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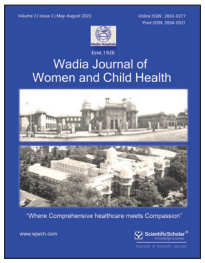

Original Article

Spectrum of World Health Organization global priority pathogens in hospitalized children - A single center experience

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ABSTRACT

Objectives: To study the spectrum of World Health Organization (WHO) global priority pathogens in hospitalized children at our center.

Material and Methods: This cross-sectional study was conducted between April 2021 to September 2022 in the Department of Pediatrics at Sri Aurobindo Institute of Medical Sciences and Post Graduate Institute (SAMC), Indore. All children admitted to the Pediatric and Adolescent Medicine Department; Ward, Pediatric Intensive Care Unit, Neonatal Intensive Care Unit, and Pediatric Surgical intensive Care Unit and with culture (Blood, urine, cerebrospinal fluid, and other body fluids/tissue) having grown at least one of the WHO priority pathogens, were studied.

Results: In this study period, 100 children had positive cultures. We found that urine specimens had the most bacterial isolations 35 (35%), followed by blood 24 (24%). *Escherichia coli* was the most often isolated organism [25 (25%)], followed by *Staphylococcus aureus* [18 (18%)]. About 80% of *E. coli* and 70.59% of *Klebsiella* spp. were resistant to third-generation cephalosporins due to extended-spectrum beta-lactamase (ESBL), while 50% of *S. aureus* were Methicillin-resistant. In all, over half of the *Enterobacteriaceae* were resistant to carbapenem (49.21%) or third generation cephalosporins (55.56%) due to ESBL. *Pseudomonas aeruginosa* carbapenem resistance was found in 11.11% cases.

Conclusion: In this study, WHO priority list pathogens, *Enterobacteriaceae, methicillin-resistant S. aureus*, *Klebsiella* species, and *E. coli* all show significant antimicrobial resistance (AMR). On the other hand, AMR trends for *Acinetobacter baumanni*, *P. aeruginosa*, and *S. aureus* (vancomycin resistant) are lower than the estimations provided by the WHO globally.

Keywords: Global priority pathogens, Pediatric, World health organization

INTRODUCTION

The World Health Organization (WHO) was requested by Member States to develop a global priority pathogens list (PPL) of antibiotic-resistant bacteria to help in prioritizing the research

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and development of new and effective antibiotic treatments. Antibiotic-resistant bacteria were defined as bacterial isolates that became resistant to the administered drug with a change from "susceptible" to "intermediate" or "resistant," or from "intermediate" to "resistant" in the susceptibility pattern.[1-3] The main drivers of antibiotic resistance (AR) are misuse and overuse of antibiotics due to presumptive treatment and inappropriate use of broad-spectrum antibiotics with erratic dosing.[4,5]

Other factors include transmission of resistant bacteria between patients, from healthcare workers to patients and vice versa, prophylactic use in animal husbandry, and lack of guidelines and policies for the use of antibiotics. A report from the World Bank forewarned that antimicrobial resistance (AMR) that includes AR could cause as much damage to the global economy as the 2008 financial crisis.[1] AMR is one of the most complex global health challenges today. The world has long ignored warnings that antibiotics and other medicines are losing their effectiveness after decades of overuse and misuse in human medicine, animal health, and agriculture.

Common illnesses such as pneumonia, post-operative infections, urinary tract infection (UTI), diarrheal, and sexually transmitted diseases, as well as the world's largest infectious disease killers-tuberculosis, human immunodeficiency virus, and malaria-are increasingly becoming untreatable because of the emergence and spread of drug resistance worsening AMR could have serious public health, economic, and social implications. The threat of AMR is also becoming a key consideration for programs addressing maternal and child health, sexual and reproductive health, foodborne diseases, water and sanitation, and infection prevention and control. Moreover, although the 21st century is being shaped by technology and innovation, humans could soon find themselves in an era where simple infections would once again kill millions every year.

Antibiotics have greatly reduced morbidity and mortality from classical and opportunistic infections in the last few decades.[1] Contrasting the gains made, the accelerated global consumption of antibiotics and lapses in the infection prevention and control practices, have hastened the frequency and severity of AR.

WHO global priority pathogen list

Priority 1: Critical

Carbapenem resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, carbapenem-resistant *Enterobacteriaceae* - carbapenem and third-generation cephalosporin-resistant.

Priority 2: High

Enterococcus faecium - vancomycin-resistant, *Staphylococcus aureus* - methicillin-resistant, intermediate and resistant vancomycin, *Helicobacter pylori* - clarithromycin-resistant, *Campylobacter* - fluoroquinolone resistant, *Salmonella* spp. - fluoroquinolone resistant, *Neisseria gonorrhoeae* – third-generation *Cephalosporin* and *fluoroquinolone-resistant*.

Priority 3: Medium

Streptococcus pneumonia - penicillin-non-susceptible *Haemophilus influenzae*- ampicillin-resistant *Shigella* spp.- fluoroquinolone-resistant.

MATERIAL AND METHODS

In this cross sectional study, all children admitted in the Paediatric and Adolescent Medicine Department i.e., Ward, Pediatric Intensive Care Unit (PICU) and neonatal intensive care unit (NICU), and Pediatric Surgical Intensive Care Unit (PSICU) of Sri Aurobindo Institute of Medical Sciences between April 2021 and September 2022 and had culture (blood, urine, cerebrospinal fluid, other body fluids/tissue) reports showing the presence of one of the WHO priority pathogens, were evaluated. The clinical syndromes associated with these pathogens were also noted.

Statistical analysis

Both descriptive and inferential statistics were used to identify the features and characteristics of the data. Continuous variable was expressed as mean ± standard deviation or range. Non-continuous variable (categorical data) was expressed as number of occurrence and percentage. Chi-square test was used to identify the association between variables. $P < 0.05$ was considered as significant. Microsoft Excel was used to prepare the master charts.

RESULTS

In this study, there were 100 children who had various cultures growing an organism. Urine specimens had the maximum bacterial isolations [35 (35%)], followed by blood [24 (24%)] [Table 1]. *Escherichia coli* was the most frequent isolated organism 24 (24%), followed by *S. aureus* 20 (20%). About 80% of *E. coli* and 70.6% of *Klebsiella* spp. were resistant to third-generation cephalosporins due to extended-spectrum beta-lactamase (ESBL), while 50% of *S. aureus* were methicillin-resistant. In all, over half of the *Enterobacteriaceae* were resistant to carbapenem (49.21%) or third-generation cephalosporins (55.56%) due to ESBL. *P. aeruginosa* carbapenem resistance was determined to be modest (11.11%). Over the past 4 years, a time trend study of selected WHO "Critical priority" pathogens revealed a

significant proportion of carbapenem resistance in *E coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae*. *E. coli,* and *K. pneumoniae* also continued to have a high prevalence of ESBL. *S. aureus* continues to have a high percentage of methicillin resistance among the WHO's "High priority" pathogens.

Three of the WHO's "High priority" infections were not discovered in our cohort - namely *H. pylori* (clarithromycin-resistant), *Campylobacter* spp. (fluoroquinolone-resistant), and *N. gonorrhoeae* (third-generation cephalosporin-resistant and fluoroquinolone-resistant). Similarly, one of the WHO's "Medium priority" pathogens, *H. influenzae* (ampicillin-resistant), was not found in this cohort, and antibiotic sensitivity data were unavailable.

DISCUSSION

The WHO advice paper from 2017 found that *A. baumannii* (91%) and *P. aeruginosa* (82%), both of which are classified as Critical Priority[6] infections, had the greatest levels of carbapenem resistance globally. Carbapenem resistance was found to be more than 50% in *A. baumannii* and between 31 and 50% in *P. aeruginosa* in the general population of the Indian subcontinent, according to the same research. Early findings from the monitoring data collected from up to 22 The Indian Council of Medical Research-Antimicrobial Resistance Surveillance and Research Network (ICMR-AMRSN) locations in India indicated that over 80% of *A. baumannii* strains were resistant to carbapenem, whereas approximately 30% of *P. aeruginosa* strains were resistant. On the other hand, a different research that was conducted on children in Mumbai, India, found that only 15% of *P. aeruginosa* strains are resistant to carbapenem.[7,8] This finding is similar to the present study. In the present investigation, the prevalence of carbapenem-resistant strains of *P. aeruginosa* among pediatric patients was found to be 11.1%.

In the general population, the WHO report found significant levels of carbapenem resistance in *E. coli* (55%), *Klebsiella* (70%), and *Enterobacter* spp. (59%), which is not too dissimilar to the results in our investigation in the pediatric population. In the general population, the results from ICMR-AMRSN indicated a prevalence of carbapenem resistance that was comparable in *K. pneumoniae* (40–50%) but much lower in *E. coli* (15–25%).[7]

In this study, the prevalence of *methicillin-resistant S. aureus* was high and comparable to that found in the WHO report. About 80% of *E. coli* and seventy-five and a half percent of *Klebsiella* spp. were resistant to third-generation cephalosporins as a result of ESBL, and 50% of *S. aureus* were resistant to methicillin. However, because of the small sample size of *Salmonella* spp., *Shigella* spp., and *S. pneumoniae*, it is possible that the findings of this research cannot be compared to those of other studies.

Over the last several years,[8-10] India has seen the publication of a number of papers on AMR. A retrospective investigation with a 5-year follow-up that was conducted in a tertiary care hospital in North India revealed rising rates of AMR in urinary tract

Table 1: Isolated organism.

Specimen	Blood	Urine	Stool	Pus	Sputum	CSF	Other body fluid aspirate	Swab	Tissue	Total
Critical priority organisms										
Acinetobacter baumannii	1	2	0	1	0	0	1	0	0	5
Pseudomonas aeruginosa	2	2	0	1	0	1	1	1	1	9
Escherichia coli	5	12	0	3	0	1	1	1	1	24
Klebsiella spp.	4	7	1	1	2	1	1	1	1	19
Enterobacter spp.	2	4	1	1	0	0	0	2	0	10
Serratia spp.	0	1	0	1	0	0	1	0	0	3
Proteus spp.	0	1	0	0	0	0	0	0	0	1
Providencia spp.	0	2	0	0	0	0	0	0	0	2
Citrobacter spp.	1	1	0	1	0	0	0	1	0	4
Others spp.	1	0	0	0	0	0	0	0	0	1
High priority organisms										
Enterococcus faecium	1	1	0	0	0	0	0	0	0	2
Staphylococcus aureus	6	1	1	2	4	1	0	4	1	20
Salmonella spp.	0	0	0	0	0	0	0	0	0	0
Medium priority organisms										
Streptococcus pneumoniae	1	0	0	0	0	0	0	0	0	1
Shigella spp.	0	1	0	0	0	0	0	0	0	1
Total organisms	24	35	3	11	4	4	5	10	4	100

CSF: Cerebrospinal fluid

infection-causing isolates.[9] However, the reported carbapenem resistance prevalence in *Klebsiella* spp. (39%) and *E. coli* (12%) were lower than what was found in the current study.[10] Increasing trends of AMR were observed among gram-negative isolates from samples collected across seven hospitals in India over the course of 4 years. About 24% of the *Enterobacteriaceae* that were isolated from a pediatric tertiary care hospital in Mumbai produced ESBL, and 27% of the *Enterobacteriaceae* that were isolated showed a lesser degree of resistance to carbapenem than the isolates in the present study.[8]

CONCLUSION

Of the WHO PPL pathogens, *Enterobacteriaceae*, methicillin-resistant *S. aureus*, *Klebsiella* species, and *E. coli* all show significant AMR in the research site. On the other hand, AMR trends for *A. baumanni*, *P. aeruginosa*, and *S. aureus* (vancomycin resistant) are lower than the estimations provided by the WHO globally. These results have the potential to influence the priorities, policies, and practices of the local community. We strongly suggest that big health institutions monitor and assess developing patterns and trends in AMR on a periodic basis to prioritize, plan, and execute health facility level policies and recommendations for the most effective use of antimicrobials.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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