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BACTERIOLOGICAL CHARACTERIZATION OF LOWER RESPIRATORY TRACT INFECTION AMONG PATIENTS ATTENDING SOME HOSPITALS IN KEBBI STATE NIGERIA

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ABSTRACT
The aetiology of lower respiratory tract infection (LRTI) is diverse and complicated, hence in most developing countries, treatment of LRTI is made usually empirically in which the etiologic agent is rarely identified. Therefore this study was designed to isolate and identify bacterial pathogens of lower respiratory tract among patients attending some hospitals in Kebbi State, Nigeria. Three hundred and fifty sputum samples were collected from six different hospitals in Kebbi State after obtaining an ethical approval from the ministry of health and informed consent from all the participants. Sputum samples were inoculated into blood agar, chocolate agar and MacConkey agar plates. The chocolate agar plates were incubated in an incubator (5% CO_2) at 37 ^oC for 24 hours while blood agar and MacConkey agars were incubated in an aerobic atmosphere at 37^oC for 24 hours. The bacterial isolates were identified using conventional biochemical tests and then confirmed using commercial biochemical test kit (MICROBACT) according to manufacturer's instruction. Antimicrobial susceptibility test were determined using disc diffusion method according to CLSI guidelines. Staphylococcus aureus was the most predominant bacteria isolated in this location followed by Klebsiella pneumoniae with an estimated percentage occurrence of 31.1% and 22.2% respectively. Other bacteria isolated include Klebsiella oxytoca (13.9%), Escherichia coli (11.1%), Pseudomonas aeruginosa (5.6%), Aeromonas hydrophila (5.6%), Acinetobacter baumannii (4.6%), Burkholderia pseudomallei (2.8%) and Proteus spp (2.8%). It was found out that, the young adults and the elderly were most at risk of a severe respiratory condition. The result also shows that LRTI were more common in males than in females. Most of the isolates were susceptible to piperacilin ((51%), trimethoprim sulphamethoxazole (61%), Azithromycin (70%), Ciprofloxacin (71%) and Gentamycin (74%), in order of ranking. High resistance were recorded in almost all the βeta-lactam antibiotics, erythromycin and vancomycin tested. In conclusion, Staphylococcus aureus was the most predominant bacteria isolated followed by Klebsiella pneumoniae while the least bacteria isolated were Burkholderia. pseudomallei and Proteus vulgaris. Lower respiratory tract infection was also more common in male and occurred mostly in young adults and elderly. Azithromycin, Ciprofloxacin, Gentamycin and piperacillin remain the useful antibiotics in the treatment of LRTIs in this location.
Keywords: Bacteria, Pathogens, Respiratory Tract, Sputum

INTRODUCTION

Lower respiratory tract infections (LRTIs) occur below the level of the larynx, i.e. in the trachea, the bronchi, or in the lung tissue. These includes condition such as tracheitis, bronchitis, bronchiectasis, lung abscess, tuberculosis and pneumonia (Kalgo *et al.*, 2016). Lower respiratory tract infection (LRTI) is considered as one of the major public health problems and a leading cause of morbidity and mortality in many developing countries (Rakshya *et al.*, 2018; GBD, 2016; LRIC, 2018). There were approximately 11.9 million episodes of severe acute lower respiratory infections (ALRI) resulted in hospital admissions in young children worldwide (Nair *et al.*, 2013).

The aetiology of LRTIs is diverse and complicated. Bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa* and other Gram-negative bacilli are widely considered the major pathogens responsible for LRTIs (Musher and Thorner, 2014). Viruses also play an important role in LRTIs, especially in infants younger than 2 years (Juvén *et al*., 2000). The common viral pathogens include respiratory syncytial virus (RSV), Human metapneumovirus (hMPV), Influenza virus (FLU) A and B, Parainfluenza virus (PIV) 1 to 3 and Adenovirus (ADV). The atypical bacterial pathogens that are recognized as childhood respiratory pathogens include *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Chlamydia trachomatis* (Pientong *et al*., 2011). Previous studies conducted in different parts of the world indicated that the leading bacterial causative agents of community acquired pneumonia (CAP) are *Streptococcus pneumoniae* and *Haemophilus influenzae* followed by *Staphylococcus aureus* (Müller *et al*., 2007; Shibl *et al*., 2010; Egbe *et al*., 2011).

World Health Organization Global Burden of Disease Study estimated that lower respiratory tract infections (LRTIs) were responsible for 429.2 million episodes of illness worldwide and also were the leading cause of disease burden measured in terms of disability adjusted life years (DALYs) (Shibl *et al*., 2010). Lower respiratory tract infection is the leading cause of death, accounting for more than 4 million fatalities annually. It is a particularly important cause of death in low- and middle income countries (Lozano *et al*., 2012). Pneumonia killed 808,694 children under the age of 5 in 2017, accounting for 15% of all deaths of children under five years old (WHO, 2019). It is also the second leading cause of years of life lost due to premature mortality (Lozano *et al*., 2012) and one of the most frequent reasons for hospitalisation. In adults aged over 59 years, 1.6 million deaths annually are attributed to community acquired pneumonia (Shibl *et al*., 2010). The burden of LRIs is highest in areas of low sociodemographic status, populations that depend on solid fuels for cooking and heating, and in malnourished and immunoimpaired populations (GBD 2015; LRIC, 2015).

Acute lower respiratory tract infection is a common cause of hospital admission in Nigeria (Akambi, 2009). Several studies were carried out from different parts of the country to determine the etiologic agents of Lower Respiratory Tract Infection and their susceptibility pattern to commonly used antibiotics (Egbage and mordi, 2006; Okesola and Ige, 2007; Taura *et al*., 2013; Iliyasu *et al*., 2015; Kalgo *et al*., 2016; Usman and Muhammad, 2017; Kolawole *et al*., 2017; Okon *et al*., 2018). But no comprehensive data has been established on the bacterial etiology of lower respiratory tract infection in Kebbi State. Therefore this study was designed to isolate and identify the bacterial pathogens of lower respiratory tract infection in Kebbi State.

MATERIALS AND METHODS

Study Area/Site

This study was conducted in Kebbi State, Kebbi State is located on latitude 11.6781° N and longitude 4.0695° E, the state is bounded by Sokoto State to the north and east, Niger State to the south, and Benin Republic to the west. The major ethnic groups are Hausa and Fulani, other ethnic groups includes Dakarkari, Zabarmawa, Dukkawa and Kambari. Kebbi State have a total land area of 36,129 sq. km. Agriculture is the main occupation of the people especially in rural areas. Crops produced are mainly grains. Animal rearing and fishing are also common. The state has the total population of 3,256,541 people as projected from the 2006 census (NPC, 2017). The study site includes: Sir Yahaya Memorial Hospital Birnin Kebbi, Kebbi Medical Centre, Aisha Buhari General Hospital Jega and General Hospital Argungu, General Hospital Yauri and Martha Bamaiyi General Hospital Zuru.

Study Population

The study population included patients from all age group that presented the clinical evidence of lower respiratory tract infection such as fever, rigors, fatigue, anorexia, diaphoresis, dyspnea, productive cough and pleuritic chest pain (Ashby and Turkington, 2007) as diagnosed by the attending physician at the General out Patient Department (GOPD) of the selected hospitals in Kebbi State.

Study Design

This is a Cross-sectional and hospital based study.

Sampling Technique

Stratified sampling technique was employed for this study until the sample size was completed.

Sample size

Sample size was calculated as 274 minimum sputum samples from patients with LRTI using Fisher's formula $N=Z^2\ pq/d^2$ for the population above 10,000, using previous estimated prevalence of LRTI which was put at 0.2319 (Ajobiewe *et al*., 2018). For this study a maximum of 350 sputum samples were collected across the six hospitals in Kebbi State.

Ethical Clearance

Ethical approval was obtained from the Ministry of Health ethical review committee in Kebbi State (see appendix II). Informed consent both oral and written (see appendix II) was obtained from all the participants while assents were obtained from parents in case of children. All data were stored anonymously and was handled only by the investigator and authorized personnel.

Inclusion Criteria

All consented patients with clinical sign and symptoms of LRTI as diagnosed by the attending physician and those who have not taken antibiotic atleast two weeks prior to sample collection were included into this study.

Exclusion Criteria

Patients who did not give their consent (see appendix I) or those that took antibiotic about two weeks prior to sample collection were excluded from this study.

Sample Collection

Early morning sputum specimens were collected aseptically from patients attending the selected Hospitals in Kebbi State after obtaining an approval from the ethical review committee. All patients were instructed on how to collect the sputum samples aseptically, i.e. they were asked to cough deeply early in the morning into a well-labeled sterile, leak proof, wide mouthed container, with tight fitting cover, which was taken to the laboratory for analysis. The data used for this study were obtained using structured questionnaire

Culture of the sputum

The sputum samples were cultured on chocolate agar, sheep blood agar (5%), and MacConkey agar plates (oxoid). On the Chocolate agar, bacitracin and optochin disks were placed at secondary inoculation to screen *S. pneumoniae*. The chocolate agar plates were incubated in anaerobic incubator (5% CO_2) at 37 ºC for 24 hours while blood agar and MacConkey agar were incubated in an aerobic atmosphere at 37ºC for 24 hours (Borkot *et al*., 2016). Suspicious colonies were sub-cultured for purification and thereafter preserved on nutrient agar slants and stored in a refrigerator (4ºC) for subsequent analysis.

Identification of the isolated bacteria

The bacterial isolates were identified based on colonial morphology, gram staining characteristics and series of biochemical tests which includes: catalase test, coagulase test, indole test, citrate test, Urease test oxidase test, Tripple Sugar Iron (TSI) agar test, Mannitol fermentation test, growth on Eosine Methylene Blue (EMB) agar, The isolates were further confirmed using commercial biochemical test kit micobact 24E (Oxoid, UK) according to manufacturer's instructions. A colony from 24 hour culture were picked and emulsified in 5ml of sterile saline solution. It was then mixed thoroughly and homogeneous suspensions were prepared. The wells of individual substrate set were exposed by cutting the end tag of the sealing strip and the back was slowly peeled. The strip were placed in the in the holding tray. Using a sterile Pasteur pipette 4 drops of the bacterial suspension were added in each of wells in the set. The black wells substrate underlined in the holding tray were then overlay with sterile mineral oil. The seal were replaced and incubated at 37^{o}C for 24 hour. It was then removed from an incubator and appropriate reagents were added i.e. 2 drops of indole were added to well 8 and read after 2 minutes, 1 drop each of VPI and VPII were added to well 10 and read within 15-30 minutes and 1 drop of TDA were added to well 12 and the result were read immediately. All the wells in the strip were interpreted by comparing the colour change of the wells to the standard chart as presented by the manufacturer.

Antimicrobial Susceptibility Pattern of the Isolated Bacteria

Antimicrobial susceptibility test were determined using disc diffusion method, the disc diffusion method that was presented in this study, was a modification of the Kirby Bauer technique that has been carefully standardized by CLSI. The colonies were suspended in saline, and then the inoculums were adjusted to a turbidity equivalent to a 0.5 McFarland standard. After adjusting the turbidity of the inoculum suspension, a sterile cotton swab was dipped into the adjusted suspension. The swab was then rotated several times and pressed firmly on the inside wall of the tube above the fluid level. This removed the excess inoculum from the swab. The dried surface of a Mueller-Hinton agar plate was inoculated by swabbing the swab over the entire sterile agar surface. This procedure was repeated by streaking two more times, rotating the plate approximately 60° each time to ensure an even distribution of inoculums. The lid was then left slightly open for 3 to 5 minutes, but no more than 15 minutes, to allow for any excess surface moisture to be absorbed before applying the drug impregnated discs (Lalitha, 2006). The following antibiotics disc was used for this research: Azithromycin, erythromycin, Ciprofloxacin, Ceftriaxone, Ceftazidime, Cefixime, Cefuroxime, Amoxicilin, Gentamycin, Cotrimoxazol, Cefotaxime, Cloxacilin, Vancomycin and Piperacillin.

The predetermined batteries of antimicrobial discs were dispensed onto the surface of the inoculated agar plate. Each disc was pressed down to ensure complete contact with the agar surface. The discs were distributed evenly so that they are no closer than 24 mm from center to centre. The plates were inverted and placed in an incubator set to 36°C within 15 minutes after the discs were applied and incubated for 18 hours. The diameters of the zones of complete inhibition (as judged by the unaided eye) were measured, including the diameter of the disc. Zones were measured to the nearest whole millimetre, using a ruler, which was held on the back of the inverted Petri-plate. The organisms were reported as susceptible, intermediate or resistant to the agents that were tested (CLSI, 2017).

RESULTS

Table 1: Number and percentage distribution of bacterial pathogens of lower respiratory tract infection in Kebbi State

Bacterial pathogens isolated	Number of occurrence	% Occurrence
Staphylococcus aureus	34	31.1
Klebsiella pneumoniae	24	22.2
Klebsiella oxytoca	15	13.9
Escherichia coli	12	11.1
Aeromonas hydrophila	6	5.6
Acinetobacter baumannii	5	4.6
Pseudomonas aeruginosa	6	5.6
Burkholderia pseudomallei	3	2.8
Proteus spp	3	2.8
TOTAL	108	100

Table 2 Number and percentage distribution of bacterial pathogens of lower respiratory tract infection across different hospitals in Kebbi State.

Bacterial Isolates	No. of isolates	SYMH No.(%) n=100	KMC No.(%) n=50	ABGHJ No.(%) n=50	GHA No.(%) n=50	GHY No.(%) n=50	MBGHZ No.(%) n=50
S. aureus	34	12(35.3)	8(23.5)	5(14.7)	7(20.6)	2(5.9)	-
K. pneumoniae	24	7(29.1)	5(20.8)	3(12.5)	2(8.3)	4(20.8)	3(12.5)
K. oxytoca	15	3(20)	2(13.3)	3(20)	1(6.7)	4(26.7)	2(13.3)
P. aeruginosa	6	-	-	-	-	2(33.3)	4(66.7)
E. coli	12	3(25)	2(16.7)	5(41.7)	1(8.3)	-	1(8.3)
A. baumannii	5	-	-	1(20)	-	4(80)	-
A. hydrophila	6	1(16.7)	-	-	5(83.3)	-	-
B. pseudomallei	3	-	-	-	1(33.3)	1(33.3)	1(33.3)
P. vulgaris	3	3(100)	-	-	-	-	-
	108	29	17	17	17	17	11

Key: SYMH- Sir Yahaya Memorial hospital Birnin Kebbi, KMC- Kalgo Medical Centre ABGHJ- Aisha Buhari General Hospital Jega, GHA- General Hospital Argungu MBGHZ- Martha Bamaiyi General Hospital Zuru

Table 3: Incidence of lower respiratory tract infection across different age groups

Years	No. of samples examined (%)	No. of positive samples (%)
0-19	39(11.1)	11 (10.2)
20-39	150(42.9)	47 (43.5)
40-59	116(33.1)	39 (36.1)
60-79	42(12.0)	11 (10.2)
80-100	3(9.0)	0 (0)
TOTAL	350 (100)	108 (100)

Table 4: Incidence of lower respiratory tract infection in relation to gender

Gender	No. of samples examined (%)	No. of positive samples (%)
Male	216 (61.7)	58 (53.7)
Female	134 (38.3)	50 (46.3)
TOTAL	350 (100)	108 (100)

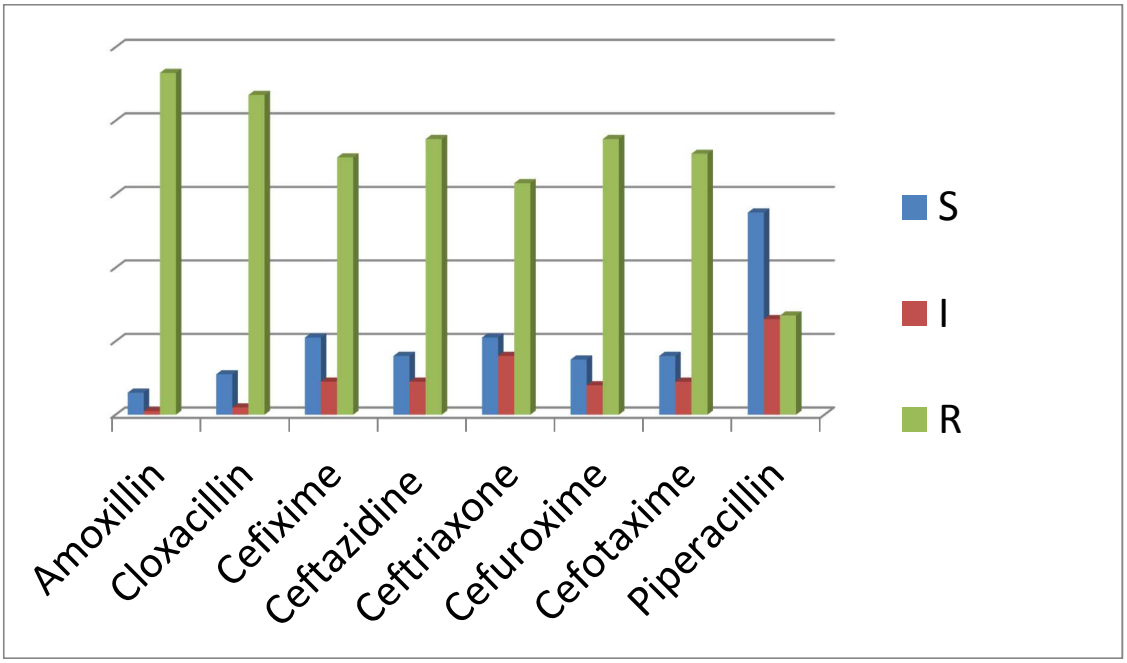

Figure 1: Antimicrobial Susceptibility Pattern of the bacterial isolates to commonly used antibiotics across the selected hospitals in Kebbi State

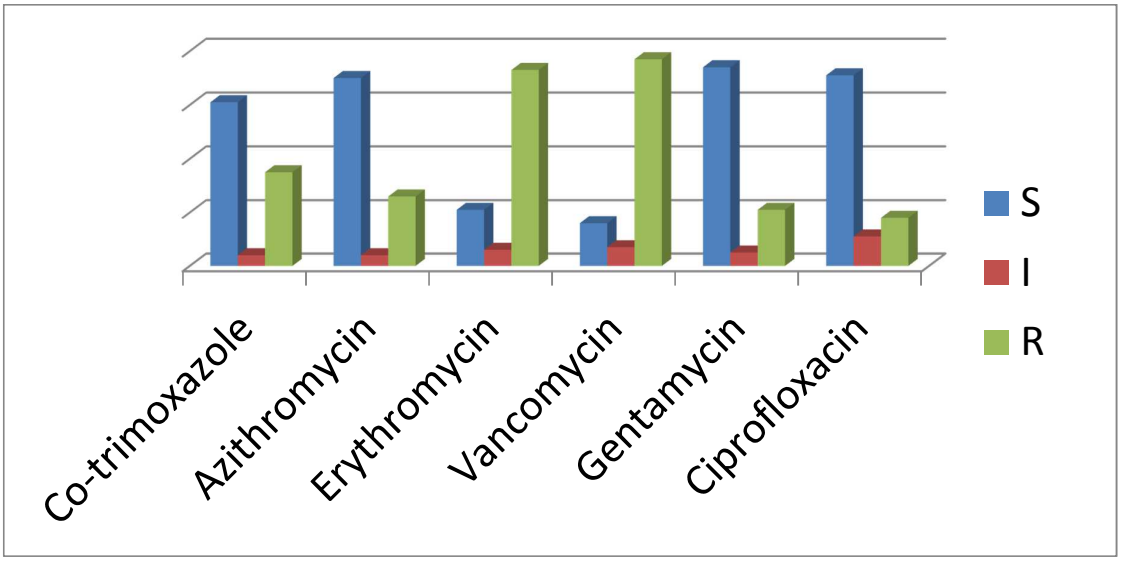

Figure 2: Antimicrobial Susceptibility Pattern of the bacterial isolates to commonly used antibiotics across the selected hospitals in Kebbi State
Key: S- Susceptible, I- Intermediate and R- Resistance

DISCUSSION

The overall incidence of bacterial pathogens of LRTIs recorded in this study was 31%. This finding is slightly higher than those of earlier studies recorded at National Hospital Abuja (14.5%), Ilorin (15.53%), Benin (18.91%), Kano (21.5%) and Nepal (24.6%) (Abdullahi and Iregbu, 2018; Kalgo *et al*., 2016; Christopher *et al*., 2011; Taura *et al*., 2013; Rakshya *et al*., 2018). Higher prevalence were reported in Bangladesh (64%) and some European countries (59%) (Borkot *et al*., 2016; Leven *et al*., 2018), this variation of incidence may be due to differences in geographical location.

Staphylococcus aureus (31.1%) is the most predominant bacteria isolated in this location followed by *Klebsieella pneumoniae* (22.2%), *Klebsiella oxytoca* (13.9%), *Escherichia coli* (11.1%), *Pseudomanas aeruginosa* (5.6%), *Aeromonas hydrophila* (5.6%), *Acinetobacter*

*baumannii (*4.6%*), Burkholderia. pseudomallei (*2.8%*)* and *Proteus spp (*2.8%*)* in order of ranking.

The distribution of aetiology of lower respiratory tract as recorded in this study is similar to the previous study at National Hospital Abuja (Abdullahi and Iregbu, 2018), study in Shanghai, China from 2013 to 2015 (Pengcheng *et al*., 2018), a multicenter Analysis from Turkey (Guclu *et al*., 2021) and Ethiopia (Dessie *et al*., 2021) except that, in addition, the current study isolated *Aeromonas hydrophila and Burkholderia. pseudomallei.* Some studies from neighbouring countries such as Yaoundé, Cameroon (Tchatchouang *et al*., 2019) and other studies in some part of Europe (Leven *et al*., 2018) documented *S. pneumoniae* as the leading pathogen of LRTIs followed by *H. influenzae* which contradict the current findings where *Staphylococcus aureus* were the most prevalent bacteria isolated followed by *Klebsiella* spp, this is similar to the findings in Bangladesh as reported by Borkot *et al*., (2016) and some studies from southern Ethiopia (Gebre *et al*., 2021)

Staphylococcus aureus were isolated predominantly in SYMH (35.3%) followed by KMC (23.5%), ABGHJ (14.7%), GHA (20.6%) and GHY (5.9%) while none were isolated at MBGHZ. *Klebsiella pneumoniae* were seen in all the hospitals with an estimated percentage of occurrences of SYMH (29.1%), KMC (20.8%), ABGHJ (12.5%), GHA (8.3%), GHY (20.8%) and MBGHZ (12.5%). *Klebsiella oxytoca* were also isolated in all the hospitals which includes SYMH (20%), KMC (13.3%), ABGHJ (20%), GHA (6.7%), GHY (26.7%) and MBGHZ (13.3%). *Pseudomonas aeruginosa* were isolated in two hospitals i.e. GHY (33.3%) and MBGHZ (66.7%). *Escherichia coli* were isolated in SYMH (25%), KMC (16.7%), ABGHJ (41.7%), GHA (8.3%) and MBGHZ (8.3%). *Acinetobacter baumannii* were found only in ABGHJ (20%) and GHY (80%). *Aeromonas hydrophila* were also seen in only two hospitals i.e. SYMH (16.7%) and GHA (83.3%). *B . pseudomallei* were isolated in three hospitals which comprised of GHA (33.3%), GHY (33.3%) and MBGHZ (33.3%) while *Proteus vulgaris* were only isolated at SYMH (100%). The aetiologic agents of LRTIs may vary from one geographical locations to another or vary from area to area within the same geographical location (Zafar *et al*., 2008; Akingbade and Ogiogwa, 2012)

Lower respiratory tract infections were more common in males (53.7%) than females (46.3%). This finding is similar to the work conducted in Kano by Taura *et al*., (2013), India (Shah *et al*., 2010), Abeokuta, Ogun State, Nigeria (Akingbade *et al.* 2012) and Bangladesh (Borkot *et al*., 2016). However, these results contradicts the data obtained by El- Mahmood *et al*., (2010), in which in a similar study, out of 232 total isolates, 114 (49.1%) were from males while 118 (50.9%) from females. This also contradicts previous findings in 11 European countries (Belgium, Spain, Poland, Slovakia, UK, Slovenia, Sweden, Italy, France, Germany, and Netherland) where 60% of the female were reported with LRTIs (Ieven *et al*., 2018). Male prevalence of LRTI may be due to their exposure to different group of population and also to some associated risk factors of respiratory tract infection such as smoking, alcohol consumption and COPD (Panda *et al.*, 2012; Borkot et al., 2016).

Most of the pathogens were isolated among patients in age range 20-39 years with the percentage occurrence of 43.5%, closely followed by age range 40-59 years with 36.1%, the lowest rate was recorded in age range 0-19 and 60-79 years with 10.2% each. From our study, it was observed that, the young adults and the elderly were most at risk of a severe respiratory condition. This finding tally with the work of Taura *et a*l., (2013) in Kano, Nigeria and some works conducted in Bangladesh (Borkot *et al*., 2016). Similar to the current study as reported by Dessie *et al*., (2021) in Ethiopia, aging is a risk factor for bacterial pneumonia. In their study, the age group >64 years was 2.4 times more likely to have bacterial pneumonia compared to the age group of 5–15 years (Almirall *et al*., 2017). Similar findings were reported from Spain (Prina *et al*., 2015; Rivero-Calle *et al*., 2016), Pakistan (Ahmad *et al*., 2017), Japan (Morimoto *et al*., 2015), and the USA (Quartin *et al*., 2013)

The bacteria isolated were susceptible to piperacilin ((51%), trimetprin sulphamethoxazole (61%), Azithromycin (70%), Ciprofloxacin (71%) and Gentamycin (74%), in order of ranking, these are supported by the findings of El-Mahmood *et al*., (2010), Taura *et al*., (2013) and a study in Kathmandu, Nepal (Rakshya *et al*., 2018). High resistance were recorded in almost all the βeta-lactam antibiotics tested such as Ceftriaxone (63%), Cefuroxime (70%), Cefotaxime (71%), Ceftazidine (75%), Oxacillin (87%) and Amoxicillin (93%). High resistance were also recorded among macrolide (Erythromycin) and Glycopeptide (Vancomycin). This findings correlate with the work carried out by Barkot *et al*., (2016) in Bangladesh. High resistance recorded in this study may be attributed to local usage and indiscriminate use of antibiotics in this location.

CONCLUSION AND RECOMMENDATIONS

Staphylococcus aureus is the most predominant bacteria isolated in this location followed by *Klebsiella pneumoniae* with an estimated percentage occurrence of 31.1% and 22.2% respectively. Most of pathogens were isolated among patients in age range 20-39 years with the percentage occurrence of 43.5%, closely followed by age range 40-59 years with 36.1%. The result also shows that LRTI were more common in males than in females. Most of the isolates were susceptible to piperacillin ((51%), trimetprin sulphamethoxazole (61%), Azithromycin (70%), Ciprofloxacin (71%) and Gentamycin (74%). High resistance were recorded in almost all the βeta-lactam antibiotics tested. Treatment of lower respiratory tract infection with β-lactam actibiotics in this centre should be discouraged, due to high level of resistance exhibited by the isolated bacteria**.** It is also recommended that, definitive diagnosis and antimicrobial susceptibility pattern should be routinely carried out on all suspected cases of LRTI in these centres while presumptive diagnosis should be discouraged. Further studies should be conducted on molecular characterization of emerging and re-emerging bacterial pathogens of lower respiratory tract in this location.

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