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SYSTEMATIC REVIEW

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Epidemiological distribution of bacterial meningitis infections in South Africa: a systematic review and meta-analysis

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Abstract

Scientific evidence from public health findings can enhance the management, treatment, and prevention policies for bacterial meningitis (BM) infections. However, comprehensive epidemiological data on BM prevalence in South Africa is limited. We aimed to assess the prevalence and characteristics of laboratory-confirmed BM cases at the national population level. Using PRISMA standards, we retrieved data from electronic databases and selected reference articles. Out of 115,626 participants, 57,964 (50.13%) were infected with BM, with the highest prevalence (7.67%) in the age group 6–17 years. Our meta-analysis of 19 studies revealed an overall pooled prevalence of 38.01%, 95% confidence interval (CI: 0.26–0.50), with significant heterogeneity (I^2 = 99.86%, Q = 13117.45, $p < 0.0001$). The Egger test indicated publication bias (z = 3.4977, $p = 0.0005$). Subgroup analyses showed a higher prevalence in studies with sample sizes over 1000 (60.22%, 95% CI: 0.3899–0.7819, I^2 = 99.92%), over long study years (37.50%, 95% CI: 0.2642–0.5005, I^2 = 99.84%), cross-sectional study design (58.69%, 95%CI: 0.4906–0.6770, I2 = 99.72%), and particularly in Gauteng province (60.42%, 95% CI: 0.4539–0.7371, I^2 = 98.45%). The infectious types included *Listeria* (83.33%, 95% CI: 0.1936–0.9905, I^2 = 0.00%) and *Neisseria* (62.64%, 95% CI: 0.6126-0.6400, I^2 = 0.00%). Significant heterogeneity was noted in study design (R^2 = 52.93%, $p < 0.0001$), sample size (R^2 = 0.00%, $p = 0.0117$), and province (R^2 = 0.0%, $p < 0.0001$). These findings underscore a high prevalence of BM infections in South Africa's epidemiological landscape, highlighting the urgent need for targeted surveillance for effective prevention and treatment strategies.

Keywords Epidemiology, Distribution, Bacterial meningitis infections, South africa, Meta-analysis

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Introduction

Bacterial meningitis (BM) infections pose a global health challenge, with incidence and case fatality rates spreading worldwide [1]. BM is the form of meningitis with the most significant fatality; according to WHO, one in six individuals dies of BM, while one in five who survive experience significant neurological difficulties [2]. In addition to neurodegenerative diseases [3], BM contributes to the worldwide neurological burden and is a significant cause of child mortality [1]. However, the impact of these life-threatening pathogens has a severe impact in middle and low-income countries, where it is associated with a high case fatality rate and substantial long-term complications.

Africa bears the highest burden of bacterial meningitis, with seasonal and geographic variations in outbreak patterns [4]. The "meningitis belt" of sub-Saharan Africa, stretching from Senegal to Ethiopia, experiences the highest incidence rates globally [4]. In these regions, *Streptococcus pneumoniae* (*pneumococcus*) and *Neisseria meningitidis* (*Meningococcus*) are the primary etiological agents of bacterial meningitis in adults and children. The most common causal agents for neonates include *Streptococcus agalactiae* (group B *Streptococcus*), *Escherichia coli*, and *Staphylococcus aureus* [4–6]. Despite extensive vaccination efforts against these pathogens, BM remains a significant cause of morbidity and mortality in Africa, with children under five years of age bearing the heaviest disease burden [4, 6].

Despite this heavy burden, detailed scientific evidence of comprehensive epidemiological data on BM infections is conspicuously lacking in many African nations. In South Africa, for example, studies over decades reported *Neisseria* meningitidis as the predominant pathogen in Johannesburg, followed by *Streptococcus pneumoniae* and *Haemophilus influenzae* [7]. In the Western Cape Province, *tuberculous* meningitis was the most prevalent infection, followed by *N. meningitidis*, *H. influenzae*, and *S. pneumoniae* [8]. Similarly, *S. pneumoniae* was the leading cause of bacterial meningitis in Swaziland [9]. There is currently no comprehensive national data on the region's epidemiological distribution of BM infections.

The persistent of BM is influenced by various circumstances, such as a higher percentage of neutrophilic polynuclei in the cerebrospinal fluid (CSF) from the initial lumbar puncture, presence of headaches before meningitis, female gender, and the occurrence of a brain abscess during the initial hospitalisation have all been linked to the severity of meningitis [10]. *N meningitidis* also displays genetic variety during asymptomatic carriage, focusing on outer membrane genes that affect bacterial adherence and immune evasion via horizontal gene transfer and hypermutation [11]. Furthermore, pharmacokinetic issues, treatment delays, and microbial virulence are all liable for the high morbidity and fatality rates associated with bacterial meningitis, which is exceptionally high in newborns, the elderly, and hospital-acquired cases [12]. Additionally, gram-positive bacterial infection, high C-reactive protein levels, and consciousness disorders are risk factors for refractory BM in children with positive infections [13]. Moreover, other factors that aggravate the BM disease burden include a deficient healthcare system, conflicts, political uncertainty, and difficulties with diagnosis that cause treatment delays, resulting in increasing rates of morbidity and death [14–16]. Also, the emergence of drug-resistant strains complicates treatment efforts. For instance, penicillin-resistant strains of meningococci have been reported, exacerbating the challenge of managing the disease effectively [17–19]. Environmental distribution of resistance genes and antimicrobial drug resistance in bloodborne pathogens presents a significant risk to the community and presents difficulties managing infectious pathogens [20–22].

National scientific evidence on BM will help understand the disease's epidemiology and inform public health resources on prevention, early diagnosis, and treatment of meningitis. Evidence from scientific data from multiple public health findings could advance BM prevention programs and policies to improve surveillance systems in low-resource settings. We set out to determine the prevalence and characterise national population-level findings on the laboratory-confirmed reported cases of BM among South Africans. We examined patterns in the frequency and highlighted the critical use of evidence data on changes in demographic and prevalence data of BM to appraise the epidemiological characteristics on a national scale. To increase knowledge about meningitis among healthcare professionals and enhance policymakers' comprehension of the need to develop solutions to alleviate the burden of meningitis in the nation.

Methodology

Search strategy

Using the standard Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA), we searched the electronic databases Web of Science (WOS), Scopus, PubMed, and article references for relevant material [3, 23, 24]. Utilising the boolean keywords "Epidemiology AND Prevalence AND Bacterial Meningitis OR Neisseria meningitidis OR meningococcus OR Streptococcus pneumoniae OR pneumococcus OR Haemophilus influenzae OR Streptococcus agalactiae OR group B streptococcus OR Meningitis infections AND South Africa" in the form of headers or title specific terms for medical themes, studies published between 1995 and March 27, 2024, were retrieved.

Studies selection criteria

Inclusion criteria

Articles that reported the diagnosis of meningitis obtained from the cerebrospinal fluid of the spinal tap samples, using bacterial latex antigen tests, polymerase chain reaction (PCR), culture of cerebrospinal fluid, or any other typically diagnostic material or methods to diagnose bacterial meningitis from the South African population were qualified for inclusion. Studies that reported or determined the bacteria (*Neisseria* meningitidis OR *Meningococcus* OR *Listeriosis* OR *Escherichia coli* OR *Streptococcus pneumoniae* OR *pneumococcus* OR

Haemophilus influenzae OR *Streptococcus agalactiae* OR group B *streptococcus*) which caused meningitis by analysing the fluid were included.

Exclusion criteria

Studies that reported co-morbidity, such as mycobacterium tuberculosis (TB) meningitis or meningococcal disease in HIV-infected populations, were excluded from the systematic review and meta-analysis. Bacterial and viral pathogens affect the brain in distinct ways. While HIV do not directly causing bacterial meningitis, but can contribute to the development of aseptic meningitis through autoimmune mechanisms. Individuals with latent HIV infection are at an increased risk of developing tuberculosis (TB), which presents differently from other forms of bacterial meningitis. Unlike rapidly progressing meningitis caused by bacterial pathogens such as *Neisseria meningitidis* or *Streptococcus pneumoniae*.

Also, articles were restricted to English-language only as detailed in Fig. 1.

Outcomes of interest

The presence or prevalence of *Neisseria meningitidis* OR *Meningococcus* OR *Listeriosis* OR *Escherichia coli* OR *Streptococcus pneumoniae* OR *pneumococcus* OR *Haemophilus influenzae* OR *Streptococcus agalactiae*

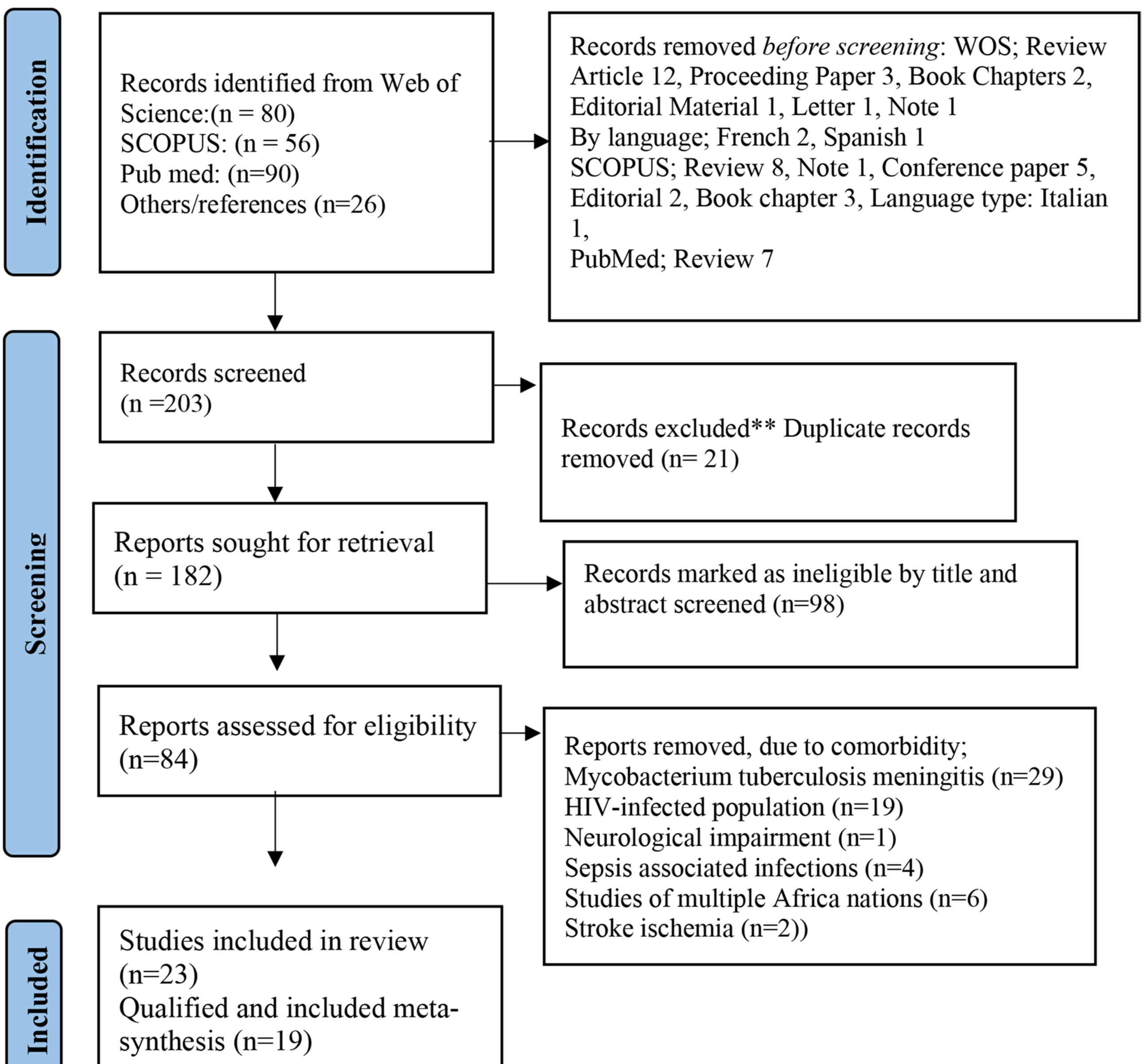

Fig. 1 Flowchart of PRISMA guideline for the study selection and meta-analysis

OR group B *Streptococcus* bacteria in meningitis cases among the South African population was the outcome of interest.

Data extraction and outcomes of interest

The first authors' names, the year the study was published, the population as a whole, the number of positive cases of bacterial meningitis, the province or region in South Africa under investigation, the study period, and the type of study were the performance indicators for this meta-analysis similar to procedure we have reported elsewhere [3, 24]. The findings or results, discussions, figures, and tables from the qualified articles were independently identified and mined as meta-data by the two groups of investigators (HO, and YEC). Furthermore, the two sets of investigators' agreements were used to evaluate the proficiencies and inconsistencies. After that, documentation of the homogeneity, consistency, and heterogeneity among the study populations was completed, and additional statistical analysis was conducted using the predefined study criteria set by the investigators.

Assessment of data quality

The data quality for this meta-analysis was assessed using the Newcastle-Ottawa Scale (NOS), which is approved by the Agency for Healthcare Research and Quality (AHRQ) (http://www.ohri.ca/programs/clinicalepidemiology/oxford.asp). Three criteria were utilised to judge the quality of the studies: outcome measurement, group comparability, and study group selection. A star system was employed to grade each category.

Statistical analysis

The 95% confidence interval and raw proportions or prevalence of bacterial meningitis were calculated using the Wilson method of confidence intervals (CIs). The weighted overall effect size (weighted average proportion) was calculated for the initial research random-effects meta-analysis based on the individual effect sizes and associated sample variances. We apply the restricted maximum-likelihood estimator with the input method= "DL". Because the proportion between studies varies from 0.005 to 1, the logit transformation was used to obtain the pooled prevalence to improve the statistical characteristics [25].

The influence of heterogeneity and homogeneity in the study population was measured using meta-regression analysis [26]. A forest plot was made after the subgroup analysis of the epidemiological distribution. Asymmetry was tested using Egger's test, and the results were funnel plots that compare publication bias. The rank correlations test and Kendall's model were then used to determine the significance of the bias. The statistical software R 4.0.5 was used for each two-tailed analysis with a significance threshold of 0.05 [27,28].

Results

Literature search summary

Summary of the included studies

The search across three databases and a review of references from 1995 to 2024 identified 252 papers on the prevalence and distribution of BM infections in the region. After removing irrelevant and duplicate articles and examining titles and abstracts, we narrowed it down to 84 articles for data mining. Ultimately, 23 met the inclusion criteria, and 19 were meta-analysed (Fig. 1).

Twenty-three studies documented the prevalence and distribution of BM infections, confirmed by laboratory procedures. Specifically, there were seven studies from Gauteng [29–35], one each from Western Cape [8], KwaZulu Natal [36], and Free State [37], as well as nine inter-provincial studies (Table 1 and supplementary Fig. 1). The inter-provincial studies included reports from Chris Hani Baragwanath Hospital (Gauteng) [38], Edendale Hospital (KwaZulu Natal), Mapulaneng and Matikwane hospitals (Mpumalanga), and Klerksdorp-Tshepong Hospital (North West) among others [38–45]. Notably, there were no specific reports on the epidemiology of BM infections from Limpopo, Mpumalanga, Northern Cape, and North West provinces. The only study from Eastern Cape [46] assessed the ability of serum to block murine subtyping monoclonal antibodies from binding in samples from 33 South African subjects with *Neisseria* meningitidis infections. However, it did not address the epidemiological distribution of BM infections and was therefore excluded. Additionally, four studies on national surveillance of BM infections in conjunction with other countries and continents [47–50] were reviewed but not included in the analysis. The reported case sizes ranged from 1 to 32,824 per study, with study periods varying from months to years across various settings, including national, public, private, and military hospitals and laboratories, as summarized in Table 1.

Our findings indicate that out of 115,626 tests conducted, 57,964 (50.131) cases of BM infection were influenced by national epidemiological data derived from the scientific evidence.

However, only nine studies included participants' age. As shown in Fig. 2, the age of 6–17 years was most affected by BM infections, with a prevalence (7.67% proportion of 4,448), followed by the age 18-years group at (6.80% proportion of 3,944). Notably, only two studies reported male participant gender [37, 47]. The infection distribution across provinces revealed Gauteng with 8,072 cases (13.93%) and Western Cape with 883 cases (1.52%). Furthermore, inter-province cases numbered 48,598 (83.84%), as detailed in Fig. 3. The leading

Table 1 Characteristics of the included studies

Authors	Region or province	Total	Cases	Prev (%)	Age	Aetiology	Study area	Study type	Study period
51	Inter-Province	263	135	51.33	< 5years	*Haemophilus influenzae* serotype b	NR	Laboratory-based surveillance	2003–2009
35	Gauteng	1000	1000	100.00	NR	*Listeria*	Steve Biko academic hospital in Pretoria	Case reports	18 months
47	NR	1	1	100.00	5years	Viridans streptococci	NR	Case reports	NR
34	Gauteng	3	3	100.00	44 & 51years	*Streptococcus pneumoniae*	NR	Experimental	I year
33	Gauteng	4770	2988	62.64	NR	*Nesisseria*	NR	Laboratory-based surveillance	2003–2013
36	KwaZulu Natal	14,327	38	0.27	< 5days	*Streptococcus*	R. K. Khan hospital	Report	9 years
8	Western Cape	2920	NR	0.00	< 13years	*N. meningitidis*, *Haemophilus influenzae*, *S. pneumoniae*	Western Cape province of South Africa	Survey	I986-I989
39	Inter-Province	2234	1447	64.77	NR	B meningococcous	Public, private, and military laboratories	NR	NR
40	Inter-Province	4733	3329	70.34	5–17 years	*Streptococcus pneumoniae*	National, laboratory-based surveillance for	Surveillance	NR
41	Inter-Province	40	24	60.00	NR	Meningococcous	Laboratory-based surveillance for	Prospective study	Months
32	Gauteng	285	18	6.32	NR	*S. pneumoniae*	South African institute for medical research	NR	NR
31	Gauteng	26	24	92.31	18years	Meningococcous	Chris Hani Baragwanath hospital	Retrospective cohort	2007–2009
37	Free State	540	236	43.70	≥ 13years	Meningococcous	NDH Bloemfontein, hospital	A retrospective, observational study	20,017–20,019
49	NR	11,680	1195	10.23	< 5years	*H. influenzae*, *N. meningitidis*, *S. pneumoniae*	South Africa's regional reference laboratory	regional reference laboratory	NR
38	Inter-Province	3937	749	19.02	NR	Pneumococcous	Chris Hani Baragwanath hospital (Gauteng), Edendale hospital (Kwazulu Natal), Mapulaneng and Matikwane hospitals (Mpumalanga), and Klerksdorp-Tshepong hospital (North West).	Prospective, hospital-based, observational study	Months
30	Gauteng	122	122	100.00	< 3 months	Group b streptococcus (GBS) is a leading cause of neonatal sepsis and meningitis.	Tertiary care public hospitals in Johannesburg.	Case-control study tertiary care public hospitals	2012–2014
48	Inter-Province	1020	NR	0.00	NR	*Streptococcus* p	The Drakenstein child health study (DCHS) in the western cape province in South Africa	Longitudinal prospective birth cohort study	NR
42	NR	3721	137	3.68	NR	Pneumococcus	National laboratory	Experimental Cross-sectional	NR
43	Inter-Province	46,485	32,824	70.61	NR	NTPn	NR	National, laboratory-based surveillance	2003–2013
50	NR	63	31	49.21	NR	Meningococcus	NR	Prospective	NR
44	Inter-Province	12,254	131	1.07	NR	*Streptococcus pneumoniae*	NR	Retrospective	1991–2016

Table 1 (continued)

Authors	Region or province	Total	Cases	Prev (%)	Age	Aetiology	Study area	Study type	Study period
[52]	Inter-Province	12,717	9959	78.31	NR	*H. influenzae, N. meningitidis,S. pneumoniae*	NR	Germs-SA national and enhanced laboratory-based	2016–2020
[29]	Gauteng	5249	3917	74.62	0-69years	Meningococcus; *Neisseria meningitidis*	National, laboratory-based surveillance	Laboratory-based surveillance	2003–2016

Prev. prevalence, *NR* Not reported, *NTPn* nontypeable pneumococci

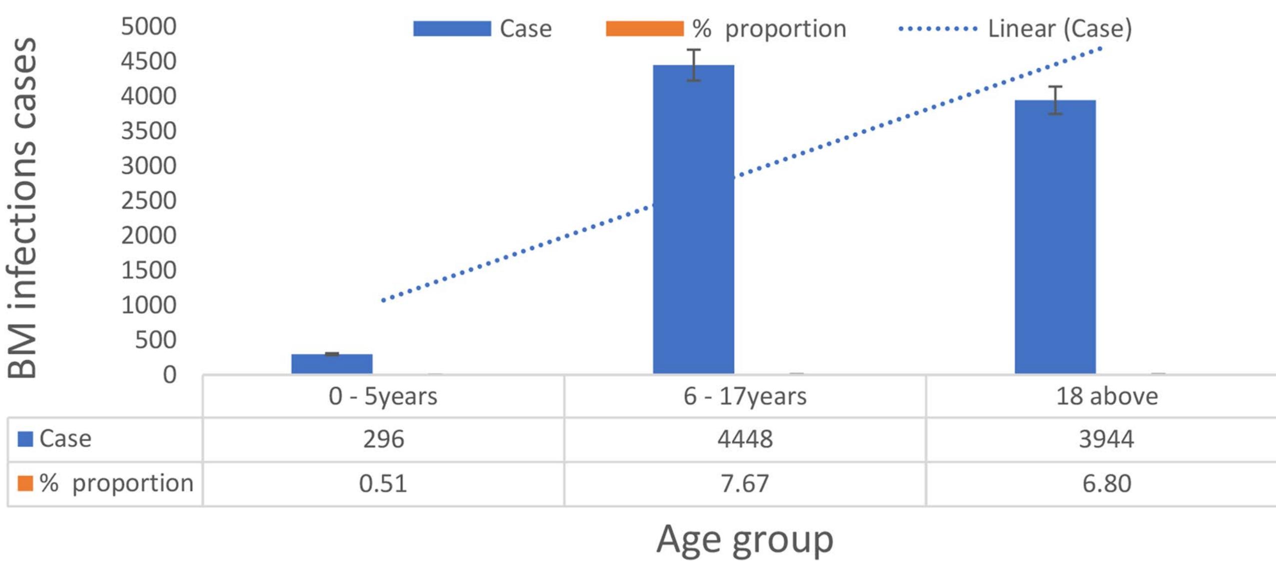

Fig. 2 Age distribution of the national prevalence estimate of BM infections

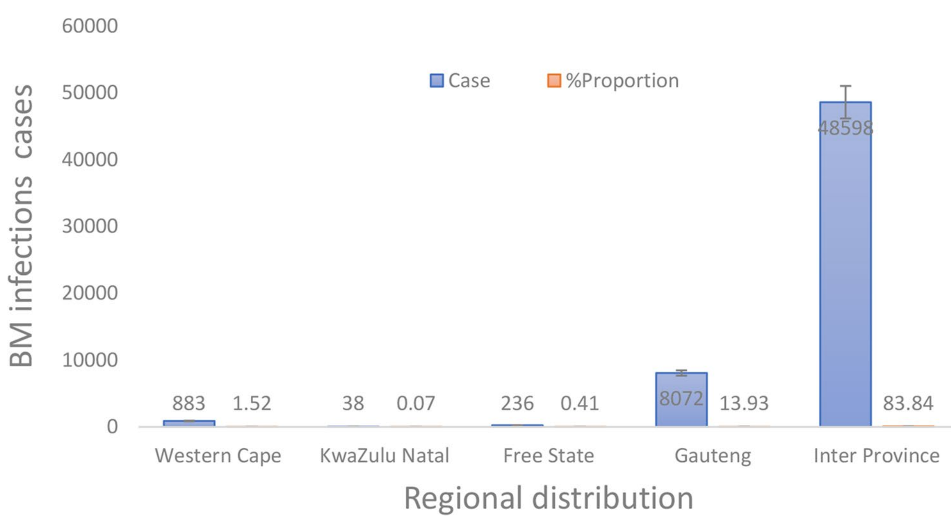

Fig. 3 Regional distribution of the national prevalence estimates of BM infections

aetiology pathogens responsible for BM infections were *Streptococcus pneumoniae* (37,351 cases; 64.44%) and *Neisseria* (4719 cases; 8.14%. Mixed BM infections, including a combination of *N. meninigtidis*, *Haemophilus influenzae*, and *S. pneumoniae*, accounted for 14,759 cases (25.46%). Additionally, *N. meningitidis* is significant, with 4,719 cases (8.14%), as presented in Fig. 4.

Quality assessment Supplementary Table 1 shows the assessment questions in each article's respective domain and the quality evaluation scores of the included articles.

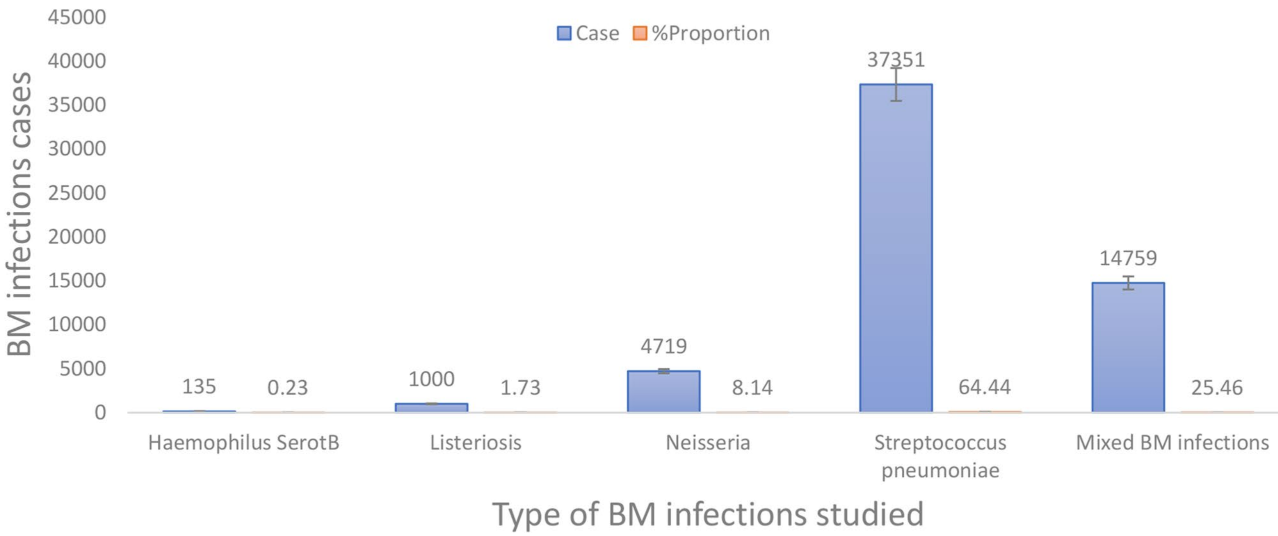

Fig. 4 Pathogens distribution of the national prevalence estimate of BM infections

Due to the lack of comparison studies in the included publications, all meta-synthesized studies rated zero stars for the NOS comparability variables. The quality scores for the remaining studies range from 5 to 7: eight studies scored seven points, five scored six, and five received five points of a possible eight.

National overall pooled prevalence distribution estimate of BM infectious

Among the 19 studies included in the meta-analysis of South Africa's national prevalence of BM infections, the pooled estimate is 38.01% (95% CI: 0.26–0.50), with high heterogeneity (I^2 = 99.86%) determined by a random-effects model, and a significant Q statistic (Q = 13117.45, $p < 0.0001$) as shown in Fig. 5. This indicates considerable variation in effect sizes and a wide distribution of BM infections. The Egger test, illustrated in Figs. 6A & B, confirmed significant publication bias ($p = 0.0005$), indicated by funnel plot asymmetry. Each point on the funnel plot corresponds to a distinct analysis, with the vertical line representing the mean effect size. The uneven distribution of scores further highlights this bias. The Egger test analyzed funnel plot asymmetry using linear regression, revealing that publication bias likely impacted the national prevalence estimate (z = 3.4977, $p = 0.0005$), as depicted in Fig. 3.

Variations in the National prevalence of BM infections: subgroup analysis

The subgroup analysis aimed to identify differences contributing to the national prevalence of BM infections. Categorical subgroup analyses included study size (≥ 1000 vs. <1000 samples) and study duration (months vs. ≥1 year). Results indicated that studies with sample sizes less than 1000 had an estimated prevalence of 27.55% (95% CI: 0.1670–0.4190, I^2 = 95.17%), while those with larger samples had a prevalence of 60.22% (95% CI: 0.3899–0.7819, I^2 = 99.92%). Studies lasting over a year estimated a prevalence of 37.50% (95% CI: 0.2642–0.5005, I^2 = 99.84%), compared to 36.61% (95% CI: 0.0859–0.7802, I^2 = 96.92%) for studies of shorter duration.

Further subgroup analysis by province/region revealed the following prevalence estimates: Gauteng (60.42%, 95% CI: 0.4539–0.7371, I^2 = 98.45%), Free State (43.70%, 95% CI: 0.3957–0.4792, I^2 = 0.00%), Inter Provinces (35.96%, 95% CI: 0.2096–0.5432, I^2 = 99.92%), Western Cape (30.24%, 95% CI: 0.2860–0.3193, I^2 = 0.00%), and KwaZulu Natal (0.27%, 95% CI: 0.0019–0.0036, I^2 = 0.00%). Regarding study design, cohort studies showed an estimated prevalence of 23.91% (95% CI: 0.0445–0.6797, I^2 = 99.69%), cross-sectional studies had a prevalence of 58.69% (95% CI: 0.4906–0.6770, I^2 = 99.72%), and mixed design indicated a prevalence of 29.87% (95% CI: 0.1167–0.5788, I^2 = 99.36%).

Among the pathogens, *Listeria* had the highest impact, with a prevalence of 83.33% (95% CI: 0.1936–0.9905, I^2 = 0.00%), followed by *Neisseria* (62.64%, 95% CI: 0.6126-0.6400, I^2 = 0.00%), and mixed infections (62.46%, 95% CI: 0.3471–0.8389, I^2 = 99.91%). *Haemophilus influenzae* Serotype B had a prevalence of 51.33% (95% CI: 0.4530–0.5732, I^2 = 0.00%), and *Streptococcus pneumoniae* showed the lowest prevalence at 19.53% (95% CI: 0.0674–0.4487, I^2 = 99.92%). Detailed forest plots for these subgroup analyses are shown in Supplementary Figs. 2–6.

In the national survey, the most impactful types of BM infections were *Haemophilus influenzae* Serotype B (*$p = 0.05$) and Neisseria (***$p = 0.001$), compared to *Streptococcus pneumoniae*. Among provinces, Gauteng (*$p = 0.05$), Free State (**$p = 0.01$), and KwaZulu Natal

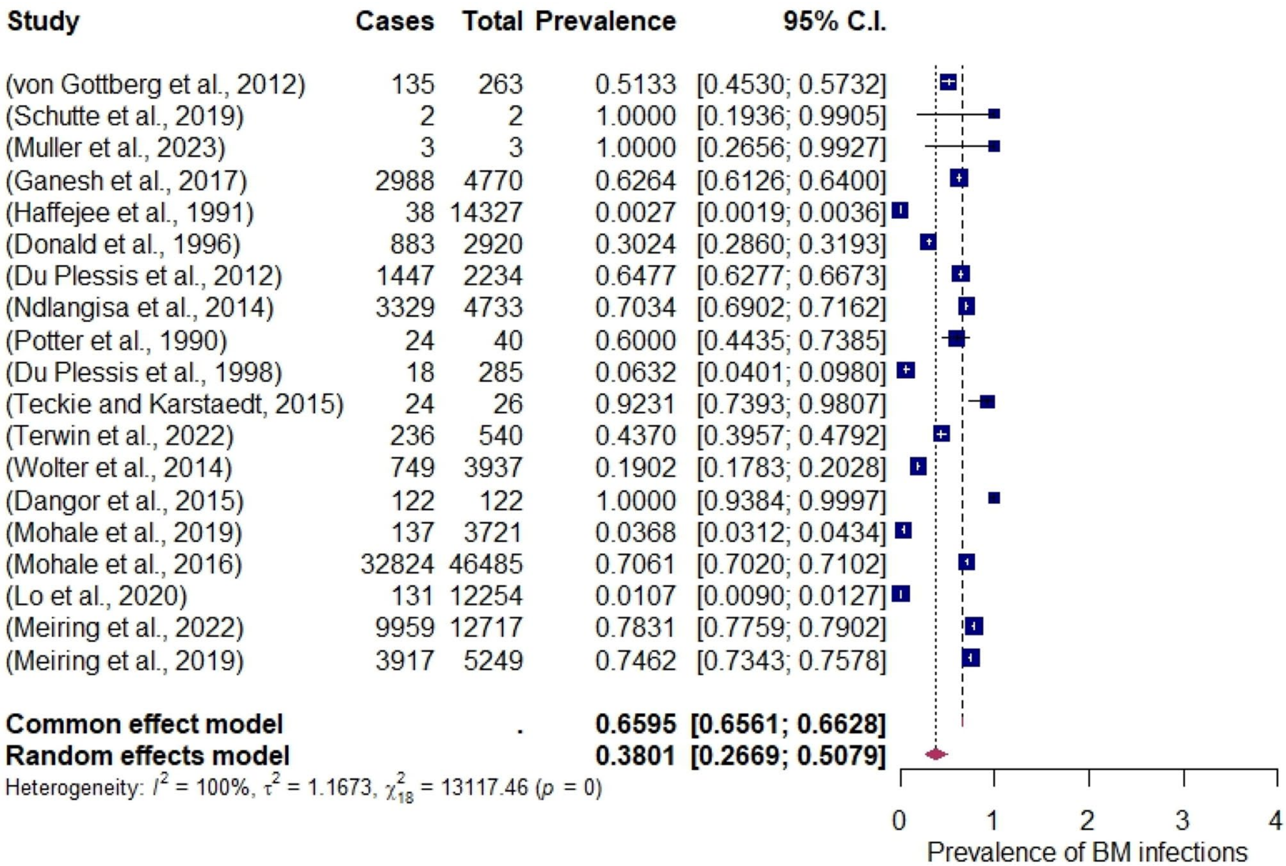

Fig. 5 Forest plot for the national prevalence of BM infections

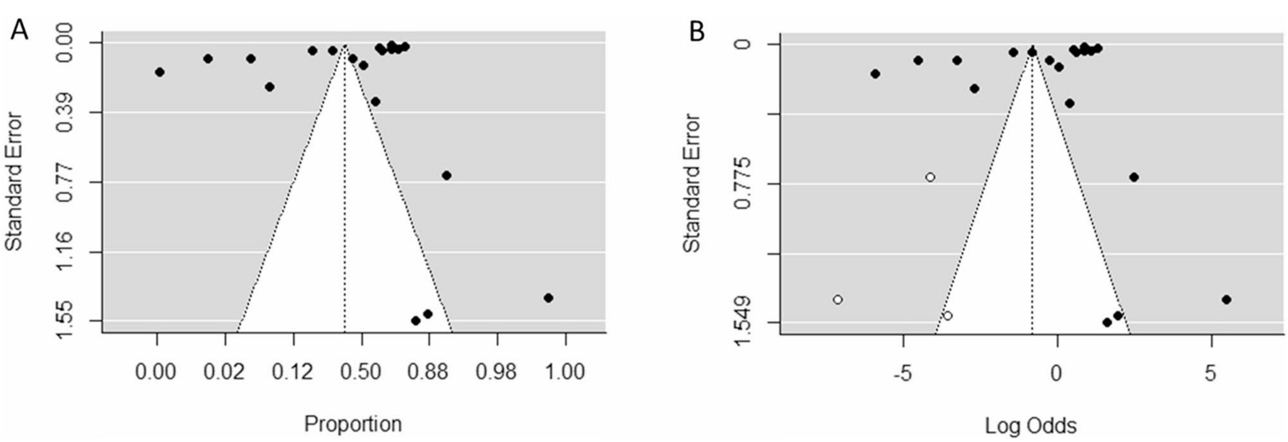

Fig. 6 (A) Proportion (B) Trimfill, of the publication bias shown in the funnel plot for the national prevalence of BM infections studies

(***$p = 0.001$) showed significant differences in infection rates compared to Inter-Provinces, as outlined in Table 2.

Source of heterogeneity analysis for the National prevalence of BM infections: meta-regression

Five covariate characteristics were analyzed to identify the primary causes of heterogeneity in the overall prevalence estimates from the included studies. The level of heterogeneity was measured using R^2 and p-values, which indicated the moderator effects and contributions of each covariate. Univariate meta-regression results showed that study design (R^2 = 52.93%, $p < 0.0001$) and sample size (R^2 = 0.00%, $p = 0.0117$) significantly contributed to the overall heterogeneity of national prevalence rates of BM infections within the studied population. In contrast, the study period (R^2 = 31.62%, $p = 0.1036$) did not significantly correlate with the overall heterogeneity. Multivariate meta-regression indicated that the observed

Table 2 Pooled estimates of the multiple categorical variables on the BM infections of the regional epidemiological characteristics

Categorical Variables	Studies	Estimate effect	95% CI	Random effect model		
				prevalence (%)	95% CI (%)	Heterogeneity (I^2)
Provinces						
InterProvinces	9	−0.3242	−2.5769–1.9285	35.96	20.96–54.32	100%
Free state	1	−0.2532	−2.3896–1.8832	43.7	39.57–47.92	-
Gauteng	7	1.1	−1.2525–3.4524	60.42	45.39–73.71	98%
KwaZuluNatal	1	−5.6765	−8.7098–2.6431	0.27	0.19–0.36	-
WesternCape	1	−0.5827	−3.6003–2.4349	30.24	28.60–31.93	-
Test for Province differences: $p < 0.001$						
Meningitis types						
Streptococcus_pneumoniae	9	−1.5734	−4.6773–1.5305	19.53%	6.74–44.87	100%
*Haemophilus_influenzae*SerotypeB	1	0.0532	−2.8736–2.9801	51.33%	45.30–57.32	-
Listeria monocytogenes	1	1.5562	−3.5716–6.6840	1	19.36–99.05	-
Meningococcous	4	0.6766	−2.6147–3.9679	62.93%	46.63–76.74	97%
Test for Meningitis types differences: $p < 0.05$						
Mixed	3	0.4558	−2.9211–3.8328	62.46%	34.71–83.89	100%
Neisseria	1	0.4636	−3.6690–4.5962	62.64%	61.26–64.00	-
Test for mixed aetiological pathogens differences: $p < 0.001$						

heterogeneity in national prevalence was not significantly associated with meningitis-causing pathogens or types (R^2 = 0.0%, $p = 0.1036$); however, region significantly contributed to the heterogeneity (R^2 = 0.0%, $p < 0.0001$).

Discussion

The first comprehensive scientific analysis of the prevalence or distribution of BM infectious in South Africa is presented in this paper. The prevalence or distribution by provinces or regions, BM infection types, and the impact of categorical variables, such as study design, sample size, and study period, as well as available evidence of demographic variables (gender and age group), are among the potential heterogeneity explored. To shed light on the national occurrence and case prevalence rates of BM, age group, provinces, and pathogen-specific variations, which may have potentially impacted the fatal illness that has long-term sequelae in mid- and low-income nations in Africa.

Our findings show up surging cases of the population infected with BM and the age (6–17years) being at high risk in this scientific evidence-based survey in agreement with previous reports [4, 52, 53]. Also, the studies report from Inter province and the province of Gauteng were the regions with high distribution of BM. Whereas the most impactful bacterial types were *streptococcus pneumoniae*, *Meningococcus*, and *Neisseria meningitidis*, the most significant was the mixed infections. Our findings support other reports of BM infectious [4, 54–57] in African nations.

Furthermore, there are apparent age-related differences in the epidemiology of BM; for example, neonates and older patients have a higher prevalence. *Escherichia coli* and *Streptococcus agalactiae*, or Group B *streptococci*, are the two primary causes of neonatal meningitis [4]. The epidemiological studies from Africa and the Netherlands [58] indicated (51% and 37%) high occurrences of community-acquired bacterial meningitis caused by *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Listeria monocytogenes*. S. *pneumoniae* and N. *meningitidis*, of which 90% of cases affect infants and children. The peculiarities of infant's immune systems and the living conditions among the vulnerable population put them at risk of being infected with BM. Nevertheless, the high prevalence of BM in infants could be attributed to an immature monocyte line resulting in poor phagocytosis, insufficient natural killer cell response, poor cytokine and chemokine secretion, and low interferon concentrations [4, 59]. In addition, there is a high tolerance to self-antigens and lower complement factor levels than in adults [60]. Immune senescence in older adults is marked by aberrant cytokine production, diminished neutrophil phagocytic and cytotoxic capacity, and absolute lymphopenia, among other things [61].

Our findings indicate that the national overall pooled estimate proportion of BM infectious has been very high among the South African population. It implies that BM infections are one of the prevalent causes of death and a widespread contagion that imposes a significant burden on the general population. This estimate is similar to the findings of [45,62], who reported a yearly incidence rate of 4/100,000 among the general population and a prevalence rate of 40/100,000 in infants in South Africa. However, this observation was not based on scientific evidence or national findings. Therefore, it is necessary to document the BM infection burden to gather comprehensive evidence and thorough epidemiological data nationally for public health engagement. Our finding depicts limited comprehensive studies on BM infections, which, unfortunately, have focused on specific regions and restricted populations and only examined certain epidemiological factors. Our survey indicates sparsity evidence from the provinces and little or no documentation on the gender and specific age impact of BM infections. The scarcity of these kinds of investigations is frequently attributed to limitations in research findings for public awareness, weakened health policy implementations, and a deficiency in connected health surveillance systems, leading to an insufficient integration of the evidence and outcomes. Accumulating evidence from diverse sources in the fields of public health burden is essential for the effectiveness of programmes and policies aimed at preventing/managing the BM burden on a national scale. Efficient monitoring and surveillance, improved immunization initiatives, and the creation of innovative treatment approaches are crucial for reducing the consequences of BM burden in South Africa. Tackling BM health challenges requires a well-coordinated endeavour to enhance regular surveillance systems or healthcare infrastructure, bolstering diagnostic capacities, advances in research for alternative treatment, and widening the availability of current medications.

South Africa National estimates of the prevalence of BM infections

This review and meta-analysis examine the current South African national prevalence of BM infections based on scientific evidence. Our findings indicate a national overall prevalence of 38.01% and a lack of adequate representation of research conducted in some provinces. Examining covariates analytics of study design, size, period, BM infection pathogens types, and provinces variables that effectively explains the heterogeneity in the national pooled prevalence. However, the reported province has a prevalence rate of BM infections ranging from 0.27% to 60.42%. This indicates that the current BM infection significantly impacts public health, as reported by mainstream researchers.

Furthermore, significant variations in study design were attributed to the substantial disparity in healthcare provision and medical health recording systems, resulting in discrepancies in data accessibility, as documented by the primary findings. It shows that most of the included studies possess extensive referral database structures and medical recording systems, which enable the execution of exceptional prevalence studies. However, several others are limited to conducting studies at a national or regional hospital level and do not have consistent surveillance data systems from primary care systems. In addition, it is clear from our findings that most evidence was reported from National, Public, private, and military hospitals and laboratories, while most of the findings from primary paediatric hospitals or primary care units were limited. This implies integrating primary healthcare data into mainstream research findings for stakeholders' engagement. At the same time, the importance of better diagnostic tools cannot be overstated due to the challenges in interpreting clinical symptoms and CSF results. This is necessary to prevent the omission of potentially life-saving diagnoses that may be lacking in primary health facilities.

The studies in this analysis exhibit significant heterogeneity in research sample sizes, making it inappropriate to directly compare case report studies with population-based observational investigations, large-scale national research, and prospective or retrospective cohort surveys. Also, the study period covers a wide range (months to years), indicating good coverage of epidemiological findings. The utilization of secondary data in prospective or retrospective cohorts may be restricted to pre-existing variables accessible in the laboratory information system (LIS) and relied on the data documented on laboratory order forms by clinicians at the source. This leads to insufficient data and sample size, resulting in selection bias.

Furthermore, our investigation revealed a diverse range of BM infection types with notable clinical implications in the region. The causing pathogens include *Haemophilus influenzae* serotype B, *Listeria*, *Neisseria meningitidis*, *Haemophilus Streptococcus pneumoniae*, and *H. influenzae* [35–38, 40, 51]. However, the most significant impactful pathogens include *Streptococcus pneumoniae*, *Nesisseria*, *Listeria* and mixed infections [62]. Nevertheless, there has been a lack of current epidemiological research that comprehensively describes the national impact of meningitis caused by specific infections. Our findings highlighted one or more specific bacteria causing the BM infections. Often, distinguishing between bacterial and viral meningitis only based on clinical symptoms may have limited the specific identification of BM infection. BM infections were significantly prevalent in provinces like Free State, Gauteng, and KwaZulu Natal compared to reports of inter-province. Meanwhile, some provinces were under-reported by mainstream research.

Africa exhibits the highest prevalence of bacterial meningitis, with outbreaks that often fluctuate according to the season and geographic location in the meningitis belt, which spans from Senegal to Ethiopia in the sub-Saharan region [63]. Globally, Pneumococcus and Meningococcus are well documented as the primary causative organisms responsible for BM infections in infants (< 1) and adults [4]. Similarly, in South Africa, our findings reveal *Streptococcus agalactiae* (group B *Streptococcus*), *Escherichia coli*, and *Staphylococcus aureus* to be responsible for the prevalence of newborn meningitis [30, 36, 38, 49, 51]. Serogroup B meningococcal illness in South Africa occurs infrequently and without a predictable pattern between 2005 and 2008. However, someone may wonder about the current trend [39]. Although attempts have been made to vaccinate against the common sources of BM infections, meningitis remains a major health burden in Africa [4].

Future engagement strategies in managing BM infections in South Africa

This study provided scientific evidence for developing policies to alleviate the burden of meningitis within the South African region. Inadequate data from some provinces or regions and the lack of complete gender or age reports in our scientific evidence highlight significant gaps in the national surveillance that are crucial for monitoring the spread of BM infectious pathogens and formulating vaccination strategies. Given the limited ability of BBB penetration and the increasing problem of antibiotic resistance, coupled with the various concerns surrounding vaccines, there is a pressing requirement for novel treatment alternatives and improved emergency medical care at national and regional scales for BM infections worldwide.

Furthermore, future engagement may involve assessing trends in neonatal infections over time for interventions' impact, regular evaluation of antimicrobial susceptibility patterns and risk factors for neonatal mortality [45]. Studies to assess the efficacy of updated treatment protocols for BM and examine the long-term consequences and complexities of treating *Listeria* meningitis could be beneficial [35]. The primary focus of our study was on infectious meningitis primarily caused by *Neisseria*, *Listeria*, *Streptococcus*, *Escherichia coli*, and *Staphylococcus aureus*. We did not investigate co-infections such as TB, HIV, HPV, or other terminal illnesses. However, it is important to explore the impact of co-morbidities on the outcomes of meningitis [37]. The relationship between war, freedom struggle, political instability and disease burden in Africa is still not well understood, and this lack of understanding may be connected to the scarcity of African data on BM infections [24], [4]. In order to tackle the difficulties associated with managing and diagnosing paediatric meningitis patients, future research should prioritize the investigation of innovative diagnostic methods that can provide accurate and fast diagnoses [62]. Furthermore, conducting studies investigating the factors contributing to the delayed diagnosis and treatment of meningitis could potentially affect the observed prevalence of the disease in South Africa and the entire African continent. Research to enhance vaccination coverage and rates in locations with a high risk of BM disease and investigations on factors that impact the integrity of the blood-brain barrier during infection based on epidemiological groups may improve the burden [65]. Studies focused on improving polysaccharide vaccines with limitations in immunologic memory and efficacy [66] are essential. Also, the PsA-TT vaccination effectively filled the need to manage group A meningococcal illness; a similarly innovative approach to vaccine development that prioritizes the precise specifications of the product and its affordability will be impactful [67].

Study limitations

The keywords, title specific and databases used for data collection may have limited the research scope and excluded literature not indexed in the utilised databases, may have offer distinctive insights or encompass upcoming trends. We are confident that the evidence compiled from Scopus, WoS, PubMed, and handpicked literature references will offer a comprehensive overview of the research landscape. The ecological character of this study restricts the ability to make causal inferences based on the data. Population-based studies can reveal disease patterns within a community and serve as a foundation for conducting more comprehensive investigations. Furthermore, as we only considered instances of meningitis (*Listeria*, *Neisseria meningitidis*, *Haemophilus Streptococcus pneumoniae*) that were confirmed in laboratories from public healthcare facilities, we have probably underestimated the actual extent of the disease.

Other limitations of this study are the scarcity of comparable and precise details in the prevalence estimates due to the exclusion of several studies. For example, studies reporting BM infections in HIV, TB or co-morbidity with other illnesses were disqualified. Also, studies from multinationals, those that did not provide essential data (total population, number of cases, expected outcome (prevalence), were not eligible for inclusion. At the same time, poor age and gender representation limited their subgroup analysis. Additionally, only studies conducted in English were included in our analysis. Consequently, this study's national estimated prevalence of BM infections may be underestimated.

Our meta-analysis on BM infections among the South African population is the first national survey; we examine the epidemiological distribution of BM infections to highlight a significant public health burden for future research. The epidemiological survey synthesis integrates data from various sources, including national, public, private, and military hospitals and laboratories. We can learn more about BM infection using the complete information that has been collected. This study establishes a framework for future epidemiologic studies that use evidence data, sheds light on preventative strategies, and emphasizes the need for more complete data to understand BM infections.

Conclusion

The findings emphasize the significant occurrence of BM infections that affect South Africa's epidemiological situation, while some provinces lack research-based data. It underscores the need for implementation of regular surveillance tailored to the South African region's specific BM infections epidemiological conditions and review of treatment guidelines at the national level. Furthermore, it informs policymakers and stakeholders of the urgent need for effective prevention initiatives and treatment strategies in the region.

Supplementary Information

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Supplementary Material 1.

Authors' contributions

Author Contributions StatementHO and YEC conceived, designed and conducted the study. HO analyzed, Interpreted the results and drafted the manuscript. HO and YEC revised the manuscript. All authors agreed for the final version to be published.

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Data availability

The datasets/information used for this study are available in the supplementary files and the manuscript.

Declarations

Ethics approval and consent to participate

Not Applicable.

Consent for publication

All the authors have read and agreed to the final copy of the findings in the manuscript.

Competing interests

The authors declare no competing interests.

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