Infection and Drug Resistance

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ORIGINAL RESEARCH

# Prevalence, Antimicrobial Drug Resistance and Associated Risk Factors of Streptococcus Pneumoniae Bacteria Infection Among Under-Five Children With Acute Lower Respiratory Tract Infection Attending Sheik Hassan Yebere Referral Hospital, Jig-Jiga, Ethiopia

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**Background:** Pneumonia is inflammation of the lung. The *Streptococcus pneumoniae* (*S. pneumoniae*) is commensal in the upper airway and can cause infection to under-five children. The bacteria is gram-positive diplococci, catalase negative, and optochin sensitive. The bacteria is the leading cause of bacterial pneumonia among under-five children. No similar data is reported from the current study area.

**Objective:** To determine prevalence, antimicrobial drug resistance and associated factors of *S. pneumoniae* infection among under-five children with acute lower respiratory tract infection attending Sheck Hassan Yebere Referral Hospital from March 1 to April 30, 2021 Jig-Jiga, Ethiopia.

**Methods:** A cross-sectional study was conducted among 374 study participants selected by convenience sampling method. A structured questionnaire was used to collect child data. Nasopharyngeal/oropharyngeal swabs were collected and diagnosed to isolate *S. pneumoniae* by using culture then identified by biochemical examination. Later antimicrobial drug resistance testing was performed by Kirby–Bauer disk diffusion method. All data were entered on epi-data 3.1 then exported to SPSS version 22 to calculate analysis. Statistically significant value was found by calculating an adjusted odds ratio with p-value $\leq 0.05$ in a multivariate logistic regression model.

**Results:** Among 374 under-five children, 180 (48.1%) were males and 109 (29.2%) were from low income families. The overall prevalence of *S. pneumoniae* infection in the study was 18% (95% CI 14.4–22.2). No window (AOR=2.8 CI 1.1–7.6), no/non-exclusive breast-feeding (AOR= 2.1 CI 1.1–4.1), and previous URTI (AOR= 3.2 CI 1.7–6.1) were significantly associated with *S. pneumoniae* infection. The isolated organism showed drug resistance for Cotrimoxazole (35%), and Tetracycline (34%).

**Conclusion:** The prevalence and antimicrobial resistance in this study were comparatively high. No window, non-exclusive breast-feeding and previous URTI were associated with *S. pneumoniae* infection. The isolated *S. pneumoniae* showed high drug resistance to cotrimoxazole and tetracycline.

**Keywords:** under-five pneumonia, antimicrobial resistance, *S. pneumoniae*

## Introduction

Pneumonia is an inflammation of alveoli and bronchioles of the lung.[1] It can be caused by either a virus or bacteria pathogen. The *S. pneumoniae* bacteria is normal flora in the upper respiratory airway and it can frequently cause



Received: 14 March 2023
Accepted: 19 May 2023
Published: 2 June 2023

respiratory tract infection for under-five children due to low or under-developed immunological status.[2] In the middle and low income countries the bacteria are commonly carried in the nasopharynx of children, which serves as a reservoir for human pathogen for the development of pneumonia disease.[3]

Airborne is the main transmission route for the bacteria respiratory infection. Therefore, this airborne transmission of *S. pneumoniae* bacteria is almost exclusively high in the home air environment in crowded living conditions as well as the using of solid fuel source for cooking that leads to poor indoor air quality.[4] *S. pneumoniae* bacteria is a gram-positive lancet-shaped diplococci, non-spore forming, catalase negative, bile soluble and optochin sensitive bacteria. Microscopically, the bacteria is seen in pairs, single cells and chains and it is found in the family member of *Streptococcus* so it is named *S. pneumoniae*.[5] The bacteria best grows on blood agar media because naturally the bacteria lack catalase enzyme which is essential for hydrogen per oxide neutralization, so the media neutralizes it and the bacteria grows as alpha hemolytic on the these blood agars.[6]

*S. pneumoniae* bacteria spreads via aerosol from infected individuals; it can also spread directly via contact with saliva and nasal secretions. It usually causes rhinorrhea.[7] According to a World Health Organization (WHO) estimation report in developing countries, each year 156 million under-five children had pneumonia; among these, annually 1.2 million deaths occur and 20 million pneumonia cases need hospital admission.[8] So these deaths in the developing world account for 90–95% of the total death rate.[9]

In Africa, especially Ethiopia, annually 3,370,00 under-five children develop pneumonia and, among these, 40,000 children will die, which accounts for 18% of the all causes of deaths reported every year.[10] Due to low coverage of controlling and preventive strategies like administration of pneumococcal conjugate vaccine (PCV) and vitamin A supplementation throughout all parts of Ethiopia, the burden of pneumonia among children is high.[11] According to the study done in some Ethiopian regions, the most common serotypes found in Ethiopian children were 15A/B/C 10A/F, 7C, 35A/B, 19A. However, the PCV 13 vaccination protects against strains of 1, 3, 4, 5,6A. 6B, 7F, 9V, 14, 19A, 19F, 18C, and 23F.[12] A study conducted in Indonesia showed the overall prevalence of *S. pneumoniae* bacterial infection among children to be 22%.[13] In Gondar city, Ethiopia, the prevalence of *S. pneumoniae* infection among children under five years of age was 12%.[10] Similarly, in the Mizan Tepi University teaching hospital prevalence was 25.3% and in Harar, in the eastern part of the country, it was 11.2%.[14,15]

WHO reported that *S. pneumoniae* bacteria is being increasing antibiotic drug resistant across the world.[16] In a prospective study conducted in Amhara region and Addis Ababa city national referral hospitals, *S. pneumoniae* showed antimicrobial drug resistance for Erythromycin (59.6%), Clindamycin (17.5%), Tetracycline (38.6%), Chloramphenicol (17.5%) and Trimethoprim-sulphamethoxazole (24.6%).[17] In a correctional study conducted in Harar among under-five children from March 1 to 30, 2020, *S. pneumoniae bacteria* showed high antibiotic resistance to Trimethoprim-sulphamethoxazole 21 (48.8%), but in contrast the bacteria showed a 95.4% susceptible rate for Ceftriaxone and a 93% susceptible rate for Amoxicillin-clavulanate.[14]

In Ethiopia, especially the Somali region, there is a lack of data available on overall *S. pneumoniae* prevalence and its antimicrobial drug resistance among children under five years of age. Therefore, to fill this gap the study was conducted to determine prevalence of *S. pneumoniae* with its associated risk factors and antimicrobial drug resistance among under-five children with acute lower respiratory tract infection.

# Methodology

## Study Area and Period

The study was conducted at Sheik Hassan Yebere Referral Hospital from March 1 to April 30, 2021. This hospital found in the Somali region capital town of Jig-Jiga, is now giving health services for people living in the town and other patients referred from different localities of the region. Jig-Jiga is located 625 km to the east of the capital city of Ethiopia, Addis Ababa, and 60 km from the western border of Somalia.[18]

## Study Design

A health facility-based cross-sectional study was carried out.

## Source Population

All children under five years of age who visited the hospital pediatric outpatient department (OPD) with acute lower respiratory tract infection.

## Study Subjects

All selected children age less than five years with lower respiratory tract infection who visited Sheik Hassan Yebere Referral Hospital pediatric outpatient department in the study period.

## Eligibility Criteria

All under-five children suspected for symptomatic lower respiratory tract infection who had persistent cough, fever and sometimes difficulty breathing and visited Sheik Hassan Yebere Referral Hospital pediatric OPD during the study period. However, all children who were on antibiotic therapy during the study period were excluded from the study because their samples may lead to false negative results.

## Sample Size Determination

Single population proportion formula was used to determine the sample size of the study by considering the prevalence rate of *S. pneumoniae* 33.3%,[19] margin of error 5%, confidence interval 95% and finally adding 10% non-response rate, the total sample size was 374.

## Sampling Procedure

There were three hospitals (Karamara general hospital, Jig-Jiga primary hospital and Sheik Hasan Yebere Referral Hospital) in Jig-Jiga town. By using simple random sampling method, the Sheik Hasan Yebere Referral Hospital was selected. Then, from pediatric outpatient department study participants who had symptoms of acute lower respiratory tract infection were selected by using convenience sampling method.

## Methods of Data Collection

Four BSc nurses and two laboratory technologists participated in the collection of data and samples. The main criteria for the selection of data collectors and supervisor was based on experience. The principal investigator gave two days training for the participating data collectors on how to collect the data and sample specimens before the actual data collection. Then there was daily onsite supervision and monitoring by supervisor and principal investigator.

## Data Collection Instruments

### For Socio-Demographic Factors and Child Clinical History

Data for patient socio-demographic factors like age, sex, and educational status of parents were collected using semi-structured questionnaires by direct interview with the child parent/legal guardian. The clinical history of the child was obtained from the pediatric physician record and similarly the vaccination status was obtained from immunization records by asking the child's parent to show the card. All data was collected during working days at the hospitals.

### For Clinical Specimens

Both nasopharyngeal and oropharyngeal swab specimens were collected using sterile swabs, which were then placed in sterile cups labeled with identification numbers.

### For Nutritional Status Measurements

Nutritional status of the child was assessed by using anthropometric measurement. The weight of the child in kilograms was measured using a standard weighing scale. The clinical nurse working at OPD measured children without shoes and wearing light clothes standing erect; those children who cannot stand erect were measured lying down on the measurement scale. The weight measurement was calibrated to zero before taking the actual weight. Weight for age Z-scores (WAZ) was used to assess the nutritional status of the child to classify them as malnourished or not. WHO

anthro-version 3.2.2 software application was used to calculate WAZ. If the WAZ score result is less than −2 standard deviations, then the child is considered underweight.[20]

## Laboratory Procedure

### Sample Collection

Specimens were collected using sterile swabs and transferred to sterile tubes. Before collecting the actual specimen, the sample tube was labeled with necessary identification. The clinically acceptable sample consists of mucoid, yellowish, which sometimes may contain blood.

## Sample Transport

The specimens were transported using Amies transport medium, inserted in leak-proof biohazard bags with maintainable cooler temperature of 2–8°C. During sample transportation specimen transport forms were included. Then, the collected samples were immediately transported to the microbiology laboratory without delay.

## Culturing the Media

Upon arrival the specimens were cultured at Jig-Jiga University Sheck Hassan Yebere Referral Hospital microbiology laboratory for the isolation of *S. pneumoniae*. The specimens obtained were inoculated on an enriched media like blood agar containing 5% sheep blood and chocolate agar. Then, using strict standard operating procedure, the inoculated plates were incubated with 5% $CO_2$ at the temperature of 37 °C for 18–24 hours. The isolated colonies that showed alpha hemolysis on the blood agar plate were further identified using Optochin disk sensitivity and biochemical tests like fermentation of glucose, lactose and sucrose. For an ambiguous result on Optochin, a disk sensitivity bile soluble test was performed to confirm the result.[21]

## Antimicrobial Sensitivity Testing

Antimicrobial drug resistance testing was performed on the isolated *S. pneumoniae* bacterial pathogens on Mueller–Hinton agar containing 5% sheep blood using disk diffusion method. The method was performed on 150 mm plate and the diameter of zone of complete inhibition including the diameter of the disk was measured with the unaided eye. Firstly, we obtained information from attending physicians on the antibacterials they were commonly ordering to treat *S. pneumoniae* bacteria, and we compared those antimicrobials to the Clinical and Laboratory Standards Institute (CLSI) guidelines. Those antimicrobials were Chloramphenicol 30μg, Vancomycin 30μg, Penicillin, Amoxacillin-clavulanate 30μg, Tetracycline 30μg, Ceftriaxone 30μg, and Trimethoprim-sulphamethoxazole 25 μg. The zone of inhibition was measured by ruler and compared with CLSI standards to identify whether samples containing isolated *S. pneumoniae* bacteria were susceptible or resistant to the drugs. For non-meningitis isolate, a penicillin MIC (minimum inhibitory concentration) of ≤ 0.06μg/mL or (zone of inhibition ≥20mm predicts susceptibility to the β- lactam). Those *S. pneumoniae* bacterias' which showed a zone of inhibition of ≤19mm were further checked by MIC before being reported as resistant.[22]

## Microscopic Examination for Morphology

The isolated and suspected *S. pneumoniae* bacteria were taken from the media, then smeared and stained by gram stain. Finally, by using 100% oil objective the diplococci bacteria was observed.

## Operational Definitions

Under-five children: children older than 2 months and younger than 59 months.
Acute respiratory infection (ARI): an infection of the airway that may interfere with normal breathing.
MDR: resistance of the bacteria to two or more antibiotics from different classes of antibiotics.

## Data Quality Control

The prepared structured questionnaire was translated into commonly used languages like Amharic and Somali and then back-translated into English for checking the consistency of the questionnaire. All data collectors took training

on how to collect, handle and transport data and specimens before the actual data collection. A pretest was performed on 5% of the sample size in non-study area at Ayerdega Health Center. Quality of prepared media was checked by incubating for 24 hrs at 37 °C without inoculation to check for the presence of contaminants. For the drug susceptibility test, we took quality control strains of *S. pneumoniae* ATCC (American-type culture control) 49619 from the regional laboratory and the diameter of zone of inhibition was compared using CLSI standard criteria.[22] The quality of Optochin disk was checked with a positive control of *S. pneumoniae* ATCC 49619 and negative controls of *Staphylococcus aureus* ATCC 25953. The results of the pretest were excluded from the actual data and the supervisor investigated all processes thoughout the study period. For some questions that were not understood by respondents, like prior antimicrobial usage, we prepared color photos for easy identification by parents of study participants. Finally, we used double data entry in statistical software SPSS 22 for the minimization of data entry error.

## Methods of Data Analysis

The collected data was coded and entered in Epi-data version 3.1 software. Then it was cleaned to check the validity of entered data. After exporting on SPSS version 22, statistical analysis was made. Descriptive statistics for independent variables were calculated and odds ratios were measured to assess the associations between dependent and independent variables. All independent variables were analyzed using bivariate analysis and then those variables with a p-value of ≤0.25 were further checked by multivariate analysis to control for the confounding variable. Both crude and adjusted odds ratios were calculated with a 95% confidence interval. A result with a p-value of ≤0.05 was considered a statistically significant association with the outcome variable. Finally, the data was formulated as figures and tables, both by SPSS and by using Microsoft Excel 2016 programs.

## Ethical Consideration

Ethical clearance ref no. (JJU-CMHS-ERC 0032/2021) was obtained from Jig-Jiga University College of Medicine and Health Sciences Institutional Health Research and Ethics Review Committee (IHRERC), in accordance with the Declaration of Helsinki. A cooperative letter written from Jig-Jiga University research and publication office was sent to Sheik Hassan Yebere Referral Hospital to get permission. All participant parents were informed that participation in the study was voluntary. Their failure to participate in the study would not result in any form of penalty. Participants were also informed of the confidentiality of the data and told that they can quit the study if they are not comfortable. Written informed consent was obtained from the child's parent/legal guardian after explaining the purpose and objective of the study. Finally, participating children with positive laboratory results of *S. pneumoniae* infection were linked to the attending physician to get appropriate treatment.

# Results

## Socio-Demographic Characteristics

In this study, 374 under-five children suspected for lower respiratory tract infection were included, with a response rate of 100% (all selected study participants got involved willingly, with no refusals). In this study there were 194 (51.9%) female participants; 170 (45.5%) of the under-five children were under one year of age; and 264 (70.6%) were Somali ethnicity (Table 1).

## Living Conditions

Of 374 study participants, the highest proportion (170, 45.5%) of them were living in a house with two rooms. Of all rooms, 69 (18.4%) do not have a window for ventilation; 185 (49.5%) children live in a family that cooks in the kitchen and the majority (197 (52.7%) use charcoal for fuel source; 118 (32.6%) children are exposed to either cigarettes or shisha in the house (Table 2).

**Table 1** Socio-Demographic Characteristics of Under-Five Children Attending Sheck Hasan Yebere Referral Hospital, Jig-Jiga, Ethiopia, 2021

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Sex | Male | 180 | 48.1 |
| | Female | 194 | 51.9 |
| Age | <1 | 170 | 45.5 |
| | ≥ 1–2 | 96 | 25.7 |
| | ≥ 2–3 | 49 | 13.1 |
| | ≥ 3–4 | 42 | 11.2 |
| | ≥ 4–5 | 17 | 4.5 |
| Parent's marital status | Married | 297 | 79.4 |
| | Single | 13 | 3.5 |
| | Divorced | 59 | 15.8 |
| | Widowed | 5 | 1.3 |
| Religion | Muslim | 287 | 76.8 |
| | Orthodox | 73 | 19.5 |
| | Protestant | 14 | 3.7 |
| Ethnicity | Somali | 264 | 70.6 |
| | Amhara | 59 | 15.8 |
| | Oromo | 34 | 9.1 |
| | Gurage | 12 | 3.2 |
| | Others | 5 | 1.3 |
| Mother's educational status | Unable to write/read | 149 | 39.8 |
| | Can read and write | 75 | 20.1 |
| | Primary school | 66 | 16.2 |
| | Secondary school | 62 | 16.6 |
| | Diploma and above | 22 | 5.9 |
| Father's educational status | Unable to write/read | 72 | 19.3 |
| | Can Read and write | 63 | 16.8 |
| | Primary | 43 | 11.5 |
| | Secondary | 84 | 22.5 |
| | Diploma and above | 112 | 29.9 |
| Mother's current occupation | Housewife | 251 | 67.1 |
| | Civil servant | 31 | 8.3 |
| | Merchant/Trader | 53 | 14.2 |
| | Daily laborer | 36 | 9.6 |
| | Others | 3 | 8 |
| Father's occupation | Agricultural worker | 93 | 24.9 |
| | Civil servant | 74 | 19.8 |
| | Merchant/Trader | 97 | 25.9 |
| | Daily laborer | 75 | 20.1 |
| | Driver | 26 | 7.0 |
| | Others | 9 | 2.4 |
| Monthly income | <3000 | 33 | 8.8 |
| | 3000–6000 ETB | 109 | 29.2 |
| | 6000–9000 ETB | 120 | 32.1 |
| | >9000 ETB | 112 | 29.9 |

**Abbreviation**: ETB, Ethiopian birr.

## Vaccination, Breast-Feeding and Supplementation Status

Among all study participants, the majority (216, 57.8) have received a PCV vaccination. But 249 (66.6%) of the children did not take zinc supplements (Table 3).

**Table 2** Living Conditions of Under-Five Children Attending Sheik Hasan Yebere Referral Hospital Jig-Jiga, Ethiopia 2021

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Number of rooms in the house | One | 93 | 24.9 |
| | Two | 170 | 45.5 |
| | Three | 84 | 22.5 |
| | Four and above | 27 | 7.2 |
| Available windows in the house | No window | 69 | 18.4 |
| | Only one window | 182 | 48.7 |
| | Two windows | 123 | 32.9 |
| Fuel source | Charcoal | 197 | 52.7 |
| | Wood | 98 | 26.2 |
| | Electricity | 69 | 18.4 |
| | Kerosene | 10 | 2.7 |
| Place of cooking | Living room | 137 | 36.6 |
| | Kitchen | 185 | 49.5 |
| | Outdoors | 52 | 13.9 |
| Child carrying while cooking | Yes | 208 | 55.6 |
| | No | 166 | 44.4 |
| Child household cigarette or Shisha exposure | Yes | 118 | 31.6 |
| | No | 256 | 68.4 |

**Table 3** Vaccination and Feeding Status of Under-Five Children Attending Sheik Hasan Yebere Referral Hospital, Jig-Jiga, Ethiopia, 2021

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| PCV vaccination | Vaccinated | 216 | 57.8 |
| | Not vaccinated | 158 | 42.2 |
| Breast-fed for first 6 months | Exclusive breast-feeding | 181 | 48.4 |
| | Non-exclusive breast-feeding | 193 | 51.6 |
| Duration of breast-feeding | Still breast-feeding | 126 | 33.7 |
| | 1–23 months | 213 | 57 |
| | 24–36 months | 35 | 9.4 |
| Zinc supplementation | Yes | 125 | 33.4 |
| | No | 249 | 66.6 |

## Clinical History of the Child

Among all under-five children involved in study, 163 (43.6%) had previous history of URTI, 19 (5.1%) had history of measles, 4 (1.1%) of them had malaria. Regarding to growth status of the children, calculated from body mass index (BMI) Z-score, 129 (34.5%) were underweight (Table 4).

## Overall Prevalence of *S. pneumoniae* Bacterial Infection

The proportion of *S. pneumoniae* infection among children age less than five years attending Sheck Hassan Yebere Referral Hospital was 68/374 (18%) (95% CI 14.4–22.2).

## Bivariate and Multivariate Analysis Results for Factors Associated with *S. pneumoniae* Bacterial Infection

Child's father's educational status, number of windows in room, type of fuel source, place of cooking, household cigarette exposure, breast-feeding, previous URTI and nutritional status of the baby showed significant associations with *S. pneumonia*

**Table 4** Clinical History and Growth Status of Under-Five Children Attending Sheik Hasan Yebere Referral Hospital, Jig-Jiga, Ethiopia, 2021

| Variable | Category | Frequency | Percentage |
|---|---|---|---|
| Previous URTI | Yes | 163 | 43.6 |
| | No | 211 | 54.6 |
| Measles | Yes | 19 | 5.1 |
| | No | 355 | 94.9 |
| Malaria | Yes | 4 | 1.1 |
| | No | 370 | 98.9 |
| Diarrhea | Yes | 177 | 47.3 |
| | No | 197 | 52.7 |
| Chronic disease CHD or | Yes | 51 | 13.6 |
| Asthma | No | 323 | 86.4 |
| Growth status of the child | Underweight | 129 | 34.5 |
| | Overweight | 29 | 7.8 |
| | Obese | 36 | 9.6 |
| | Healthy weight | 180 | 48.1 |

infection in a binary logistic regression model. These variables were subjected to multivariate analysis and the majority remained significantly associated with *S. pneumoniae* infection. In the multivariate regression analysis, children who lived in a home with insufficient ventilation due to absence of windows (p-value=<0.04 AOR=2.8; 95% CI 1.1–7.6), children who did not exclusively breast-feed (p-value=<0.03 AOR=2.1; 95% CI 1.1–4.1), and children who encountered previous URTI (AOR=3.2; 95% CI 1.7–6.1); p-value=<0.01) were associated with *S. pneumoniae* infection (Table 5).

## Antimicrobial Drug Susceptibility Testing

Among all *S. pneumoniae* isolated bacteria, 24 (35%) were resistant to Cotrimoxazole, 23 (34%) were resistant to Tetracycline, and 10 (14%) were resistant to penicillin. Whereas 61 (89%), 68 (100%), 64 (94%) and 64 (94%) were susceptible to Chloramphenicol, Ceftriaxone, Vancomycin and Amoxicillin-clavulanate, respectively (Table 6).

Multi-drug resistant *S. pneumoniae* is increasing worldwide, as reported from many studies across the globe. An increased number of antimicrobial treatments are at increased risk of drug resistance to commonly used antibiotics.[23] In our study, from all isolated *S. pneumoniae* bacteria, 28 (41.2%) were resistant to only one antibiotic, 15 (22.1%) were resistant to two antibiotics and 3 (4.4%) were resistant to three or more antibiotics (Table 7).

# Discussion

Pneumonia is an inflammatory disease which mainly affects the parenchymal structure of the lung like alveoli and bronchioles.[1] The bacteria named *S. pneumoniae* is found as a normal flora in the upper respiratory airway but these bacteria can cause a serious infection for children aged less than five years due to their lower immunological status.[2]

According to this study, the overall prevalence of *S. pneumoniae* bacterial infection was 18%, which showed a lower prevalence from other studies conducted in Niger and Indonesia, with reported prevalence rates of 39.6% and 22%, respectively.[13,24] This difference might be due to the detection method; the latter study was conducted using a highly sensitive molecular technique known as PCR. BThe results of the PCR technique are not dependent on the lab technician's ability or the time it takes to grow the bacteria in the culture dish, which results in highly compressed, accurate and fast data sets. Similarly, the prevalence rate of *S. pneumoniae* infection reported in our study was also lower compared to similar studies conducted in Belgium, Mozambique, Ghana and Indonesia, which reported prevalence rates of 21%, 80.5%, 48.9% and 46%, respectively.[25–28] This difference could be the result of the duration of the study period, study area and detection method. For example, the study conducted in Belgium involved 12 months of data collection, the Mozambique study was carried out in three different areas of study, and the Ghanaian study was carried out by molecular detection method that made the prevalence of infection higher. In another way, the prevalence of *S. pneumoniae* infection showed a higher prevalence rate than the study conducted in United States,

**Table 5** Results of Bivariate and Multivariate Analysis of *S. pneumoniae* Infection Associated Factors Among Under-Five Children Attending Sheik Hasan Yebere Referral Hospital, Jig-Jiga, Ethiopia, 2021

| Variables | Category | *S. pneumoniae* | | Bivariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|---|---|---|
| | | Positive n (%) | Negative n (%) | COR (95% CI) | P-value | AOR (95% CI) | p-value |
| Father educational status | Unable to write/read | 28(38.8%) | 44(61.2%) | 6.5(2.9–14.5) | 0.01 | 1.8(0.5–6.2) | 0.37 |
| | Can read and write | 14(22%) | 49(78%) | 2.9(1.2–70) | 0.02 | 0.8(0.2–2.9) | 0.74 |
| | Primary school | 8(19%) | 35(81%) | 2.3(0.9–6.3) | 0.09 | 0.9(0.3–3.9) | 0.7 |
| | Secondary school | 8(9.9%) | 76(90.1%) | 1.1(0.4–2.8) | 0.88 | 0.6(0.2–2.0) | 0.43 |
| | Diploma and above | 10(8.9%) | 102(91.1%) | 1 | | | |
| No. of windows | No windows | 27(39.1%) | 42(60.9%) | 5.4(2.6–11.5) | 0.01 | 2.8 (1.1–7.6)* | 0.04 |
| | Only one window | 28(15.4%) | 154(84.6%) | 1.5(0.7–3.1) | 0.23 | 0.9 (0.4–2.3) | 0.88 |
| | Two windows | 13(10.6%) | 110(89.4%) | 1 | | | |
| Place of cook | Living room | 34(24.8%) | 103(75.2%) | 0.89(0.4–1.8) | 0.77 | 0.83(0.3–2.3) | 0.72 |
| | Kitchen | 20(10.8%) | 165(89.2%) | 0.3(0.2–0.7) | 0.01 | | 0.61 |
| | Outdoors | 14(26.9%) | 38(73.1%) | 1 | | | |
| Cigarette or Shisha exposure in household | Yes | 32(25.9%) | 86(74.1%) | 2.2(1.3–3.9) | 0.003 | 1.8 (0.9–3.4) | 0.08 |
| | No | 36(14.1%) | 220(85.9%) | 1 | | | |
| Breast-feeding | Non-exclusive | 51(26.4%) | 142(73.6%) | 3.4(1.9–6.2) | 0.01 | 2.1(1.1–4.1)* | 0.03 |
| | Exclusive | 17(9.4%) | 164(90.6%) | 1 | | | |
| Previous URTI | Yes | 46(28.2%) | 117(71.8%) | 3.4(1.9–5.9) | 0.01 | 3.2 (1.7–6.1)* | 0.01 |
| | No | 22(10.4%) | 189(89.6%) | 1 | | | |
| Nutritional status by BMI | Underweight | 36(27.9%) | 93(72.1%) | 3.2(1.8–6.0) | 0.01 | 1.5(0.7–0.3.1) | 0.20 |
| | Overweight | 6(20.7%) | 23(79.3%) | 2.2(0.8–6.1) | 0.12 | 2.2(0.7–7.2) | 0.17 |
| | Obese | 7(19.5%) | 29(80.5%) | 2(0.8–5.3) | 0.14 | 2(0.7–6.5) | 0.15 |
| | Healthy weight | 19(10.6%) | 161(89.4%) | 1 | | | |

**Notes**: *Means those variables that showed significant association with S. *pneumoniae* bacterial infection (P-value ≤0.05).


https://doi.org/10.2147/IDR.S409919

**Table 6** Antibiotic Susceptibility Pattern of Isolated *S. pneumoniae* Among Under-Five Children Attending Sheik Hasan Yebere Referral Hospital, Jig-Jiga, Ethiopia, 2021

| Antimicrobial Drugs | Susceptible | Intermediate | Resistant |
|---|---|---|---|
| Amoxicillin clavulanate | 64(94%) | 2(3%) | 2(3%) |
| Cotrimoxazole | 36(53%) | 8(12%) | 24(35%) |
| Chloramphenicol | 61(89%) | – | 7(10%) |
| Tetracycline | 41(60%) | 4(6%) | 23(34%) |
| Penicillin | 52(77%) | 6(9%) | 10(14%) |
| Ceftriaxone | 68(100%) | – | – |
| Vancomycin | 64(94%) | 4(6%) | – |

**Table 7** MDR (Multi-Drug Resistant) *S. pneumoniae* Isolated from Under-Five Children Attending Sheik Hasan Yebrere Referral Hospital, Jig-Jiga, Ethiopia, 2021 (N=68)

| Antibiotics | Resistance |
|---|---|
| Cotrimoxazole + Tetracycline | **11(16.2%)** |
| Cotrimoxazole + penicillin | 3(4.4%) |
| Penicillin + Chloramphenicol | 1(1.5%) |
| Cotrimoxazole + Tetracycline + Chloramphenicol | 1(1.5%) |
| Augmentin + Cotrimoxazole + Tetracycline | 1(1.5%) |
| Augmentin + Cotrimoxazole + penicillin + Chloramphenicol | 1(1.5%) |

Laos PDR and in Gondar city, Ethiopia, which reported prevalence rates of 16.2%, 15.7% and 12%, respectively.[10,29,30] The possible reason could be that the US study was conducted in a clinic rather than in a hospital, in Laos PDR the study participants were under-five children who have received a PCV vaccination, and in Gondar city the study was conducted in a community-based setting that may contribute for to low prevalence of *S. pneumoniae* bacteria infection. Similarly, our study finding had a higher prevalence rate than the study conducted in Haramaya University Hiwot Fana Specialized University Hospital, with the prevalence of S. *pneumoniae* infection among under-five children at 11.2%[14]; the difference might be living conditions.

Earlier prevalence studies carried out in different areas of Ethiopia showed a high prevalence rate of *S. pneumoniae* infection when compared to our study finding. This study finding revealed a lower prevalence than that of another study conducted in Wondo Genet and Mizan Tepi University Teaching Hospital, with prevalence of *S. pneumoniae* of 33.33% and 25.3%, respectively;[15,19] this difference might be due to geographical variation. Similarly, this study has much lower prevalence than the study carried out in Jima Shaman Gibe Hospital and Debre Berhan Referral Hospital, with total prevalence of *S. pneumoniae* infection of 43.8% and 39.6%, respectively.[31,32] The disagreement could happen as a result of differences in the geographical areas and geographical settings of studies.

The finding of this study showed that children who were living in houses with no windows had a 2.8 times increased risk of *S. pneumoniae* infection than their counterparts, which is more or less similar to previous studies conducted in Alexandria, where children who were living in poorly circulated air due to no window in the rooms had a 3.5 times increased risk of *S. pneumoniae* infection than children who were living in houses with 2 or more windows.[33] Similarly, on the other side of Munesa district, children living in houses with more than two windows were 95% protected from *S. pneumoniae* infection.[15] Poor ventilation can

have a serious health impact due to prolonged exposure to bacteria, which means that lower air exchange rate might increase the concentration of the *S. pneumoniae* bacteria.

In this study, under-five children who had a previous upper airway infection in the last month were 3.2 times more likely to develop *S. pneumoniae* infection than under-five children who did not have the illness. This result was higher than previous studies conducted in East Africa and Munesa district where under-five children with history of respiratory infection in the upper airway was significantly associated with infection of *S. pneumoniae* with an AOR of 2.62 and 4.2, respectively.[15,34] This difference from the study done in East Africa could be due to the study design used; our study was done using a cross-sectional design but the previous study was done by systematic review and meta-analysis. The other difference regarding the study done in Munesa was that it was conducted in a community-based setting but our study was hospital based.

In this study, under-five children who were not exclusively breast-fed for 6 months were 2.1 times more likely to develop *S. pneumoniae* infection than children who were exclusively breast-fed. But our results were lower than those of a study conducted in Kersa district: among 378 children, those who were not exclusively breast-fed below the age of six months were more likely to develop pneumonia infection, with an AOR of 3.3.[35] This difference could be the result of study design because our study was cross-sectional but the earlier study used a case control approach. In a study conducted in Achefer district, Northwest Ethiopia, under-five children who were exclusively breast-fed were 83 times less likely to be infected with *S. pneumoniae* bacteria than those who were not.[36] Again, this difference may be explained by the fact that our study used a case control approach. According to immunological science, breast-feeding protects infants from infections and inflammation, mainly via secretory IgA antibodies and some other anti-inflammatory components; thus, breast-feeding for the first six months of life is advisable until the infant begins to produce their own antibodies. The secretory IgA obtained from breast-feeding has ability to modify the virulence of the surface protein A of S. *pneumoniae* bacteria.

The isolated *S. pneumoniae* bacteria in the present study showed drug resistance for commonly used antimicrobials. Those antimicrobials were Cotrimoxazole 35%, Tetracycline 34%, penicillin 14% and Chloramphenicol 10%. The finding of this study was compared with different studies across the globe. A study conducted in Tehran revealed that *S. pneumoniae* bacteria showed antibiotic drug resistance to Tetracycline (69.85%), Azithromycin (54.9%), Cotrimoxazole (11.8%), penicillin (9.2%), and Vancomycin (1.5%);[37] further, regarding resistance to Tetracycline, Vancomycin and Cotrimoxazole, these figures are higher than those in our study. This may be due to geographical variation. In this study, *S. pneumoniae* showed lower resistance patterns when compared to a study conducted in Gondar, where *S. pneumoniae* showed resistance patterns of 33.2% to Erythromycin and Tetracycline and 14.6% to Chloramphenicol.[38] The isolated *S. pneumoniae* bacteriain our study showed similar 10% antibiotic drug resistance to Erythromycin to that found in a study conducted in Harar and Gondar, Ethiopia.[14,38]

A study conducted in Hawassa, Ethiopia showed 64.6% and 42.6% resistance of *S. pneumoniae* to Cotrimoxazole, and Tetracycline, respectively, which is higher than the resistance pattern reported in our study; however, Chloramphenicol showed 8.8% resistance, which is lower than that found in our study.[39] Similarly, a study in Jima town Shanan Gibe Hospital revealed that *S. pneumoniae* showed resistance to Tetracycline (53.2%), Cotrimoxazole (43.7%), penicillin (36.1%), and Chloramphenicol (13.3%),[32] which is higher antibiotic resistance than that in our study area. This difference could be the result of variation in geographical, area, study season and implementation of immunization. A study conducted at Harar Hiwot Fana Specialized Hospital revealed that *S. pneumoniae* showed resistance to Chloramphenicol (14%), Tetracycline (42%), Ceftriaxone (2.3%) and Cotrimoxazole (46.5%), which are higher than those from our study. Amoxicillin-Clavulanate showed similar resistance pattern from our study,[14] which might result from a variation in study period.

## Limitation

This study used convenience-sampling method, which may limit the generalizability of the findings.

## Conclusions

The prevalence and antimicrobial drug resistance of *S. pneumonia* in this study were comparatively high. The overall prevalence rate among under-five children attending the hospital was 18%. No window in the house, non-exclusive breast-feeding and previous URTI were associated with *S. pneumoniae* bacterial infection in under-five children. The

identified organisms showed drug resistance to Cotrimoxazole (35%), Tetracycline (34%) and Chloramphenicol and Erythromycin (both 10%).

## Abbreviations

CLSI, Clinical Laboratory Standard Institute; LRIs, lower respiratory infections; MDR, multi-drug resistance; OPD, outpatient department; PCV, pneumococcal conjugate vaccine; URTI, upper respiratory tract infection; WAZ, weight for age Z-score; WHO, World health organization.

## Data Sharing Statement

The data used in this research study is available from the corresponding author upon reasonable request.

## Acknowledgment

We would like to thank Jig-Jiga University research directorate for funding us to conduct this research project. Our special thanks also to Jig-Jiga University College of Medicine and Health Science Faculty for their continuous support and tremendous follow up during the study. We would like to thank Sheck Hassan Yebere Referral Hospital Laboratory staff and pediatric nurses who participated during collection and examination of data and samples, respectively.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

The funding for this research project was obtained from Jig-Jiga University Research Directorate.

## Disclosure

All authors declare that they have no competing interests.

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