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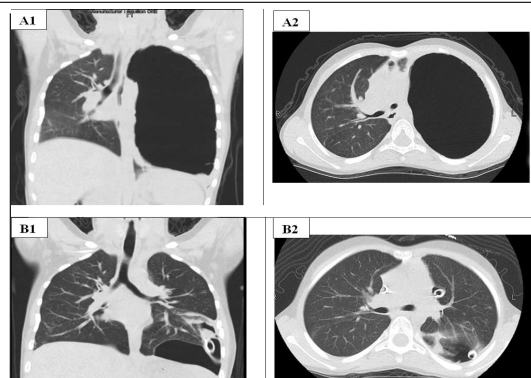
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A 10 year old child with recurrent chest infection and failure to thrive. Flow cytometry and IgA was normal. His IgE was very high. His post-procedure bronchoalveolar lavage showed *Aspergillus nodularis*.

Images A1 and A2 – At presentation (Large bulla with few loculations and thin septations within it along with minimal compressed residual left lung parenchyma and associated mediastinal shift of the right side. Right lung appears unremarkable)
Images B1 and B2 – Post-procedure (Interval introduction of 2 left-sided chest tubes resulting in reduction in the size of the bulla, improved aeration/re-expansion of the collapsed lung and resolution of contralateral mediastinal shift.)

Courtesy: Ali Faisal Saleem, Asst professor, Paediatric Infectious Disease, Aga Khan University.

Antimicrobial Stewardship – An urgent need of Pakistan.

Antimicrobials were used for management of microbial infections in ancient time worldwide. Alexander Fleming discovered penicillin in 1928 and antimicrobial resistance was major concern even at that time, which was later evident in 1940.¹ Initial elation which came with a discovery of many antibiotics and antifungal agents in succeeding years was overcome by emergence and propagations of resistant bacterial strains, some of them are now resistant to all available antibiotics. At least 23,000 people die and at least 2 million people become infected as a direct result of multidrug resistant bacteria in United States.² Many more people die from other conditions that were complicated by an antibiotic-resistant infection. Though it is difficult to calculate the full social and economic costs of AMR, the combined impact of disability and death, loss of labor productivity, cost to health systems, and the burden of care on communities has extensive consequences. A recent review estimated that 700,000 deaths occur each year worldwide due to AMR. If appropriate action is not taken now, then by 2040 AMR will kill 300 million people worldwide. This figure is higher than today's cancer death and the estimated cost is 100 trillion US dollars.³

There are many factors responsible for increasing resistant of antimicrobial among microorganisms like irrational or inappropriate use of antimicrobial agents, lack of awareness about proper use and antibiotic resistance, easy availability of all the antimicrobial over the counter without prescription, absence of policies on manufacturing and utilization of antimicrobial and use of antibiotics in animal food and agriculture. Poor infection control practices both in health care as well as in community leads to rapid spread of these deadly organisms not even between countries but also across globe. During the past few decades, development of new antibiotics has slowed considerably and our options for treating increasing resistant infections are becoming more and more limited. CDC estimates that 30 percent of all antibiotics prescribed in outpatient clinics and in hospitals in United States are unnecessary. Using appropriate and identifying best combination is essential. A targeted approach towards pathogen and drug sensitivity is the key using first-line drugs recommended by national guidelines.⁴ A coordinated approach including all stakeholders to improve the judicious use of antibiotics can only be achieved through antibiotic stewardship. Antimicrobial stewardship has been defined as “the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance”.⁵ Joseph and Rodvold wrote about the “4 D's of optimal antimicrobial therapy”: right Drug, right Dose, De-

escalation to pathogen-directed therapy, and right Duration of therapy.⁶ The world health assembly has endorsed a global action plan to tackle the issue of antimicrobial resistance in 2015. The goal of the plan is to ensure continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality assured, used in a responsible way and accessible to all who need them.⁷ It has provided framework to develop their nation action plan to battle AMR.

Pakistan is also facing challenges of increase spread of multidrug resistance organisms, in healthcare setting as well as in community, and antimicrobial resistance with major contributions made by antibiotic misuse and lack of national health policies. From ESBL enterobacteriaceae and drug resistance Salmonella in last decade, to carbapenem resistance enterobacteriaceae, multidrug resistant salmonella, MDR TB and MRSA, problems has now become very frightening.^{7,8} There is lack of national policies to optimize use of antimicrobial therapy through antimicrobial stewardship. Although few initiative has been taken for increasing awareness about antibiotic stewardship at individual level, there is need of national action plan for AMR which can be implemented in all healthcare facilities and sectors across Pakistan. There should be policies for infection control, improved diagnostic facilities at all level, antibiotic policies including its use in animal and agriculture industries, pharmacy regulation for over the counter availability of all type of antimicrobials, national antimicrobial resistant network, plans to increase awareness and education of not only healthcare professional but also at community level and support for ASP from public and private sectors.

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Frequency and Level of Exposure of Health Care Workers to Hospitalized Crimean-Congo Hemorrhagic Fever Cases and Their Management: A Descriptive Study from a Tertiary Care Hospital

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ABSTRACT

Background

Crimean-Congo hemorrhagic fever (CCHF) is a life threatening zoonotic infection. The virus is transmitted either by tick bite or through contact with infected blood or body fluid. Nosocomial transmission and outbreaks in health care is widely reported. Health care workers (HCWs) are at a higher risk of exposure to CCHF.

Methods

It is a descriptive study conducted from January 2015-September 2017 at Aga Khan University Hospital. The study aims to estimate the frequency of exposure of HCWs to confirm cases of CCHF and the efficacy of Ribavirin for prophylaxis use. Demographics, level of exposure, efficacy of Ribavirin prophylaxis and clinical outcome were studied.

Results

During January 2015 till September 2017, 9 cases of CCHF were admitted at our hospital. A total of 65 HCWs were exposed to CCHF cases amongst which there were 18 doctors, 33 nurses and 14 other supportive staff. Nine HCWs had a high-risk of exposure and were given Ribavirin prophylaxis. All of these exposures remained clinically asymptomatic for CCHF.

Conclusion

Hospitalized cases of CCHF virus pose a significant risk of exposure to HCWs which can be prevented by strict adherence to infection control practices. Although efficacy of Ribavirin for prophylaxis is not definitive and very little data exists on its prophylactic use, but since none of our high-risk exposures developed symptomatic infection after Ribavirin prophylaxis, our study supports its role in prevention.

Key words

CCHF; HCWs; Exposure; Ribavirin prophylaxis

Objective

The objective of this study was to calculate the frequency, level

of exposure amongst HCWs exposed to the cases of CCHF and to assess the role of Ribavirin in post exposure prophylaxis (PEP).

Background

Crimean-Congo hemorrhagic fever virus [CCHFV] belongs to the family *Bunyaviridae*, which can cause deadly viral hemorrhagic fever (VHF). It was first described in Crimea in the Soviet Union in 1944.¹ In Pakistan, it was first reported in 1976, when a laparotomy was performed on a patient with symptoms of gastrointestinal bleed at a general hospital in Rawalpindi.² Since then it has become endemic in Pakistan with sporadic outbreaks. Humans can get the infection either by the tick bites or through contact with the blood or body fluids of the infected animals or human. CCHF incubation period varies from one to nine days.³

CCHF cases pose a high risk of transmission to HCW and because of the disease high case fatality rate (10-50%), it remains a major public health concern and challenge for hospital Infection Control. In this study, we have evaluated the frequency and risk of HCWs exposure during providing care to cases of CCHF.

Methods

Hospital Setting and Patients

The study was conducted as a descriptive study on nine index cases of CCHF with sixty five HCWs that were exposed at the Aga Khan University Hospital (AKUH). AKUH is a 600-bed tertiary care referral hospital located in Karachi, Pakistan. All HCWs who were exposed to confirmed cases of CCHF from January 2015–September 2017 were enrolled in the study.

Clinical Data Collection and Definitions

Demographic data including age, gender, profession, date and type of exposure, location of unit where exposure occurred, Ribavirin prophylaxis, its side effects and outcomes of exposed HCWs were collected using data collection forms.

High-risk exposure comprised of HCWs who had direct skin or mucosal contact with contaminated blood or body fluids, those participated in CPR and without adequate precautions and were exposed to needle stick injury or blood or body fluids spill.

Moderate -risk exposure included HCWs who performed

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high risk procedures with adequate PPE, hence had no direct contact with contaminated blood or body fluids.

Low-risk exposure included HCWs who were involved in the patients care but had no direct contact with the patient or did not get closer than 1 meter to the patient.

Analysis

The collected data was analyzed to report results in frequencies and percentages. To preserve confidentiality, we coded each exposed HCW and removed their original identifications.

Results

In the two years of study 2015 till 2017, 65 HCWs were exposed to 9 confirmed cases of CCHF. Nine exposures were reported from 2 patients (14%) in 2015, 38 exposures from 4 patients (58%) in 2016 and 18 exposures from 3 patients (28%) in 2017, till the month of September. Therefore, the number of exposures per patient per year were 4.5, 9.5 and 6 in 2015, 2016 and 2017 respectively. The median age of exposed HCW was 29.53 (23-45) years of which 43 (66%) were males. Amongst the 65 HCWs exposed 18 (28%) were doctors, 33 (51%) were registered nurses while 14 (22%) were other health care associates. Most of the exposures occurred in the Emergency Department. Table 1 describes the professional role of health care workers exposed to index cases.

Amongst the 65 HCWs exposed, 9 (14%) had high-risk exposure, 35 (54%) had moderate-risk exposure while low-risk exposure was seen in 21 (32%). In the high-risk exposure group, 4 (44%) were doctors, 4 (44%) were nurses and 1 (11%) was a health care associate. In the moderate-risk exposure group 8 (22.8%), 18 (51%) and 9 (25%) were doctors, nurses and health care

Table 1. Role of health care workers exposed to 9 CCHF cases

Index CCHF Cases	Physicians	Nurses	Support Staff*	Total n (%)
Index Case 1	0	4	2	6 (9)
Index Case 2	1	2	0	3 (5)
Index Case 3	11	9	3	23 (35)
Index Case 4	0	1	2	3 (5)
Index Case 5	3	5	3	11 (17)
Index Case 6	0	1	0	1 (2)
Index Case 7	0	7	4	11 (17)
Index Case 8	2	1	0	3 (5)
Index Case 9	1	3	0	4 (6)
Total n (%)	18 (28)	33 (51)	14 (22)	65 (100)

*Support staff: stretcher-bearer, nurse's aid, cleaning staff, security agent

associated respectively. Among low-risk exposure 6 (29%) were doctors, 11 (52%) were nurses and 4 (19%) were health care associates, Table 2. In the high-risk exposure group one had needle stick injury whereas other exposures included blood spill during central line Cannulation, exposure to blood or body fluid without gloves and extubation without personal protective equipment. The HCWs with high-risk exposure were offered Ribavirin prophylaxis whereas those with moderate-risk exposure were kept under close surveillance for monitoring of symptoms of CCHF for up to 14 days. HCWs with low-level exposure were neither offered treatment nor follow up. None of the exposed HCWs developed clinical symptoms of CCHF.

In the high-risk exposure group only one physician developed jaundice after consuming 4 doses of Ribavirin due to which Ribavirin had to be discontinued and the exposed HCW was counseled for strict surveillance of clinical symptoms of CCHF.

Table 2. Role of health care worker and the level of risk of exposure

Role of Health Care Worker	Level of risk associated with exposure		
	High (%)	Moderate (%)	Low (%)
Physicians (n=18)	4 (22)	8 (44)	6 (33)
Nurses (n=33)	4 (12)	18 (55)	11 (33)
Support staff (n=14)	1 (7)	9 (64)	4 (29)
Total n=65	9 (14)	35 (54)	21 (32)

n: number of contacts, %: percentage

Discussion

The study shows a significant risk of exposure for HCWs to the cases CCHF. All the exposures could have been prevented by adhering to the Standard Precautions. Registered Nurses were more commonly exposed to the cases of CCHF, thus emphasizing the need for education, reinforcement and reminders for adopting Standard Precautions for this group of HCWs. The study showed that about a quarter of exposures were low risk that could have been prevented by staff education and by restricting the movement of HCW in the designated area for CCHF cases.

The health care workers in the high risk exposure group did not take adequate precautions nor used required Personal Protective Equipment (PPE) when performing procedure that mandate barrier precautions. Education on PPE usage and ensuring their availability can prevent future exposures. Nurses and physicians had the most of the high-risk exposures that could be justified as they perform many emergency interventions that could lead to high risk exposure. Regardless, all the HCW exposures in our study were due to breach in following standard

practices for Infection Control, although Nurses and Physicians being the most aware class of HCW are expected to be most responsible.

There were three index CCHF cases which had the longest hospital stay and despite having prolonged stay had interestingly contributed to the least number of HCW exposures. This advocates that prolong hospital stay may not be a risk factor for CCHF exposure. Most of the exposures of HCWs occurred before the confirmation of CCHF diagnosis in suspected patients except in index case 3 in which it was found that majority of exposures occurred after the confirmation of diagnosis of CCHF and all these exposures were secondary to breach in the infection control practices which is a concern.

During our study period we did not identify any case of Nosocomial transmission of CCHFV from CCHF patients to HCWs, although cases of transmission of CCHFV from infected patient to other patients and to HCWs have been reported from numerous other countries.^{6,7}

There is a growing concern regarding the effectiveness of Ribavirin in prophylaxis among CCHF exposures. All our high-risk exposures were treated with Ribavirin and remained clinically asymptomatic for CCHF which supports its use in PEP as also suggested by Guner *et al* a finding which requires further advocacy.⁸

Conclusion

From this study we have concluded that hospitalized CCHF cases pose a significant risk of exposure to HCWs which can entirely be prevented by strict adherence to Standard and Transmission Based Precautions. There is a higher level of exposure amongst the Emergency Unit staff where the patient

is initially managed without a confirmed diagnosis. Therefore, HCWs should be educated, trained and monitored regarding the adherence to Standard and Transmission Based Precautions with proper use of PPE especially when performing high risk procedures. The role of Ribavirin for PEP is supportive in our study but needs further study to warrant effectiveness.

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Antimicrobial Susceptibility Pattern of *Staphylococcus aureus* Isolated from PNS Shifa Hospital, Karachi, Pakistan.

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Abstract

Objective

To determine antimicrobial susceptibility pattern of *Staphylococcus aureus* in a tertiary care hospital, Karachi.

Study design

Descriptive cross sectional.

Place and Duration of study

The study was carried out in Department of Microbiology, PNS Shifa hospital, Karachi from June 2014 to May 2016.

Materials and Methods

A total of 2240 samples are selected for the study among which 1132 samples revealed the growth of different microorganisms. Samples of pus, blood, body fluids, and sputum and wound swabs are included and different biochemical reactions are performed in order to identify *Staphylococcus aureus* isolates. The antimicrobial susceptibility of these isolates are performed by disk diffusion method using cefoxitin (30µg) and different antibiotics are tested against methicillin resistant and sensitive staphylococcus isolates as outlined by Clinical Laboratory Standard International Guidelines.

Results

Among different samples, total 592 samples showed the growth of *Staphylococcus aureus*. Among them n=377 (64%) isolates were methicillin resistant *Staphylococcus aureus*, and n=215 isolates were methicillin sensitive (36%). Out of 377 isolates of methicillin resistant *staphylococcus aureus* (MRSA) from different clinical samples, 79% (n=298) isolates are from pus samples. We have also isolated 215 MSSA, 82% (n=176) are isolated from pus. Out of 377 isolates of MRSA, 41% (n=153) are susceptible to tigecycline, 15% (n=57) susceptible to erythromycin, 46% (n=172) sensitive to clindamycin, 28% (n=106) sensitive to cotrimoxazole, 66% (n=250) sensitive to doxycycline, 72% (n=272) sensitive to chloramphenicol, and 17% (n=65) sensitive to ciprofloxacin. Among 215 isolates of *staphylococcus aureus* (methicillin sensitive), 50% (n=108) of

isolates were sensitive to tigecycline, 41% (n=88) were sensitive to erythromycin, 55% (n=118) were sensitive to clindamycin, 53% (n=113) were sensitive to cotrimoxazole, 74% (n=160) were sensitive to doxycycline, 71% (n=152) were sensitive to chloramphenicol, 58% (n=125) were sensitive to ciprofloxacin. All strains of *Staphylococcus aureus* (methicillin resistant and sensitive) are found susceptible to vancomycin and linezolid, 100% (n=592).

Conclusion

The antibiotic susceptibility pattern obtained from the above study showed a lot of antimicrobial choices available for *staphylococcus aureus*, so the use of Vancomycin and linezolid should be the last resort for treating such infections. It also draws attention towards increasing resistance among the widely used antibiotic such as ciprofloxacin so its overuse should be discouraged.

Key words

Antimicrobial susceptibility, Methicillin resistant *Staphylococcus aureus*, *Staphylococcus aureus*.

Introduction

Staphylococcus aureus is one of the most prevalent and shared pathogen involved in human infections.¹ It causes a broad range of infections which includes skin and soft tissue infections, pneumonia, infective endocarditis leading to septicemia.¹ It has been implicated as one of the most common organisms involved in post-operative wound infections.² Nasal carriage among health care workers is the main source of nosocomial infections. Colonization rate of healthcare personals is greater, most likely due to increased exposure.³

In recent past there has been an alarming increase in methicillin resistant *Staphylococcus aureus* (MRSA) in hospital settings.⁴ The rise in hospital admission for CAP (community acquired pneumonia), VAP (ventilator associated pneumonia) and surgical site infections are linked with increased prevalence of MRSA.⁵

Before the discovery of penicillin, staphylococcal septicemia was a major threat.¹ Within a short span bacteria developed resistance to penicillin and therefore rendered ineffective.^{2,7,8} In 1960s beta lactamase penicillin's emerged as revolutionary

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drugs, but soon they failed after the emergence of methicillin resistant *Staphylococcus aureus* (MRSA). Against MRSA vancomycin is the suitable antibiotic and the drug of choice.^{9,10} The present predicament is the emergence of vancomycin resistant strains of *staphylococcus aureus*, and thus the treatment options are also available for such resistant strains.^{11,12}

The rationale of our study is to detect the antimicrobial susceptibility pattern of *Staphylococcus aureus* both methicillin resistant and sensitive isolated in a tertiary care hospital, Karachi and to limit the unnecessary usage of broad spectrum antibiotics.

Materials and Methods

This study was conducted in the Department of Microbiology, PNS Shifa Hospital, Karachi. The study protocol was approved by institutional ethical and research committee. The duration of study is from June 2014 to May 2016. A total of 2240 samples received for culture and sensitivity among which 1123 samples were positive for the growth of microorganisms. Around 592 samples showed the growth of *Staphylococcus aureus*. These isolates further studied for beta-lactamase production, and 377 isolates found to be methicillin resistant.

Samples were inoculated on blood and MacConkey agar plates and incubated at 37°C aerobically for 24 to 48 hours. On the basis of beta-hemolytic colonies sample selection made with yellowish pigment found on blood agar. Further test were performed for confirmation of *Staphylococcus aureus*. These test include catalase test, slide coagulase test and tube coagulase test, DNase test.¹²

Antimicrobial susceptibility testing was carried out by Kirby-bauer disc diffusion method as outlined by Clinical Laboratory Standard International Guidelines.¹³

Methicillin resistance was confirmed by Kirby-bauer disc diffusion method using Mueller Hinton agar plate, supplemented with 7% NaCl and 30µg ceftioxin disc (OXOID). An isolate observed methicillin resistant if zone of inhibition of 30µg ceftioxin is ≤21mm. Results were evaluated on the basis of criteria found in CLSI and the ATCC control used in this procedure is *Staphylococcus aureus* (ATCC29213).¹³

The antibiotics tested for susceptibility includes ceftioxin (30µg), gentamycin (10µg), amikacin (30µg) erythromycin (15µg), clindamycin (2µg), trimethoprim-sulfamethoxazole (1.25µg), chloramphenicol (30µg), doxycycline (30µg), ciprofloxacin (5µg) and linezolid (30µg).(OXOID).

Data analysis was done using IBM SPSS and regressions were applied to find any association between independent and dependent variables.

Results

Among different samples, total 592 samples showed the growth of *Staphylococcus aureus*. Among them n=377 (64%) isolates were methicillin resistant isolates, and n=215 isolates were methicillin sensitive (36%). Out of 377 isolates of methicillin resistant *Staphylococcus aureus* (MRSA) n=298 (79%) isolates are from pus samples, n=56 (15%) from blood, n=11 (3%) from tip, n=4 (1%) from cerebrospinal fluid and n=7 (2%) from pleural and ascitic fluid as shown in Figure 1. Out of 215 MSSA isolates of *staphylococcus aureus* n=176 (82%) are from pus samples, n=21 (10%) are from wound swab, n=15 (7%) are from blood and n=2 (1%) from tip as shown in Figure 1.

Among 377 isolates of MRSA, 41% (n=153) are susceptible to tigecycline, 15% (n=57) susceptible to erythromycin, 46% (n=172) sensitive to clindamycin, 28% (n=106) sensitive to

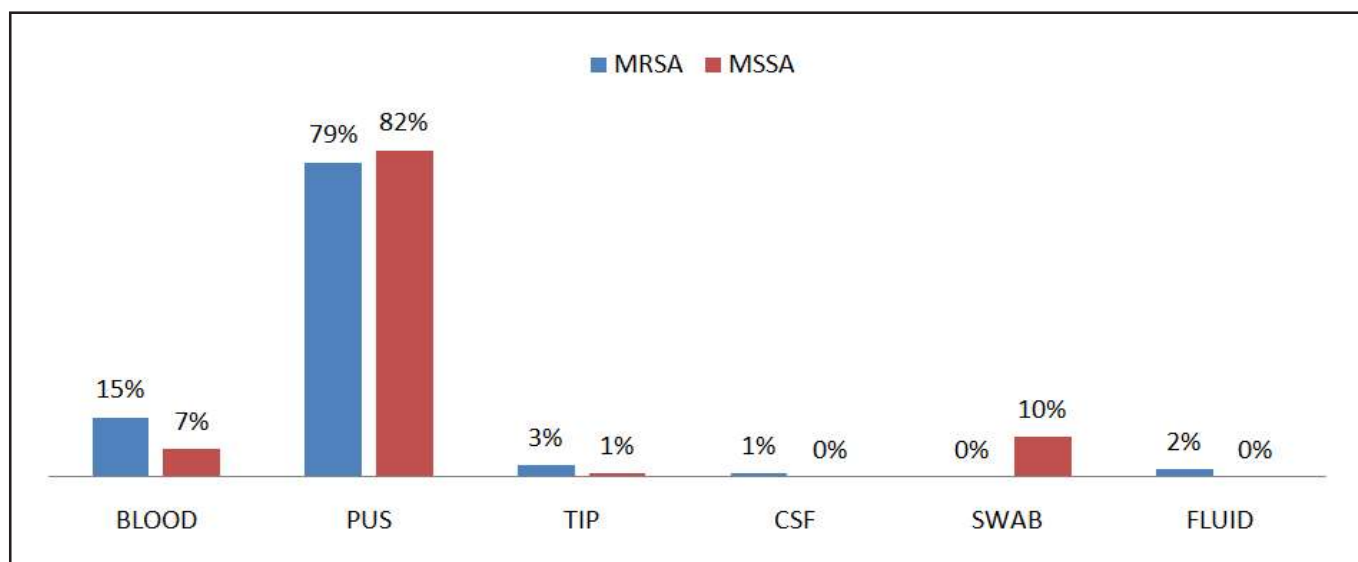


Figure 1: Percentage of MRSA (n=377) and MSSA(n=215) isolates

cotrimoxazole, 66% (n=250) sensitive to doxycycline, 72% (n=272) sensitive to chloramphenicol, 42% (n=158) sensitive to gentamicin, 37% (n=139) sensitive to amikacin and 17% (n=65) sensitive to ciprofloxacin. Antibiogram is shown in Figure 2.

Among 215 isolates of MSSA, all are sensitive to oxacillin, amoxicillin and cephradine, 100% (n=215), 50% (n=108) of isolates were sensitive to tigecycline, 41% (n=88) were sensitive to erythromycin, 55% (n=118) were sensitive to clindamycin, 53% (n=113) were sensitive to cotrimoxazole, 74% (n=160) were sensitive to doxycycline, 71% (n=152) were sensitive to chloramphenicol, 90% (n=193) were sensitive to gentamicin, 81% (n=174) were sensitive to amikacin, 58% (n=125) were sensitive to ciprofloxacin as shown in Figure 3.

All strains of MSSA and MRSA are found susceptible to Vancomycin and linezolid (100%).

Discussion

One of the most common causes of nosocomial infections in the current research setting is methicillin resistant *Staphylococcus aureus* (MRSA). Its increasing prevalence is a major threat to

our healthcare system as it not only increases the hospital admissions but also linked with increased mortality rates.¹⁴

The prevalence of MRSA and its antibiotic susceptibility pattern is a substantial aid for a clinician to treat such infections.¹⁵ The prevalence of MRSA found in the above study is 63.38%, which is in agreement with the Iranian study showing the prevalence around 60%.¹²

The prevalence of MRSA in a recent study conducted in Peshawar, Pakistan was 36%, which is less than found in our study.¹⁶ This difference is due to the change in the environmental conditions, seasonal variations, difference in blood culture system, and type of patient population.¹⁶

The progressive increase in the emergence of methicillin resistant *Staphylococcus aureus* (MRSA) and its association with non-judicial use of antimicrobials is a matter of concern not only for clinicians but also for microbiologist and constitute a major global risk. The frequency of MRSA in our study is highest in pus (79%), followed by blood (15%), while the frequency of MSSA is 82% in pus and 10% in wound swab. This is comparable to a study conducted in Ethiopia, where incidence

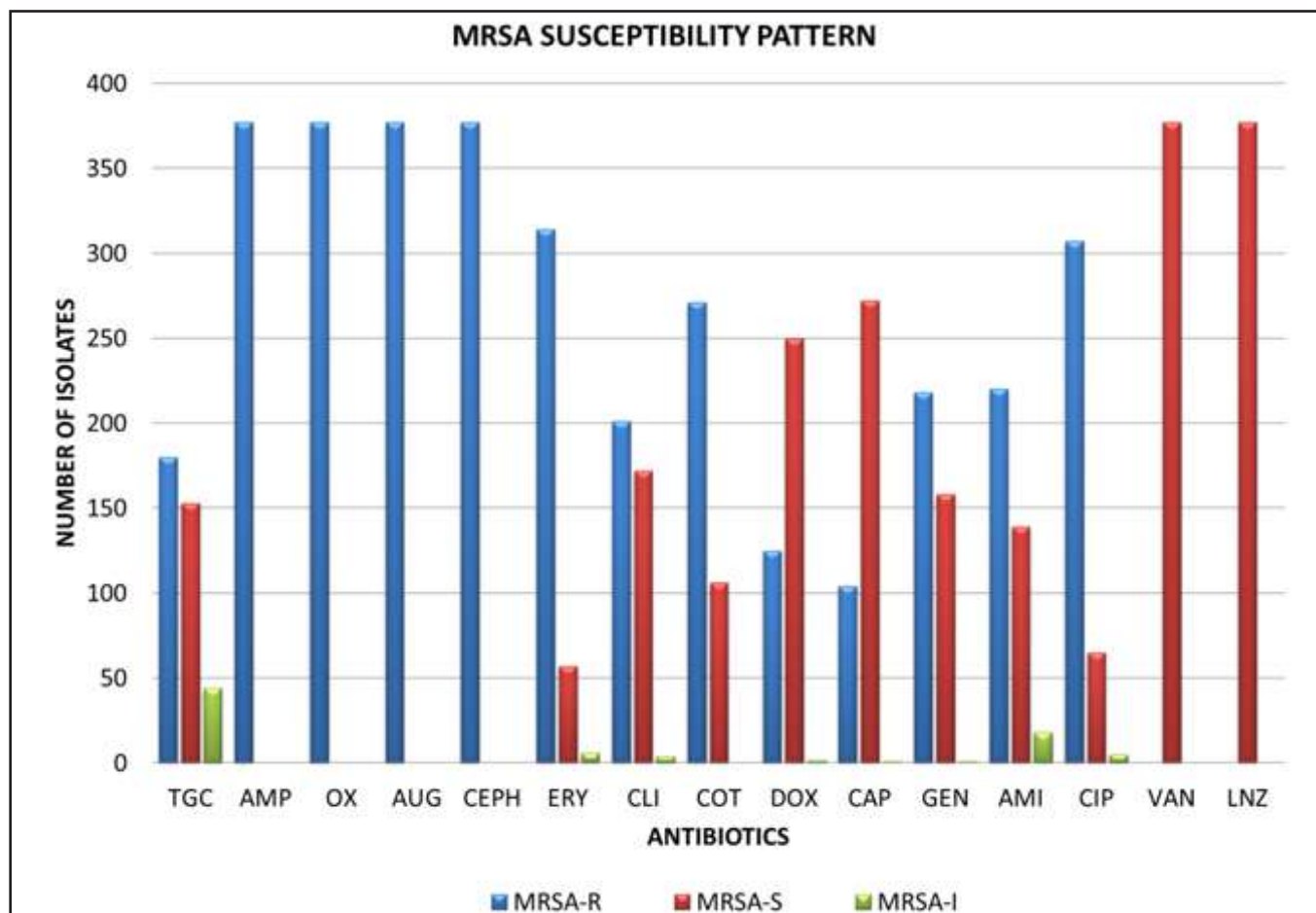


Figure 2: Antibiogram of MRSA isolates (n=377).

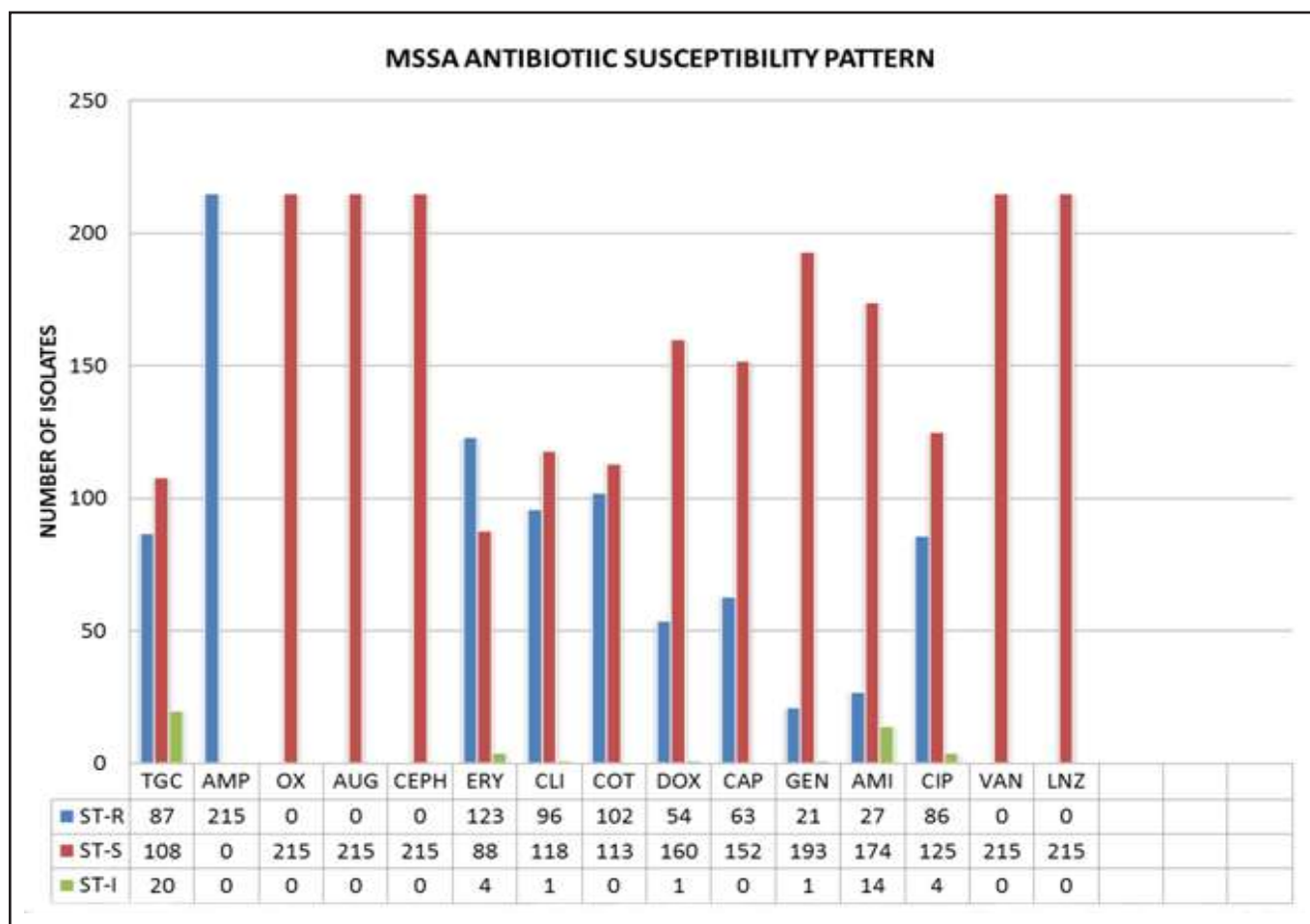


Figure 3: Antibigram of MSSA isolates (n=215).

of *staphylococcus aureus* both methicillin resistant and sensitive is highest in pus (55%).¹⁷ The result is also in concordance with Indian studies reporting highest prevalence of MRSA in pus followed by blood.^{19,20}

Among antibiotics, majority of *staphylococcus aureus*, both methicillin resistant and methicillin sensitive is susceptible to chloramphenicol, (72% for MRSA) and (71% for MSSA). Antibiotic susceptibility against doxycycline is also high as comparable to other antimicrobials. All isolates are 100 percent sensitive to Vancomycin and linezolid. Similar results are also obtained in a study carried out in Northern areas of Jordan in 2015.¹⁸

Vancomycin and linezolid are the only antimicrobials showing 100% sensitivity to all staphylococcus isolates, which is also observed in studies carried out in different regions of Asia.^{1,2} Same pattern of sensitivity against Vancomycin was also found in a recent study carried out in Namibia.²³

One of the most striking point concluded from the above data is the increasing resistance of ciprofloxacin (17% sensitive) for

MRSA. The emergence of resistance of ciprofloxacin (17% sensitive) is a characteristic feature of the current research. This may presumably be related to the inappropriate antibiotic use in hospital setup and outpatient departments.²²

The reason behind this resistance is mainly the overuse of this antibiotic in hospital setup and outpatient departments in our country, same pattern of resistance is also observed in a recent study conducted in Iraq.^{21,22} A recent study carried out in Namibia showed different susceptibility pattern of ciprofloxacin.²³

This variation may be related to the change in the targeted population, culture techniques and different preferences of clinicians to choose the appropriate antimicrobials.

Antibiotic resistance is a major global threat, and one of the most unsolved problem in public health. This is a point of concern for clinicians, microbiologist and pharmacist. It leads to the efforts of pharmaceutical companies in manufacturing new antimicrobials effective against the resistant microorganisms. After a certain period of time, those antimicrobials again become ineffective either due to their overuse or the emergence of new

resistance mechanisms developed by the pathogens. These organisms continuously acquire new antibiotic resistance and virulent factors.

The limitations of this study are that all the samples included are obtained after admission and from outpatient department who already may have been taking antibiotics. Detailed clinical evaluation was done in order to correlate the results and to obtain their clinical significance.

Conclusion

The antimicrobial susceptibility pattern obtained from the above study displayed the increasing resistance in overly prescribed drugs especially ciprofloxacin against *staphylococcus aureus*. Attention should be given to restrict the non-judicial use of antimicrobials such as vancomycin and linezolid, used among admitted patients.

Conflict of interests

We have no conflict of interest.

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Clinical Spectrums of *Salmonella Bacteriuria* in Renal Transplant Recipients

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Introduction

Pakistan is an endemic area for *salmonella* infection.¹ Enteric fever and salmonellosis are the most common clinical presentations. Asymptomatic carriers are found to be associated with shedding of antigens usually through the gastrointestinal tract and rarely through the urinary tract.² Chronic carrier state of *Salmonella* has been associated with immunosuppression, stone disease, structural abnormalities and associated infection e.g. Schistosomiasis.³

Our center is the largest renal transplant facility in Pakistan where over 3400 live related renal transplant have been performed. Infection in renal transplant recipients contributes significantly to their mortality and morbidity.⁴ *Salmonella bacteriuria* is a rare finding even in endemic regions and reports in renal transplant recipients are scarce.⁵ We have observed variable clinical findings in patient having *Salmonella* species in their urine cultures. The purpose of this study is to observe the incidence of *Salmonella bacteriuria* and its clinical spectrum in our renal transplant recipients.

Material and Method

This was an observational retrospective study conducted over a period of two years from July 2009 to July 2011 in renal transplant recipients with positive urine culture. Culture reports were retrieved from the laboratory data base. Each positive urine culture report with *salmonella* species was considered as a separate episode. Urine cultures, if repeatedly positive within 15 days in the same patient were excluded.

Urine culture and urinalysis are part of routine laboratory testing for all transplant patients at their follow up clinic visit at our center.

Patients' files were reviewed for history of fever, dysuria, graft tenderness, antibiotic treatment and its duration at the time of each episode. Laboratory parameters including pyuria, total leukocyte count, serum creatinine level and blood culture positivity were noted.

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All mid-stream urines (MSU) were processed for quantitative analysis using calibrated 0.001ml (1 μ l) disposable plastic loops and inoculated by Quadrant Technique on CLED (Cystine Lactose Electrolyte-Deficient) Agar. Plates were incubated overnight at 37°C at ambient air. With 0.001 ml loop, one colony equals 1,000CFU/ml and 100 colonies would be equal to 100,000 CFU/ml. Bacterial count of $\geq 10^5$ CFU/ml of single morphotype were considered significant. Routine biochemical tests and serotyping using conventional antisera were used for *Salmonella* species identification. Antibiotic susceptibility testing was performed with Kirby-Bauer disc diffusion method using Clinical laboratory standard institute (CLSI) standards.

Definitions

Salmonella bacteriuria

Urine culture positive for *Salmonella* species with or without clinical sign and symptoms and abnormal laboratory parameters.

New episode

Positive urine culture at least 4-6 weeks after enteric fever or salmonellosis or last positive urine culture positive for *Salmonella* species.

Asymptomatic bacteriuria

Isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen from an individual without symptoms or signs of urinary tract infection.

Inclusion criteria

All urine samples collected as mid-stream specimen and positive for *Salmonella* species from all age groups.

Exclusion criteria

All urine cultures which came positive within recent (4-6 weeks) documented episodes of enteric fever (positive blood cultures)

Result

Eighteen renal transplant recipients were found to have *Salmonella bacteriuria*, representing 0.06% of total positive urine culture in this time period.

Out of 18 patients, urine cultures of 16 patients were positive for typhoid causing *Salmonella* species (*S.typhi* and *S.paratyphi*) while non-typhoidal *Salmonella* species were detected in the

urine of 2 patients.

Two patients had blood culture proven typhoid infection while other 2 had Salmonellosis with stool culture positive with in last 2 months duration.

Total 34 episodes were recorded from 18 patients during the study duration (Table 1).

Clinical presentations and laboratory parameters were variable in all episodes of patients (Table 2).

Clinical features of pyelonephritis, fever with chill, dysuria and graft site tenderness with positive blood cultures were present in only 3 patients. Graft biopsy was not performed in these patients However; histopathological proven florid pyelonephritis

Table 1. Description of symptomatic and asymptomatic episodes (N=34)

No. of Patients	No. of symptomatic episodes (N)	No. of asymptomatic episodes (N)
9	1	0
3	1	2
3	2	0
1	4	0
1	0	4
1	1	1
18	23 (68%)	11(32%)

Table 2. Summary of clinical features and laboratory parameters

Clinical Features	N (%)
Fever with dysuria	09 (39)
Only fever	06 (26)
Fever, graft tenderness, dysuria	06 (26)
Only dysuria	02 (09)
Laboratory Parameters	N (%)
Pyuria, rise in creatinine	05 (22)
Pyuria, rise in creatinine, rise in TLC, positive blood culture	04 (17)
Pyuria, rise in creatinine, rise in TLC	03 (13)
Only rise in creatinine	04(13)
Only pyuria	02 (09)
Only rise in TLC	01 (04)
Pyuria,, rise in TLC	01 (04)
No laboratory finding	03 (13)

supported by the relevant clinical findings and laboratory parameters was found in two patients (11%).

Patients with all symptomatic episodes were treated for an average duration of 14 days. Five patients have recurrent episodes despite adequate treatment. Only a single episode of asymptomatic bacteriuria was treated because no other cause of elevated creatinine was identified.

Among 16 typhoid causing *Salmonella* species, 11(69%) were resistant to ciprofloxacin, whereas MDR (resistant to ampicillin, Co-trimoxazole and chloramphenicol) strain were 4 (25%). No ceftriaxone resistant strain was detected in any episode during the study duration.

Discussion

Infections of *Salmonella* species could be intestinal and extra intestinal. High incidence of UTI in renal transplant recipient is due to abnormal structure, high immunosuppression⁶ and instrumentation. The incidence of *salmonella bacteriuria* in our renal transplant recipients is 0.06%. Variable incidence rate has been observed among different population with different levels of immune status. Hsu *et. al* reported the incidence of 1.5% in heart transplant recipients.⁷ The incidence of *Salmonella bacteriuria* by Nwadioha *et.al* in Nigerian general population is 2%.⁸ Tena D *et.al* had reported 0.056% non-typhoidal *Salmonella* urinary tract infection in immunosuppressed hospitalized population.⁹

In most studies, non-typhoidal *Salmonella* (NTS) strains have been reported causing urinary tract infection.^{10, 11} However, typhoid causing *Salmonella* was the dominant pathogen in our study population.

Spectrum of clinical features in renal transplant recipients could be variable. In this study, we found that it ranges from simple asymptomatic bacteriuria to florid pyelonephritis. Fever and dysuria was the most common presenting feature, however, fever could be the only presenting symptom without localized systemic sign symptoms and abnormal laboratory parameters. Graft tenderness with fever and dysuria suggesting graft pyelonephritis was the next most common presenting feature. These clinical findings of graft pyelonephritis were supported by laboratory parameters such as pyuria, rise in creatinine, rise in TLC, positive blood culture.

Recurrent symptomatic episodes might be possibility due to abnormal urinary tract along with severe immunosuppression.¹² Biofilm formation could be the possible reason of chronic carrier and delayed clearing according to Raza A *et.al*.¹³ Renal stones in native kidney, obstructive uropathy and post-transplant stenting may be the nidus for biofilm formation and hence causing chronic carrier and delayed clearance. We observed symptomatic and asymptomatic episodes in our patients as well.

Pakistan is categorized as a highly-prevalent area of *Salmonella enterica* serovar, having significant carrier rate.² High immunosuppression and surgical intervention can activate and lead to overt infection. In this study group, only four patients has history of blood and stool culture proven *salmonella* infection with in last 4-6 weeks, but the rest did not have any recent history of fever of unknown origin or abdominal discomfort suggestive of enteric and Salmonellosis.

Presence of multi-drug resistance bacteria including high resistance rate against Ciprofloxacin in our study also reflect overall resistance pattern in Pakistan.¹⁴ All isolates were susceptible to ceftriaxone. Most of patients were treated for average 14 days, however, symptomatic episodes were observed in 5 patients despite adequate treatment. Therefore, in case of relapse, clinician can consider to extend the total treatment duration.

Impact of level of immunosuppression and recurrence was not evaluated and therefore a major limitation of study and need to evaluate in further studies.

There are some limitations of our study. It was a retrospective study and patient's clinical details were gathered from their files, in which some time have patchy and inconsistent details.

It was only two years data, in which sample size was scarce and therefore the pattern of frequency and details of episodes is not dependable for a clinician to take any decision.

Conclusion

Effect of *Salmonella* species, especially typhoid strains, is variable from asymptomatic episode to simple cystitis and graft pyelonephritis. If not treated properly, it may lead to serious consequences such as deteriorating graft function and even graft rejection. Due to its high resistance against *salmonella* species, ciprofloxacin should be avoided as empirical therapy.

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Antimicrobial Resistance Profile in Complicated Intra-abdominal Infections

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Abstract

Background

Early administration of appropriate empirical antibiotics is integral part of early management of complicated intra-abdominal infections. Selection of empiric antibiotics relies upon microbiologic profile and resistance patterns of commonly encountered organisms in hospital and community. In developing countries, limited microbiological susceptibility information can result in either under treatment or unnecessarily broad coverage.

Objectives

To find out frequency of various micro-organisms and their resistance profiles to help decide empiric antibiotics to be used in complicated intra-abdominal infections.

Methods

We conducted review of medical records of adult patients admitted from Jan 2012 to Dec 2015 with complicated intra-abdominal infections.

Results

Mean age of 317 patients included in the study was 51+/-18 years. Healthcare associated infections were present in 57% of patients. Most common source of infection was large bowel and appendix accounting for 22% of cases, followed by pancreatic infection (20%). Common organisms reported were *E. Coli* (56%), *Enterococci* (28%) and *Klebsiella Pneumoniae* (15%). Extended Spectrum Beta Lactamase (ESBL) producers were 75% of *E Coli* and 55% of *Klebsiella Pneumoniae* isolates. Carbapenem resistance was present in 8% of *Klebsiella Pneumoniae* isolates.

Conclusion

High prevalence of ESBL producing gram negative rods and resistance to other broad spectrum antibiotics especially in healthcare associated infection needs to be kept in mind while planning empiric antibiotics therapy in complicated intra-abdominal infections. Antibiotic stewardship program is proposed to avoid emergence of multi-drug resistant organisms.

Key Words

Intra-abdominal Infections, Antibiotics, Microbiology, Bacteria

Introduction

Intra-abdominal infections (IAIs) include a wide variety of pathological conditions, ranging from cholecystitis to fecal peritonitis. In complicated IAIs, the infectious process proceeds beyond a single organ, causing either localized or generalized peritonitis.¹ Examples of complicated intra-abdominal infections are perforation of large or small intestine with abscess formation or fecal contamination and appendicitis complicated by perforation or abscess formation. Complicated IAIs are further classified into community-acquired intra-abdominal infections (CAIAIs) which are acquired in community, and healthcare associated intra-abdominal infections (HA-IAIs) which are acquired in hospitalized patients or residents of long-term care facilities. HA-IAIs are common and are usually associated with increased mortality, multi drugs resistant organisms and fungal infections.^{2,3}

Complicated IAIs can cause frequent hospital readmissions, reoperation or radiological interventions, increased length of hospital stay and increased cost of care.⁴ Mortality rates associated with complicated intra-abdominal infections range from 7% to up to 30% in different studies.^{5,6} Management of complicated IAIs include hemodynamic support, source control and early appropriate empirical antibiotics administration.² Surviving Sepsis Campaign Guidelines recommend administration of effective empirical intravenous antimicrobials having activity against all likely pathogens, within first hour of recognition of sepsis.⁷ Knowledge of prevalence of pathogens and local resistance patterns play key role in selection of empirical antibiotics.⁸

There is no data available from our country regarding prevalence and resistance patterns of organisms involved in complicated intra-abdominal infections. Hospital infection control surveillance reports and antibiograms report overall prevalence of organisms and their resistance patterns without clinical correlation. So objective of present study was to determine frequency of various organisms involved in complicated intra-abdominal infections and to find out their resistance patterns to guide selection of empirical antibiotics.

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Material and Methods:

We reviewed files of all adult patients who were admitted in the Aga Khan University Hospital (AKUH) Karachi Pakistan with diagnosis of complicated intra-abdominal infection from July 2012 to Jun 2015. Patients who did not have abdominal fluid culture or those who did not grow any organisms in cultures were excluded from analysis. Data was collected on a preformed questionnaire regarding demographics, source of infection, community acquired vs. healthcare associated infection, organisms reported and their resistance profiles. Infections were labeled as healthcare associated if acquired after at least 48 hours of hospitalization. Data was analyzed using SPSS version 19.⁹ Qualitative data was reported in percentages while quantitative data was reported as mean +/- SD. Chi Square test was used to test association between qualitative variables. P value of less than 0.05 was considered significant.

Results

Of the 317 patients included in the study, 211 (66%) were males and 116 (34%) were females. Mean age of patients was 50 +/- 18 years. Healthcare associated infections were present in 181 (57%) patients and community acquired infection was present in 127 (40%) patients. State of health care vs. community acquired could not be determined for 9 patients. Generalized peritonitis was present in 58 (18%) patients at the time of presentation. Post laparotomy cases accounted for 25% (79) of cases, while pancreas was source of infection in 20% of cases. Contribution by other sources of infection is given in table 1. Most common organisms involved were *E. Coli* and Enterococci infecting 56% and 28% of the patients respectively. Fungal growth was seen in 13% of cases. Pseudomonas infection and fungal infection were significantly more common in hospital acquired settings. Other organisms and their frequencies are given in table 2. Extended Spectrum Beta Lactamase (ESBL) producing *E. Coli* were 75% and ESBL producing Klebsiella Pneumoniae (*KPneumoniae*) were 54%. Carbapenem resistance in *K. Pneumoniae* was reported in 8% of isolates. Frequency of Vancomycin Resistant Enterococci was 13%. Detailed antibiotic sensitivity of various gram negative rods is reported in table 3. Analyzing antibiotic coverage of commonly used

Table 1. Source of Infection in Complicated Intra-abdominal Infections

Source of Infection	Number of Patients (317)	Percentage (100%)
Post Laparotomy	79	25%
Pancreas	64	20%
Large Bowel and Appendix	69	22%
Biliary Ducts	59	19%
Liver	35	11%
Gastro-duodenal and Small Bowel	18	6%

Table 2. Organisms involved in complicated intra-abdominal infections

Organisms Involved	Number of Patients (317)	Percentage (%)
Gram Negative Bacteria		
<i>E. Coli</i>	178	56%
<i>KlebsiellaPneumoniae</i>	48	15%
<i>Pseudomonas</i>	45	14%
<i>Enterobacter</i>	21	07%
<i>Acinetobacter</i>	15	05%
<i>Proteus</i>	16	05%
Other Gram Negatives	29	09%
Gram Positive Bacteria		
Enterococci	90	28%
Staph Aureous	23	07%
<i>Streptococcus Milleri</i>	17	05%
Other Streptococci	40	13%
Anaerobes		
<i>Bacteroids</i>	17	05%
<i>Clostridium</i>	1	0.3%
Fungal Infection		
Fungal Infection	32	13%
<i>Candida Albicans</i>	15	47%
<i>Candida Non-Albicans</i>	16	50%
<i>Aspergillus</i>	1	03%

Table 3. Percentage Sensitivity of Gram Negative Rods

Organisms	CTX	CTZ	CBP	PTZ	AKN	CIP	PMX
<i>E. Coli</i>	25.3	-	96.1	74.7	95.5	28.3	100
<i>K. Pneumoniae</i>	45.8	-	91.7	83.3	87.5	62.2	66.7
<i>Pseudomonas</i>	-	72.1	57.1	84.6	85.4	75.0	100
<i>Acinetobacter</i>	13.3	-	20.0	33.3	26.7	20.0	100

CTX: Ceftriaxone, CTZ: Ceftazidime, CBP: Carbapenems, PTZ: PiperacillinTazobactam, AKN: Amikacin, CIP: Ciprofloxacin, PMX: Polymyxin

antibiotics, we found that more than 90% of gram negative rods and anaerobes were covered by carbapenems alone as compared to less than 90% for piperacillin/tazobactam (pip/tazo) or amikacin if used alone. Coverage of combination of amikacin with pip/tazo or combination of amikacin with carbapenems was more than 90% against prevalent gram negative rods and anaerobes. Activity of pip/tazo against *Pseudomonas* (85%)

was better than carbapenems (57%), while in community acquired complicated IAIs combination of Carbapenems with amikacin had better coverage.

Discussion

Knowledge of common organisms encountered in various clinical situations and their resistance profile is necessary prerequisite to select appropriate empirical antibiotics. Lack of this information on one hand can result in inadequate antimicrobial coverage and resulting unsuccessful outcomes.^{10,11} While on the other hand, unnecessary broad antimicrobial coverage can result in antibiotics associated toxicities, acquisition of more resistant organisms and higher costs of treatment.¹² Extended spectrum beta lactamase (ESBL) producing enterobacteriaceae are becoming increasingly common in both community-acquired and hospital acquired infections worldwide.¹³ Reports also show that resistant to fluoroquinolones has increased over time in both *E. coli* and *K. Pneumoniae*.¹⁴ Our results also show increased prevalence of ESBL producing *E. Coli* and *K. Pneumoniae* but as compared to western data which reports prevalence to be 15-35% in *E. Coli* and 34 – 52% in *K. Pneumoniae*^{5,14}, it was 75% and 54% respectively in our study. Reported from India also showed comparable prevalence of ESBL producing *E.Coli* and *K. Pneumoniae* viz. 61 – 80% and 63 – 74% respectively.^{15,16} This shows regional trends of high prevalence of ESBL producing organisms. This is the reason that cephalosporins as empirical antibiotics in complicated intra-abdominal infections have gone out of favor worldwide.¹⁷

There is evidence of recent and rapid spread of serine carbapenemases especially in *Klebsiella Pneumoniae* Carbapenemase (KPC) and it has become an important concern when administering antimicrobial therapy in hospitals worldwide.¹⁴ Prevalence of carbapenem resistant *K. Pneumoniae* in western countries is 0.5-1%¹⁴ which in our study population turned out to be 8%. Studies from India report it to be from 20-30%.^{15,16} Thus though there is regional trend of high resistance of *K Pneumoniae* to carbapenems, our study population profile is still better than neighboring country. Irrational use of antibiotics could be the underlying cause of higher resistance profiles in resource constrained countries.

Antibiotic coverage against Enterococci in intra-abdominal infections is not routinely recommended. But in specific clinical conditions like critically ill patients and healthcare associated infections, coverage against Enterococci may be required. Antibiotic coverage against Enterococci infections pose challenge due to both intrinsic and acquired resistance to many antibiotics. Our study showed prevalence of Vancomycin Resistant Enterococci (VRE) to be 11% which is similar to those reported from Europe and India i.e. 10% and 12% respectively.^{5,15} Our study showed fungal infection in up to 13% of patients which is almost double as compared to reported frequencies (7%) in

complicated intra-abdominal infections.¹⁸

Literature guidelines for management of complicated intra-abdominal infection, including those from Surgical Infection Society (SIS) and the Infectious Diseases Society of America (IDSA)¹⁹ and 2013 WSES guidelines²⁰ have made evidence based recommendations for empirical antimicrobial coverage in intra-abdominal infections. These guidelines recommend administration of either single agent (Carbapenems or Pip/Tazo) or combination of antibiotics (metronidazole with ciprofloxacin or co-amoxiclav) as empirical coverage in intra-abdominal infections. While analyzing these recommendations for our study population, we found inadequate coverage by Pip/Tazo alone. Though Carbapenems alone had adequate coverage for community acquired IAIs, combination of Amikacin with Carbapenems had even better coverage. For HA-IAIs pip/tazo in combination with amikacin can be 1st line empirical therapy in patients high risk for *Pseudomonas* infection. There is no recommendation of empirical antifungal therapy. In view of higher prevalence of fungal infections in our study population, further research is needed to evaluate need of empirical antifungal therapy in critically ill patients in our region. Fluconazole covers 98% of candidal species and can be used as empiric antifungal agent in critically ill patients.²¹

Conclusion

This study identifies higher resistance profile of microorganisms in complicated intra-abdominal infections in our country. These results can be employed for appropriate selection of empirical antibiotics in complicated IAIs. Presuming irrational use of antibiotics as the underlying factor for relatively higher prevalences, antibiotic stewardship program needs to be applied in hospitals.

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Septic Abortion due to *Streptococcus pneumoniae*: a rarity - Case report

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Abstract

It is very rare to find *Streptococcus pneumoniae* causing septic abortion. This case report describes a case of septic abortion attributed to *S. pneumoniae*. The pathogen was isolated from high vaginal swab and blood cultures of the patient. The patient was treated successfully and discharged in stable condition. This case report highlights the significance of pneumococcus in septic abortion and emphasizes upon microbiology laboratory personnel the importance of correlating cultures with clinical findings of patients.

Key words

case report, septic abortion, *Streptococcus pneumoniae*

Introduction

Streptococcus pneumoniae is a gram positive, capsulated, lancet shaped diplococcus. It causes serious infections of various organ systems including, pneumonia, bacteremia, sepsis and meningitis, which may be life threatening. On rare occasions, it may be isolated from unusual sites such as causing necrotizing fasciitis and deep seated abscesses of different organs e.g. spleen, liver, pancreas, brain and others.¹⁻³ *S. pneumoniae* causing septic abortion is very rare. Literature review identifies only a few cases of septic abortion caused by *S. pneumoniae*.^{4,5} Here we report a case of *S. pneumoniae* septic abortion, a rare presentation.

Ethical Review

The study was provided an exemption of ethical approval by the Institutional Ethical Review Committee.

The Case Report

A 31-year-old woman, gravida 8, para 6+1, at 11 weeks gestation, presented in emergency department in November 2013 in our hospital with lower abdominal pain and fever for 24 hours. She also had off and on vaginal bleeding for 17 days. She did not have symptoms related to urinary, bowel, respiratory systems. There was no sore throat or ear infection or any other systemic illness. Patient denied history of intervention or attempt for induced miscarriage.

On examination, she was febrile (38°C), pulse was 115beats/min, respiratory rate 22/min and blood pressure 110/63mmHg. There was no ear discharge or neck rigidity and chest examination was normal. Abdomen was soft but she had diffuse tenderness in lower abdomen. Per speculum examination revealed brownish discharge and a high vaginal swab was taken for culture. On bimanual examination, uterus was 12 weeks size, cervical os was closed, tenderness on cervical excitation was positive and no adnexal mass was felt.

Her baseline investigations and septic workup were sent. Complete blood count report showed haemoglobin 10.1 g/dl and WBC count 11,500 /mm³ (normal range: 4000-10000) with 90% polymorphonuclear leukocytes. Her CRP was 3.6 mg/dL (normal range: 0-0.5) on admission. Pelvic ultrasound showed a single intrauterine fetus with crown rump length of 2.8 cm, corresponding to 9 weeks and 4 days, cardiac activity was absent and there was no perigestational sac abnormality.

On the basis of clinical presentation and laboratory work up, provisional diagnosis of septic abortion was made. She was started on broad spectrum intravenous antibiotic (piperacillin-tazobactam). Medical termination of pregnancy was attempted but was not successful. Her CRP rose to 12.9 mg/dL in 48 hours. She underwent dilatation and evacuation at 72 hours of starting her on antibiotics. Evacuated material was sent for histopathology which confirmed it as products of conception.

Blood cultures grew *Streptococcus pneumoniae* (penicillin minimum inhibitory concentration: 0.03 µg/ml). Antibiotics were de-escalated to ceftriaxone and metronidazole. High vaginal swab taken on admission showed heavy growth of *S. pneumoniae* with the same sensitivity as that of blood isolate. Products of conception were also sent for culture but did not yield any growth. Patient recovered fully and discharged home in a stable condition.

Despite all the advances in the field of medicine, *S. pneumoniae* still remains a major pathogen causing high morbidity and mortality and may be isolated from unusual sites.

It is very rare for *S. pneumoniae* to cause septic abortion. Literature shows very few cases of septic abortion due to *S. pneumoniae*.^{4,5} In postpartum women, peritonitis, endometritis and tuboovarian abscess caused by pneumococcus have been

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described.⁶⁻⁸ *S. pneumoniae* is usually not a part of normal vaginal flora but it may be found in low numbers as a transient colonizer without causing disease. People at risk of getting pneumococcal infection include those with chronic medical conditions (hepatic, heart & renal failure), asplenia, steroids, immunoglobulin & complement deficiency, neutropenia or neutrophil functional defects, malnutrition, alcoholism and history of gynecological instrumentation.⁹ None of these were found in this patient. *S. pneumoniae* possesses several virulence factors that enable it to cause disease. These include polysaccharide capsule (prevents opsonization and phagocytosis), IgA protease (cleaves immunoglobulin A), pneumolysin (cytotoxic, activates complement), autolysin (causes bacterial disintegration and release of pneumolysin) and pneumococcal surface proteins A & C (inhibit phagocytosis) among others.⁹ The fine balance between microbial virulence (affected by absolute number of that pathogen), host immune system and the presence of other microflora determines the ability of a pathogen to cause disease.¹⁰ Here we suggest that this case represents an ascending infection of the reproductive tract since there were no localizing signs for other organ systems. Literature shows a similar case report of a septic abortion caused by pneumococcus where source of infection was presumed to be uterine in origin.

In our patient, *S. pneumoniae* infection resulted in septic abortion. Obstetrical procedures and septic abortion are associated. This patient did not have prior history of intervention or illness. *S. pneumoniae* was isolated from blood culture and also from high vaginal swab in almost pure culture. However, *S. pneumoniae* was neither observed on Gram stain of products of conception nor isolated from its culture. This is most likely due to the fact that patient had been receiving antibiotics for

the last 72 hours before dilatation and evacuation was performed.

Conclusion

This case illustrates a rare presentation of *S. pneumoniae* infection. Though rare, but *S. pneumoniae* may be isolated from high vaginal swab and if the growth is predominant, it should not be disregarded. An attempt must be made to clinically correlate its significance.

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Instructions to Authors

Scope

The Infectious Diseases Society of Pakistan sponsors the Infectious Disease Journal of Pakistan (IDJ). The Journal accepts Original Articles, Review Articles, Brief Reports, Case Reports, Short Communications, Letter to the Editor and Notes and News in the fields of microbiology, infectious diseases, public health; with laboratory, clinical, or epidemiological aspects.

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Manuscripts must be formatted according to submission guidelines given below, which are in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (originally published in *N Engl J Med* 1997;336:309-15). The complete document appears at www.icmje.org. Please submit one complete copy of the manuscript and all enclosures to **The Managing Editors, Infectious Diseases Journal of Pakistan, Department of Pediatrics & Child Health, The Aga Khan University, Stadium Road, P.O. Box 3500, Karachi 74800, Pakistan**. An electronic copy of the manuscript must also be sent to pak_idj@yahoo.com. All manuscripts submitted to IDJP must be accompanied by an Authorship Declaration stating that '*The authors confirm that the manuscript, the title of which is given, is original and has not been submitted elsewhere. Each author acknowledges that he/she has contributed in a substantial way to the work described in the manuscript and its preparation*'. Upon submission a manuscript number will be assigned which should be used for all correspondence.

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Abstract should not exceed 250 words and must be structured in to separate sections headed *Background, Methods, Results and Conclusions*.

Please do not use abbreviations or cite references in the abstract. A short list of four to five key words should be provided to facilitate.

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The section must clearly state the background to the research and its aims. Controversies in the field should be mentioned. The key aspects of the literature should be reviewed focusing on why the study was necessary and what additional contribution will it make to the already existing knowledge in that field of study. The section should end with a very brief statement of the aims of the article.

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Please provide details of subject selection (patients or experimental animals). Details must be sufficient to allow other workers to reproduce the results. The design of study and details of interventions used must be clearly described. Identify precisely all drugs and chemicals used, including generic name(s) and route(s) of administration. All research carried out on humans must be in compliance with the *Helsinki Declaration*, and animal studies must follow internationally recognized guidelines. The authors are expected to include a statement to this effect in the Methods section of the manuscript. A description of the sample size calculation and statistical analysis used should be provided.

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Present results in logical sequences in the text, tables and illustrations. Articles can have a maximum of 5 illustrations (in a combination of figures and tables) per article. The results should be in past tense and repetition of results presented in the tables should be avoided. Exact *P*-values should be reported along with reporting of OR and RR with their Confidence Intervals where applicable.

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Emphasize the new and important aspects of the study and conclusions that follow from them. Do not repeat the details from the results section. Discuss the implications of the findings and the strengths and limitations of the study. Link the conclusions with the goals of the study but avoid unqualified statements and conclusion not completely supported by your data.

Acknowledgments

Acknowledge any sources of support, in the form of grants, equipment or technical assistance. The source of funding (if any) for the study should be stated in this section. Please see below for format of **References, Figures and Tables**.

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Authoritative and state of the art review articles on topical issues are also published, with a word limit of 2000. It should consist of critical overview of existing literature along with reference to new developments in that field. These should be comprehensive and fully referenced. Articles should contain an Abstract; Main Text divided into sections, Conclusions and References.

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Short clinical and laboratory observations are included as Brief Reports. The text should contain no more than 1000 words, two illustrations or tables and up to 10 references.

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Announcements of conferences, symposia or meetings may be sent for publication at least 12 weeks in advance of the meeting date. Details of programs should not be included.

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Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by Arabic numerals (in superscript). References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification of the particular table or illustration. Bibliography should be given in order. Authors, complete title, journal name (Abbr), year, vol, issue, page numbers. According to "Uniform

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Illustrations should be numbered, given suitable legends and marked lightly on the back with the author's name and the top edge indicated. Original drawings may be submitted although high quality glossy photographs are preferable. They should be kept separate from the text. If possible, figures should be submitted in electronic format as either a TIFF (tagged image file format) or JPEG format. Minimum resolution for scanned artwork is:

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Those who have contributed sufficiently to the conceptualization, design, collection and analysis of data and writing of the manuscript should be granted authorship. Ideally all authors should be from the same department except for studies that are multi center or multispecialty.

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