Original Article

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ACTIVE SURVEILLANCE FOR ASYMPTOMATIC COLONIZATION WITH MULTI-DRUG RESISTANT GRAM-NEGATIVE BACILLI IN PRE-OPERATIVE PAEDIATRIC CONGENITAL CARDIAC DISEASE PATIENTS; PRELIMINARY RESULTS

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ABSTRACT

Objective: To carry out active surveillance for Gram negative Multi drug resistant Bacilli in pre-operative congenital heart disease patients.

Study Design: Prospective cohort study.

Place and Duration of Study: This study was conducted at Department of Paediatric Cardiac Surgery AFIC-NIHD, Rawalpindi from 1st Jan 2015 to 28th Feb 2015.

Methodology: It is an ongoing study, but a preliminary analysis has been conducted on a sample size of 50 patients. Informed consent was taken from patient's parents before sample collection. Samples included throat and rectal swabs which were processed for culture and antibiotic sensitivity of gram negative bacilli isolated.

Results: A total of 14 (28%) patients were identified who were colonized with Multi drug resistant gram negative bacteria (MDR-GNB). Nine isolates were ESBL producers. None of the strains showed Carbapenem resistance. Isolated MDR-GNB were *Escherichia* coli (n=10), Proteus species (n=01), *Acinetobacter* species (n=1) and *Klebsiella pneumoniae* (n=02).

Conclusion: The presence of MDR GNB in preoperative paediatric patients addresses the need for antibiotic stewardship programmes and judicious use of antimicrobials in community based settings.

Keywords: Gram negative bacilli (GNB), Multi drug resistance (MDR), Pre-operative.

INTRODUCTION

Multi drug resistant (MDR) gram- negative infections (resistance to three or more than three groups of antibiotics)are associated with increased length of hospital stay, mortality and colossal hospital costs in comparison with infections due to susceptible gram negative bacilli (GNB)[1,2]. Injudicious antibiotic use has been associated with MDR gram-negative infections[3]. MDR GNB infection is also associated with resistance of endogenous flora attained as a result of antibiotic pressure or transmission of resistant GNB from the hospital environment[4]. The aim of this study is to determine the frequency of paediatric congenital heart disease pre-operative patients colonized with MDR GNB in our set-up.

PATIENTS AND METHODS

This Prospective cohort study is being conducted at Department of Paediatric Cardiac Surgery AFIC-NIHD, Rawalpindi in collaboration with Pathology Department AFIC NIHD. Patients undergoing congenital Cardiac Surgery less than 18 years of age are included in this ongoing study. Patients who have length of stay greater than 3 days in current admission were excluded. A preliminary analysis has been conducted on a sample size of 50. The study was approved by the Institutional Ethical and Review Board AFIC/NIHD. Formal approval and informed consent was taken from the parents before sample collection. An especially designed data collection form was used for data collection which included patient demographics, history of prior hospital admissionand use of antibiotics. Saline moistened throat and rectal swabs were taken and cultured on blood and MacConkey's agar (Oxoid UK). Gram negative bacilli identified on Gram staining, if yielded were identified using API 20NE (Biomerieux, France). Antimicrobial susceptibility testing was carried out on Mueller-Hinton Agar (Oxoid, UK) by using modified kirby-Bauer disc diffusion technique as per CLSI 2014 criteria[5]. The production of Extended spectrum beta lactamase (ESBL) was

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detected phenotypically by using double disc synergy test using a susceptibility disk (Oxoid UK) containing amoxicillin-clavulanate (20/10 ug), placed in the center of the plate, and disks containing oxyimino-β-lactam the standard ceftazidime (30 ug), ceftriaxone (30 mg), aztreonam (30 mg) or cefpodoxime (10 mg) are placed 20 mm (center to center) from the amoxicillin-clavulanate disk. Plates were then incubated overnight at 35 ± 2°C. Positive result was indicated when the inhibition zones around any of the cephalosporin discs was augmented in the direction of the disc containing clavulanic acid[6].

The data was entered and analyzed in SPSS version 21 (IBM). Frequencies and percentages were calculated for qualitative variables while mean and standard deviation (SD) were calculated for quantitative variables. Statistical significance between various variables was analyzed using Fisher's Exact Test with a *p* value of <0.05 considered as statistically significant.

RESULTS

Active surveillance of MDR-GNB is an ongoing study. This is a preliminary analysis of 50 patients who were assessed as per inclusion criteria from 1st Jan 2015 to 28th Feb 2015. The mean age of the patients was 4.5 ± 2.21 yrs. Out of 50 patients 34 (68%) were Male and 16 (32%) were female.

A total of 14 (28%) patients were identified, who were colonized with Multi drug resistant gram negative bacteria (MDR-GNB). As shown in fig no.1, 13 (26%) isolates were rectal and 1(2%) from throat, 9 (64.2%) were ESBL producing all were isolated from rectal swabs. None of the strains showed Carbapenum resistance. Isolated MDR-GNB were Escherichia coli (n=10), Proteus species (n=01), Acinetobacter species (n=01) and Klebsiella pneumoniae (n=02).

Table-1: Correlation of Patients history with MDR-GNB colonization.

History of Patients having colonization of MDR-GNB	MDR-GNB	*p*-value*
H/o Previous Hosp admission n=10	4(40%)	0.643
Use of Antibiotics in last month n=15	6(40%)	0.243
Use of Antibiotics at the time of admission n=45	18(40%)	0.340
Chest Infection at the time of admission n=7	1(14.2%)	0.357
Fever at the time of admission n=6	2(33.3%)	0.510

*Fisher's exact test

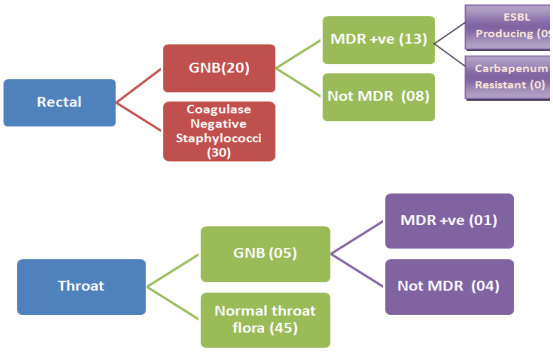

Figure-1: Presence of MDR-GNB in rectal and throat.

Table-2: Antibiogram of multi drug resistant gram negative bacteria n=14.

Antibiotics	Resistant	Sensitive
Trimethorprim sulfamethoxazole	11	03
Minocycline	04	10
Gentamycin	06	08
Amikacin	03	11
Ciprofloxacin	07	07
Cefotaxime	05	09
Ceftriaxone	05	09
Colistin	01	13
Imipenum cilastatin	0	14
Meropenum	0	14
Cefoperazone/ Sulbactum	2	12
Piperacillin/ Tazobactum	3	11

10 (20%) Patients had history of previous hospital admissions, out of which 3(30%) were colonized with MDR-GNB. 14% (n=7) and 12% (n=6) had chest infection and fever at the time of admission respectively all of whom were receiving antibiotics at time of admission. 30%

(n=15) patients had history of antibiotic usage prior to congenital cardiac surgery, and 90% (n=45) patients were given antibiotics at the time of admission. Previous history of fever, antibiotic usage, hospital admissions and other infections was not significantly associated with MDR-GNB colonization as shown in Table1 (P values >0.05). Majority of the MDR GNB were susceptible to Carbapenums and Colistin as shown in Table-2.

DISCUSSION

Patients in pediatric intensive care Units (PICU) are prone to develop infections with MDR organisms. A retrospective cohort study by Siddiqui et al shows increased rates of carbapenem resistant gram negative isolates in children admitted in the intensive care unit[7]. Although all the MDR isolates were resistant to Cephalosporins in our preliminary analysis; so far, none of the isolates are resistant to Carbapenums. Due to increased colonization and infection by multidrug-resistant gram-negative bacilli (MDR GNB), many military hospitals in USA the have instituted infection control processes inclusive of active surveillance cultures detection of MDR GNB colonization[1].

Predominantly MDR *Klebsiella pneumonia, Escherichia coli* and Acinetobacter species have been implicated in colonization[3].

Extended Spectrum β-lactamases (ESBLs) convey resistance to all penicillins, Cephalosporins and Monobactams[6]. More than 50% of the MDR GNB isolates in our study were ESBL producers in contrast to the findings of Villar et al, who detected 18.9% ESBL producers from faecal samples in Argentina which was a community based setting, and 4.9% Carbapenem - resistant GNB were isolated[8]. In another large multicenter study of hospitalized paediatric patients in France, most of the MDR GNB isolates were Enterobacter cloacae and Escherichia coli with a prevalence of ESBL producing GNB being 5.2% mostly isolated from younger children consistent with our findings[9]. A high prevalence of ESBL GNB colonization has also been reported in Spain[10].

Although this is a preliminary analysis and the sample is limited, no statistically significant association was found with history of previous hospital admission unlike the findings of Patel et al who demonstrated multiple MDR GNB colonizations associated with previous hospital stays in paediatric patients[11]. The sensitivity of surveillance cultures of ICU pateints for MDR GNB in detecting positive clinical cultures for MDR GNB has been reported as 58.8% (95% confidence interval, 48.6 to 68.5%)[12].

The injudicious use of broad-spectrum antibiotics even in community settingspaucity of antibiotic stewardship and lack of adherence to antibiotic policies in hospitals has led to increased prevalence of MDR GNB[13]. Major risk factors associated with MDR GNB colonization include older age, hospital admission and antibiotic usage within the last three months and presence of medical devices like Central venous catheters, urinary catheters and mechanical ventilation[13,14]. The presence of colonization with MDR GNB in this paediatric sample advocates the need for further population based studies to determine the actual burden of MDR GNB in the community. Usage of amoxycilllin-clavulanic acid and prolonged hospitalization were significantly associated with carriage of Carbapenemase resistant enterobacteriacae and majority of the isolates were producing ESBL in Pakistan[15]. NDM1 enzyme conferring Carb-apenum resistance and a forerunner for pan drug resistance has also been reported from Pakistan; mostly from commensal Escherichia coli[16].

CONCLUSION

The presence of MDR GNB in pre-operative paediatric patients addresses the need for antibiotic stewardship programmes, judicious use of antimicrobials in community based settings, hand hygiene compliance and use of risk based contact precautions to prevent cross infection.

Conflict of Interest

This study has no conflict of interest to declare by any author.

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