Review

Opportunistic Pathogens in Malnourished African Children: A Scoping Review

Bassey Ekeng *, Olufunke Adedokun, Vivien Otu, Stella Chukwuma, Agatha Okah, Osamagbe Asemota, Ubokobong Eshiet, Akpan Morgan, Rosa Nwagboso, Eti Ebiekpi, Emmanuella Umoren, Edet Usun

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Opportunistic Pathogens in Malnourished African Children: A Scoping Review

Bassey Ekeng [1,*], Olufunke Adedokun [2], Vivien Otu [2], Stella Chukwuma [3], Agatha Okah [4], Osamagbe Asemota [2], Ubokobong Eshiet [2], Akpan Morgan [5], Rosa Nwagboso [6], Eti Ebiekpi [7], Emmanuella Umoren [8] and Edet Usun [2]

1 Department of Medical Microbiology and Parasitology, University of Calabar Teaching Hospital, Calabar, Nigeria
2 Department of Paediatrics, University of Calabar Teaching Hospital, Calabar, Nigeria
3 Department of Medical Microbiology, College of Medicine, Enugu State University of Science and Technology, Enugu, Nigeria
4 Department of Paediatrics, University Hospitals Coventry and Warwickshire, UK
5 Department of Paediatrics, University of Uyo Teaching Hospital, Uyo, Nigeria
6 Department of Family Medicine, University of Calabar Teaching Hospital, Calabar, Nigeria
7 Department of Community Medicine, University of Uyo Teaching Hospital, Uyo, Nigeria
8 Department of Paediatrics, Leeds Teaching Hoospital Trust, UK
* Correspondence: basseyewaekenggmail.com; +2348037361816

Abstract: Understanding the interplay between infections and severe acute malnutrition is critical in attaining good clinical outcomes in managing malnourished children. However, review studies describing the profile of the associated pathogens in the malnourished African pediatric population are sparse in the literature. We aimed to identify the spectrum of pathogens from studies reporting infections in malnourished African children, as well as the antibiotic resistance pattern and clinical outcomes. A systematic literature of the PubMed database was conducted following PRISMA guidelines from January 2001 to June 2024. The search algorithm was ((marasmus) OR (kwashiorkor) OR (severe acute malnutrition) OR (protein energy malnutrition)) AND (Africa). For a more comprehensive retrieval, an additional search algorithm was deployed: (HIV OR tuberculosis) AND (severe acute malnutrition). We included 67 studies conducted between 2001 and 2024. Most of the studies were from East Africa (n=53, 79.1%) and Southern Africa (n=5, 7.4%). A total of 7,056 pathogens were identified comprising 3,030 Viruses, 2,381 bacteria, 1,452 parasites and 193 fungal pathogens. The predominant pathogens were HIV, *Mycobacterium tuberculosis*, and malaria parasites accounting for 42.5%, 25.2%, and 17.1% respectively. Antibiotic susceptibility testing was documented in only three studies. Fatality rates were reported in 49 studies and ranged from 2% to 56% regardless of the category of pathogen. This review affirms the deleterious effect of infections in malnourished patients and suggests a gross underdiagnosis as studies were found from only 17 (31.5%) African countries. Moreover, data on fungal infections in malnourished African children was nearly absent despite being at risk. There is also a need to prioritize research investigating African children with severe acute malnutrition for fungal infections besides other opportunistic pathogens and improve the availability of diagnostic tools and the optimized usage of antibiotics through the implementation of antimicrobial stewardship programmes.

Keywords: severe acute malnutrition; tuberculosis; HIV/AIDS; immunocompromised; Africa

1. Introduction

Severe acute malnutrition (SAM) is a significant global health issue, defined by the World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) based on specific criteria: a weight-for-height z-score (WHZ) below -3, a mid-upper arm circumference

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(MUAC) under 115 mm, or the presence of nutritional edema [1]. According to UNICEF (2022), 45 million children under five were impacted by wasting, with 13.7 million categorized as severely wasted [2]. The burden of SAM is predominantly concentrated in South Asia and sub-Saharan Africa, where factors such as drought, armed conflict, poverty, food insecurity, inadequate healthcare infrastructure, and socioeconomic instability exacerbate the prevalence of malnutrition [3]. Despite global efforts, the continent continues to struggle with high rates of undernutrition, micronutrient deficiencies, obesity, and non-communicable diseases. According to a recent report by United Nations agencies, nearly 282 million people in Africa, or about 20% of the population, were undernourished in 2022 [4]. Malnutrition rates vary significantly across African regions, with sub-Saharan Africa bearing the heaviest burden. In Eastern Africa, countries such as Ethiopia, South Sudan, and Somalia have some of the highest stunting rates, often exceeding 30% [5].

The role of climate change in exacerbating SAM is particularly concerning. The Intergovernmental Panel on Climate Change (IPCC) reports that global warming is intensifying food insecurity, especially in tropical regions where 95% of malnourished individuals reside [6]. Rising temperatures and more frequent extreme weather events, such as droughts, lead to reduced agricultural productivity, directly contributing to increased rates of malnutrition. The interconnectedness of climate change and food security highlights the need for comprehensive approaches that address environmental factors in the fight against malnutrition.

SAM leads to physical wasting and severely compromises the immune system, increasing susceptibility to infections. These infections—whether bacterial, viral, parasitic, or fungal—tend to be more frequent and severe in SAM patients, further elevating metabolic demands and depleting already scarce nutrient reserves. This creates a vicious cycle where malnutrition and infection exacerbate each other, complicating recovery and worsening health outcomes [7]. Infectious diseases pose significant health risks, particularly in regions afflicted by high rates of malnutrition, such as sub-Saharan Africa. The widespread prevalence of malnutrition and opportunistic infections in sub-Saharan Africa underscores the formidable health challenges facing the region. The immune dysfunction associated with SAM can lead to a higher risk of morbidity and mortality from common childhood illnesses such as diarrhea and pneumonia [7]. It is a major public health issue in Africa, affecting millions of people, particularly children under five [8]. However, large-scale reviews describing the spectrum of pathogens in children with SAM are lacking in the literature, particularly for the African setting. In addition, data on the susceptibility profile of these pathogens are fragmented in the literature. Previous reviews focused on undernutrition and associated factors among HIV-infected children in sub-Saharan Africa [9], while reviews summarizing data on pathogens in African children with SAM have largely been focused on HIV [10,11]. Studies on other groups of pathogens in this at-risk group and their antimicrobial-resistance pattern are lacking. Thus, the overarching aim of this review was to highlight the burden of pathogens reported in African children with SAM, and the need to drive antimicrobial stewardship practices in this setting and invariably improve clinical outcomes.

2. Materials and Methods

2.1. Study Design

We conducted a scoping review of literature adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines [12].

2.2. Search Strategy

We conducted a systematic literature search of the PubMed database between January 2001 to June 2024 (BEE). The search algorithm was ((marasmus) OR (kwashiorkor) OR (severe acute malnutrition) OR (protein energy malnutrition)) AND (Africa). An additional search algorithm was deployed for a more comprehensive retrieval: (HIV OR tuberculosis) AND (severe acute malnutrition). No language restrictions were applied.

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2.3. Inclusion and Exclusion Criteria

All articles with primary data on pathogens in malnourished African children were eligible for inclusion. Studies reporting infections in malnourished children outside Africa or in children who were not classified as 'malnourished' were excluded. Review articles were also excluded.

2.4. Selection Process

Two authors (BEE and OFA) conducted the initial screening of titles and abstracts, focusing on studies reporting pathogens in malnourished African children. Selected studies were further screened, and duplicates were removed as more than one search algorithm was deployed. Full-text assessment was thereafter performed and followed by data extraction. Discrepancies in inclusion/exclusion decisions were resolved through a discussion.

2.5. Data Extraction

Data on study authors, study location, (country and region in Africa), study period, study design, age range, pathogens, clinical presentation, investigation/diagnostic measures, and treatment outcomes (fatality/mortality rates) were extracted. Four authors (BEE, OFA, UIE, and AGO) performed data extraction, and any indifferences revolved by a consensus. Descriptive statistics was used to summarize the findings.

3. Results

3.1. Search Results

Our initial search yielded 1,023 articles and 311 articles following an additional search, amounting to a total of 1,334. After the selection process, 91 articles were identified as having met the inclusion criteria. Others were excluded for several reasons including lack of information regarding this review, clinical trial studies, reviews, guidelines, studies reporting infections in the non-African paediatric population, studies reporting infection in adults, amongst others. Of the 91, 31 duplicates were removed, remaining 60 articles. Seven articles were added from other sources, thus a total of 67 articles were included in this review, Figure 1.

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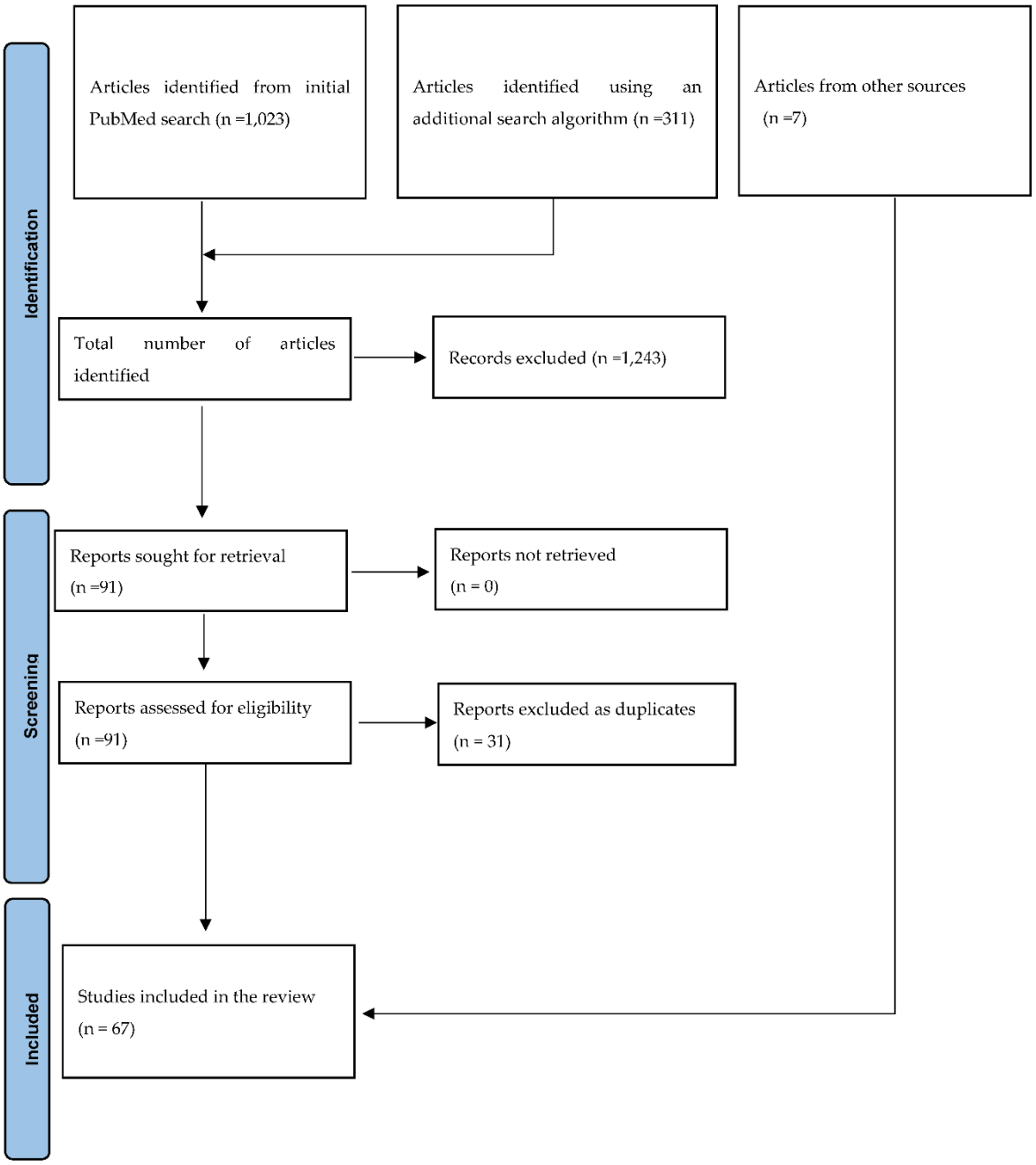

Figure 1. PRISMA flow diagram.

3.2. Demographics

We included 67 studies conducted between 2001 and 2024. Data was found from only 17 (31.5%) of the 54 African countries including Ethiopia (n=25), Uganda (n=10), South Africa (n=5), Zambia (n=5), Malawi (n=3), Mozambique (n=3), Kenya (n=2), Sudan (n=2), Nigeria (n=2), Niger (n=2) and Cameroon, Senegal, Zimbabwe, Sierra Leone, Democratic Republic of Congo and Ghana (one study each). Two studies were conducted in centres located in two different countries: Kenya/Tanzania and Zambia/Zimbabwe. When stratified by regions, most of the studies were from East Africa (n=53, 79.1%) and Southern Africa (n=5, 7.4%).

3.3. Study Designs

Of the sixty-seven, the study designs were retrospective (47.8%, n=32), prospective (28.4%, n=19), cross-sectional (n=20.9%, n=14), and case-control (3%, n=2). 95.5% (n=64) were hospital-based studies, 3% (n=2) were community-based studies and 1.5% (n=1), an outpatient therapeutic programme. The

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study population was children with SAM in fifty-seven studies, complicated SAM in seven, a combination of SAM and moderate acute malnutrition (MAM) in two studies, and undernourished children in one study.

3.4. Pathogens

A total of 7,056 pathogens were identified. Viruses comprised 42.9% (n=3,030) and predominantly HIV (99.1%, n=3,002), bacteria, 33.7% (n=2,381), majorly *Mycobacterium tuberculosis* (74.7%, n=1,779), parasites, 20.6% (n=1,452), commonest amongst which was malaria parasite (83.4%, n=1,207) and fungal pathogens (2.7%, n=193). HIV infection, TB, and malaria accounted for 42.5%, 25.2%, and 17.1%. Figure 2 shows a snapshot of the number of all pathogens identified in their respective categories. Cases of infections without a mention of associated pathogens were excluded from the analysis of pathogens identified in this review. Overall, Viruses were majorly implicated followed by bacteria and parasites. Fatality rates were reported in 49 studies and ranged from 2% to 56% regardless of the category of pathogen, Table 1.

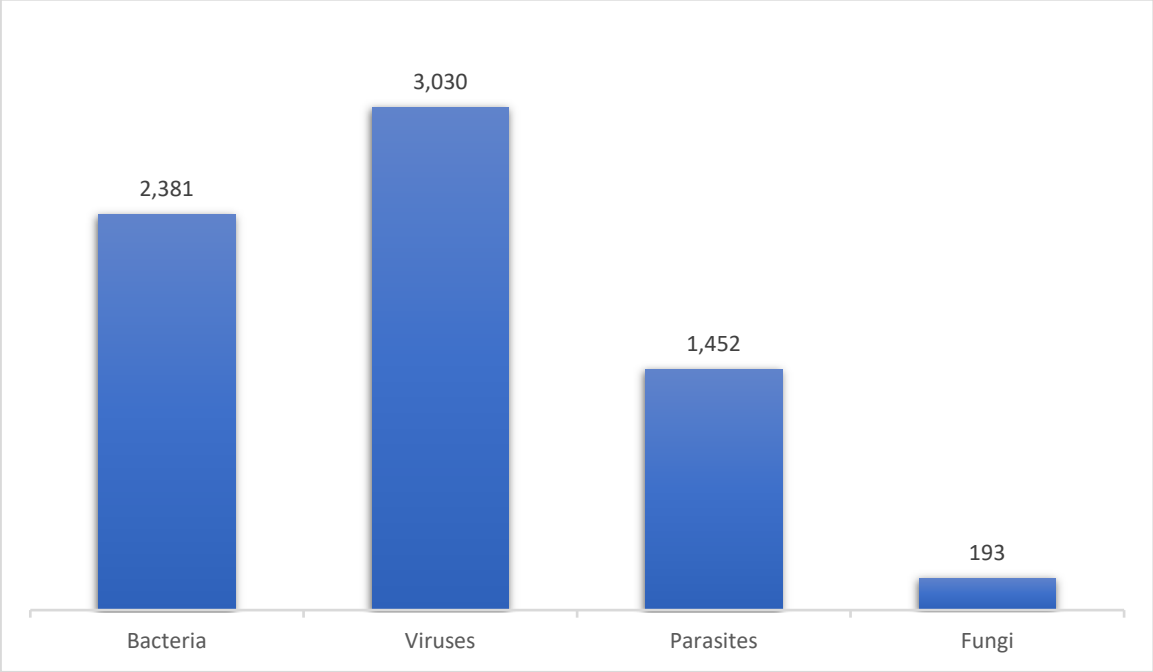

Figure 2. A pictorial representation of pathogens in malnourished African children.

Table 1. Summary of original studies reporting pathogens in malnourished African children.

Location/ Country	Type of Study	HB/CB/ OTP	Study period	Study population	Sample size (n)	Age range or Median age	Number of Pathogens/Infection cases (n)	Fatality rates	Authors/ Year of publication	No. of reference
South Africa	Prospective, observational study	HB	NS	SAM	113	< 5 years	HIV (n=58), TB (n=27)	11.5 % (n=13)	De Maayer et al 2011	[13]
[a]Ethiopia	Retrospective	HB	2013 to 2015	SAM	545	< 5 years	Malaria (n=37),	9.3 %	Girum et al 2017	[14]

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	cohort study						TB (n=41)	(n=51)		
Sierra Leone	Descriptive cross-sectional study	HB	Over 6 months in 2018	SAM	74	Median age of 11 months	TB (n=20)	-	Ide et al, 2019	[15]
Zambia	Retrospective study	HB	2009 to 2013	SAM	9,450	0 to 59 months	TB (n=151)	56% (n=84)	Munthali et al 2017	[16]
Mozambique	Retrospective study	HB	February to August 2018	SAM	45	0 to 59 months	TB (n=17)	-	Osorio et al. 2020	[17]
[a]South Africa	Cross-sectional study	HB	2014 – 2018	SAM	956	Children under 5 years	HIV (n=181) TB (n=127) Malaria (n=4)	25.9 % (n=248)	Gavhi et al.2019(2020)	[18]
Uganda	Cross-sectional study	HB	June 2021 to December 2022	SAM	797	1 month to 5 years	HIV (n=76)	-	Musiime et al. 2024	[19]
[b]Zambia/ Zimbabwe	Prospective cohort study	HB	July 2016 and March 2019	SAM	649	1 to 59 months	HIV (n=130)	8.5 % (n=55)	Bwakura-Dangarembizi et al, 2021	[20]
Malawi	Prospective cohort study	HB	NS	SAM	454	6 to 59 months	HIV (n=79)	14.8 % (n=67)	Chinkhumba et al, 2008	[21]
[a]Niger	Prospective study	HB	November 2007 to July 2008	Complicated SAM	311	6 to 59 months	Bacteremia, n=79, malaria parasite, n=44, enteric pathogens isolated from stool (bacteria, n=36, viruses, n=23,	9% (n=29)	Page et al, 2013	[22]

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							intestinal parasites, n=6), TB (n=4), pathogens isolated from the urinary tract (bacteria, n=48), pathogens identified from nasal swabs (viruses, n=5)			
Mozambique	Retrospective observational study	HB	March 2016 to February 2017	SAM	1,231	0 to 5 years	HIV (n=157)	-	Calgaro et al, 2021	[23]
Ethiopia	Cross-sectional study	HB	April – June 2020	SAM	208	6 to 59	HIV (n=11)	-	Teshale et al, 2023	[24]
[a]Ethiopia	Retrospective cohort study	HB	January 2012 to December 2015	SAM	500	Under 5 years	TB (n=15)	7% (NS)	Yohannes et al, 2017	[25]
[a]Mozambique	Cross-sectional study	HB	January 2018 to March 2020	Undernourished children	449	1 to 14 years	HIV (n=120), malaria (n=12), intestinal parasitic infections (n=90)	-	Cossa-Moiane et al, 2024	[26]
Zambia	Retrospective study	CB	October 2009 and September 2012	SAM (n=1,195) MAM (n=664)	1,859	Median age of 16 months	HIV in children with SAM (n=134) HIV in children with MAM (n=51)	2.9 % (n=53)	Amadi et al, 2016	[27]

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[a]South Africa	Retrospective cohort study	HB	October 2014 to December 2018.	SAM	126	0 to 59 months	HIV (n=23), TB (n=17)	15.1% (n=19)	Heydenrych et al, 2024	[28]
[a]Ghana	Cross-sectional prospective study	HB	February 2010 to October 2010	SAM	246	3 months to 13 years	HIV (n=67), TB (n=23), malaria (n=34), bacteremia (n=85)	17.5% (n=43)	Asafo-Agyei et al 2013	[29]
[a]Ethiopia	Retrospective follow-up study	HB	March to April, 2018	SAM	398	6 to 59 months	HIV (n=1), malaria (n=76), TB (n=27)	-	Wondim et al, 2020	[30]
[a]Ethiopia	Retrospective cohort study	HB	September 2017 to March 2020.	Complicated SAM	665	0 to 59 months	HIV (n=5), TB (n=23), malaria (n=2)	9% (60)	Oumer et al, 2021	[31]
Sudan	Prospective hospital-based study	HB	April to October 2018	SAM	376	6 to 59 months	Malaria (n=131), intestinal parasites (n=24)	3.7% (n=14)	Bilal et al, 2020	[32]
Kenya	Prospective descriptive study	HB	June 2005 to June 2009	SAM	1,206	6 to 12 years	HIV (n=229), malaria parasitemia (n=227), bacteremia (n=86)	16% (194)	Talbert et al, 2012	[33]
Malawi	Cross-sectional observational study	HB	February to May 2012	SAM	300	6 to 60 months	HIV (n=52), TB (n=2)	9.7% (n=29)	LaCourse et al. 2014	[34]
[b]Kenya/Tanzania	A retrospective study	HB	2004 to 2005	SAM	1121	NS	Malaria (n=404), candidiasis (n=119), TB (n=293)	19% (n=64)	Sunguya et al, 2006	[35]

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								28% (n=222)		
Niger	Cross-sectional study	HB	2016 to 2017	SAM	202	< 5 years	TB (n=90)	19.6 % (n=20)	Schramm et al. 2021	[36]
[a]Uganda	Prospective study	HB	September-November 2003 and September-December 2004	SAM	450	< 60 months	HIV (n=151), bacteremia (n=76)	28.9 % (n=22)	Bachou et al, 2006	[37]
Zambia	Retrospective	CB	2012 to 2014	SAM	858	6 to 59 months	HIV (n=63), malaria (n=7)	5.6 % (n=48)	Moramarco et al, 2016	[38]
Nigeria	Cross-sectional study	HB	-	SAM	400	< 5 years	HIV (n=31)	-	Sudawa et al, 2013	[39]
[a]Ethiopia	Retrospective cross-sectional study	HB	2018 – 2020	SAM	414	< 5 years	Malaria (n=7), HIV (n=20), TB (n=43)	-	Atalell et al, 2021	[40]
[a]South Africa	A retrospective multicohort study	HB	2009 – 2013	SAM	454	6 to 60 months	HIV (n=196)	24.4 % (n=108)	Muzigaba et al, 2017	[41]
[a]Ethiopia	Retrospective	HB	2012 - 2016	SAM	1690	The majority of the participants were < 2 years	TB (n=107), HIV (n=54)	-	Baraki et al, 2020	[42]

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[a]Democratic Republic of Congo	Retrospective	HB	2017 - 2018	SAM	633	1 month to 18 years	HIV (n=14), malaria (n=33), bacteremia (n=38)	9.2 % (n=58)	Kambale et al, 2020	[43]
[a]Ethiopia	Retrospective cohort study	HB	2012 – 2019, (may to June 2019)	SAM	515	Majority were < 24 months	TB (n=71)	9% (n=46)	Bitew et al, 2020	[44]
[a]Ethiopia	Retrospective cross-sectional study	HB	2015 - 2017	SAM	205	1 month – 14 years	HIV (n=21), TB (n=16), malaria (n=30)	4.4 % (n=9)	Mena et al, 2018	[45]
[a]Ethiopia	Retrospective study	HB	2013 - 2015	SAM	196	Median age: 12+8.5 months.	TB (n=27), malaria (n=2)	16% (NS)	Kabeta et al, 2017	[46]
[a]Uganda	Analytical and Descriptive Prospective Cohort Study	HB	July to September 2019	SAM	338	< 5 years	Malaria (n=72), bacteremia (n=23), HIV (n=20), TB (n=17)	14.5 % (49)	Banga et al, 2020	[47]
[a]Ethiopia	Retrospective cohort study	HB	2015 to 2017	SAM	420	6 to 59 months	HIV (n=3), TB (n=87), malaria (n=10)	10.8 % (n=41)	Fikrie et al, 2019	[48]
[a]Ethiopia	Cross-sectional study	HB	2010 to 2012	SAM	298	2 to 59 months	HIV (n=5)	11.7 % (n=35)	Abeje et al 2016	[49]
[a]Ethiopia	A Retrospective Cohort Study	HB	2011 to 2013	SAM	415	0 to 59 months	TB (n=9), HIV (n=17), malaria (n=77)	28.7 % (n=119)	Desta et al, 2015	[50]
[a]Ethiopia	A Retrospective	HB	2013 to 2016	Complicated SAM	259	6 to 59 months	TB (n=18), HIV (n=11)	12.2 %	Negussie et al, 2020	[51]

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	Cohort Study							(n=37)		
[a]Nigeria	Prospective cohort study	HB	2017 to 2019	SAM	100	Mean age: 14.28 ± 14.04 months	HIV (n=81), TB (n=79)	7.7 % (NS)	Ikobah et al, 2022	[52]
[a]Ethiopia	Retrospective cohort study	HB	2014 to 2016	SAM	253	6 to 59 months	TB (n=19)	5.5 % (n=14)	Mekuria et al, 2017	[53]
[a]Uganda	Prospective cohort study	HB	2014 to 2015	SAM	400	6 to 59 months	HIV (n=43)	9.8 % (39)	Nabukeera-Barungi et al, 2017	[54]
[a]Ethiopia	Cross-sectional study	HB	2012 to 2016	SAM	401	6 to 59 months	TB (n=37), HIV (n=26), malaria (n=13)	8.5 % (n=34)	Desyibelew et al 2017	[55]
[a]Cameroon	Retrospective study	HB	2006 to 2015	SAM	179	< 15 years	Malaria (n=27)	15% (n=27)	Chiabi et al, 2016	[56]
[a]Senegal	Descriptive and analytical cross-sectional study	HB	March to November, 2021	Complicated SAM	103	6 to 59 months	TB (n=2), HIV (n=6)	2.9 % (n=3)	Ba et al, 2023	[57]
Uganda	Cross sectional study	HB	2023 - 2024	SAM	137	6-59 months	TB (n=32)	-	Asiimwe et al, 2024	[58]
[a]Ethiopia	Cross sectional study	HB	Not stated	SAM	351	0.5-14 years	HIV (n=9), TB (n=17), malaria (n=9)	-	Girma et al 2013	[59]
[a]Ethiopia	Retrospective study	HB	2015 - 2019	SAM	454	6 – 59 months	HIV (n=15), TB (n=35)	-	Bizuneh et al 2022	[60]
[a]Ethiopia	Retrospective cohort study	OTP	2016 - 2019	SAM	600	Birth to 59 months	HIV (n=12), TB (n=12)	2.0 % (n=12)	Abate et al 2020	[61]

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South Africa	Prospective	HB	2012 - 2015	SAM	82	1 month to 10.6 years	HIV (n=82), Bacteria (n=51)	-	Archary et al, 2016	[62]
[a]Ethiopia	A retrospective cohort study	HB	January to February, 2021	SAM	162	6 – 59 months	Malaria (n=9), HIV (n=12)	6.8 % (n=11)	Aye et al, 2023	[63]
[a]Ethiopia	A prospective cohort study	HB	March to July, 2018	SAM	133	6 – 59 months	TB (n=24), HIV (n=3), malaria (n=3)	3.8 % (NS)	Adem et al, 2020	[64]
Uganda	A prospective cohort study	HB	2010 - 2011	SAM	74	6 months – 5 years	HIV (n=18), malaria (n=7)	12% (n=9)	Mody et all, 2014	[65]
Ethiopia	A Retrospective Cohort Study	HB	2015 – 2017	SAM	375	6 – 59 months	HIV (n=15), TB (n=54), malaria (n=21)	12.3 % (n=43)	Kabthymer et al, 2020	[66]
Malawi	Prospective observational study	HB	2021 - 2022	Complicated SAM	131	6 – 59 months	TB (n=4)	-	Vonasek et al, 2024	[67]
Ethiopia	Retrospective cohort study	HB	2018 - 2022	SAM	247	< 5 years	TB (n=24)	-	Wake et al, 2024	[68]
[a]Ethiopia	Retrospective, Cohort study	HB	2016 to 2019	SAM	476	< 5 years	HIV (n=31) TB (n=61)	11.3% (n=54)	Kassaw et al 2021	[69]
Uganda	Prospective cohort study	HB	June to August 2015	SAM	122	Children under 5 years	HIV (n=9) Malaria (n=25)	-	Nduhukire et al.2020	[70]
Kenya	Retrospective	HB	2007-2016	SAM	3090	5-12yrs	HIV (n=197)	3.4% (n=132)	Ngari et al, 2021	[71]

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	cohort study									
Zambia	Cross-sectional study	HB	19982000	SAM	200	6 to 24months	HIV (n=106), TB (n=27), bacteremia (n=26), Intesstinal infection [*Cryptosporidium parvum* (n=47), *Isospora belli* (n=4), *Giardia intestinalis* (n=11), *Blastocystis hominis* (n=4), *Microsporidia* (n=1), *Salmonella spp.* (n=35), *Shigella spp.*(n=4), *Vibrio cholerae* (n=6), *Hookworm* (n=3), *Ascaris lumbricoides* (n=10), Yeast cells (n=74)	19.5% (39)	Amadi et al, 2001	[72]
Uganda	Prospective cohort study	HB	November 2007 to July 2008	SAM	270	<5yrs	HIV (n=33)	25% (n=67)	Nwalanga et al 2020	[73]

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[a]Sudan	Case control study	HB	1992-1993	SAM	81	0 to 5 years	TB (n=8), intestinal parasitic infection (n=24), UTI [(*E. coli*, (n=6), *Proteus* species (n=2), *Klebsiella* species (n=2)]	-	Sulaiman et al, 2011	[74]
[a]Uganda	Prospective observational study	HB	2012 - 2013	SAM	120	6 – 59 months	HIV (n=20)	14% (n=17)	Rytter et al, 2017	[75]
[a]Ethiopia	Retrospective cohort study	HB	December 10-30, 2021	SAM	712	6 months to 59 months	TB (n=43), HIV (n=3)	5.9%	Ahmed et al, 2023	[76]
[a]Ghana	Prospective observational study	HB	2013 to 2018	SAM	601	0 to 59 months	HIV (54), TB (n=32), malaria(n=110)	16.5% (n=99)	Asare et al, 2021	[77]
Zambia	Cohort study	HB	August - December 2009	Complicated SAM	430	6 months to 59 months	HIV (n=161) TB (n=6)	40.5% (n=174)	Irena et al 2013	[78]
Uganda	Retrospective observational study	HB	January to December 2017	Complicated SAM	330	1-5yrs	HIV (n=86)	22% (70)	Muwanguzi et al, 2021	[79]

SAM: Severe acute malnutrition, MAM: Moderate acute malnutrition, OTP: Outpatient Therapeutic Program, HB: Hospital base, CB: Community base, HIV: Human immunodeficiency virus, UTI: Urinary tract infection, TB: Tuberculosis, a: studies reporting other infections, but pathogen not identified, b: Multicenter study.

4. Discussion

SAM poses a significant public health concern, particularly affecting children under the age of five. It is characterized by extreme thinness and severe deficiencies in essential nutrients. The World Health Organization (WHO) reports that almost 16 million children globally are impacted by SAM, with a higher prevalence in sub-Saharan Africa [80]. The clinical indicators of SAM encompass substantial weight loss, low weight-for-height, and frequently, edema. The criteria for identification include mid-upper arm circumference (MUAC) and weight-for-height Z-score evaluations [1]. Children afflicted by SAM face a significantly heightened risk of mortality due to compromised

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immune function stemming from malnutrition [16]. Malnutrition undermines the body's defence against infections by compromising physical barriers such as the skin and mucous membranes, facilitating pathogen entry, and increasing infection risk. It also disrupts immune cell production and function, resulting in reduced T cell and B cell counts and activity, which are pivotal for an effective immune response [80]. In addition, SAM can incite an imbalance in cytokine production, thus increasing vulnerability to various diseases including pneumonia, diarrhea, tuberculosis, and opportunistic infections [81]. Also, SAM may yield long-term developmental issues, affecting physical growth and cognitive development [82]. In contrast, infections can also predispose to malnutrition in children with diarrheal disease following gastrointestinal infection. Cachexia and anaemia can also result from infections like HIV/AIDS and TB, and nutrient deprivation resulting from parasitic infections [81]. Our review highlights over five thousand cases of opportunistic infections in malnourished children living in Africa over the past two decades with HIV, *Mycobacterium tuberculosis* and malaria parasite being the predominant associated pathogens. A significant proportion of these data was obtained from studies conducted in East African countries and Southern Africa with few cases from West and North Africa which suggests an underestimation of the burden of infectious diseases in this at-risk group.

4.1. Viral Infection

The predominance of HIV amongst pathogens reported in malnourished African children may be associated with the high burden of HIV in Africa. As of 2022, about 25.6 million people were living with HIV in Africa accounting for more than two-thirds of the people living with HIV worldwide (WHO). Malnutrition exerts a deleterious effect on the production and functionality of immune cells, thereby diminishing the body's capacity to combat infections such as HIV. Concomitantly, economic challenges impede access to nourishing sustenance and healthcare, exacerbating malnutrition and elevating the susceptibility to HIV infection, creating a cycle that further weakens the immune system [3].

The high prevalence of HIV among SAM children may also be linked with vertical transmission [83]. Malnourished pregnant women with HIV are more likely to have higher viral loads, increasing the risk of passing the virus to their children during pregnancy, childbirth, or breastfeeding [84]. Furthermore, in regions affected by severe poverty and malnutrition, individuals may engage in high-risk behaviours such as transactional sex to obtain food or income, increasing the risk of HIV transmission [85]. HIV worsens malnutrition by causing loss of appetite, poor absorption of nutrients, and increasing metabolic demands. This sets in motion a challenging cycle where malnutrition worsens HIV outcomes, and HIV further deteriorates nutritional status, leading to rapid health decline [86]. This scenario is buttressed in a study to ascertain 52-week mortality in children discharged from hospitals for management of complicated SAM, conducted in three hospitals in Zambia and Zimbabwe. Children with underlying HIV infection were observed to have an almost 4-fold higher mortality compared with children without underlying HIV infection [20]. In Nigeria, HIV was shown to drive undernutrition as the prevalence of stunting, underweight, and wasting among the HIV-infected subjects was significantly higher compared with the controls [39]. Similarly, a Mozambican study evaluating the adherence of malnourished children to nutritional rehabilitation programs reported a higher prevalence of SAM amongst participants with underlying HIV infection [23]. Thus, besides predisposing to malnutrition, HIV infection in malnourished children is associated with fatal clinical outcomes.

4.2. Bacterial Infection

Next to HIV are bacterial infections presenting as TB, pneumonia, diarrheal disease, and urinary tract infections. The commonest among these clinical conditions was TB. TB and SAM are a major cause of mortality especially in resource-limited settings for children under the age of five years. The coexistence of both further worsened morbidities and clinical outcomes with fatality rates reaching up to 56% [16]. Moreover, children under five years have the highest risk of progressing from Mycobacterium tuberculosis infection to disease, and to disseminated forms of TB [87]. The

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relationship between TB and malnutrition exists in a bidirectional manner. Malnutrition heightens susceptibility to active TB by undermining cell-mediated immunity, pivotal for controlling Mycobacterium tuberculosis, or by inciting the reactivation of latent TB infections [88]. On the other hand, TB worsens malnutrition as it causes increased metabolic demands, nutrient malabsorption, and chronic inflammation. Thus, the risk of TB disease increases with undernutrition and TB can cause or worsen undernutrition [81]. One study estimated that 26% of overall TB cases in 22 high-burden countries are attributable to undernutrition [89]. Similarly, a recent review of 51 cohort studies with over 27 million participants from the six WHO regions reported undernutrition probably increases the risk of TB two-fold in the short term (< 10 years) and may also increase the risk in the long term (> 10 years) [90]. In contrast, studies included in this review revealed delayed recovery from SAM and high fatality rates in malnourished children with coexisting TB disease compared with cohorts without TB disease [16,30,31].

The high prevalence of TB in malnourished African children can be linked to several socioeconomic factors. Low socioeconomic status, overcrowded living conditions, and food insecurity are common in regions with high rates of SAM and thus contribute to the spread of TB. Additionally, natural or man-made disasters, such as conflicts and displacement, exacerbate food insecurity and poor living conditions, further increasing the risk of TB and other infectious diseases. These factors create an environment where communicable diseases can thrive, especially among individuals with compromised immune systems.

Children afflicted by both TB and SAM frequently present with chronic cough, weight loss, and fever—symptoms that conflate with those of severe malnutrition—thereby rendering diagnosis challenging [87,88]. Besides this is the difficulty in making a confirmatory diagnosis using Gene Xpert or cultures as most studies have shown these methods to be unreliable. The diagnosis of TB in the African paediatric population hinges on the ability of the attending physician to make a clinical diagnosis based on presenting symptoms and radiological presentations of the index patient with or without a confirmatory result from the laboratory. Authors opined guidelines should be designed for the diagnosis of TB in malnourished children especially in a resource-limited setting where proven diagnostic tools are often limited [15,34].

Besides *Mycobacterium tuberculosis*, other respiratory pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae* also contributed to morbidities [37,62], frequently precipitating pneumonia in malnourished children. Consequently, malnourished children often experience protracted illness owing to compromised infection clearance, due to weakened respiratory muscles and diminished secretion of protective lung fluids. Furthermore, the weakened immune system in children with SAM amplifies their susceptibility and the gravity of pneumonia. In one study, lower respiratory tract infections were the most common complications second to diarrheal disease with a frequency of 42.4% (405/ 956) and associated with 1.6 times higher odds of dying compared to those who did not have lower respiratory tract infections [18]. Thus, malnutrition induces deficiencies in essential nutrients crucial for a robust immune response, further impeding the body's ability to combat respiratory infections.

4.3. Parasitic Infection

Parasitic infections were also associated with morbidities in malnourished children with malaria parasites accounting for over 80% of the cases. Besides malaria parasites, other parasites were also documented including Ascaris lumbricoides, Cryptosporidium species, Trichuris trichiura, Trichomonas intestinalis, Entamoeba histolytica, Entamoeba dispar/histolytica, Giardia intestinalis, Strongyloides stercoralis, Schistosoma haematobium, Schistosoma mansoni, and Endolimax nana [22,26,31,72]. Overall, only one study reported a significant correlation between parasite infection with clinical outcomes; a study from Ethiopia aimed at assessing the time to recovery from SAM and its predictors reported a high chance of recovery for children who had no anaemia, TB, or malaria infection at admission compared with their counterparts [30].

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4.4. Fungal Infection

Data on fungal infections in children with SAM was found in only two studies further affirming the gross neglect of fungal diseases, especially in the paediatric population including Africa. As previously narrated, malnutrition not only results in nutritional deficiencies but also compromises immune function, disrupts the gut microbiota, and alters host defense mechanisms [81]. Consequently, it creates an environment conducive to fungal colonization and infection, heightening the risk for vulnerable populations. Several factors contribute to malnourished children's increased susceptibility to fungal infections; poor hygiene standards, congested living situations, limited access to clean water and sanitation facilities, and malnutrition-related immunological dysfunction, all contribute to fungal colonization and infection in children. In addition, comorbid illnesses like HIV infection raise the risk of fungal infections in malnourished children, emphasizing the importance of integrated healthcare methods that address the complex determinants of health. Despite these myriad factors, the cognizance for fungal infections is yet low compared with bacterial and viral infections as seen in this review. Contrastingly, recent estimates showed invasive fungal infections have an annual incidence of 6·5 million and account for about 3·8 million deaths globally [91]. This seeming neglect may be accounted for by the sparse data on fungal infections in malnourished children particularly in the African setting. We recommend prioritizing research investigating malnourished children for invasive mycoses to ascertain the burden of IFIs in this at-risk population, drive awareness of fungal diseases, and decrease morbidity.

4.5. Susceptibility Testing of Pathogens

The hallmark of antimicrobial stewardship (AMS) is to ensure the optimized usage of antibiotics and invariably improve clinical outcomes. Its role in preserving and protecting the currently available antibiotics and tackling antimicrobial resistance cannot be over-emphasized. Adherence to AMS strategies implies the indication for antimicrobial therapy is stated and the antibiotic sensitivity pattern of the associated pathogen is provided and deployed to manage an index case. However, in this review, we identified only three studies reporting the antibiotic susceptibility profile of the associated pathogens (bacteria). This is yet indicative of the existing gaps regarding antimicrobial usage in a resource-limited setting like Africa and the need to prioritize funding for innovative studies seeking to explore mechanisms or approaches to limit the exposure of malnourished patients to infectious diseases while setting up and ensuring adherence to AMS programs.

In one of the three, authors reported a high level of resistance to commonly used antibiotics and advocated for clinical trials to determine the most feasible combination of antibiotics for managing bacteraemia in severely malnourished children [37]. In another study, authors suggested an increased investment in antibiotic stewardship programmes, in the face of increasing rates of drug-resistant bacterial infections amongst HIV-infected children with SAM [62]. On the other, the authors emphasized the need to tackle the emergence of antibiotic-resistant bacteria by improving diagnostics, ensuring infection control practices, and reinforcing regional antimicrobial resistance surveillance [22].

4.6. Clinical Outcomes and Treatment Relapse

Regardless of the setting, whether studies were hospital or community-based, the treatment outcomes were largely influenced by comorbidities and predominantly of infectious origin [13,14,16,20,21,25,27,28,31,32,33,35,44,45,54]. Regarding treatment relapse, an Ethiopian study reported the odds of SAM relapse was significantly higher in children with mothers who had no exposure to education and promotion about infant and young child feeding practices, children who were not fully immunized for their age, and children with mid-upper arm circumference of < 12.5 cm at discharge than their counterparts [24]. Similarly, another study reported a lower chance of recovery among children who were not fully vaccinated [30]. Yet in another study, the time to recovery from SAM was delayed in children with comorbidities such as HIV, TB and pneumonia [42]. The authors recommend the provision of supplementary food for children with low MUAC at discharge, the

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promotion of nutrition education, and the improvement of child immunization services and coverage to help reduce SAM relapse [24]. In addition, Special emphasis should be given to prevent and treat comorbidities [42].

5. Limitations

Some studies reported comorbidities such as pneumonia, diarrhoea, anaemia, gastroenteritis, urinary tract infections, respiratory tract infections, dysentery, meningitis or sepsis without specifying the associated pathogen which may have undermined the burden of pathogens identified in this review. Also, the diagnosis of TB was presented in some studies as a clinical diagnosis. A confirmatory diagnosis like the Gene Xpert test or culture or lipoarabinomannan assay was lacking. However, having reviewed a significant number of cases from over 60 studies in Africa within the past two decades, we affirm that the findings from this index review can be applied to encourage research on pathogens in African children with SAM, strengthening antimicrobial stewardship programmes in this setting and invariably decrease morbidity and mortality.

6. Conclusion

Ensuring early and accurate diagnosis and treatment of infections in severely malnourished patients is critical to obtaining good clinical outcomes. Strengthening healthcare systems, particularly in resource-limited settings, is crucial to ensuring that SAM patients receive timely and effective treatment for infections. In addition, public health strategies that integrate nutrition and infection control, such as immunization programs and improved sanitation, are essential components in reducing the global burden of SAM.

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