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Prevalence and risk factors for Lower Respiratory Tract Infection: a Multicenter study, at Kebbi State, Nigeria

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ABSTRACT Lower respiratory tract infections are one of the major public health concerns responsible for morbidity and mortality in low and middle income countries. Improved surveillance of the causative agents as well as identification of risk factors might enable targeted intervention. The aim of this study was to establish the incidence and risk factors of lower respiratory tract infection in Kebbi State. Three hundred and fifty sputum samples were collected from consented patients with the symptoms of LRTI attending six different hospitals in Kebbi State. The samples were all screened for bacterial pathogens using standard microbiological techniques. The bacterial isolates were identified using conventional biochemical tests and then confirmed using commercial biochemical test kit microbact 24E (Oxoid UK) according to manufacturerer's instruction. *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%), B. pseudomallei (2.8%)* and *Proteus* spp *(2.8%)* in order of ranking. 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. A significant number (32%) of patients who are exposed to either agricultural or industrial chemicals have positive bacterial growth. The present study found that prior antibiotic treatment was also a significant risk factor for LRTIs. In conclusion, it was found out that, *Staphylococcus aureus* is the most predominant bacteria isolated. Exposure to smoke from firewood and chemicals from both agricultural or industrial chemicals as well as indiscriminate use of antibiotics were the risk factors for LRTIs in this location.

Keywords: Prevalence; Respiratory Tract; Sputum; Pathogens; Risk factors

I. 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 include conditions such as tracheitis, bronchitis, bronchiectasis, lung abscess, tuberculosis, pneumonia [1]. 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 [2], [3], [4]. There were approximately 11.9 million episodes of severe lower respiratory infections (LRI) resulted in hospital admissions in young children worldwide [5]. 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 [6]. Viruses also play an important role in LRTIs,

especially in infants younger than 2 years [7]. 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* [8]. 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* [9], [10], [11].

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) [10]. 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 [12]. Pneumonia killed 808,694 children under the age of 5 in 2017, accounting for 15% of all deaths of children under five years old [13]. It is also the second leading cause of years of life lost due to premature mortality [12] 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 [10]. The burden of lower respiratory tract infection is highest in areas of low sociodemographic status, populations that depend on solid fuels for cooking and heating, and in malnourished and immunoimpaired populations [14]. Acute lower respiratory tract infection is a common cause of hospital admission in Nigeria [15]. Several studies were carried out from different part of the country to determine the etiologic agents of Lower Respiratory Tract Infection and their susceptibility pattern to commonly used antibiotics [16], [17], [18], [19], [1], [20], [21], [22]. The etiologic agents of LRTIs may vary from one geographical locations to another or vary from area to area within the same geographical location [23], [24]. But no comprehensive data has been established on the prevalence and risk factors of lower respiratory tract infection in Kebbi State. Therefore the aim of this study was to establish the prevalence and risk factors of lower respiratory tract infection in Kebbi State.

II. MATERIALS AND METHODS

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. 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. 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 [25] as diagnosed by the attending physician at the General out Patient Department (GOPD) of the selected hospitals in Kebbi State. This is a Cross-sectional and hospital based study. Stratified sampling technique was employed for this study until the sample size was completed. Ethical approval was obtained from the Ministry of Health ethical review committee in Kebbi State (see appendix IV). Informed consent both oral and written (see appendix II) was obtained from all the participants while ascents were obtained from parents in case of children.

All data were stored anonymously and was handled only by the investigator and authorized personnel. 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. 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 size was calculated as 274 sputum specimen asminimum from patients with LRTI using Fisher's formula $N=Z^2 pq/d^2$ for the population above 10,000

$N= 1.96^2 * 0.2319 (1-0.2319)/ 0.05^2$
$= 3.8416*0.2319 (0.7681)/ 0.0025$
$= 0.6843/ 0.0025$
$= 274 = 350$

Ethical approval was obtained from the Ministry of Health ethical review committee in Kebbi State. Informed consent both oral and written were obtained from all the participants. All data were stored anonymously and was handled only by the investigator and authorized personnel. The sputum samples were collected at the general out patients department (GOPD) of the selected hospitals after being examined and suspected of having lower respiratory tract infection by the attending physician. Each patient were given a well-labeled sterile, leak proof, wide mouthed container, with tight fitting cover, and they were instructed to go home and provide early morning sputum samples (as soon as the patient wake up in the morning before eating). Each patient were asked to rinsed his mouth with clean water and then cough deeply until sputum came up into his mouth which he then spit into the sample container aseptically. The samples were then taken to the laboratory for analysis without delay.

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 a 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 [27]. Suspicious colonies was sub-cultured for purification and thereafter preserved on nutrient agar slants and stored in a refrigerator (4ºC) for subsequent analysis. 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, TSI, Mannitol fermentation, growth on 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 well substrates underlined in the holding tray were then overlay with sterile mineral oil. The seal were replaced and incubated at 37ºC 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.

The risk factors associated with Lower Respiratory Tract in Kebbi State were determined using a structured questionnaire. Information such as Age, sex, occupation, place of residence, use of tobacco, use of alcohol and other relevant data were obtained as described in Appendix III. Each patient was asked to carefully fill the questionnaire correctly and information obtained were analysed using SPSS version 20. Statistical analysis was performed using SPSS version 20 to evaluate the data obtained from the centres. The difference between the ratios was evaluated using chi-square test and $p < 0.05$ was considered as significant.

III. RESULT AND DISCUSSION

The etiology of lower respiratory tract infection is diverse and complicated, hence in most developing countries, treatment of LRTI is made usually empirically in which the etiologic agent is rarely identified (TABLE 1). Therefore this study was designed to determine the incidence and risk factors of lower respiratory tract infection in selected hospitals, Kebbi State. The distribution of bacteria isolated from patients with lower respiratory tract infection where *Staphylococcus aureus (*31.1%*)* was 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%*), B. pseudomallei (*2.8%*)* and *Proteus spp (*2.8%*)* in order of ranking (TABLE 2). The distribution of aetiology of lower respiratory tract as recorded in this study is similar to the previous study at National Hospital Abuja [28], study in Shanghai, China from 2013 to 2015 [29], a multicenter Analysis from Turkey [30] and Ethiopia [31] except that, in addition, the current study isolated *Aeromonas hydrophila and B. pseudomallei.* Some studies from neighbouring countries such as Yaoundé, Cameroon [32] and other studies in some part of Europe [33] documented *S. pneumoniae* as the leading pathogen of LRTIs followed by *H. influenzae* which contradict the current findings where *Staphylococcus aureus* were the most prevalence bacteria isolated followed by *Klebsiella* spp, this is similar to the findings in Bangladesh as reported by Borkot *et al.,* [27] and some studies from southern Ethiopia [34] (TABLE 3).

This study also demonstrated the incidence of bacteria isolated from patients with lower respiratory tract infection in the selected hospitals where *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 geagraphical location . [23], [24].

LRTIs were more common in males (53.7%) than that of females (46.3%). This finding is similar to the work conducted in Kano by Taura *et al*., [18] India [35], Abeokuta, Ogun State, Nigeria [36] and Bangladesh [27] but however, these results contradicts the data obtained by El- Mahmood *et al*., in which in a similar study, out of 232 total isolates, 114 (49.1%) were from males while 118 (50.9%) from females [37]. 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 [33]. Male prevalence of LRTI may be due to their exposure to different group of population and also to some associated

Table 1
Distribution of bacteria isolated from patients with of lower respiratory tract infection in some hospitals, Kebbi State.

S/N	Bacterial Isolates	No. of isolates (%)	SYMH No.(%) n=100	KMC No.(%) n=50	GHA No.(%) n=50
1	*Staphylococcus aureus*	34(31.5)	12(35.3)	8(23.5)	7(20.6)
2	*Klebsiella pneumoniae*	24(22.2)	7(29.1)	5(20.8)	2(8.3)
3	*K.lebsiella oxytoca*	15(13.9)	3(20)	2(13.3)	1(6.7)
4	*Pseudomonas aeruginosa*	6(5.6)	-	-	-
5	*Escherichia coli*	12(11.1)	3(25)	2(16.7)	1(8.3)
6	*Acinetobacter. baumannii*	5(4.6)	-	-	-
7	*Aeromonas hydrophila*	6(5.6)	1(16.7)	-	5(83.3)
8	*Burkholderia. pseudomallei*	3(2.8)	-	-	1(33.3)
9	*Proteus vulgaris*	3(2.8)	3(100)	-	-
	TOTAL	108(100)	29	17	17

where SYMH- Sir Yahaya Memorial hospital Birnin Kebbi, KMC- Kalgo Medical Centre, GHA- General Hospital Argungu MBGHZ

TABLE 2
Distribution of bacteria isolated from patients with of lower respiratory tract infection in some hospitals, Kebbi State.

No	Bacterial Isolates	No. of isolates (%)	ABGHJ No.(%) n=50	GHY No.(%) n=50	MBGHZ No.(%) n=50
1	*Staphylococcus aureus*	34(31.5)	5(14.7)	2(5.9)	-
2	*Klebsiella pneumoniae*	24(22.2)	3(12.5)	4(20.8)	3(12.5)
3	*Klebsiella oxytoca*	15(13.9)	3(20)	4(26.7)	2(13.3)
4	*Pseudomonas aeruginosa*	6(5.6)	-	2(33.3)	4(66.7)
5	*Escherichia. Coli*	12(11.1)	5(41.7)	-	1(8.3)
6	*Acinetobacter baumannii*	5(4.6)	1(20)	4(80)	-
7	*Aeromonas hydrophila*	6(5.6)	-	-	-
8	*Burkholderia. pseudomallei*	3(2.8)	-	1(33.3)	1(33.3)
9	*Proteus vulgaris*	3(2.8)	-	-	-
	TOTAL	108(100)	17	17	11

Where ABGHJ- Aisha Buhari General Hospital Jega, MBGHZ- Martha Bamaiyi General Hospital Zuru

risk factors of respiratory tract infection such as smoking, alcohol consumption and COPD [38], [27]. It was revealed that, most of pathogens were isolated among patients in age range 20-39 years with the percentage occurrence of 41.7%, 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% and 9.3% respectively. 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., in Kano, Nigeria [18] and some works conducted in Bangladesh [27]. Similar to the current study as reported by Dessie *et al*., in Ethiopia [31], 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 [39]. Similar findings were reported from Spain [40], [41] Pakistan [42], Japan [43], and the USA [44]

This study demonstrated that, exposure to indoor smoke from use of hydrocarbon and solid domestic fuel were seen as environmental risk for respiratory tract infections, the current study documented positive bacterial growth of over 92% from the patients who used firewood as the source of energy for cooking this is similar to the findings of [45] in lucknow district who also recorded higher among children from biomass fuels using homes, but exposure to smoking from tobacco and alcohol consumption were low in this study, this is consisted with the finding in Ethiopia [34]. A significant number (32%) of patients who are exposed to either agricultural or industrial chemicals have positive bacterial growth. It was found out from this study that, patients with respiratory tract infection in this location had visited either traditional healer, pharmacy or engaged in self medication before coming to hospital for proper treatment and that happened only when their infection persisted. Therefore the present study found that prior antibiotic

Table 3
Prevalence of lower respiratory tract infection in relation to age and gender

Age range	Positive male Samples	Positive female samples	Total positive samples (%)
0-19	5	6	11(10.2)
20-39	26	19	45(41.7)
40-59	20	19	39(36.1)
60-79	7	3	10(9.3)
80-100	0	3	3(2.7)
TOTAL	58 (53.7%)	50 (46.3%)	108(100)

Table 4
Risk factors associated with the occurrence of infection from patients attending some hospitals, Kebbi State

Characteristics	No. of Sample (%)	No. of positive cases(%)	Chi- square value	P –value
Participant Occupation Employed Unemployed	350 (100) 99 (28.3) 251 (71.7)	 42(38.9) 66(61.1)	 1.256	 0.869
Education Illiterate Primary Secondary Tertiary	 185 (52.9) 53 (15.1) 84 (24) 28 (8)	 62(57.4) 12(11.1) 28(25.9) 6(5.6)	 5.834	 0.442
Alcohol Consumption Yes No	 12 (3.4) 338 (96.6)	 2(1.9) 106(98.1)	 0.522	 0.971
Cigarette Smoking Yes No	 58 (16.6) 292 (83.5)	 19(17.6) 89(82.4)	 1.656	 0.799

Table 5
Risk factors associated with the occurrence of infection from patients attending some hospitals, Kebbi State

Characteristics	No. of Sample (%)	No. of positive cases (%)	Chi- square value	P –value
Comobidity Healthy HIV Tuberculosis Hypertension Stroke Diabetes	 248 (70.9) 11 (3.1) 52 (14.9) 26 (7.4) 8 (2.3) 5 (1.4)	 76(70.4) 4(3.7) 13(12.0) 8(7.4) 0(0) 7(6.5)	 2.904	 0.984
Types of treatment before coming to hospital None Traditional healer Pharmacy Another Doctor Praying Self-medication	 13 (3.7) 61 (17.4) 97 (27.7) 57 (16.3) 23 (6.6) 99 (28.3)	 3(2.8) 18(16.7) 33(30.5) 13(12.0) 9(8.3) 32(29.6)	 12.307	 0.265

Table 6
Risk factors associated with the occurrence of infection from patients attending some hospitals, Kebbi State

Characteristics	No. of Sample (%)	No. of positive cases (%)	Chi- square value	P –value
Energy for cooking				
Wood	308 (88)	99(91.7)		
Electricity	4 (1.1)	1(0.9)	2.055	0.979
Kerosine	10 (2.9)	3(2.8)		
Gas	14 (4.0)	3(2.8)		
Charcoal	14 (4.0)	2(1.9)		
Exposure to Agric/ Industrial chemicals				
Yes	127 (36)	35(32)	0.626	0.731
No	223(64)	73(68)		

treatment was a significant risk factor for developing MDR bacteria in LRTIs (TABLE 4, TABLE 5 and TABLE 6). Other Studies have consistently reported that inappropriate antibiotic therapy, such as overuse or underuse of empirical antibiotics, could result in an increase in drug-resistant bacteria [46], [47], [48], [49] and generate new disease. burdens [50]. Educational level was assessed among the patients with lower respiratory tract infection where illiterate has the highest number of positive growth followed by those with secondary education, least bacterial growth were recorded among participants with tertiary education. Employment were also seen to be a contributing factor for lower respiratory tract infection in which 61% of the unemployed patients display positive bacterial growth.

IV. 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 41.7%, 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. Exposure to smoke from firewood and chemicals from either agricultural or industrial chemicals were the risk factors for LRTIs while indiscriminate use of antibiotics remain the risk factor for developing multidrug resistance isolates in this location. It is recommended that, definitive diagnosis/ antimicrobial susceptibility testing should be routinely carried out on all suspected cases of LRTI in these centres while presumptive diagnosis should be discouraged.

Limitation of the study : This study is limited to lower respiratory tract infection caused by bacteria

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