=77$). About 111 studies out of all the accessed papers were rejected because they were duplicates. Besides, 146 studies were removed after reading the abstract and title because they did not fit the purpose of the review and had methodological flaws. Following the full-text review process, 80 articles were ultimately reviewed; 15 of these studies (sample size=1,295) were included in the systematic review and meta-analysis (Fig. 1).

Characteristics of included studies

In this review, fifteen [15] studies with a total sample size of 1,295 patients who met eligibility criteria were included in systematic review and meta-analysis. The included studies' minimum and maximum sample sizes, with respect to the sample size variations, were 15 and 320 cases, respectively, within a range of 350. In addition, the response rate in each included study was evaluated, and it was found that the response rate ranged from 88 to 100%, and almost all the studies had a good response rate, having a response rate of above 80% (Table 1).

Since HA exclusively affects male populations, all included studies in this review revealed a percentage of the disease among male patients only (100%). Thirteen of the fifteen papers that made up the final analysis were published, and nearly all of them employed cross-sectional study designs. Regarding the studies' geographic distribution, six of them came from countries in northern Africa and four from countries in eastern Africa. In respect to study quality status, the studies' quality scores vary from between seven and nine points out of 10 (Table 1).

The prevalence rate of hemophilia A in Africa

This systematic review and meta-analysis finding revealed that the overall pooled prevalence rate of HA cases in Africa was estimated to be 6.82 cases per 100,000 persons (95% CI: 5.16, 8.48), with heterogeneity of ($I^2=0.00\%$, $p<0.001$), as shown in the forest plot (Fig. 2).

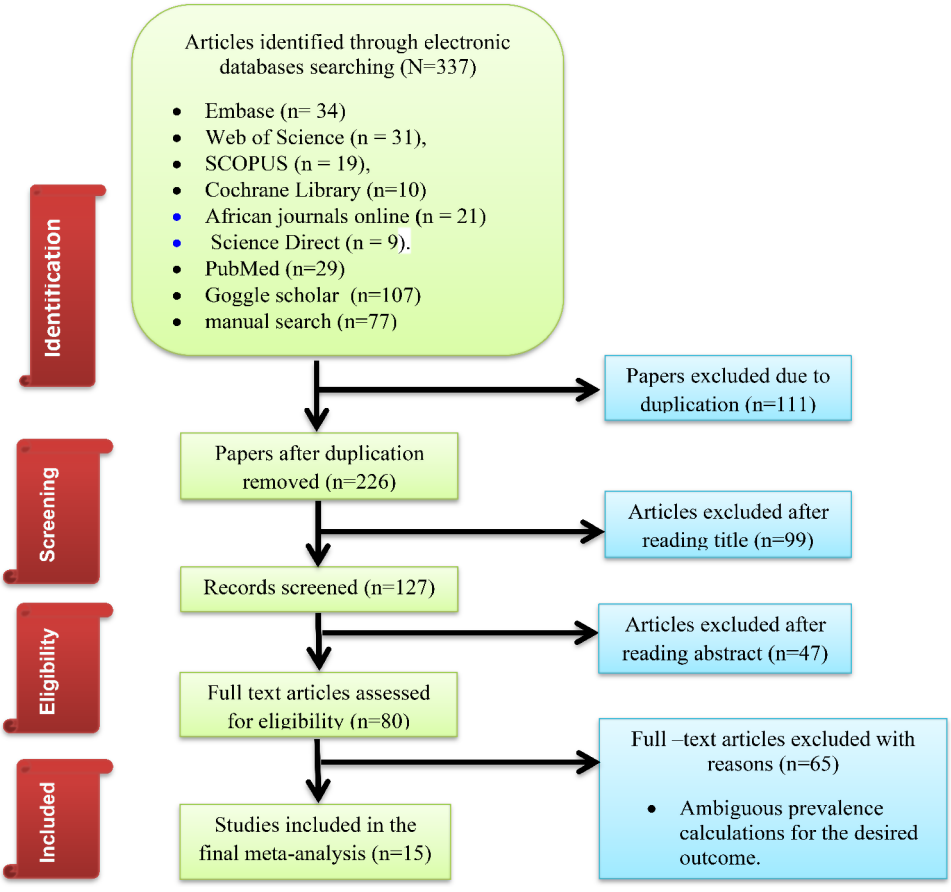


Fig. 1 PRISMA flow diagram for study selection for systematic review and meta-analysis of the prevalence of hemophilia A in Africa in 2024 ($n=15$)

Table 1 Overview of included studies in the systematic review and meta-analysis of the prevalence of hemophilia an in Africa, 2024 ($n=15$)

First author/ Year	Country	Region	Study design	Sample size	Events	Key findings: (prevalence rate per 100,000)	Quality score
Eyebe S et al., 2022 [26]	Cameroon	western	Cross-sectional	55	42	7.6	8
Nathalie L et al., 2019 [27]	Ivory coast	western	Cross-sectional	57	49	8.5	7
Youssef Al et al., 2010 [28]	Egypt	Northern	Cross-sectional	72	44	6.1	8
Tihitina M et al., 2018(unpublished) [29]	Ethiopia	eastern	Cross-sectional	153	149	9.7	8
Imen K et al., 2016 [30]	Tunisia	Northern	Cross-sectional	32	20	6.2	8
E. Hejer et al. 2012 [31]	Tunisia	Northern	Cross-sectional	320	146	4.5	8
Tarig O et al. 2021 [32]	Sudan	Northeast	Cross-sectional	30	25	8.3	9
Lethukuthula M et al., 2022 [4]	South Africa	southern	Cross-sectional	44	36	8.1	7
Sokhna A et al., 2022 [33]	Senegal	western	Cross-sectional	15	13	8.6	9
Amina K et al., 2022 [34]	Morocco	Northern	Cross-sectional	120	22	1.8	8
Mzikamanda R Eet.al, 2016 [35]	Malawi	southeastern	Cross-sectional	46	14	3.4	8
Sitina et al., 2023 [17]	Ethiopia	eastern	Cross-sectional	105	76	7.2	8
Noufissa B et al., 2014 [36]	Morocco	Northern	Cross-sectional	16	15	9.3	8
Raida O et al., 2020 [37]	Egypt	Northeast	Cross-sectional	165	165	10	8
Lucy NY et al., 2017 (unpublished) [38]	Kenya	eastern	Cross-sectional	65	61	9.3	8

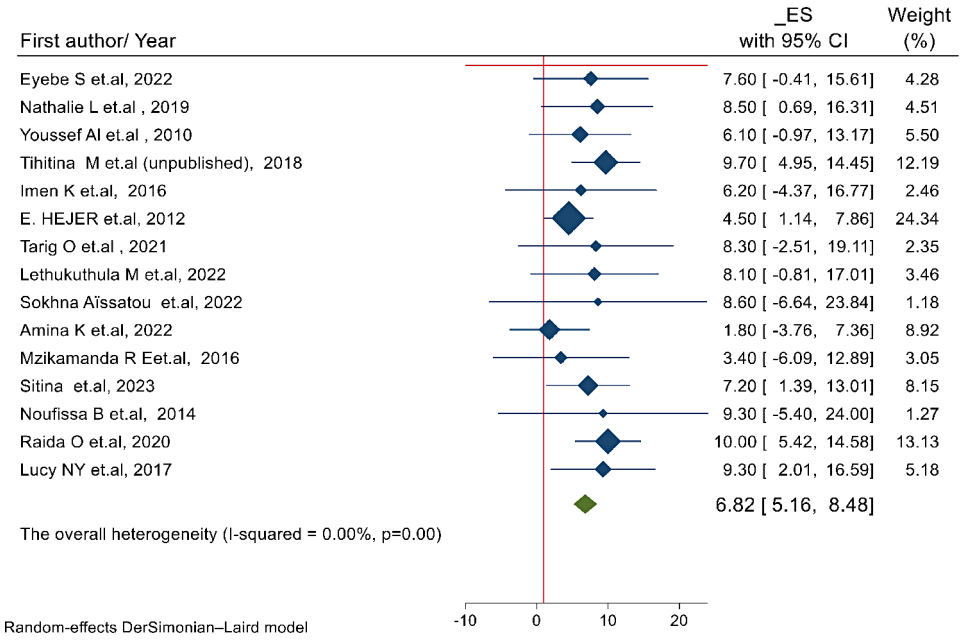


Fig. 2 Forest plot of the pooled prevalence of HA in Africa, 2024 ($n=15$)

Publication bias

In this systematic review and meta-analysis, the funnel plot was assessed for asymmetry in the distribution of the prevalence of HA. As defined below in the funnel map, all the studies' effect sizes were normally distributed around the center of a funnel plot, suggesting that there was no evidence of publication bias (Fig. 3).

Galbraith plots were used to assess the heterogeneity of the studies and detect potential outliers. Thus, this study demonstrated that the amount of variation between studies was absent (Fig. 4).

Discussion

For the purpose of influencing policy and providing evidence-based quality healthcare, reliable evidence of disease prevalence is vital [39]. Systematic reviews and meta-analyses are helpful design to give a general overview of particular variables for this goal [39]. These tools, which rely on predetermined, systematic, and repeatable methods, aid in the correct and dependable synthesis of evidence in addition to summarizing the data that is currently available [40]. This systematic review and meta-analysis aimed to summarize the results of several studies

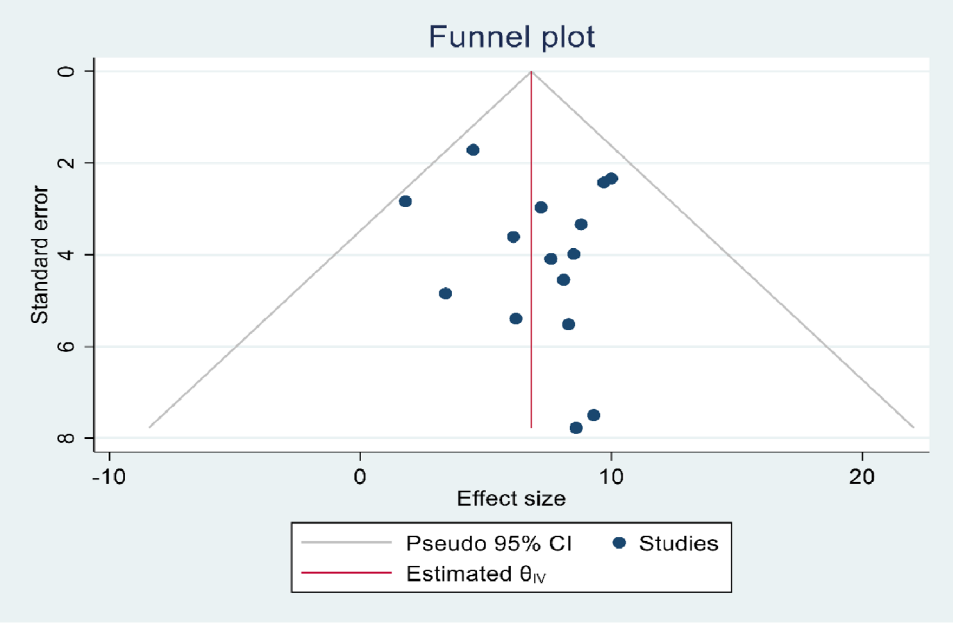


Fig. 3 Funnel plot with 95% confidence limits of the prevalence of HA in Africa, 2024 ($n=15$)

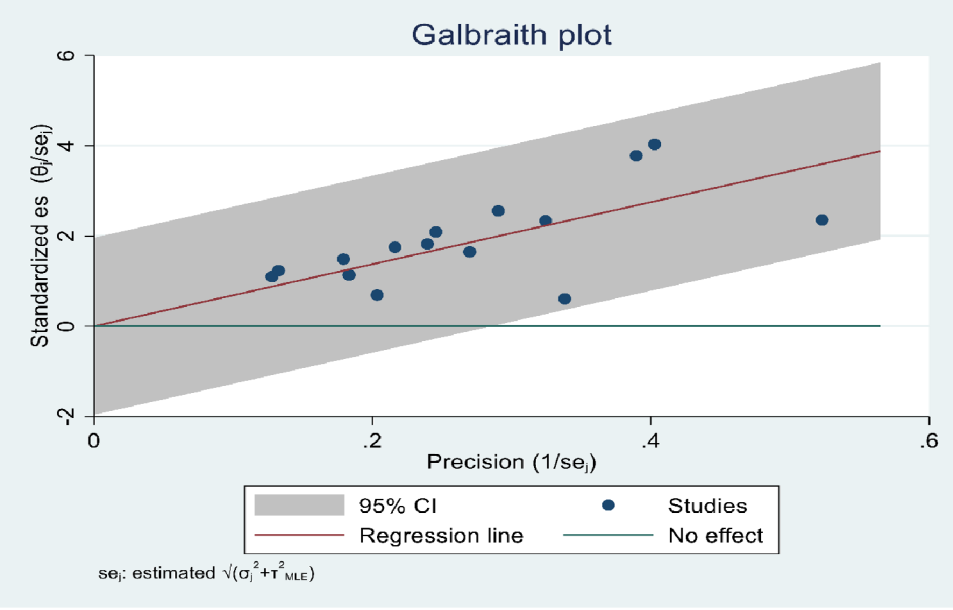


Fig. 4 The Galbraith plot shows a graphical display of the amount of heterogeneity from a meta-analysis

reporting the prevalence of HA into a single estimate on African continents.

In our scope of searching, comprehensive evidence is limited to the pooled prevalence of HA elsewhere. As a result of the aforementioned situation, we compared our findings with a few pieces of related literature. The overall pooled prevalence of HA in the present study location is disagreed with the meta-analysis findings from China, which reported 3.6 per 100,000 people with HA [41]. A plausible rationale for the discrepancy in HA prevalence could be related to the number of sites examined. This indicates that, in contrast to the findings from China, which came from a small number of jurisdictions, we were able to obtain data from big African countries using a legitimate methodology. As a result, it can be suggested to raise the disparity in the illness burden estimates. The additional considerable possibility could be linked to the span of the study and a slight enhancement in the regions' disease reporting and documentation systems.

Furthermore, the results of our investigation were inconsistent with the meta-analysis results that details the prevalence of hemophilia in India, Russia, Taiwan, and Turkey, which documented 2.27 per 100,000, 5.12 per 100,000, 3.61 per 100,000, and 4.93 per 100,000 person, respectively [42]. The findings of our study demonstrate that the magnitude of HA in Africa may be higher than in India, Russia, Taiwan, and Turkey, which could be the reason for discrepancies in the pooled prevalence of HA. We speculated that cases of hemophilia may go undetected or unreported in the mentioned countries, which would account for part of the discrepancy in the summary estimate of the disease. This might be due to two factors: first, it's possible that the awareness of medical professionals on hemophilia and its symptoms is improved in Africa. Second, it's possible that the setting for the laboratory tests needed to identify hemophilia might be relatively improved with its weakness in the Africa. The lack of inclusion of bleeding disorders in national health policy road maps in many African nations may make it challenging to estimate the disease's burden.

Also, our results were inconsistent with the global prevalence of HA in 2016, which was reported to be 2.8/100,000 populations [43, 44] ' as well as the 4.8–13.2/100,000 males diagnosed with HA in upper middle-income countries [45]. The observed discrepancy in the combined prevalence may be attributed to various factors such as improved reporting practices, upgraded diagnostic facilities, increased survival rates, or patient migration to better-care areas in the current study locations relative to prior settings.

Additionally, the burden of HA as determined by our investigation does not align with the results of systematic reviews and meta-analyses conducted in Australia, Canada, France, Italy, New Zealand, and the United Kingdom that documented the prevalence of HA as 17.1 cases per 100,000 [46]. The possible explanation for the disparity in HA prevalence between the present study locations and Australia, Canada, France, Italy, New Zealand, and the United Kingdom could be related to the variation in geographical location investigated (the sample size), the difference in access to diagnostic setup, tools for identification, and differences in the patient registry that are very essential for tracking the identification and diagnosis of HA. Since many cases of the disease remain uncovered, an additional explanation for the discrepancy could be the iceberg phenomenon of the disease, which is expected in many African regions. All of the above-mentioned contexts in the present study are considerably challenging, which could increase the discrepancy in disease prevalence.

Our review findings offers more precise estimates of the pooled prevalence of the disease in Africa rather than depending on estimates from outside sources, which has consequences for theory, practice, or policy. Our findings also show that for the past ten years, the prevalence has been rising. This study gave the local ministry of health a reliable database and will be helpful in determining the quantity of treatment supplies and other resources that are currently appropriately estimated for the African nations with remarkably high rates of sickness. Our understanding of the trends and patterns of HA in the study settings has improved as a result of examining these regional pooled burdens of the disease.

Strengths and limitations of the review

This systematic review and meta-analysis's thorough search and exacting methodology were among its strong points. We reviewed a vast geographic area during the evaluation process, reporting hemophilia epidemiology despite variations in disease load. As a result, our meta-analysis's findings were most likely representative of the entire continent of Africa.

This systematic review and meta-analysis had some limitations: Due to the fact that HA is the most common bleeding disorder as compared to hemophilia B, the present systematic review and meta-analysis didn't incorporate hemophilia B burden. The other limitations of this review were that we didn't pool HA based on its severity (mild, moderate, and severe) as data on mild and moderate HA aggregated with severe HA in the published literature. The language bias may also be a limitation of this review, as we only included articles published in English. Selection bias may have occurred in this study since we did not include all papers that were not publicly available from the electronic database. Another drawback was that, due to inadequate sample sizes, type II errors can potentially have an impact on the review results. This may have to do with the nature of the illness and the region's restricted diagnostic settings.

Conclusions

This systematic review and meta-analysis revealed that HA is an alarming problem that may pose a future threat to public health in Africa. Knowing the disease's epidemiological burden will be more vital to making the problem more visible to relevant authorities and is a first step toward developing innovative solutions to target the disease. Our results have important implications for HA control and better care. Given the detrimental effects of the disease on health and the complications involved, we recommended that African regions immediately increase patient access to factor VIII medication, improve carrier detection rates, and take an initiative toward the development and access to gene therapy. We also recommended that the Africa region quickly revise their health policy to incorporate bleeding disorders (hemophilia), into regional health policy. This approach can facilitate the

establishment of electronic disease surveillance systems and to shorten the waiting period for factor VIII medication collected from donors.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20165-w.

Supplementary Material 1

Acknowledgements
The authors thank English language professionals for their contribution in removing any grammatical errors, tenses, and punctuation.

Author contributions
All authors contributed to data extraction, critical appraisal and analysis, drafting or revising the article, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work. Conceptualization: MBD.Data curation: MBD, KB, and DZ.Formal analysis: MBD, DZ, and KB.Investigation: MBD, KB and DZ.Methodology: MBD, KB, and DZ.Software: MBD, and DZ .Validation: KB and DZ.Visualization: MBD, KB, and DZ.Writing original draft: MBD, and DZ Writing– review and editing: MBD, and DZ.

Funding
This review project did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability
Data reported in this manuscript are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
No ethical approval was necessary because data was collected and analyzed for previously reported research in which primary investigators was obtain informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 8 May 2024 / Accepted: 23 September 2024
Published online: 27 September 2024

References

1. Mazepa MA, Monahan PE, Baker JR, Riske BK, Soucie JM. Men with severe hemophilia in the United States: birth cohort analysis of a large national database. Blood J Am Soc Hematol. 2016;127(24):3073–81.
2. Gholami MS, Valikhani M, Dorgalaleh A, Mousavi SH, Pezeshkpoor B, Hemophilia A. Congenital Bleeding Disorders: Diagnosis and Management. 2018:103 – 37.
3. Mehta P, Reddivari AKR. Hemophilia. 2019.
4. Mafisa L, Dlova AN, Moodley V. The profile of patients with haemophilia managed at a haemophilia treatment centre in Pretoria, Gauteng. South Afr Family Pract. 2022;64(1):5551.
5. Castaman G, Matino D. Hemophilia A and B: molecular and clinical similarities and differences. Haematologica. 2019;104(9):1702.
6. Mbanya DN, Diop S, Ndoumba Mintya AN, El Kiaby M. Hemophilia care in Africa: Status and challenges. Transfus Clinique et biologique: J De La Societe francaise de Transfus Sanguine. 2021;28(2):158–62.
7. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key N, Kitchen S, Llinas A, et al. Guidelines for the management of hemophilia. Haemophilia: Official J World Federation Hemophilia. 2013;19(1):e1–47.
8. Coffin D, Gouider E, Konkle B, Hermans C, Lambert C, Diop S, et al. The World Federation of Hemophilia World Bleeding Disorders Registry: insights from the first 10,000 patients. Res Pract Thromb Haemostasis. 2023;7(8):102264.
9. Azhar AAM, Raj AA, Izam F, Mokhtar MD, Zakaria NAIA, Banerjee KG. The key complications of hemophilia and recent advancements in their management: an update. Int J Res Med Sci. 2021;9(6):1800.
10. Kadhim KAR, Al-Lami FH, Baldawi KH. Epidemiological profile of hemophilia in Baghdad-Iraq. INQUIRY: J Health Care Organ Provis Financing. 2019;56:0046958019845280.
11. Shim Y-J, Lee K-S. Genetic risk factors of Hemophilia A. J Genetic Med. 2010;7(1):1–8.
12. Al Mahmasani L, Finianos A, Bou-Fakhredin R, Elias J, Taher A. Acquired hemophilia A: when an overlooked autoimmune disorder causes significant bleeding. Expert Opin Orphan Drugs. 2020;8(2–3):79–89.
13. Gitschier J, Kogan S, Levinson B, Tuddenham E. Mutations of factor VIII cleavage sites in hemophilia A. 1988.
14. Diop S, Seck M, Sy-Bah D, Faye BF, Sow-Ndoye A, Gueye YB, et al. Implementing haemophilia care in Senegal, West Africa. Haemophilia: Official J World Federation Hemophilia. 2014;20(1):73–7.
15. Mbanya D, Diop S, Mintya AN, El Kiaby M. Hemophilia care in Africa: status and challenges. Transfus Clin Biol. 2021;28(2):158–62.
16. Bouyadmar M, Khorassani ME, Kababri ME, Kili A, Hessissen L. The prevalence of anti-factor VIII and anti-factor IX antibodies among patients with hemophilia in Rabat, Morocco: a single center experience. Pan Afr Med J. 2022;41:126.
17. Iyar S, Gebremariam GT, Beyene DA, Gebremedhin A, Tadesse TA. Health-related quality of life and its associated factors among hemophilia patients: experience from Ethiopian Hemophilia Treatment Centre. J Pharm Health Care Sci. 2024;10(1):3.
18. Editorial. Unresolved problems in haemophilia. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 1973;47(48):2312.
19. Mafisa L, Dlova AN, Moodley V. The profile of patients with haemophilia managed at a haemophilia treatment centre in Pretoria, Gauteng. South African family practice. Official J South Afr Acad Family Practice/Primary Care. 2022;64(1):e1–7.
20. Nations U. African Populations by country: https://www.imf.org/en/Publications/fandd/issues/2023/09/PT-african-century. 2023.
21. Njoroge EK. Factors Impacting Universal Health Care Implementation in Kenya: a case study of Bomet County. J Med Nurs Public Health. 2024;4(1):1–16.
22. Odipo E, Jarhyan P, Nzinga J, Prabhakaran D, Aryal A, Clarke-Deelder E, et al. The path to universal health coverage in five African and Asian countries: examining the association between insurance status and health-care use. Lancet Global Health. 2024;12(1):e123–33.
23. Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: advantages and limitations of the Newcastle Ottawa Scale. World J Meta-Analysis. 2017;5(4):80–4.
24. Modesti PA, Reboldi G, Cappuccio FP, Agyemang C, Remuzzi G, Rapi S, et al. Panethnic differences in blood pressure in Europe: a systematic review and meta-analysis. PLoS ONE. 2016;11(1):e0147601.
25. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Archives Public Health. 2014;72:1–10.
26. Eyebe ES, Chedjou KJP, Fomboh TC, Chendjou A, Mabopda V, Tayou C, et al. HindIII and MseI in the Biomolecular Profile of Hemophilia in Cameroon: a primer study. J Biosci Med. 2022;10(6):8–19.
27. Lambert C, Lannoy N, Meité ND, Sanogo I, Eeckhoudt S, Hermans C. Inhibitor epidemiology and genetic-related risk factors in people with haemophilia from Côte d'Ivoire. Haemophilia: Official J World Federation Hemophilia. 2020;26(1):79–85.
28. Zaki MES. Descriptive epidemiology of Hemophilia Mansoura. Egypt: Retrospective; 2010.
29. MUSSE T, PREVALENCE OF HEMOPHILIA AMONG PATIENTS VISITING BLACK, ETHIOPIA. LION SPECIALIZED TEACHING HOSPITAL, ADDIS ABABA,. 2018.
30. Kraiem I, Hadhri S, El Omri H, Sassi R, Chaabani W, Ennabli S, et al. editors. Frequency of specific coagulation inhibitors and antiphospholipid antibodies in Tunisian haemophiliacs. Annales de biologie clinique; 2012.
31. HEJER E, AMEL C, FATMA B, KAOUTHER WIJDENB, MOEZ Z. Regional registry of bleeding disorders in Tunisia. Haemophilia: Official J World Federation Hemophilia. 2012;1:3.

32. Ahmed TOK, Khair SAO, Agabeldour AA, Awadelkareem H, Fadl O, Babker AM. Prevalence of antibody inhibitors among Sudanese patients with Hemophilia. Prevalence. 2021;5(8):12–7.
33. Touré SA, Seck M, Sy D, Senghor AB, Faye BF, Diop S. Clinical outcome and incidence of inhibitor development in severe hemophilia patients receiving low-dose prophylaxis: a 3-year follow-up study in Senegal, West Africa. Hematology, Transfusion and Cell Therapy. 2023;45:S95-S100.
34. Bouyadmar M, El Kababri M, Kili A, Hessissen L. The prevalence of anti-factor VIII and anti-factor IX antibodies among patients with hemophilia in Rabat, Morocco: a single center experience. Pan Afr Med J. 2022;41(1).
35. Mulanje L, MZIKAMANDA R, MKWENEMBERA F, MAKUTI S, OZUAH N, editors. Haemophilia in the Central and Northern Regions of Malawi–an Epidemiological Study. Haemophilia: the official journal of the World Federation of Hemophilia; 2022: WILEY 111 RIVER ST, HOBOKEN 07030 – 5774, NJ USA.
36. Benajiba N, Boussaadni YE, Aljabri M, Bentata Y, Amrani R, Rkain M. Hémophilie: état des lieux dans un service de pédiatrie dans la région de l'oriental du Maroc. Pan Afr Med J. 2014;18(1).
37. Oudat R, Al-Maharmeh M, Al-Ghrayeb R, Ogeilat T, Mustafa MK. Prevalence of FVIII inhibitors among children with Hemophilia A: experience at the Jordanian Royal Medical Services. Med Archives. 2020;74(3):187.
38. Nyachae L. The prevalence of and risk factors Associated with development of factor Viii inhibitors in patients with Hemophilia a seen at the Kenyatta. National Hospital: University of Nairobi; 2022.
39. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. JBI Evid Implement. 2015;13(3):147–53.
40. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med. 2009;151(4):W–65.
41. Qu Y, Nie X, Yang Z, Yin H, Pang Y, Dong P, et al. The prevalence of hemophilia in mainland China: a systematic review and meta-analysis. Southeast Asian J Trop Med Public Health. 2014;45(2):455.
42. Qu Y, Zhan S, Dong P. PSY12 the Prevalence and Treatment Status of Hemophilia in India, Russia, Taiwan and Turkey: a systematic review and Meta Analysis. Value Health. 2012;15(7):A679.
43. Hemophilia WFo. Report on the annual global survey. World Federation of Hemophilia Montreal^ eQuebec Quebec; 2011.
44. WFo H. Report on the Annual Global Survey 2014. Montréal, Canada: World Federation of Hemophilia. 2015:1–54.
45. Stonebraker JS, BOLTON-MAGGS PH, Michael Soucie J, Walker I, Brooker M. A study of variations in the reported haemophilia a prevalence around the world. Haemophilia: Official J World Federation Hemophilia. 2010;16(1):20–32.
46. Iorio A, Stonebraker JS, Chambost H, Makris M, Coffin D, Herr C, et al. Establishing the prevalence and prevalence at birth of hemophilia in males: a meta-analytic approach using national registries. Ann Intern Med. 2019;171(8):540–6.

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