

Prevalence, Distribution and Antimicrobial Susceptibility Pattern of Bacterial Isolates from a Tertiary Hospital in Malawi

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Abstract

Background

Bacterial infections are a significant cause of sickness and death in sub-Saharan Africa. This study aimed at establishing the prevalence, distribution and antimicrobial susceptibility pattern of major bacterial isolates from patients attending a tertiary hospital in Malawi.

Methods

We retrospectively reviewed bacteria culture and antibiotic sensitivity records for 4,617 patients from 2002 to 2014 at Mzuzu Central Hospital (MCH). No inclusion and exclusion criteria were followed. Data was analysed using excel and SPSS programs.

Results

The most prevalent isolates were *S. aureus* (34.7%, n= 783), *Klebsiella* species (17.4%, n= 393) and *Proteus* species (11.4%, n = 256). Most pathogens were isolated from adults (88.3%, n=3889) and pus was the main source (69.3%, n = 1224). *S. pneumoniae* was predominantly isolated from cerebrospinal fluid (60.3%, n = 44) largely collected from children (88.2%, n =64). Overall, most bacteria exhibited high resistant to all regularly used antibiotics excluding ciprofloxacin.

Conclusions

Our report demonstrates an increase in bacteria burden in sites other than the blood stream and subsequent increase in prevalence of antimicrobial resistance for all major isolates. Creating an epidemiological survey unit at MCH will be essential to help inform better treatment and management options for patients with bacterial infections.

Background

Bacterial diseases remain the major cause of morbidity and mortality worldwide[1]. Most of these infections and deaths predominantly occur in sub-Saharan Africa (sSA) which has vulnerable population and poor health delivery systems [1]. Inadequate funding, poor microbiology services, limited technical experts and scarce epidemiological data to inform better preventive and treatment strategies all contribute to the rise in burden of bacterial infections in sSA [2, 3]. Regrettably, the increase in burden of bacterial infections in sSA is also accompanied by high incidences of antimicrobial resistance (AMR)[4]. As a low income country in sSA, Malawi is no exception to these challenges [5].

Across sSA, AMR has been reported in different countries. Apart from the emergence of Meticillin-resistant *Staphylococcus aureus* (MRSA), Malawi has reported a rapid increase of *non-Salmonella* Enterobacteriaceae with extended spectrum beta-lactamase (ESBL) and fluoroquinolone resistance among common Gram-negative pathogens [5]. In Zimbabwe, Gram-negative bacteria showed high

resistant to Cotrimoxazole (68.5%) and Ampicillin (84.5%) while Gram-positive bacteria demonstrated resistance to Cotrimoxazole (69%) and Nalidixic acid (81%) [6]. A study in Ghana revealed that *Neisseria gonorrhoeae* isolates were resistant to tetracycline (100%), benzylpenicillin (90.9%) and ciprofloxacin (88.6%) [7]. In general, key Gram-negative (including *Klesbsiella*, *E. coli*, *Salmonella*, *Shigella*) and Gram-positive bacteria (such as *S. pneumoniae*, *S. aureus*, *S. agalactae*, *MRSA*) across sSA have acquired resistance to the common essential antimicrobials being used in the region [8].

Management of invasive bacterial infections in sSA is becoming increasingly difficult because of the rise in AMR to commonly used drugs. The rise in AMR can be attributed to several factors such as bad clinical practices, poor public perception and behaviour towards antimicrobial use, increase in adverse agricultural practices etc. [9]. Most importantly, irresponsible widespread use of antimicrobials creates a sturdy selective pressure that propels the adaptive and evolutionary response by microbes, hence the emergence of various AMR phenotypes [9]. Worse still, today's global economy allows people to travel and interact worldwide in a process spreading the pathogens across the world [9]. The rise in AMR not only threatens the public health sector but also the already fragile economies in sSA through prolonged hospitalization and use of expensive and specialised treatment and care for the sick.

It is generally accepted that AMR is a global threat mostly affecting low-income countries, however most data available on bacterial pathogen surveillance and AMR profile is from high-income countries [8]. Nevertheless, most countries in sSA use syndromic approach to treat bacterial infections. In order to be effective, empirical treatment requires better knowledge of local AMR profile. The aim of this study was to determine the prevalence, distribution and antimicrobial susceptibility patterns of commonly isolated pathogenic bacteria at Mzuzu Central Hospital, a referral hospital for six district hospitals in Northern Malawi.

Methodology

Research Design

We conducted a retrospective audit of records for bacterial culture and sensitivity testing results beginning 2002 to 2014 from MCH microbiology laboratory department. No inclusion and exclusion criteria were applied. The MCH Laboratory participates in international microbiology quality assessment programs such as the UK External Quality Assessment program (UKNEQAS) and Zimbabwe Quality Assurance Program (ZIMQAP). Ethical approval for the study was obtained from National Health Science Research Committee (NHSRC), (approval number NHSRC # 1206).

Bacterial Identification and Characterisation

Specimens from outpatient department and clinical wards were transported to microbiology department laboratory for analysis within 2 hours of collection. Conventional microbiology culture methods were employed to isolate and identify bacteria. Media was prepared in-house as per procedures stipulated in Cheesbrough [10].

About 10 mL and 3 mL of blood collected from adults and paediatric patients, respectively were inoculated into BD bactec plus aerobic culture vials™ for incubation at 35 - 37°C in BD Bactec™ 9050 Blood Culture System (BD, USA). Positive cultures were sub-cultured onto Blood Agar Plate (BAP), MacConkey Agar Plate (MAP) or Chocolate Agar Plate (CAP) if any fastidious organism was suspected. Inoculated plates were incubated at 37°C, 5% CO₂ for up to 3 days.

Swabs collected from wounds, skin and soft tissue infection were gram stained, cultured on either BAP/CAP or MAP, and, incubated at 37°C, 5% CO₂ for up to 72 hours [10]. Cerebrospinal fluid (CSF) and other fluids, were gram stained, cultured on BAP and CAP for incubation at 37°C, 5% CO₂ for up to 72 hours [10]. Urine samples were inoculated on CLED agar and incubated at 37°C for up to 48 hours [10]. A specimen was considered positive for UTI if the number of enumerated colonies were greater than $\geq 10^5$ CFU/mL [10, 11].

Isolates were identified and processed according to standard techniques summarised in Table 1. Antibiotic susceptibility was determined by disc diffusion technique on Mueller Hinton agar except for *Streptococcus pneumonia* and other fastidious organisms, Mueller-Hinton agar was supplemented with 5% human blood. Data was interpreted according to the CLSI guidelines [12]. Major bacterial isolates were evaluated for their susceptibility against the most commonly used antibiotics during the study period. Antibiotics analysed included Ciprofloxacin, Ceftriaxone, Penicillin, Tetracycline, Ampicillin, Chloramphenicol, Amoxicillin, and Gentamycin.

Data Analysis

Data was analysed using Excel (Microsoft office, USA) and GraphPad Prism 7 software programs. Graphs or pie chart were used to show the prevalence and distribution of the isolated bacteria against gender (male and female), age groups (Children and adults) and specimens (Pus, ear swab, V. Blood, Cerebral Spinal Fluids, High Vaginal Swabs, Urine and Other fluids). In addition, a frequency table expressed in percentage and absolute numbers was used to display the susceptibility patterns of the six commonly isolated bacteria against the six commonly used antibiotics.

Results

Study population and demographics

To understand the demographics of the patient population, clients were characterised according to their sex and age group. Out of 4,617 patients who submitted samples for microbiology analysis, 2246 (49%) were male and 2,371 (51%) were female (Figure 1). We observed that adult patients (>12 years old (3889 (88.3%)) were more than children (≤ 12 years old (517 (11.7%)) (Figure 1). Overall, more patients were registered in 2002 (626) and 2012 (618) but much less numbers were recorded in 2006 (130), 2008 (175) and 2014 (84) (Figure 2B).

Analysis of isolates by source of specimen and hospital department

To analyse the dynamics of bacterial infections, total number of specimens collected and isolates recovered were determined for each hospital department. Most samples were collected in the Out Patient Department (OPD; 1,885, 43%; Figure 2A). Pus from wound and ear infections was the most abundant sample and the majority of it was collected in the OPD, Male surgical ward, Paediatric ward and Female surgical ward (Figure 2A). Corresponding to the high number of samples collected, the OPD had the highest number of bacterial isolates (784, 44.5%; Figure 2A). TB department had the least number of isolates (20, 1.1%). Across the departments, *S. aureus* was the most isolated pathogen (67, 43.5%) followed by *Klebsiella* species (387, 22%) (Figure 2B).

Absolute number of (A) specimens and (B) isolates recovered per department were determined.

Prevalence of bacterial isolates

To evaluate the prevalence of bacteria pathogens over the 13-year period, we determined the overall numbers of individual isolates and established the comprehensive figure of pathogens per year. *Staphylococcus aureus* was the most commonly isolated bacterium (783, 34.7%) (Figure 3A). Other common isolates included *Klebsiella* species (393, 17.4%), *Proteus* species (256, 11.4%), *Coagulase-Negative Staphylococcus* (193, 8.6%), *Escherichia coli* (169, 7.5%) and *Pseudomonas* species (131, 5.8%; Figure 3A). The pattern of the number of positive cultures matched the pattern of number of patients who submitted microbiology samples (Figure 3B). Altogether, the culture positivity rate was approximately 48.9% (2258/4611). Assuming that each patient submitted one sample, the highest culture positivity rate was recorded in 2011 (212/367; 57.7%) whereas the lowest rate was registered in 2005 (85/284; 29.9%; Figure 3C). In 2011, 54.2% (115/212) of the bacteria isolates were Gram negative with *Klebsiella* species being in majority (25/115; 21.7%).

Distribution of bacterial isolates according to demographics

To identify the most susceptible group from bacterial infections, isolates were distributed according to gender and age groups of the patients. The percentage of male and female patients whose samples were positive for bacterial culture was roughly the same i.e. 51% and 49% respectively (Figure 4A). A significant number of bacterial isolates were isolated from patients aged more than 12 years (Figure 4B). Largely, the distribution of isolates among male and females was fairly similar with prevalence rates of within 50% except for *Pseudomonas* species which were isolated more in males than females (63.1%, 36.9% respectively; Figure 4A). Most of the isolates were recovered from patients older than 12 years excluding *S. pneumoniae* which was isolated predominantly in clients younger than 12 years (88.2%; Figure 4B).

Antibiotic susceptibility profiles of major bacterial isolates

To assess antimicrobial resistance, the most commonly isolated bacteria were tested for their susceptibility to the most commonly used antibiotics at the hospital during the 13-year period. In comparison to other pathogens, *S. pneumoniae* demonstrated the highest rate of sensitivity to most of

the antibiotics except for gentamicin where 40% of the strains showed resistance (Table 1). In this study, Ciprofloxacin followed by Gentamicin and Cotrimoxazole proved to be the most effective antibiotics with overall pathogen sensitivity rates of 84%, 75% and 70% respectively (Table 1). Nonetheless, worrying levels of antibiotic resistance were registered in the study. On the whole, *Pseudomonas* species exhibited relatively the highest resistance to most antibiotics. For instance, our data shows that 75%, 62%, and 40% of *Pseudomonas* strains were resistant to Chloramphenicol, Nalidixic acid and Cotrimoxazole, respectively (Table 1). *Klebsiella* species were second with antibiotic resistance rates of 62%, 49% and 43% to Chloramphenicol, Cotrimoxazole and Nalidixic acid, respectively. Overall, high rates of antibiotic resistance to Erythromycin (49%), Chloramphenicol (47%), and Nalidixic acid (42%) were recorded (Table 1)

Table 1. Antimicrobial susceptibility patterns of major bacterial pathogens against commonly used antibiotics during 2002-2014 period. The numbers in the table represent isolates found to be sensitive and resistant to the antibiotics

BACTERIA	ANTIBIOTICS											
	CHLORAMPHENICOL		COTRIMOXAZOLE		GENTAMICIN		NALIDIXIC ACID		ERYTHROMYCIN		CIPROFLOXACIN	
	S	R	S	R	S	R	S	R	S	R	S	R
<i>S. aureus</i>	340 (66%)	177 (34%)	281 (76%)	90 (24%)	346 (77%)	103 (23%)	NA	NA	233 (47%)	258 (53%)	211 (81%)	51 (19%)
<i>S. pneumoniae</i>	44 (92%)	4 (8%)	27 (96%)	1 (4%)	30 (60%)	20 (40%)	NA	NA	38 (88%)	5 (12%)	20(87%)	3 (13%)
<i>Klebsiella</i> species	87 (38%)	145 (62%)	81(51%)	77 (49%)	174 (73%)	66 (27%)	109 (57%)	83 (43%)	NA	NA	113 (84%)	21 (16%)
<i>Proteus</i> species	64 (42%)	90 (58%)	76 (76%)	24 (24%)	127 (83%)	26 (17%)	75 (59%)	52 (41%)	NA	NA	74 (91%)	7 (9%)
<i>E. coli</i>	45 (49%)	47 (51%)	40 (69%)	18 (31%)	72 (73%)	27 (27%)	56 (72%)	22 (28%)	NA	NA	64 (88%)	9 (12%)
<i>Pseudomonas</i> species	22 (25%)	66 (75%)	38 (60%)	25 (40%)	73 (74%)	25 (26%)	20 (38%)	32 (62%)	NA	NA	31 (84%)	6 (16%)
Total	602 (53%)	529 (47%)	543 (70%)	235 (30%)	822 (75%)	267 (25%)	260 (58%)	189 (42%)	271 (51%)	263 (49%)	513 (84%)	97 (16%)

Discussion

Understanding distribution of microbial pathogens and their associated infections is essential for controlling infectious diseases and monitoring of antibiotic resistance. The current study aimed at establishing the prevalence of common pathogenic bacteria including their antibiotic susceptibility pattern and distribution according to specimens, age groups and sex at Mzuzu Central Referral hospital. We report a high prevalence of bacteria isolates with variability in susceptibility to key antibiotics used during the study period. Most isolates displayed high resistant to Erythromycin, Gentamycin,

Chloramphenicol, Nalidixic acid and Cotrimoxazole. Conversely, majority of the isolates were sensitive to Ciprofloxacin.

While a significant number of similar studies in Malawi were limited to investigating blood stream bacterial infections [5, 13-18], our study demonstrated the spread of bacterial infections when other body sites were surveyed (Figure 2A-B). The high prevalence of bacteria isolates observed in this study (Figure 3A) highlights the need for effective monitoring and surveillance of bacterial infections in resource-limited health care settings.

Similar to previous investigations [19-24], our findings revealed that *S. aureus* was the predominant cause of bacterial infections (Figure 3A). *S. aureus* is the common cause of skin and soft tissue infections [25, 26]. Hence it is not surprising that we observed considerably high number of isolates from OPD, male surgical ward and female surgical ward following culture of pus obtained from wound and surgical site infections. The subsequent prevalent pathogens in the study were *Klebsiella* and *Proteus* species (Figure 3A), which were also mostly recovered from wound pus. Likewise, this observation is comparable to investigations conducted in other countries [22, 23, 26-28].

The fluctuations in the number of patients that were provided microbiology services correspond with the number of positive cultures. As the number of patients increased, positive cultures also increased and vice versa (Figure 3B). The relatively high bacterial culture positivity rates observed (Figure 3C) in this study could suggest good culture and bacterial isolation techniques. On the other hand, this could also be as a result of more contaminants being isolated, as most of the isolates i.e. *S. aureus* were isolated from pus, which can easily be contaminated with skin flora.

Except for *S. pneumoniae* most of the pathogens were isolated from adults (Figure 4B). The study registered more adults than children hence the observation that more isolates were recovered from adults corresponds with the high number of adult clients registered. *S. pneumoniae* is a common cause of bacterial meningitis in children[29], as such, our finding is consistent with literature. Correspondingly, our study showed that *S. pneumoniae* was predominantly isolated from CSF largely collected from children (data not shown).

In general, all major isolates showed relatively high resistance to essential antibiotics used during the study period (Table 1). Similar to previous studies [19, 30], our investigation showed higher rates of *S. aureus* resistance to chloramphenicol and erythromycin. Methicillin-resistant *Staphylococcus aureus* (MRSA) has significantly contributed to antimicrobial resistance globally [31], hence the drawback in this investigation is that *S. aureus* isolates were not tested to determine if some of the isolates were MRSA.

S. pneumoniae is a significant cause of pneumonia, sepsis, bacterial meningitis and death in Malawian children and adults [32-35]. Chloramphenicol is one of the antibiotics used in the treatment of bacterial meningitis including invasive pneumococcal diseases in Malawi. Contrary to the current study, previous investigations in Malawi reported higher rates of *S. pneumoniae* resistance to chloramphenicol [5, 19]. Our observation needs to be interpreted with care since the number of isolates analysed in the current

study is much smaller than previous studies, hence, comparing the rates of antibiotic resistance may not give a true reflection of the real situation. However, in general all major isolates exhibited high resistance to chloramphenicol with *Pseudomonas* species recording the highest rate of resistance. This finding concurs with previous studies where *Pseudomonas aeruginosa* is reported to be highly resistant to chloramphenicol [36-38].

The high rates of resistance to chloramphenicol, cotrimoxazole and nalidixic acid by major gram-negative organisms in the study is worrying as we observed a large population of patients affected during the study period. This is of importance as studies have shown an increased risk of subsequent infection and mortality after hospital discharge following colonisation with drug resistant Gram-negative bacteria [39]. Whilst drug resistant Gram-negative bacteria is recognised as a global problem in resource limited countries, the threat is much higher in areas with poor healthcare infrastructure and poor surveillance for antimicrobial resistance.

According to the Malawi Standard Treatment Guidelines, the antibiotics used in the study are essential in treatment of several conditions including sepsis, chronic diarrhoea and infant bacillary dysentery respectively [40]. In addition, cotrimoxazole is used as a prophylactic treatment for bacterial infections in HIV positive clients in the WHO clinical stages II, III and IV [40]. Overall, it is encouraging that ciprofloxacin proved to be relatively effective against most pathogens. In Malawi, ciprofloxacin is used in the treatment of bacillary dysentery in adults, sepsis, and also as a prophylactic treatment for meningococcal meningitis in adults [40].

Some of the limitations of this study include lack of patient history on previous antibiotic use. Consequently, this might have an influence on the observed rate of antibiotic resistance. . Secondly, due to limited availability of raw data, we were not able to capture an in-depth analysis of critical epidemiological data such as name of referral hospitals for the patients, onset of disease, occupation, and HIV status. Lastly, laboratory data on pathogen isolation, identification and susceptibility testing was generated using conventional methods, hence the results may be limited.

Conclusions

As a result of several social and public health interventions, Malawi has over the years recorded a marked decline in the incidence of bacterial bloodstream infections [5]. However, this study has demonstrated an increase in bacteria burden in sites other than blood stream as well as a concurrent increase in prevalence of antimicrobial resistance. The increased rates of antimicrobial resistance revealed in the study could be due to poor clinical practices or irrational use of antibiotics by the public. Nevertheless, to fight against antimicrobial resistance, a local epidemiological surveillance program is needed to guide in generation of evidence-based guidelines for the treatment and management of bacterial infections.

Abbreviations

AMR Antimicrobial Resistance

BAP Blood Agar Plate

CAP Chocolate Agar Plate

CSF Cerebral Spinal Fluid

ESBL Extended Spectrum beta-lactamase

MAP MacConkey Agar Plate

MCH Mzuzu Central Hospital

MRSA Methicillin Resistant Staphylococcus Aureus

NHSRC National Health Science Research Committee

OPD Out Patient Department

sSA Sub-Saharan Africa

UKNEQAS UK National External Quality Assessment System

ZIMQAP Zimbabwe Quality Assurance Program

Declarations

Ethics approval and consent to participate

Ethical approval for the study was obtained from National Health Science Research Committee (NHSRC), (approval number NHSRC # 1206). No consent was obtained from participants since this was a retrospective study

Consent for publication

None

Availability of data and materials

All data related to this study can be accessed at Mzuzu Central hospital upon consent is given from the authorities

Competing interests

None

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Authors' contributions

Study conception: MC, PK, MN, PSK, JW,; study design: MC, PK, MN, PSK, JW,; data collection: MC, PK, MN, PSK, PK, JW,; data analysis: MC, PK, PSK, ECA, EST, VCU; manuscript preparation: MC, PK, MN, PSK, PK, JW, ECA, EST, VCU. All the authors contributed adequately towards the completion of this study. Their career background played important roles. All authors read and approved the manuscript.

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Authors' information (optional)

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Figures

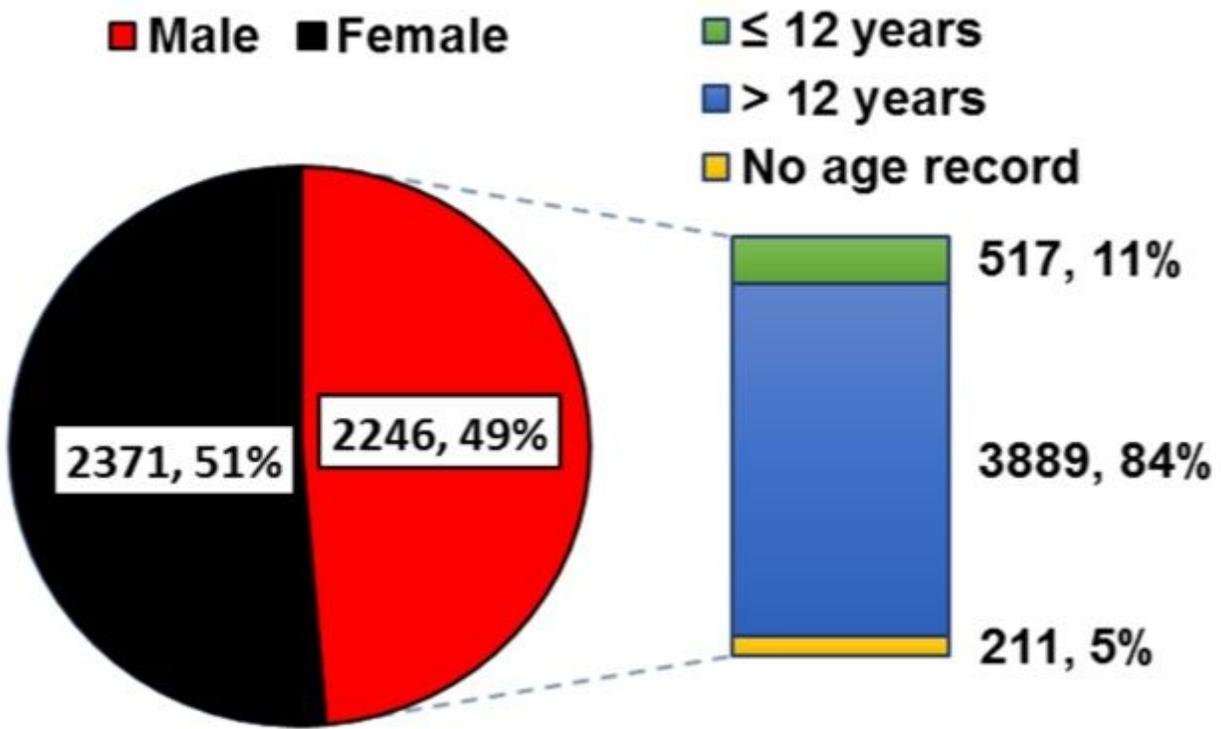


Figure 1

Demographics of the study population. Patients were categorised by gender and age group.

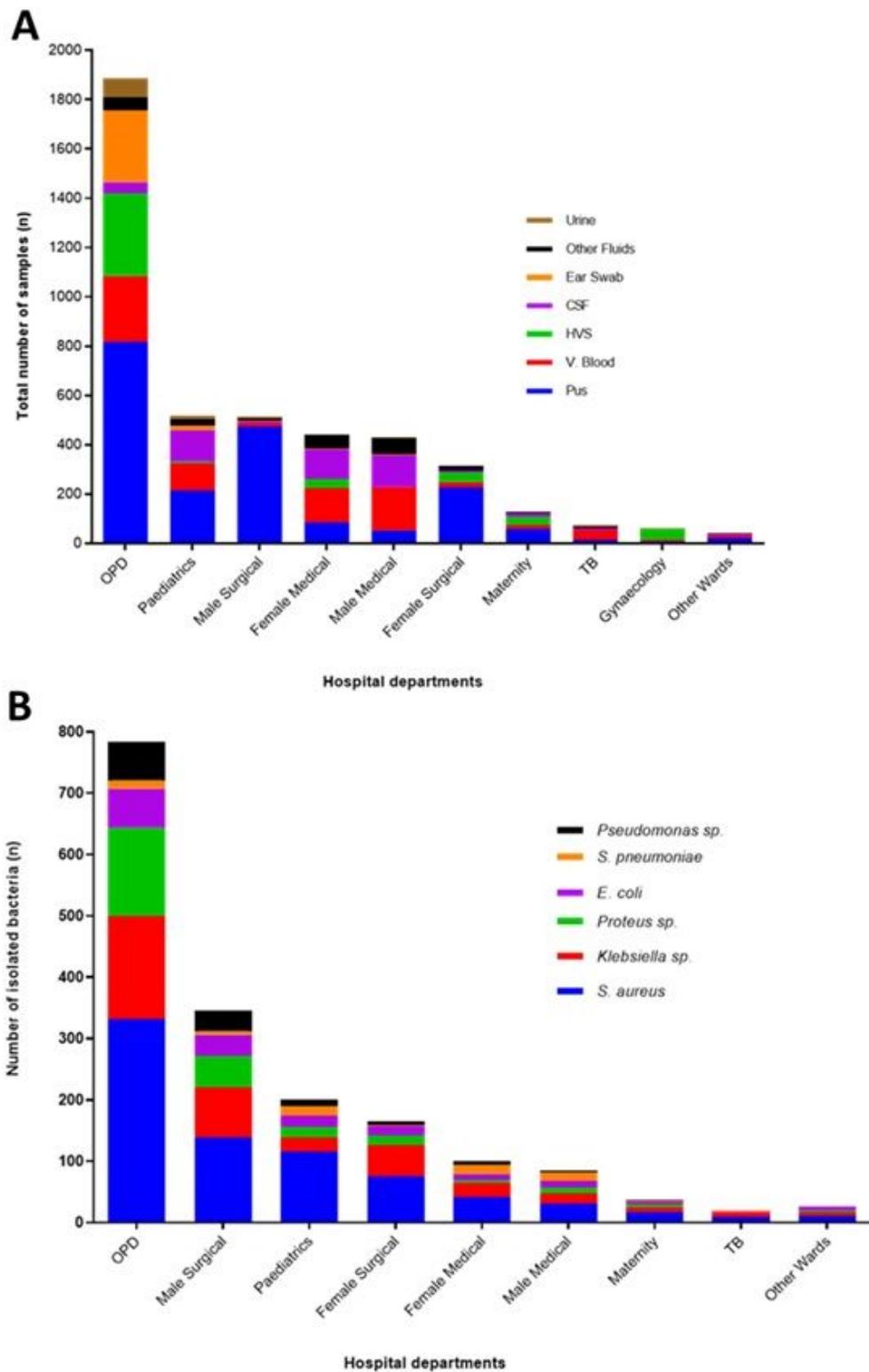


Figure 2

Distribution of isolates by specimen source and hospital department.

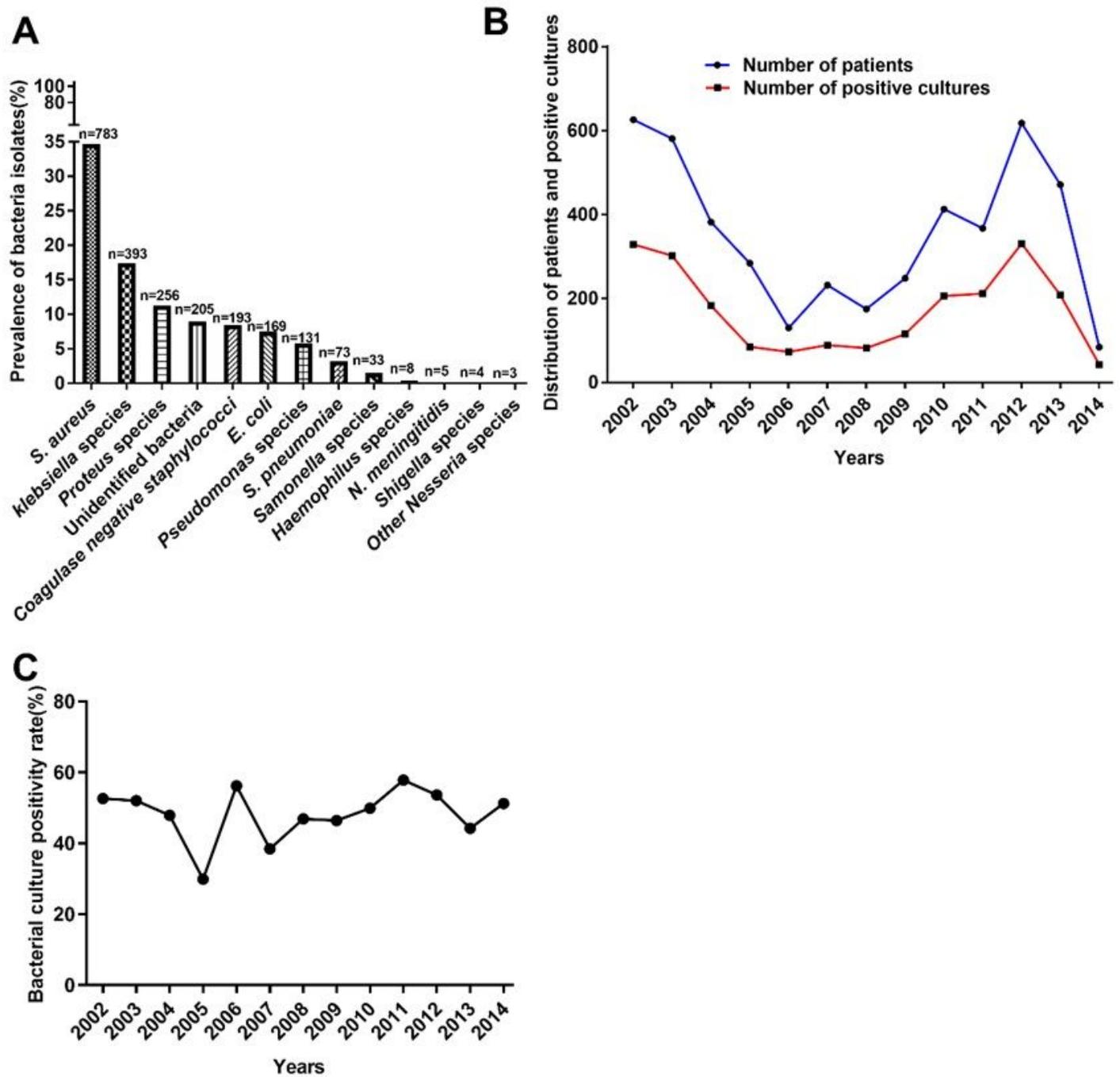


Figure 3

Prevalence of bacterial pathogens over the 13-year period. (A) Shows the prevalence of isolates during the study period. (B) Describes the distribution of patients alongside positive cultures throughout the study period. (C) Demonstrate the culture positivity rates in different years of the investigation period.

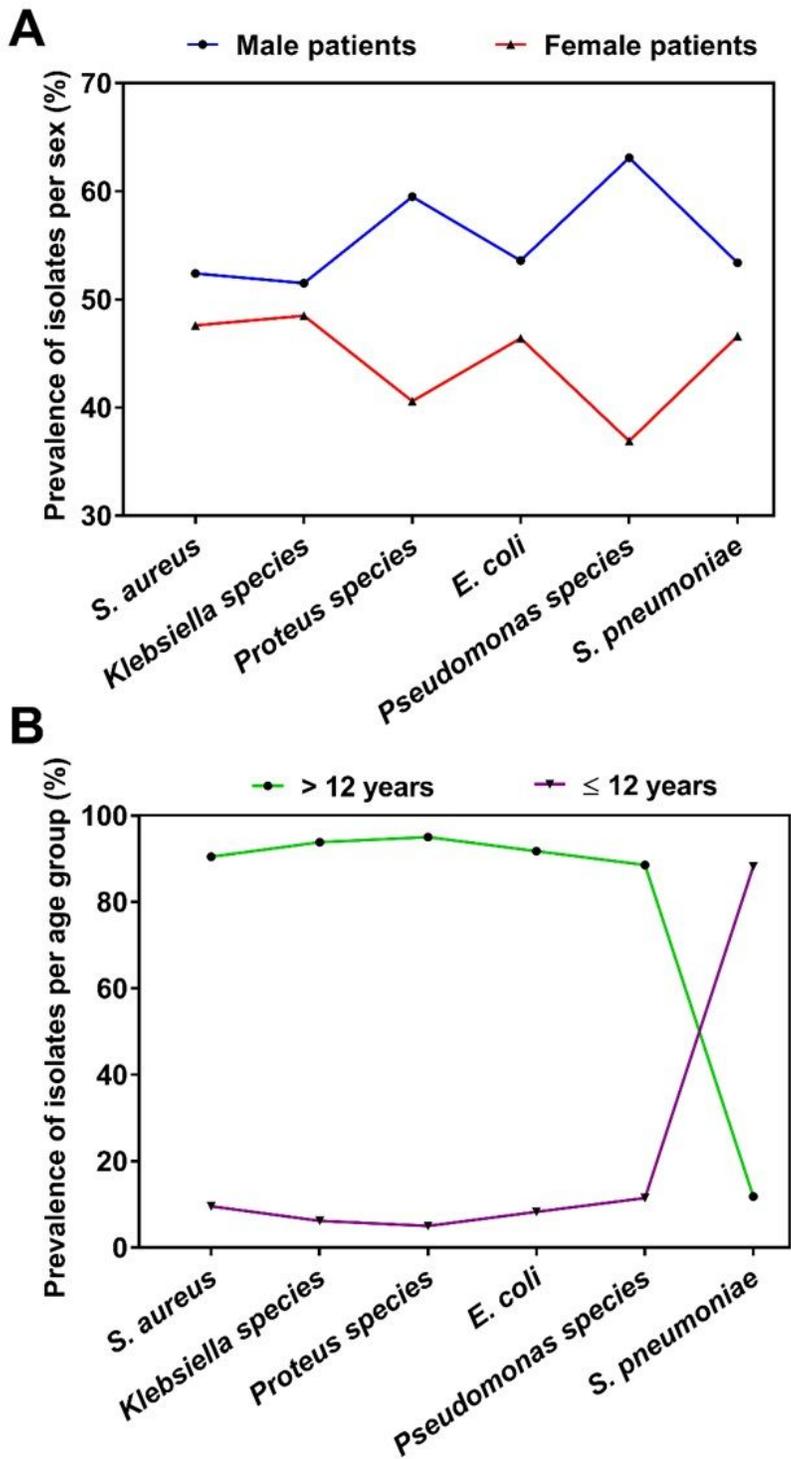


Figure 4

Prevalence of bacterial isolates per gender and age group. Isolated bacteria were distributed according to sex (A) and age group (B) of the patients.