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ANALYSIS OF DISTRIBUTION AND RESISTANCE OF ANTIBIOTIC TO PATHOGENS ISOLATED FROM THE PEDIATRIC PATIENTS

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Abstract:
Aim: *The aim of the study was to investigate the epidemiology and changes in children's sensitivity to antibacterial drugs, and to lay the foundations for rational drug use.*
Place and Duration: *In the Department of Pediatrics Unit-II of Holy Family Hospital, Rawalpindi and POF Hospital Wah Cantt for three-year duration from November 2017 to October 2020.*
Methods: *The distribution and pattern of drug resistance of pathogenic bacteria isolated from children were analyzed retrospectively.*
Results: *A total of 573 strains of pathogens were grown. A total of 201 (35.07%) strains of gram-positive cocci and 183 (31.93%) strains of gram-negative cocci were detected. A total of 189 (32.98%) fungal strains were detected. The Staphylococcus resistance rate to penicillin was 100% and to erythromycin 90.69%. There were varying degrees of resistance to other drugs, but no single strain showed resistance to vancomycin. Gram-negative rods were generally resistant to ampicillin, but showed low resistance to complex preparations of enzyme inhibitors, quinolones and aminoglycosides, and were very sensitive to imipenem and meropenem.*
Conclusion: *Gram-negative rods are the main pathogens of bacterial infections in the pediatric ward. Enhancing the monitoring of the clinical distribution of bacteria in pediatric clinical isolates and understanding changes in drug resistance are important to guide rational use of antibiotics. These measures can also prevent the emergence and spread of resistant strains.*
Key words: *epidemiology, pattern of drug resistance, isolated pathogenic bacteria.*

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INTRODUCTION:

Antimicrobial resistance is the ability of a microorganism (e.g, bacteria, viruses, and some parasites) to suppress an antimicrobial effect (eg, antibiotics, antiviral, and antimalarial). As a result, standard treatments become ineffective, infections persist, and infections can become serious and can spread to other people as well [1-2]. Antimicrobial resistance is an internationally documented health risk. Bacterial infections that are resistant to antibiotics can limit the availability of effective treatment options, making some common bacterial infections difficult to treat [3-4]. Antibiotic-resistant infections are also twice as likely to suffer from morbidity and mortality, and are associated with increased healthcare costs. Antibiotics play a key role in treating bacterial infections, and children receive them more often than other medications. However, the inappropriate and unnecessary use of antibiotics in recent decades has increased the emergence of resistant bacterial strains. Children receive many primary care services and, as such, receive too many antibiotics compared to middle-aged populations [5-6]. Children are also the main causes of infection in communities and can contribute to the human-to-human transmission of bacteria. Nearly 80% of childhood urinary tract infections in poorer countries are resistant to amoxicillin and 60% to amoxiclav. More than a quarter of children are resistant to ciprofloxacin (Cipro) and 17% to nitrofurantoin [7-8]. All of the above-mentioned factors require clinicians to be responsible for the proper diagnosis and treatment of affected children as soon as possible to avoid unnecessary disability and death. Despite this, few studies have been published describing the microbial spectrum and the antimicrobial resistance profile of bacteria in pediatric patients in Pakistan. Therefore, it is imperative to understand the pathogens and antibiotic resistance associated with pediatric infections in our hospital and surrounding regions. In this study, we selected clinical data from patients admitted to the Pediatric Department for a retrospective analysis of bacterial species distribution and changes in drug resistance [9-10]. The purpose of this study was to determine the profile and susceptibility patterns of bacterial pathogens associated with infections in children.

MATERIALS AND METHODS:

This study was held in the Department of Pediatrics Unit-II of Holy Family Hospital, Rawalpindi and POF Hospital Wah Cantt for three-year duration from November 2017 to October 2020. Pathogens were isolated from samples taken from all children admitted to the hospital. A total of 573 strains were isolated from 419 males and 154 females. The isolation and cultivation of the bacteria was performed according to the "National Guidelines for Clinical Practice". The bacteria were identified using the VITEK-2 automated bacteria analyzer, identification system and manual method.

In order to test the drug susceptibility, a fully automatic instrument for identifying bacteria VITEK - 2 MIC and the K-B diffusion method (Kirby Bauer) Paper Slice were used. Absorbent paper disks impregnated with an antibacterial agent are provided. Test methods and criteria were performed in accordance with the latest standards of the Clinical and Laboratory Institute. The choice of antimicrobials was as follows: penicillin (10 U), ampicillin (10 mg), piperacillin (100 mg), oxacillin (1 mg), ampicillin / sulbactam (10 mg / 10 mg), amoxicillin (20 mg / 10 mg)), cefoperazone / sulbactam (75 mg / 30 mg), cefazolin (30 mg), cefuroxime (30 mg), cefotaxime (30 mg), amikacin (30 mg), gentamicin (10 mg), high concentration of gentamicin (120 mg)), ciprofloxacin (5 mg), vancomycin (30 mg), erythromycin (15 mg), clindamycin (15 mg), meropenem (10 mg), imipenem (10 mg), sulfamethoxazole / trimethoprim (1.25 mg / 23.75 mg) and aztreonam (30 mg). Mueller-Hinton media was used for drug susceptibility testing. M-H agar supplemented with 5% defibrinated sheep blood was used to determine the susceptibility of Streptococcus pneumoniae, Streptococcus pyogenes and other Streptococcus spp. Hemophilus spp. Were used as a supplement to the basic culture medium for Hemophilus influenzae. Beta-lactamase strains with extended spectrum were confirmed by the double disc method. The antimicrobials used were cefotaxime / clavulanic acid (30 mg / 10 mg) and ceftazidime / clavulanic acid (30 mg / 10 mg), both provided by the hospital. The VITEK-2 identification system software was used to analyze and process all original test data. IBM Statistics SPSS 21 Premium (Chicago, IL, USA) and GraphPad Prism 6 (La Jolla, CA, USA) were used for statistical analysis.

RESULTS:

573 strains of pathogens were isolated from 73.2% (419) men and 26.8% (154) women. The Fisher - Irwin test showed a significant difference in the number of isolates between the sexes (2¼ 246.514, p <0.0001). When we divided this period into three quantum zones of 20 months each, we found that the percentage of male children was increasing steadily over time (Kruskal - Wallis 2¼ 25.20, P <0.01). A total of 73 (12.8%) children were under 28 days of age, 254 (44.4%) were aged between 29 days and 1 year, 124 (21.6%) were aged 1 to 3 years, 67 (11.7%) were

between 3 and 6 years of age and 55 (9.6%) were older than 6 years. The mean length of hospital stay was 6 days, and the mean standard deviation was 7.8 - 4.0 days (Table 1).

Table 1. Demographic representation of the isolated pathogens.

	Jan 2017 to Aug 2018	Sept 2018 to April 2019	May 2019 to Nov 2020	Total
Children, n (%)	82 (14.3)	194 (33.8)	297 (51.8)	573 (100)
Males, n (%)	58 (70.7)	140 (72.3)	221 (74.5)	419 (73.2)*
Age group, n (%)				
Age 28 days	7 (8.5)	21 (10.7)	45 (15.2)	73 (12.8)
29 days to 1 year	31 (38.0)	95 (48.5)	128 (43.4)	254 (44.4)
1 to 3 years	16 (19.1)	37 (18.9)	71 (24.1)	124 (21.6)
3 to 6 years	13 (15.8)	21 (11.0)	33 (11.0)	67 (11.7)
>6 years	15 (18.8)	21 (10.8)	19 (6.1)	55 (9.6)
Hospital stay (days)				
Median (interquartile range)	6 (7–9)	5 (7–8)	5 (7–8)	6 (4–8)
Mean standard deviation	(7.8 4.0)	(7.2 3.5)	(2.5 3.2)	(6.8 3.8)

The distribution of the pathogens included 285 respiratory samples, 68 blood samples, 26 CSF samples, 24 urine samples, and 11 stool samples (Table 2).

Table 2. Composition ratio of pathogen specimens.

Specimens	Strains, n	%
Respiratory	285	49.80*
Blood	68	11.90
Cerebrospinal fluid	26	4.50
Urine	24	4.20
Faeces	11	1.90
Wound secretions	14	2.40
Eye exudates	17	2.97
Other	128	22.20
Total	573	100.00

The distribution of pathogens by the different samples is shown in Table 3.

Pathogens	Total n	Respiratory tract n (%)	Urine n (%)	Blood n (%)	CSF n (%)	Stool n (%)	Others n (%)
Escherichia coli	57	29 (50.8)	8 (14.0)	10 (17.5)	2 (3.5)	3 (5.2)	5 (8.7)
Klebsiella pneumoniae	42	32 (76.2)	1 (2.3)	4 (9.5)	–	3 (7.1)	2 (4.7)
Acinetobacter spp.	12	10 (83.3)	–	1 (8.3)	–	–	1 (8.3)
Pseudomonas aeruginosa	12	6 (50)	–	2 (16.6)	–	–	4 (33.3)

Enterobacter cloacae	16	14 (87.5)	–	–	–	2 (12.5)	–
Staphylococcus aureus	16	5 (31.2)	–	3 (18.7)	–	–	8 (50)
CoNS	30	8 (26.6)	2 (6.6)	9 (30)	7 (23.3)	–	4 (13.3)
Staphylococcus haemolyticus	27	8 (29.5)	5 (18.5)	8 (29.6)	–	–	6 (22.2)
Streptococcus pneumoniae	9	4 (44.4)	–	1 (11.1)	3 (33.3)	–	1 (11.1)
Streptococcus pyogenes	11	10 (90.9)	–	–	–	–	1 (9.1)
Other streptococci	71	43 (60.5)	–	19 (26.7)	–	–	9 (12.6)
Enterococcus	17	4 (23.5)	2 (11.7)	5 (29.4)	4 (23.5)	–	2 (11.7)
Fungus (yeast-like fungi þ Candida albicans)	189	73 (38.6)	–	–	5 (2.6)	1 (0.5)	110 (58.2)
Other non-fermenting bacteria	24	17 (70.8)	3 (12.5)	2 (8.3)	–	2 (8.3)	–
Others	40	22 (55)	3 (7.5)	4 (10)	5 (12.5)	–	6 (15)
Total	573	285	24	68	26	11	159
Lower 95% CI of the mean		8.515*	0.296	1.672*	0.385	0.089	4.709
Upper 95% CI of the mean		29.484	2.903	7.394	3.081	1.377	25.909

Among macrolides, the rate of erythromycin resistance was> 80%, but no vancomycin-resistant staphylococci were found (Table 4).

Table 4. Resistance of Gram-positive bacteria to commonly used antimicrobial agents.

Antibiotics	Staphylococcus aureus		Staphylococcus haemolyticus		Streptococcus pyogenes		Streptococcus pneumoniae (N_T¼ 16)		(N_T¼ 27)	
	N_A	R/R (%)	N_A	R/R (%)	N_A	R/R (%)	N_A	R/R (%)	N_A	R/R (%)
Penicillin	15	100	25	100	9	77.78	6	33.33		
Erythromycin	16	81.25	27	96.30	11	100	8	100		
Clindamycin	16	81.25	27	88.89	8	87.5	6	83.33		
Rifampicin	16	56.25	27	77.78	9	11.11	5	0.00		
Vancomycin	16	100	27	100	10	0.00	7	0.00		
Tetracycline	15	80.00	25	80.00	–	–	–	–		
Oxacillin	15	33.33	25	100	–	–	–	–		
Cefoxitin	11	27.27	21	100	–	–	–	–		
Linezolid	14	0.00	18	100	–	–	–	–		
Cotrimoxazole	12	50.00	25	20.00	4	50.00	–	–		
Nitrofurantoin	16	0.00	25	0.00	–	–	–	–		
Levofloxacin	16	25.00	27	74.07	7	14.29	5	0.00		
Moxifloxacin	15	6.67	25	56.00	–	–	–	–		
Gentamicin	16	43.75	27	85.19	–	–	–	–		
Piperacillin/tazobactam	10	20.00	20	100	–	–	–	–		
Cefuroxime	–	–	–	–	9	33.33	7	14.29		

Pseudomonas aeruginosa resistance to levofloxacin, gentamicin, amikacin, imipenem and meropenem was <10%, while its resistance to piperacillin / tazobactam was 30%. Escherichia coli was not resistant to imipenem and meropenem (Table 5).

Table 5. Resistance of Gram-negative bacteria to commonly used antimicrobial agents.

Antibiotics used per specimen	Escherichia (N_T¼ 42)		Klebsiella pneumoniae spp. (N_T¼ 12)		Acinetobacter (N_T¼ 16)		Enterobacter cloacae (N_T¼ 12)		Pseudomonas aeruginosa coli (N_T¼ 57)	
	N_A	R/R (%)	N_A	R/R (%)	N_A	R/R (%)	N_A	R/R (%)	N_A	R/R (%)
Levofloxacin	49	57.14	37	5.41	12	0.00	14	0.00	11	0.00
Gentamicin	54	38.89	42	35.71	12	0.00	14	14.29	10	0.00
Imipenem	51	0.00	38	0.00	12	0.00	14	0.00	11	0.00
Meropenem	51	0.00	42	7.14	–	–	14	0.00	11	0.00
Ampicillin	48	85.42	38	97.37	12	100	4	100	11	100
Cefazolin	52	75.00	42	61.90	12	100	14	100	11	90.91
Cefuroxime	48	75.00	38	57.89	12	91.67	14	71.43	11	90.91
Ceftazidime	49	69.39	38	52.63	12	8.33	14	35.71	10	0.00
Cefotaxime	36	72.22	26	38.46	10	100	10	10.00	5	100
Ceftriaxone	53	69.81	42	57.14	12	91.67	14	35.71	10	90.00
Cefepime	52	67.31	42	54.76	12	0.00	14	35.71	11	0.00
Amikacin	48	4.17	38	5.26	–	–	14	7.14	11	0.00

Piperacillin/tazobactam	54	37.04	42	7.14	12	8.33	14	14.29	10	30.00
Aztreonam	53	66.04	42	57.14	12	91.67	14	35.71	5	0.00
Nitrofurantoin	50	8.00	37	75.68	12	100	14	85.71	11	90.91
Cefotetan	48	45.83	38	26.32	12	91.67	14	100	11	90.91
Piperacillin	50	84.00	38	97.37	12	8.33	14	42.86	11	27.27
Cefoperazone/sulbactam	50	10.00	38	11.23	–	–	8	100	–	–

DISCUSSION:

Coal mining caused severe smoke-laden air pollution, which worsened air quality. This caused a huge increase in respiratory infections in hospitalized children. There is an upward trend in annual pathogen detection, but the overall number of pathogens detected during the year has decreased [9-10]. Our study showed that the main pathogens of infection in children were gram-positive bacteria, accounting for 35.07%, while gram-negative bacteria accounted for 31.93% and fungi accounted for 32.98%. These numbers of infected pathogens are consistent with the majority of national reports. The predominance of Gram-negative bacteria in nosocomial infections is likely due to the fact that patients are treated with antibacterial agents prior to admission to hospital [11-12]. In addition, in many individual clinics, allergy tests are not performed, and therefore macrolides are used, the main spectrum of antimicrobial activity of which is gram-positive bacteria. This results in a low detection rate for gram-positive bacteria, while gram-negative bacteria have become the dominant pathogen study in hospitalized patients. Our study found that the detection of coagulase-negative staphylococcal infection was the highest of any nosocomial infection, with a detection rate much higher than that of other bacteria. This finding is in line with previous research. The pathogenicity of coagulase negative staphylococci is lower than that of golden staphylococcus. However, immunocompromised patients may still be infected, especially increasing resistance to these strains (e.g. methicillin-resistant coagulase negative staphylococci), suggesting that coagulase negative staphylococci are an important pathogen of nosocomial infections. Our study showed that the susceptibility of Escherichia coli to amikacin, cefoperazone / sulbactam and nitrofurantoin was> 90.0% [13]. The susceptibility of Klebsiella pneumoniae to fluoroquinolones and amikacin was> 92.0%. Pseudomonas aeruginosa was 100% sensitive to ceftazidime, cefepime, amikacin, fluoroquinolone and aztreonam. Enterobacter cloacae was also very sensitive to fluoroquinolones, cefoperazone / sulbactam, cefotaxime and amikacin [14]. Overall, the situation with resistant childhood pathogens is serious. There is an urgent need to strengthen the monitoring of pathogen distribution and bacterial resistance. Strict implementation of antimicrobial management and a good use of consultation and approval systems are also required to ensure a rational use of antibiotics. At the same time, food and drug regulatory agencies and health departments should strengthen their oversight of antimicrobial purchases and closely monitor prescription drugs, especially in private clinics and drug outlets. Publicity on antimicrobial health education should be increased in the press and social media to avoid the pre-hospital, over-the-counter, irrational use of antibiotics [15]. In short, preventing and controlling bacterial resistance to drugs in standard pediatric treatment is an important task.

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