Review

Viral and Bacterial Etiology of Common Respiratory Infections in Sub-Saharan Africa: A Review

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Posted Date: 14 August 2023

doi: 10.20944/preprints202308.0995.v1

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Viral and Bacterial Etiology of Common Respiratory Infections in Sub-Saharan Africa: A Review

Jordy Exaucé DEMBOUX [1], PEMBE ISSAMOU MAYENGUE [1,2,3,*], Felix KOUKOUIKILA-KOUSSOUNDA [1,2], Eric Maurice LEROY [4], Pierre BECQUART [4] and Fabien Roch NIAMA [1,2]

[1] Faculté des Sciences et Techniques, Université Marien Ngouabi, Brazzaville BP69, République du Congo
[2] Laboratoire National de Santé Publique, Brazzaville BP120, République du Congo
[3] Institut National de Recherche en Sciences de l'Ingénieur, Innovation et Technologie; Cité Scientifique de Brazzaville, route de l'Auberge de Gascogne, Brazzaville, République du Congo
[4] Institut de Recherche pour le Développement, Unité Mixte de Recherche Mivegec, Montpellier BP34090, France
* Correspondence: author: PEMBE ISSAMOU MAYENGUE/ email:pmayengue@yahoo.fr/ Tel: +242 06 616 22 66

Abstract: (1) **Background**: Respiratory infections are a major public health problem worldwide, with potentially serious consequences. Indeed, these infections remain one of the main causes of morbidity and mortality in children under 5 years old in developing countries. Etiological information on respiratory infections is crucial for prevention and case management strategies. This systematic review aims to describe the etiology of respiratory infections reported in studies carried out in sub-Saharan African countries; (2) **Methods**: Using PubMed, HINARI and Google scholar search engines, a systematic search was carried out to identify published articles on the etiology of viral and/or bacterial respiratory infections in sub-Saharan Africa in patients of all ages. We have only considered data from sub-Saharan Africa. Papers published from 2010 to 2021, in English or French have been included in this review; (3) **Results**: After reviewing 115 articles reporting studies carried out in the African continent, only 32 articles were selected of which, studies were conducted in 15 sub-Saharan African countries, including 6/32 (18.75%) in Cameroon. Twenty (62.5%) were cross-sectional studies, and twenty-four (75%) were hospital-based investigations. In these studies, RT-PCR and culture methods were respectively used for viruses and bacteria investigations. Respiratory syncytial virus was the most frequently identified, with prevalence ranging from 0.6% to 59%, followed by rhinovirus (9.3% -73%), influenza virus (flu) A/B (0.9%-69.1%), and human adenovirus (0.9% - 30.8%). *Streptococcus pneumoniae* (14.2% - 96%), followed by *Haemophilus influenzae* type *b* (2.5% - 54%), and *Klebsiella pneumoniae* (1.4% - 49.9%) were the most frequently detected bacteria; (4) **Conclusions**: This review has reported that many pathogens, mainly viruses, are associated with acute respiratory infections in sub-Saharan Africa in both children and adults. Unfortunately, the limited geographical distribution of data across sub-Saharan Africa does not allow most of countries to develop an effective strategy for the prevention and treatment of respiratory infections.

Keywords: respiratory infection; etiology; viruses; bacteria; sub-Saharan Africa

1. Introduction

Respiratory viral infections are increasingly recognized as major contributors to hospitalization and mortality in all age groups of populations worldwide [1]. Most epidemiological knowledge is based on data from developed countries. In contrast, the burden of acute respiratory infections (ARI) is particularly heavy among children in developing countries, with high rates of hospital admissions and mortality [2,3]. Indeed, it is estimated that about 126 to 156 million cases of acute lower respiratory tract infections (ALRI) such as pneumonia and bronchiolitis occur in children worldwide

 doi:10.20944/preprints202308.0995.v1

each year, causing around 1.4 million deaths, with over 95% of which occur in Africa and Southeast Asia [4].

Upper respiratory tract infections are commonly caused by viruses or bacteria. Respiratory viruses are more often responsible for upper tract ARIs than bacteria in children under 5 years of age [3]. Common symptoms include nasal congestion, cough, sore throat, and fever. However, bacteria are less identified because of low sensitivity of bacterial culture in patients with community-acquired pneumonia [5]. Respiratory viruses such as respiratory syncytial virus, influenza viruses (A and B), parainfluenza viruses, human adenovirus, human coronaviruses OC43 and 229E, rhinovirus and metapneumovirus are currently recognized as common etiologies of ARI in young children in developed countries [2].

Recent use of molecular diagnostic techniques has identified other respiratory viruses associated with ARI, including human metapneumovirus, human Boca virus, human coronavirus NL63 and human coronavirus HKU1. In addition, human rhinovirus is implicated in the majority of cold cases and often induces lower respiratory tract infections [3].

A better understanding of the range of pathogens responsible for ARI is therefore essential for clinical cases management and the design of preventive strategies aimed at reducing childhood morbidity and mortality.

Lower respiratory tract infection (LRTI) is common in the elderly, children under five years of age and people who are immunocompromised or suffering from comorbidity [6]. People with symptoms suggestive of LRTIs can contract tuberculosis (TB) and/or other bacterial and viral infections [7]. Over the years, the most severe cases of pneumonia have been associated with *Mycobacterium tuberculosis*, with little information on other relevant bacterial pathogens [8]. Some common pathogens causing LRTIs other than *Mycobacterium tuberculosis* include: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Klebsiella pneumoniae* and *Staphylococcus aureus* [8].

The viral and bacterial etiologies of ARIs have been well documented in Northern Hemisphere countries. However, few studies are available in Africa [9]. Thus, the present study aimed at summarizing the literature related to the etiology of respiratory infections, in sub-Saharan African countries and to identify information gaps in order to improve essential knowledge on the subject.

We focused our research on sub-Saharan Africa, as epidemiological, socioeconomic and vaccine policy factors in North Africa would probably be very different [10].

2. Methods

The Materials and Methods should be described with sufficient details to allow others to replicate and build on the published results. Please note that the publication of your manuscript implicates that you must make all materials, data, computer code, and protocols associated with the publication available to readers. Please disclose at the submission stage any restrictions on the availability of materials or information. New methods and protocols should be described in detail while well-established methods can be briefly described and appropriately cited.

2.1. Search strategy

This review considers data from documents published online (articles, review, report, etc...) that reported information on both viral and bacterial etiology of ARIs in Africa, by searching the online bibliographic databases PubMed, HINARI and Google Scholar using the following key terms: “Acute respiratory infections”, “Upper respiratory infections”, “Lower respiratory infections”, “Viruses”, “Bacteria”, “Respiratory syndrome”, “Influenza syndrome”, “Africa”, “Prevalence”, and “etiology”. The reference list of selected articles was used as a lead for identifying further studies. The Boolean operators “AND” and “OR” were used to combine two or more terms. The search was limited to studies published in English or French, involving patients of any age in sub-Saharan Africa, in which pathogens were identified using immunofluorescence assays (IFA), Polymerase Chain Reactions (PCR), viral cultures, bacterial cultures or a combination of these methods.

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2.2. Study selection

This review compiles studies focused on ARIs caused by viruses and/or bacteria. We only considered data from sub-Saharan Africa reported in papers published between 2010 and 2021, in English or French.

2.3. Inclusion criteria

Studies included were cohort, case-control, prospective, retrospective, and cross-sectional investigations reporting the prevalence of respiratory viruses in hospital and/or community settings. In the case of repeated studies, where the same population was recruited and examined over the same period, only the most recent or most complete study was included.

2.4. Exclusion criteria

There were no age or gender restrictions (Figure 1). Exclusion criteria were mainly: i) respiratory infections of non-human infections; ii) comparison of PCR kits for identification of respiratory pathogens and iii) studies on respiratory infection management policy.

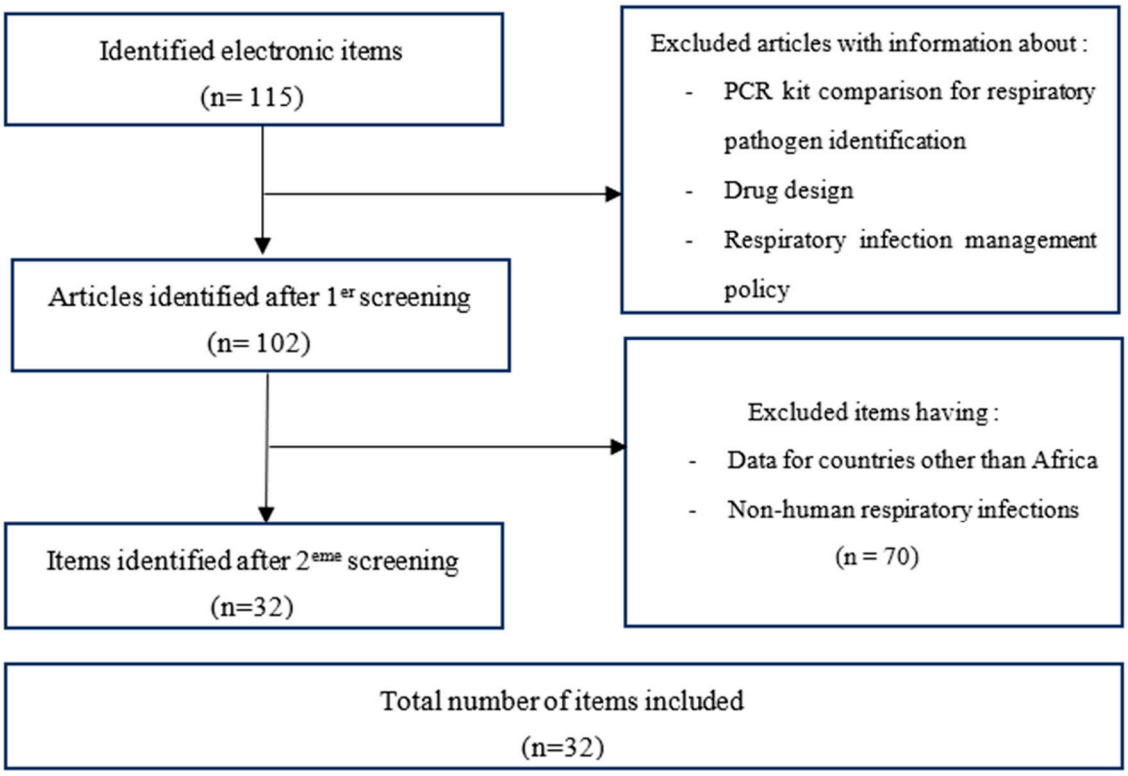

Figure 1. Summary of search strategy.

2.5. Data extraction

Full versions of selected articles were downloaded and reviewed by two study authors. Data were extracted using a predefined form with the following information: i) references; ii) sample collection period; iii) year of publication; iv) study country; v) target population (age); vi) study area; vii) sample size; viii) sampling type; ix) prevalence of identified pathogens and; x) study type.

2.6. Data summary

We synthesized the data by summarizing the main findings of each study. Given the variety of study types included in the review, ranging from simple descriptive to analytical studies, we have considered a synthesis more appropriate rather than a formal meta-analysis. A table was created to

 doi:10.20944/preprints202308.0995.v1

list all the pathogens found in each study, together with relevant study information as mentioned above on data extraction.

2.7. Ethics and distribution

This work is based on published data and therefore does not require ethical approval. This systematic review should serve as a basis for developing strategies to prevent and control respiratory infections in sub-Saharan Africa, and as a foundation for future research that can focus on identifying the gaps found. We also plan to update the study in the future to track changes and guide solutions for health services and policies.

3. Results

3.1. Literature review

The published articles included in this review were those from studies with samples collected from 2010 to 2021. In order to filter articles for this review, we initially identified a total of 115 articles from PubMed, HINARI and Google Scholar that fit with our initial search strategy. Of these, 32 articles were included and 83 were excluded, after screening each article (Figure 1).

Of the 32 articles included, 5 (three for bronchiolitis and two for influenza) focused on viral and/or bacterial strains responsible for pneumonia in children and the elderly [11–15] and 27 focused on the surveillance and epidemiology of viral and/or bacterial strains responsible for respiratory infections (Table 1).

Table 1. Summary of published articles included in the review.

References	Collection period	Year of publication	Study country	Age range	Zone / Sample size	Type of sampling	Prevalence of pathogens	Type of study
[16] Lekana-Douki et *al.*	2009 - 2011	2013	Gabon	No limit	Urban/966	Nasal	Flu A (61%); Flu B (39%)	Cross-sectional/ Prospective
[17] Lekana-Douki et *al.*	2010 - 2011	2014	Gabon	No limit	(Urban) /1041	Nasopharyngeal	HAdV (17.5%), HPIV 1-4 (16.8%), EV (14.7%), HRSV (13.5%), and Flu A (11.9%).	Cross-sectional
[2] Ouédraogo et *al.*	2010 - 2011	2014	Burkina Faso	< 3 years	(Urban) /209	Nasopharyngeal	HRV (59.1%); EV (25.5%); HRSV (16.1%); HMPV (9.4%)	Prospective
[9] Lagare et *al.*	2010 -2012	2015	Niger	< 5 years	(Urban) /160	Nasopharyngeal	HRSV (35%); HRV (29%); HPIV (24%); *S. pneumoniae* (56%); *H. inflenzae* (12%)	Retrospective
[18] Breiman et *al.*	2007 - 2011	2015	Kenya	< 5 years	2592	Naso/ Oro - pharyngeal	HRV/EV (42%); HRSV (25%); HAdV (20%); HMPV (13,7%), Flu A (10,8%)	Cross-sectional
[19] Serengbe et *al.*	2013	2015	CAR	< 5 years	361	Nasopharyngeal	HRV(47,5%);FluA/B (26,6%);HPIV-3(9,3%);HRSV(5,8%); EV(4,3%); HAdV (2,9%); HBoV (1,4%); HCoV (1,4%)	Cross-sectional
[20] Kenmoe et *al.*	2011 - 2013	2016	Cameroon	≤15	(Urban) /347	Nasopharyngeal	HRSV (13.2%), HAdV (27.3%), HboV (10.6%), Flu A/B (9.8%); HPIV (6.6%); HCoV (5.7%); HMPV (2.3%); HRV/EV (11.5%)	Prospective
[21] Uzoamaka et *al.*	2014 - 2016	2017	Nigeria	No limit	(Peri-urban) / 954	Expectoration	*Klebsiella pneumonia (49,9%); Klebsiella spp/ Pseudomonas aeruginosa, (1.4%)*	Cross-sectional
[22] Niang et *al.*	2012 - 2015	2017	Senegal	No limit	(Urban) /6381	Naso/ Oro - pharyngeal	HAdV (30,8%); FluA/B (53,1%); HRV (30%); Ev (18,5%); HRSV (13,5%)	Cross-sectional, Prospective
[23] Famoroti et *al.*	2011 - 2015	2018	South Africa	0 - 5 years	(Urban) /2172	Expectoration /Nasopharyngeal	HRSV (32.1%), HAdV (21.8%), HRV (15.4%), FluA swl (5.1%)	Retrospective
[24] Kadjo et *al.*	2013	2018	Ivory Coast	< 5 years	(Urban) /1340	Nasopharyngeal	HRV (31.92%), HRSV (24.4%), HPIV (20.5%), HCoV 229E (12.05%)	Cross-sectional
[25] Sanou et *al.*	2014 - 2015	2018	Burkina Faso	< 5 years	(Urban) / 924	Nasopharyngeal	Flu A/B (15.1%), A(H3N2) (69.1%) A(H1N1) pdm09 (30.9%)	Cross-sectional
[26] Obodai et *al.*	2006, 2013-2014	2018	Ghana	< 5 years	(Urban) /552	Nasopharyngeal	HRSV (23%)	Cross-sectional
[27] Lekana-Douki et *al.*	2018	2018	Gabon	< 5 years	(Urban) / 810	Nasopharyngeal	HBoV (4,4%)	Retrospective
[28] Kabego et *al.*	2016	2018	DRC	< 5 years	(Urban) / 146	Nasopharyngeal	HRSV (21.2 %); HRV (16.4 %); HPIV-3 (13.7%) and HAdV (4.79 %).	Cross-secctional, analytical/ Prospective
[14] Mhimbira et *al.*	2013 - 2015	2018	Tanzania	No limit	(Urban) /972	Nasopharyngeal	HRV (9.3%); Influenza A (3.1%); HRSV A/B (1.9%); *H. influenzae* (26.1%); *S. pneumoniae* (21.5%)	Prospective cohort
[29] Kenmoe et *al.*	2011 - 2014	2018	Cameroon	< 15 years	(Urban) / 811	Nasopharyngeal	HAdV(27.12%)	Cross-sectional
[15] Razanajatovo et *al.*	2010 - 2013	2018	Madagascar	No limit	(Urban) / 876	Nasopharyngeal, Expectorations Blood	HRSV (37,7%) ; FluA (18,4%) ; HRV (13,5%) ; HAdV (8,3%) ; *S. Pneumoniae* (50,3%) ; *H. Influenzae b* (21,4%) ; *Klebsiella* (4,6%)	Prospective

doi:10.20944/preprints202308.0995.v1

[12] Lagare, et *al.*	2015	2019	Niger	< 5 years	(Urban) / 638	Expectoration /Nasopharyngeal	HRSV (23,3 %), HPIV (12,2%), HRV (9,4 %), HAdV (9,4 %), Flu A (8,1 %) / *S. pneumoniae* (39%) , *Staph. aureus* (12,2%), *H. influenzae B* (2,5%)	Prospective
[11] Tchatchouang et *al.*	2019	2019	Cameroon	No limit	(Urban) /141	Branco-alveolar lavage (BAV)	*S. pneumoniae/ H. infuenzae* (14.2%); *K. pneumoniae* (9.2%); *Staph. aureus,* (7.1%)	Foresight
[30] Adema et *al.*	2017 - 2018	2020	Kenya	< 20 years	(Urban) /781	Nasopharyngeal	HRV (16.7%); HPIV (2.7%) ; HCoV (229E,NL63, OC43) (2.0%) ; HAdV (0.9%) ; HRSV (0.6%)	Longitudinal/ Cohort
[31] Kengne-Nde et *al.*	2019	2020	Cameroon	No limit	1426	Naso/ Oro - pharyngeal	HRV (35,6%); HRSV (31,0%); HBoV (8,1%); HAdV (7,7%); Flu A/B (6,5%); HMPV (5,8%); EV (4,3%); HPIV 1-4 (3,8%); HCoV (2,2%)	Cohort, Case-control, Cross-sectional
[49] Kenmoe et *al.*	2019 - 2020	2020	Cameroon	< 2 years	51	Naso/ Oro - pharyngeal	HRSV (59%); HRV (19,3%); HBoV (8,2%); HAdV (6,1%); HMPV (5,4%); HPIV (5,4%); Flu A/B (3,2%); HCoV (2,9%); Ev (2,9%)	Cross-sectional
[32] Buchwald et *al.*	2011 - 2013	2020	Mali	< 2 years	(Urban) /1333	Naso/ Oro - pharyngeal	HRSV (37%)	Cohort
[33] Obe et *al.*	2021	2021	Nigeria	< 5 years	(Urban) /200	Nasopharyngeal	HRSV (22.5%)	Cross-sectional
[8] Deberu et *al.*	2018 - 2019	2021	Ghana	No limit	(Urban) /264	Expectoration	*Klebsiella spp. (28%); M. tuberculosis* (6.5%); *Pseudomonas spp.*(15.2%)	Retrospective
[34] Kouakou et *al.*	2021	2021	Ivory Coast	≤ 5 years	(Urban/rural) / 5648	Nasopharyngeal	HRSV (10%)	Cross-sectional/ descriptive
[35] Kenmoe et *al.*	2011 - 2014	2021	Cameroon	No limit	(Urban) / 974	Nasopharyngeal	HRV/EV (16.4%)	Cross-sectional
[13] Birindwa et *al.*	2015 - 2017	2021	DRC	≤ 5 years	(Urban) /2322	Nasopharyngeal	*H. influenzae* (54%); *S. pneumoniae* (96%); HRV (73%); EV (17%); HRSV (7%);	Cross-sectional
[36] Baillie et *al.*	2011 - 2014	2021	South Africa	≤ 5 years	(Urban) /4232	Naso/ Oro - pharyngeal	HRV (21%) ;	Cross-sectional
[37] Ntagereka, et *al.*	2021	2022	DRC	No limit	(Urban) /1352	Oro-pharyngeal	SARS-CoV-2 (13.9%), Flu A (5.6%), Flu B (0.9%)	Cross-sectional
[38] Kafintu-Kwashie et al.	2015 - 2016	2022	Ghana	< 5 years	(Urban) /188	Nasopharyngeal	HRSV (11.4); HMPV (1.7 %);	Cross-sectional

ABBREVIATIONS: **HRSV**: Human Respiratory Syncytial Virus; **HRV**: Human Rhinovirus; **HAdV**: Human Adenovirus; **Flu A/B**: Influenza viruses A/B type; **HPIV 1-4**: Human Parainfluenza viruses 1-4 types; **EV**: Enterovirus; **hCoV:** Human Coronavirus ; **hMPV**: Human Metapnemovirus; **hBoV**: Human Bocavirus; **SARS-CoV-2**: Severe acute respiratory syndrome coronavirus 2 ; **S. pneumoniae**: Streptococcus pneumoniae; **S. aureus**: Staphylococcus aureus; **H. influenza b**: Haemophilus influenzae b type; **K. pneumoniae**: Klebsiella pneumoniae; **P. aeruginosa**: Pnseudomonas aeruginosa; **M. tuberculosis**: Mycobacterium tuberculosis.

doi:10.20944/preprints202308.0995.v1

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Many of these studies were carried out among children under 5 years of age. Articles excluded were related to comparisons of amplification kits, respiratory infection management policy, data from countries other than Africa, and those concerning non-human respiratory infections.

3.2. Features of included items

The 32 articles involved a total of 41,164 patients. Sample size ranged from 51 to 6,381 ARI patients per study. The included studies were obviously conducted in 15 sub-Saharan African countries (Figure 2).

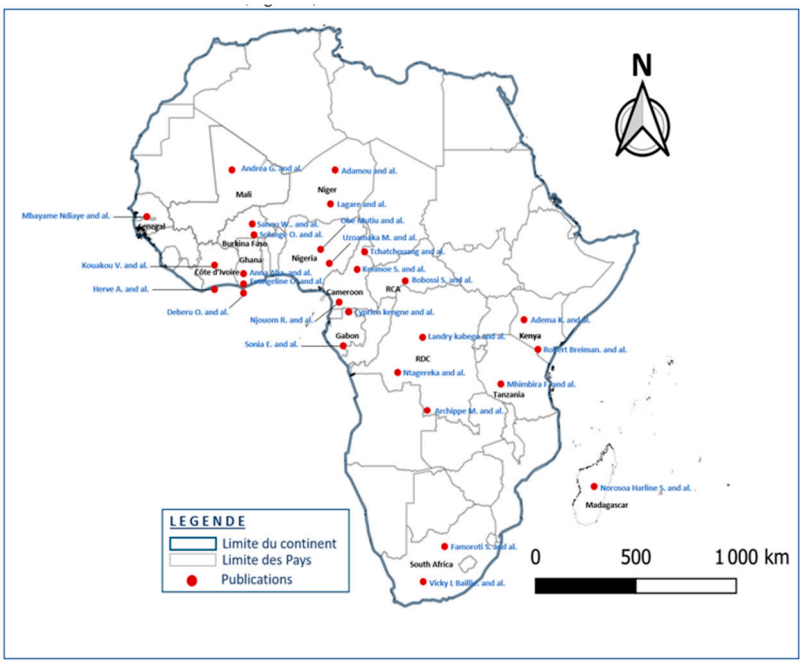

Figure 2. Geographical identification of the 32 included studies (map generating with QGIS 3.16.0).

A total of 6 published studies were conducted in Cameroon, 3 in the Democratic Republic of Congo (DRC), Ghana, and Gabon; two studies in Burkina Faso, South Africa, Côte d'Ivoire, Kenya, Niger and Nigeria respectively, and one study in each of the following countries: Senegal, Tanzania, Mali, Central African Republic (CAR) and Madagascar.

We identified 20 (62.5%) cross-sectional studies, 9 (28.12%) prospective studies, 4 (12.5%) retrospective studies and 4 (12.5%) cohort studies. We also noted case-control, analytical, longitudinal, and descriptive studies (Table 1).

Considering settings in which these published studies were focused, there were 24 (75%) hospital-based studies and 8 (25%) community-based studies. The study setting was urban in 27 (84.37%) studies, and mixed (rural, semi-rural and pre-urban) in 5 (15.62%) studies.

Pathogens were identified in a variety of respiratory samples, including nasal swabs, oropharyngeal swabs, nasopharyngeal aspirates, induced sputum, tracheal aspirates, bronchoalveolar lavage swabs and pulmonary aspirates.

Respiratory viruses were detected using immunofluorescence tests, multiplex RT-PCR, conventional PCR and viral cultures. RT-PCR was the most frequently used diagnostic method. For the detection of individual bacteria, only bacterial cultures were performed.

3.3. Etiology of pathogens detected

All the respiratory pathogens identified in these studies were viral and bacterial (Table 1). Among 32 articles reviewed, human respiratory syncytial virus was the most frequently identified, with a prevalence ranging from 0.6% - 59%, followed by human rhinovirus (9.3% - 73%), influenza A/B virus (0.9% - 69.1%), human adenovirus (0.9% - 30.8%), human parainfluenzavirus 1-4 (3.8% -

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24%), enterovirus (2.9% - 25.5%), human coronaviruses (1.4% - 13.9%), human metapneumovirus (1.7% - 13.7%), and human bocavirus (1.4% - 10.6%) (Table 2).

Table 2. Proportion of pathogens identified in the 32 articles studied, conducted in several countries.

	Prevalence (%)	Number of studies	Number of countries
VIRUS			
Human Respiratory Syncytial Virus	0,6 - 59	23	15
Human rhinovirus	9,3 - 73	17	11
Influenza virus A/B	0,9 - 69	18	11
Human adenovirus	0,9 - 30,8	14	9
Para Human Influenza virus	3,8 - 24	10	7
Human Enterovirus	2,9 - 25,5	9	7
HCoV NL63	1,4 - 5,7	7	3
HCoV OC43	1,4 - 5,7	7	3
HCoV 229E	2,0 - 12,05	7	4
HCoV HKU-1	1,4 - 5,7	6	2
Human metapneumovirus	1,7 - 13,7	6	4
Human bocavirus	1,4 - 10,6	5	3
BACTERIA			
***Streptococcus* pneumoniae**	14,2 - 96	6	5
***Haemophilus influenzae* type b**	2,5 - 54	6	5
Klebsiella pneumoniae	1,4 - 49,9	5	4
Staphylococcus aureus	7,1 - 12,2	2	2
Pnseudomonas aeruginosa	1,4 - 15,2	2	2
Mycobacterium tuberculosis	0 - 6,5	1	1

Among the bacteria detected (Table 1), the most prevalent were *Streptococcus pneumoniae* (14.2% - 96%), followed by *Haemophilus influenzae* type b (2.5% - 54%), and *Klebsiella pneumoniae* (1.4% - 49.9%). Other bacterial species, notably *Staphylococcus aureus* (7.1% - 12.2%), *Pnseudomonas aeruginosa* (1.4% - 15.2%), and *Mycobacterium tuberculosis* (6.5%) were the least identified (Table 2).

4. Discussion

This review updates known information on respiratory infections of viral and/or bacterial etiology, in sub-Saharan Africa over the last twelve years. The overall aim of this systematic review was to inform public health actors and researchers on the etiology of respiratory infections (viral and bacterial) in Africa, and to provide information that can support actions to optimize decision-making by health authorities for the control of these infections.

A wide variety of detection techniques have been found in this review, including molecular viral detection, bacterial culture which are universal and reference methods for the characterization of respiratory infection pathogens. The results highlight a predominance of human respiratory syncytial virus and a strong association between human rhinovirus and influenza A/B virus in children aged under 5 years old presenting with influenza-like illness. The other most frequently detected viruses were adenovirus and all four types of human Parainfluenzae virus. This study also showed respiratory infections of bacterial origin, with the most frequently identified species being *Streptococcus pneumoniae* and *Haemophilus influenzae* in bacterial culture mainly as well as on sputum and Branco-alveolar lavage (BAL) samples in adults.

Little or no data were found on the etiology of respiratory infections in many sub-Saharan African countries. Of the 48 countries in sub-Saharan Africa (wikipedia.org/wiki/Afique_sub-saharienne), the 32 articles included in this review were carried out in only 15 countries, the majority of which were in Central and West Africa (Figure 2). No published studies were carried out in the Republic of Congo, although it borders with two (Cameroon and DRC) of the five countries where

the number of deaths from childhood pneumonia is or was highest [39]. This lack of data could probably be due to the poor implementation of respiratory infection surveillance activities.

The pattern of predominance of human respiratory syncytial virus in this study is consistent with that reported by several previous narrative reviews [3,40]. Regardless of various factors, including screening test, type of sample tested, age of children, type of education and severity of infection, most studies indicated that human respiratory syncytial virus is the predominant causative agent of cases of respiratory diseases such as bronchiolitis, asthma, and wheezing with an incidence of between 50 and 80% [41]. Rhinovirus and influenzae A/B, the second most common viruses observed, have long been considered a cause of benign respiratory tract infections such as the common cold [9].

We found five studies that presented cases of viral and bacterial co-infections at rates of around 14% in our review [9,12–15]. Although Streptococcus pneumoniae is known to be more prevalent in superinfection in some respiratory syndromes, such as influenza [42,43], *Haemophilus influenzae*, and *Klebsiella spp* were also identified mostly in co-infection. This observation correlates with the review by Lansbury et al. who also showed that *Klebsiella pneumoniae* and *Haemophilus influenzae* were among the most frequent co-infecting bacterial pathogens [44]. *Staphylococcus aureus* was one of the least present, as expected [11]. Irrespective of testing issues, co-infection with other respiratory pathogens has important implications for diagnosis and prognosis.

Seasonality and study duration could clearly also lead to variability in the prevalence of viruses/bacteria responsible of respiratory infections.

5. Conclusion

This review shows that a number of viruses are associated with ARIs in children and adults in sub-Saharan Africa. The WHO's global strategy for the control of ARI in children under 5 years of age must rigorously consider the importance of both viral and bacterial cases. Moreover, the results highlight the lack of data for several sub-Saharan African countries. Further high-quality studies are needed to determine the role of viruses and bacteria in ARI.

6. Study limits

This study has several limitations. Firstly, only publications in English or French were taken into account, excluding data published in Portuguese, which is the official language of five African countries (Angola, Cape Verde, Guinea-Bissau, Mozambique and Sao Tome and Principe), and in Spanish, the official language of Equatorial Guinea. Secondly, unpublished literature also constitutes an information bias in this systematic review. Finally, we did not assess the statistical quality of the studies by meta-analysis, but included all articles that met the inclusion criteria.

Author Contributions: DJE and PIM conceived, designed the study, and initiated the manuscript, KKF, BP, LE and NFR supervised the study. All authors read and approved the manuscript.

Acknowledgments: This review is a prelude to the activities of the COPANFLU project funded by IRD as part of the "Jeunes Equipes Associées à l'IRD" program. Many thanks to Donatien MOUKASSA, Grace FILA-FILA, Hosanna LEGUIYA, Henri OBA, aldi MANDIANGOU, Novy BOBOUAKA, Dachel EYENET, Yann MAVOUNGOU, Georcil AHOUET, Isaac ONYANKWANG, Reiche ELENGA, Durel BABISSAT, Valchy MIEGAKANDA, Jordy DONIAMA, Stéphane VEMBE, George TSOUMOU, Ines BAKOUMA, Laureate MADINGOU, Amour MOUANDA for their assistance with documentary research and reading of the manuscript.

Conflicts of Interest: The authors declare no competing interests.

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