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ORIGINAL RESEARCH

Magnitude of *Streptococcus pneumoniae* Among Under-Five Children with Symptom of Acute Respiratory Infection at Hiwot Fana Specialized University Hospital, Harar, Ethiopia: Associated Risk Factors and Antibacterial Susceptibility Patterns

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Dejene Bayu[1]
Abiyu Mekonnen[2]
Jemal Mohammed[3]
Dagne Bodena[1]

[1]Hiwot Fana Specialized University Hospital, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia; [2]Department of Medical Laboratory Sciences, Menelik-II College of Health and Medical Sciences, Kotobe Metropolitan University, Addis Ababa, Ethiopia; [3]Department of Medical Laboratory Sciences, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia

Purpose: *Streptococcus pneumoniae* is the major cause of pneumoniae infection among under-five children that leads to high morbidity and mortality. Thus, the aim of this study was to determine the magnitude of *Streptococcus pneumoniae* in under-five children of an acute respiratory infection, assess its antimicrobial susceptibility patterns, and define the associated factors.

Methods: An institutional-based cross-sectional study was conducted on a total of 384 under-five children of acute respiratory infection attending outpatient department of Hiwot Fana Specialized University Hospital, Harar, Ethiopia, from March 1 to 30, 2020. Socio-demographic and clinical data were collected from the study participants using a structured questionnaire. Sputum samples were collected and processed to identify *Streptococcus pneumoniae* pathogen using the culture and biochemical tests as per the standard procedures. The Kirby–Bauer disk diffusion method was used for antimicrobial susceptibility testing. Data were entered into Epi-data version 3.1 and analyzed by using Statistical Product and Service Solutions version 22.

Results: The proportion of *Streptococcus pneumoniae* in under-five children with acute respiratory infection was 11.2%. About 50% of isolated *Streptococcus pneumoniae* was resistant to tetracycline and cotrimoxazole, whereas more than 90% of it was susceptible to Ceftriaxone and amoxicillin-clavulanate. Children who lived in rural areas were 3.6 times more likely to have *S. pneumoniae* compared to children who lived in urban areas (AOR: 3.6, 95% CI: 1.2–11) and children with familysmokers in a house were 3 times at risk to be infected with *S. pneumoniae* (AOR: 3, 95% CI: 1.8–8.0).

Conclusion: High antimicrobial resistance of *S. pneumoniae* against tetracycline and cotrimoxazole was observed and children who lived in rural areas and live with a family of cigarette smoker are factors associated with *Streptococcus pneumoniae*. Therefore, providing health educations to the family of children rural residents and isolating smokers from the house where children lived are recommended actions to reduce bacteria caused by *Streptococcus pneumoniae*.

Keywords: antibiotic susceptibility, children under-five, *S. pneumoniae*, Hiwot Fana Specialized University Hospital, Harar, Ethiopia

Correspondence: Dagne Bodena
Hiwot Fana Specialized University Hospital, College of Health and Medical Sciences, Haramaya University, PO Box 235, Harar, Ethiopia
Tel +251 910127241
Email dagne2004bodena@gmail.com

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Background

Streptococcus pneumoniae is one of the most usual causes of childhood serious invasive infections, like pneumoniae, meningitis, and bacteremia. It is present in the commensal bacterial community in the human nasopharynx that is responsible for a public health problem and economic impact in both developed and developing countries.[1,2]

Host, socio-economic and environmental factors including daycare attendance, living in a household with other young children and symptoms of an upper respiratory tract infection are responsible for pneumococcal carriage.[3]

S. pneumoniae is the leading cause of bacterial pneumoniae and secondary pneumoniae following flu infection that kills more than under-five years of age each year than any other illness such as AIDS, malaria, and measles combined together world wide. Over 9 million cases of the pneumococcal disease were reported in children under five years, and more than 300,000 died due to these cases in 2015 and the majority of the cases occur in low- and middle-income countries.[4,5]

Moreover, the cost of antibiotic treatment for all children with pneumoniae in 42 of the world's poorest countries is around US$ 600 million per year and around US$ 200 million incurred due to treating pneumoniae in South Asia and sub-Saharan Africa.[6] Even though effective and inexpensive treatments are available, about 30% of children in Africa, particularly in sub-Saharan Africa of rural areas, receive antibiotics that cause bacterial pneumoniae remains a major cause of morbidity and mortality globally.[7,8]

Most of the developing countries with a high burden of morbidity and mortality associated with the acute respiratory infection including Ethiopia still lack the necessary data on the real burden, epidemiology, and etiology of ARI within their territories. Actually, in most of these countries, the estimation of the burden of ARI is based on specific surveys at the national or regional level.[9]

Lack of rapid diagnostic testing and limited data on antibiotic use for suspected childhood plays a major role in the continual existence of pneumoniae in the developing countries especially in vulnerable groups, like girls, rural-dwelling children, and poor communities.[10,11]

Despite a high burden of pneumoniae, there was no study done to determine pneumoniae among under-five children in Harar town, Ethiopia. Therefore, this study aimed to assess the magnitude, associated risk factors, and drug susceptibility patterns of *Streptococcus pneumoniae* among under-five children with a symptom of the acute respiratory infection in Hiwot Fana Specialized University Hospital, Harar, Ethiopia.

Materials and Methodology

Study Area, Design, and Period

Harar is the capital city of Harari Regional State, located 526 km away from East of Addis Ababa, the capital city of Ethiopia. Hiwot Fana Specialized University Hospital is one of the referrals and a teaching hospital, which was established during the occupation of Ethiopia by Italian soldiers. Currently, the hospital serves to about 5.2 million communities around Harari regional state and neighboring regions. The hospital has a total of 899 workers, 434 health professionals, and 465 administrative staff.[12]

Study Design and Period

An institutional cross-sectional study was conducted from March 1 to 30, 2020, in Hiwot Fana Specialized University Hospital, Harar, Ethiopia.

Study Population

All under-five children suspected of respiratory tract infection who visited Hiwot Fana Specialized university hospital pediatrics outpatient department were included. We have excluded children age of less than five years who start antibiotic treatment.

Sample Size Determination

The sample size was calculated by using a single population proportion formula

$$n = Z^2 p(1-p)/d^2$$

By considering the prevalence 48.6%, anticipated population proportion of *S. pneumoniae* from a study conducted in hospitals of Bahir Dar city, Ethiopia,[13] at 95% confidence interval= 1.96 and 5% margin of error (d) =0.05

n= estimated sample size

$$n = (1.96)^2 \text{ x } 0.486(1-0.486)/(0.05)^2 = 384$$

After adding 5% of non-response rate, the final sample size was 403.

Sampling Technique

A convenient sampling technique was used to select study participants until the required sample size was achieved.

Data Collection Methods

Data Collection by Face-to-Face Interview

The parents of the children were consented and interviewed for socio-demographic variables like age, gender, and factors of housing condition, vaccination status of the child, and a residence which was adopted from different literatures.[14,15] Data were collected by trained data collectors after testing by pre-structured questionnaire. On-site supervision was carried out by a supervisor and principal investigator on a daily basis.

Sample Collection, Handling, and Transportation

A well-labeled, leak-proof, sterilized, wide mouth screw-cap universal container was given to the child's parents to collect 5 mL of morning sputum, after that child's parents were instructed to cleanse the area around the mouth opening with clean water. A deep breath was taken through the mouth and coughed up mucous with deep coughing. To avoid contamination, each individual was instructed on how to collect a cough specimen by laboratory personnel. All sputum specimens reached the laboratory as soon as collected.[16] For those who cannot give sputum samples, lung aspiration was done by inserting a needle blindly over the top of a rib and applying a suction to the plunger of the syringe, and the needle was withdrawn while maintaining constant suction. The procedure was performed under sterile conditions by experienced nurses or doctors.

Conventional Identification of *S. pneumoniae* and Antimicrobial Susceptability Test

Conventional identification of *S.pneumoniae* and antimicrobial susceptibility testing (AST) should be done according to appropriate standards and Erythromycin (15 µg), Cotrimoxazole (25 µg), Ceftriaxone (30 µg), Tetracycline (30 µg), Chloramphenicol (30 µg), and Amoxicillin-clavulanate (5 µg) were used for AST.[17]

Operational Definition

Acute respiratory tract infection is an infectious cause disease of the upper or lower respiratory tract of *Streptococcus pneumoniae*.[4]

Data Quality Control

To ensure the quality of data, training of data collectors was undertaken and administration of pre-test among 5% of the total sample size to assess its clarity, length, completeness, and consistency. Also, the skip patterns were corrected and questions found to be difficult or misleading were rephrased. Supervisor and principal investigator were closely following the data collection process. Checking for completeness and accuracy of completed data collection forms was done at the end of each day of data collection and gaps identified were addressed with the respective research assistants. Sterility of culture media was checked by incubating 3–5% of the batch at 37°c and control each new batch of agar by testing it with a reference strain *E. coli* ATCC 25922.

Methods of Data Analyses

Data were entered and edited into EPI-data version 3.1, clean, and analyzed by using SPSS 22. Descriptive statistics of different variables were determined and the result was presented in texts and tables and summarized by using percentages. Logistic regression was carried out to identify the associated factors between variables and *Streptococcus pneumoniae*. Variable with *P*-value ≤0.25 was a candidate for the multivariate analysis. Finally, multivariate logistic regression analysis was performed for adjusted odds ratio with 95% confidence intervals and variables with a *P*-value <0.05 were declared as statistically significant.

Ethical Consideration

The study protocol was approved by the Health Research Ethics, and Review Committee (HRERC) of the College of Health and Medical Sciences, Haramaya University. Information on the study was explained to the participants, including the procedures, potential risks, and benefits of the study. Participants' confidentiality of information was assured by excluding names and identifiers in the questionnaire. Informed written consent was obtained from all Childs' parent prior to the study and there was a compliance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

Socio-Demographic Characteristics of the Respondents

Of 403 participants, 384 under-five children were included in the study with a response rate of 95%. 19 participants refused to give sputum samples and were excluded from the study. Among 384 under-five children patients, 206 (53.6%) of them were males. The majority of study participants 301 (78.4%) were Oromo and among all study participants, 247 (64.3%) were residents of rural areas (Table 1).

A Behavioral Factors of the Study Participants

Among all study participants, 258 (67.2%) of the children's families were cigarette smokers. Majority of them, 227

Table 1 Socio-Demographic Characteristics of Under-Five Children Patients (n=384) at Hiwot Fana Specialized University Hospital, Harar, Ethiopia, March 1–30, 2020

Variables	Category (in Years)	Frequency	Percent
Age	<1	77	20%
	2–3	208	54.2%
	4–5	99	25.8%
Sex	Male	206	53.6%
	Female	178	46.4%
Resident	Urban	137	35.7%
	Rural	247	64.3%
Ethnicity	Oromo	301	78.4%
	Amhara	33	8.6%
	Harari	32	8.3%
	Gurage	15	3.9%
	Others	3	0.8%

(59.1%), had diarrhea during the study period and frequency of diarrhea once, twice, three times, and more than three times per day were 7 (1.8%), 50 (13%), 108 (28%), and 62 (16.1%), respectively, and 3 (0.8%), 26 (6.8%), 53 (13.8%), 92 (24%) of their mothers have breastfeeding habit once per day, twice per day, three times per day, and more than three times per day, respectively (Table 2).

Factors Associated with the Presence of *S. pneumoniae* Among Children Patients

The overall prevalence of *S. pneumoniae* among under-five children years of age with acute respiratory infection attending Hiwot Fana Specialized University Hospital was 11.2% (95% CI: 8.1–14.8).

Variables that showed association in the binary logistic regression of *P*-value of less than 0.25 were a family with Cigarette smoking habit, those children who were rural residents, those with a history of previous measles infection, and those who prepare their food within unsepareted kitchen. Cigarette smoking habit of family and children who were rural residents remained significantly associated after taken to the multiple logistic regressions (Table 3).

Antimicrobial Susceptibility Testing

About 23 (53.5%) of isolated *Streptococcus Pneumoniae* were resistant to Tetracycline and 21 (48.8%) to cotrimoxazole, whereas 95.4% and 93% of them were susceptible to Ceftriaxone and amoxicillin-clavulanate, respectively (Table 4).

Table 2 Under-Five Children Duration of Diarrhea, Cough and Habit of Fuel Use of Their Family for a Cooking (N=384) at Hiwot Fana Specialized University Hospital, Harar, Ethiopia, March 1–30, 2020

Variables	Category	Frequency	Percent
Duration of cough	For one day	36	9.4%
	For two days	132	34.4%
	For three days	96	25%
	For weeks	120	31.3%
Cigar smoker	Yes	275	71.6%
	No	109	28.4%
Breast feeding habit*	Once a day	3	0.8%
	Twice a day	26	6.8%
	Three times a day	53	13.8%
	>3 times per day	92	24%
Fuel used for cooking	Wood	268	69.8%
	Charcoal	34	8.9%
	Electricity	82	21.3%
Place of cooking	Main house	25	6.5%
	Kitchen	359	93.5%
Separate kitchen	Yes	210	58.5%
	No	149	41.5%
Window in the kitchen	Yes	26	7.2%
	No	333	92.8%
Diarrhea	Yes	227	59.1%
	No	157	40.9%
Frequency of diarrhea*	Once per day	7	1.8%
	Twice a day	50	13%
	3 times a day	108	28%
	3> times a day	62	16.1%
History of measles	Yes	65	16.9%
	No	164	42.7%
	Unknown	155	40.4%

Notes: *Breast feeding habit (n=174). *Frequency of diarrhea (n=227).
Abbreviation: N, total number of participated children.

Discussion

Streptococcus pneumoniae is a major pathogen of humans, causing diseases such as pneumoniae and meningitis that makes patients difficulty in breathing, wheezing, fever, irritability, chest pain, and chill.[1] In this study, the proportion of *S. pneumoniae* was 11.2% (95% CI: 8.1–14.8), which was similar to a study conducted in 2018 in the northern part of Ethiopia (10.3%).[18] But the present finding was lower than studies conducted in 2014 at northern part of Ethiopia by Fekadu et al, (16.1%),[19] Jimma, Ethiopia (43%),[20] and Southern Ethiopia (33.5%),[15]

Table 3 Bivariate and Multivariable Analyses for Factors Associated with *S. Pneumoniae* (N=43) Among Under-Five Children Patients at Hiwot Fana Specialized University Hospital, Harar, Ethiopia, March 1–30, 2020

Variables		*S. pneumoniae*		Bivariate Analyses		Multivariate Analyses	
		Positive n %	Negative n %	COR (95% CI)	*P*- value	AOR (95% CI)	*P*- value
Presence of Cigarette smokers	Yes No	41 (10.7%) 2 (0.5%)	234 (60.9%) 106 (27.6%)	3.1 (2–4) Ref	0.021	3 (1.8–8) Ref	0.03*
Residents	Rural Urban	37 (9.6%) 6 (1.6%)	210 (54.7%) 131 (34.1%)	3.68 (1.5–9.3) Ref	0.014	3.6 (1.2–11) Ref	0.02*
History of measles	Yes No Unknown	11 (2.9%) 17 (4.4%) 15 (3.9%)	54 (14.1%) 147 (38.3%) 140 (36.5%)	0.7 (0.4–1.1) Ref	0.17	0.9 (0.5–1.4) Ref	0.6
Separate kitchen	Yes No	15 (4.2%) 23 (6.4%)	195 (50.8%) 151 (39.3%)	Ref 2.4 (1.2–4.7)	0.21	Ref 1.3 (0.6–2)	0.42

Notes: The presence of cigarette smokers, and living in rural were associated factor. AOR*Statistically significant at *p*-value < 0.05.
Abbreviations: CI, confidence interval; OR, odds ratio; Ref, reference.

Table 4 Antimicrobial Susceptibility Pattern of *S. Pneumonia* Isolated from Children Under Five Age Patients (N=43) Who Attended at Hiwot Fana Specialized University Hospital, Harar, Ethiopia. March 1–30, 2020

Antimicrobial Agents	Resistant n (%)	Susceptible n (%)	Intermediate n (%)
Erythromycin	5 (11.6)	36 (83.7)	2 (4.7)
Cotrimoxazole	20 (46.5)	21 (48.8)	2 (4.7)
Ceftriaxone	1 (2.3)	41 (95.4)	1 (2.3)
Amoxicillin-clavulanate.	1 (2.3)	40 (93)	2 (4.7)
Tetracycline	18 (41.8)	23 (53.5)	2 (4.7)
Chloramphenicol	6 (14)	29 (67.4)	8 (18.6)

Abbreviations: N, isolated organism; n, number.

(28.1%),[21] however, higher than the studies reported from Spain (5.6%),[22] Indian (3.7%),[23] and Bangladesh (4.4%).[24] This deference might be due to variation in the study of season, age, the difference in geography, site of study, and in implementation of vaccination status.

In this study, we have assessed various factors that could possibly cause the presence of *S. pneumoniae*. Children in the family of cigarette smokers were 3 times at risk to be infected with *S. pneumoniae* (AOR: 3, 95% CI: 1.8–8.0). This finding was in line with a study conducted by Vanker et al that antenatal environmental tobacco smoke exposure was associated with *Streptococcus pneumoniae* carriage in mothers (ARR: 1.73, 95% CI: 1.03–2.92) while postnatal environmental tobacco smoke exposure was associated with carriage in infants (AOR: 1.14, 95% CI: 1.00–1.30).[24] However, the present study was not similar to the study reported from other part of Ethiopia (p=0.225).[25]

Children who lived in rural areas had 3.6 times more likely chance to be infected with *S. pneumoniae* compared to children who lived in urban areas (AOR: 3.6, 95% CI: 1.2–11). However, there was no significant association between the residence of rural and urban areas (AOR: 0.69, 95% CI: 0.33–1.4) in a study conducted in Gondar University Hospital, Ethiopia.[25] This could be the fact that there was a difference in lifestyle between urban and rural areas in different places. In some urban dwellers, utilization of health-care services in time or better access to health-care facilities may be the reason; hence, childhood illnesses could receive a timely diagnosis that makes largest contributions to the rural–urban inequality in under-five children.[26]

In this study, the results of the antimicrobial susceptibility test revealed that 41 (95.4%) and 40 (93%) of *S. pneumoniae* were susceptible to Ceftriaxone and Amoxicillin-clavulanate, respectively, whereas 23 (53.5%) of Tetracycline and 21 (48.8%) of cotrimoxazole were resistant to it. This study was similar to the study reported from Hawassa, southern Ethiopia, in which 44 (64.6%) of cotrimoxazole and 29 (42.6%) of Tetracycline were resistant to *S. pneumoniae*.[27] Another study revealed that 22.9% of Cotrimoxazole, in Ethiopia, 77.5% in Dakar, Senegal, and 100% in south Bangalore, India, were resistant to the isolated *S. pneumoniae*.[26,28,29]

On the other hand, a study conducted in Tanzania showed that the isolated 58.33% of *S. pneumoniae* were susceptible to erythromycin which was lower than this study.[30] In contrary to this study, a study conducted in

Kenya revealed that 100% of tetracycline was susceptible to isolated *S. pneumoniae*.[31] In the present study, 40 (93%) of amoxicillin-clavulanate was the most active antibiotic against *S. pneumoniae* that was similar to a study conducted in Dakar, Senegal, in which 97.05% of amoxicillin-clavulanate was susceptible to *S. pneumoniae*.[3] In this study, about 83.7% of Erythromycin was susceptible to the isolated bacteria that were similar to the study conducted at Hawassa, southern Ethiopia, that 85.3% of Erythromycin was susceptible to S. *pneumoniae*.[25] The difference of antimicrobial susceptibility compared to other studies might be due to different bacterial strains, empirical treatment practice, use of antibacterial as a prophylactic, easy availability of some drugs without a prescription, a dose of the drug, and indiscriminate/prolonged use of common antibiotics.

Limitation of the Study

Since the study is cross-sectional, it was not able to sufficiently establish causality and the study may be subjected to response bias from the respondents.

Conclusion and Recommendations

The proportion of *S. pneumoniae* among studied children was high with 11.2%. Cotrimoxazole and Tetracycline were not enough effective to treat *S. pneumoniae*. Children in the family of cigarette smokers and rural residents were at risk to be infected with *S. pneumoniae*.

Based on the findings of this study, the following recommendations are made:

Health education should be provided for families on the identified predisposing factors that needs screening and early treatment of children with *S. pneumoniae*. Ceftriaxone, amoxicillin-clavulanate, and Erythromycin can be used for the treatment of infected patients with isolated bacteria in this finding at Hiwot Fana Specialized University Hospital. Further studies should be conducted with different possible associated factors by using advanced laboratory tests.

Abbreviations

ARI, Acute Respiratory Infection; HRERC, Institutional Health Research Ethics, and Review Committee; HFSUH, Hiwot Fana Specialized University Hospital.

Data Sharing Statement

The raw data set used/analyzed during the current study is available from Mr. Dejene Bayu on a reasonable request.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; and agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors report that there is no potential conflicts of interest for this work.

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