

Review Article**Antibiotic resistance in Bangladesh: A current epilogue and a systematic review****Md. Jannatul Islam Polash, Rashni Agarwala, Khadija Tul Simran, Thashina Tasnim Tisha, Arghya Prosun Sarkar***

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Abstract

Background: Antibiotic resistance can truly be considered as one of the greatest public health difficulties in worldwide as well as in Bangladesh because of the widespread misuse and overuse, inadequate surveillance, scanty healthcare standard, and unaffordability of costly drugs. This review was displayed, to sum up, the contemporary scenario of ABR in Bangladesh to recognize inadequacies of surveillance, to deliver methodological information, and ultimately suggest some recommendations based on the review. **Materials and Methods:** This systematic review gathered information from 36 different articles relevant to ABR in Bangladesh published from 01 January 2015 to 30 September 2020. **Results:** The mean resistance and susceptibility testing pattern of antibiotics were categorized into 4 segments (Urinary tract infection-UTI, Bloodstream infection-BSI, Intestinal infection-II & Wound infection-WI). The review has revealed that (Gr-) *Escherichia coli* was the most prevalent pathogen causing UTIs; And, identified the most effective antibiotics against UTIs were Imipenem (95.7%), Amikacin (93%), Meropenem (79%) & Nitrofurantoin (76.3%), but the highest resistance showed to Nalidixic acid (91.4%), Amoxicillin (97.4%), and moderately Cephalosporin. Bloodstream-infection, which was usually caused by *Salmonella Typhi*, *Acinetobacter*, & *Staphylococcus spp.*, was the most resistant to Nalidixic acid (98%), Cotrimoxazole (65.2%), Cefotaxime and Tobramycin (100%); Otherwise, Gentamicin, Vancomycin and Polymyxin B (100%) were the most effective antibiotics. *Vibrio cholerae*, *E. coli*, & *S. Typhi* were the most predominant pathogen for Intestinal-infection and utmost sensitivity was found to Gentamicin (93.6%), Chloramphenicol (91.1%), and Ceftriaxone (86.8%). And, resistance to Nalidixic acid (86%) & Cotrimoxazole (84%). *Staphylococcus aureus* and *E. coli* were the most causative organism associated with surgical Wound-infection; and the most effective antibiotics were Azithromycin, Imipenem, & Cefuroxime (100%). **Conclusion:** It's high time to control the misuse and overuse, and appropriate initiatives should be taken to reinforce the new policy of rational prescription use to minimize antibiotic resistance.

Keywords: Antibiotics (Antimicrobials), Antibiotic Resistance (ABR or AMR), Sensitivity, Pathogens, Infections.

Introduction

The earth is on the edge of reverting to the 'pre-antibiotics era' because of developing resistance to life-saving antimicrobial medicines, with significant consequences for both individual and public health (Hoque et al., 2020). "Antibiotic resistance is one of the major public health issues, particularly in developing countries where relatively easy access and higher consumption of medicines have resulted in a disproportionately higher incidence of inappropriate antibiotic use and higher levels of resistance compared to developed countries" (Kumar et al., 2013). The widespread usage of antibiotics both therapeutically and non-

therapeutically has led to the development and dissemination of microbial resistance, and resistance genes are the determinants both in the clinical and non-clinical settings (Igbiosa and Odjadjare, 2015). The most prominent causes of antibiotic resistance are a constant inability to enhance or discover new antibiotics, as well as the indiscriminate use of antibiotics (Aslam et al., 2018). AMR poses a substantial risk of mortality and economic instability worldwide. "In contrast, the developing countries are more affected because of the widespread misuse of antibiotics, nonhuman antibiotic use, low quality of drugs, inadequate surveillance, and factors associated with individual and national poverty (poor healthcare standards, malnutrition, chronic and recurring infections, unaffordability of efficient and expensive medications)" (Ayukekbong et al., 2017; Sosa et al., 2010).

The Asia-Pacific region consists of more than 70% of the world's population (Kang & Song, 2013), while Southeast

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Asia is a diversified region with a significant (but uneven) economic expansion that has been identified as an epicenter for new infectious diseases and ABR (Zellweger et al., 2017). Bangladesh, a low-income developing country of Southeast Asia with a high level of ABR, poses a regional and global threat. Due to the high accessibility of antibiotics in Bangladesh, unqualified personnel in a 'pluralistic' healthcare system, unethical marketing tactics by pharmaceutical companies, and insufficient technological and logistical capability to monitor the huge market, this growing problem has emerged (Hoque et al., 2020).

In a study performed in Sylhet in 2012- 2015 where women were reported as one in 11 have a UTI in pregnancy and the antibiotic resistance was widespread, with just two-thirds of *Escherichia coli* were susceptible to 3rd generation Cephalosporins (Lee et al., 2019). Also, according to a 2003 report from Chittagong, typhoid patients did not respond to second-line therapy (Ciprofloxacin). Due to existing resistance, 1st line therapy was not even attempted. Moreover, this is not infrequent at all in Bangladesh like therapeutics failures (Asna et al., 2003; Ahmed et al., 2019). Even though antibiotic resistance has been emphasized as a major public health problem by multiple international agencies such as World Health Organization (WHO), the European Centre for Disease Control, and the United Nations World Health Assembly, but the policymakers and health care professionals will face significant challenges in combating the problem (Kumar et al., 2013). Internationally, it is estimated that more than 700,000 fatalities each year on account of ABR worldwide and if adequate procedures are not taken to halt its progress, approximately 10 million fatalities will be caused by AMR that result in a cost of US\$100 trillion per year by 2050 (Tadesse et al., 2017).

So, it is important to identify the gaps in surveillance, comprehend the present state of ABR, and needed effective interventions to the reinforcement of antimicrobial policies and legislation for appropriate and rational antibiotics use. The objective of this systematic review is to consolidate all accessible information about the current situation of ABR in Bangladesh. The dynamic relationship between pathogenic bacteria and antimicrobials resistance patterns as well as antibiotic susceptibility profiles in four infections (Urinary Tract Infection-UTI, Bloodstream Infection-BSI, Intestinal Infection-II & Wound Infection-WI) have been revealed in this systematic analysis. This review was also sought to address the inadequacies of surveillance and make suggestions based on worthwhile results. The aim was to offer a reference for future study as well as give direction towards the policymakers and prescribers on how to adopting and executing the best approach to reducing the degree of ABR and alleviating the difficulties caused by fast resistance.

Materials & methods

Literature search

To select articles relevant to antibiotic resistance (ABR) in Bangladesh published from 01 January 2015 to 30 September 2020, searches were conducted. Multiple searches were performed using relevant keywords (Antibiotics OR Antimicrobials) (Resistance OR Sensitivity) AND Bangladesh; (Antibiotics OR Antimicrobials) AND Bangladesh; Antibiotics AND Infections AND Bangladesh; and pathogen-specific searches were conducted from several databases (Google Scholar, PubMed, and Scopus).

Study selection

According to the following criteria, relevant articles were considered for this review: 1) ABR in humans reported from Bangladesh; 2) were published after January 01, 2015; 3) article record after duplicates were removed; 4) full-text articles were assessed for eligibility; 5) had a sample size >10; 6) were identified from four infection types, the total number of specimens besides the number/percentage of resistance/susceptible frequency was documented. Demographics, locations, urinary tract infection, bloodstream infection, intestinal infection, wound infection, antibiotic situation, sensitivity & resistance of bacteria in a human were studied.

Data extraction and analysis

To accumulate data, the selected articles were evaluated using parameters e.g., publication year, study year duration, patient type, location, total specimen, pathogen, type of infection, prevalence, susceptibility test standard, resistance, and so forth have been evaluated. Quantitative data were also gathered on antibiotic resistance as well as overall effect determined for mixed pathogenic studies. The resistance and susceptible pattern of each bacteria to various antibiotics is demonstrated as the mean resistance & sensitivity. Data extraction and examination were performed independently by more than one person to nullify any minor possibility of error, and if hadn't any corresponding results together, the studies co-examined jointly to resolve the dispute. After data extraction, all related data were entered in Microsoft Word and the results were analyzed using Microsoft Excel 2013.

Results

Study characteristics

Finally, 36 articles were included in the review from a preliminary selected 106. The majority of the findings were carried out mostly in hospitals were published between 2015 and 2020. The bulk of the studies (66.0%, 24/36) were

done in Dhaka, the capital district. Out of the two susceptibility testing methods (disk diffusion & agar dilution) employed, disk diffusion was performed in 83.4% (30/36) of the studies. The data interpretation of antimicrobial susceptibility testing was mostly followed by Clinical and Laboratory Standards Institute (CLSI) guidelines 83.4% (30/36). Our study is divided into four sections in this review is based on infection attacks. The majority of the isolates, 13 of the 36 studies (36.1%) samples were collected from urinary tract infection; while cultures from

bloodstream infection wound infection & multiple sample type intestinal infection were analyzed in 25% (9/36) and 11.1% (4/36) & 27.8% (10/36) of the studies, respectively. The majority of the isolates came from hospital in-patient 55.6% (20/36), where only 8.3% (3/36) were from out-patient and 30.5% (11/36) were from both. An overview of the characteristics of the studies comprised in this systematic review is provided in Table 1.

Table 1. Characteristics of the articles comprised in the review

Published Year	Frequency (% ^a)	References
2020	7 (19.0)	Noman et al., 2020; Tabassum et al., 2020; Hossain et al., 2020a; Hossain et al., 2020b; Dasgupta et al., 2020; Parvin et al., 2020; Houpt et al., 2020; Baddam et al., 2020
2019	7 (19.0)	Lee et al., 2019; Hooda et al., 2019; Zereen et al., 2019; Ahsan and Rahman, 2019; Islam et al., 2019; Farzana et al., 2019
2018	9 (25.0)	Nazme et al., 2018; Yu et al., 2018; Saha et al., 2018; Ahmed et al., 2018; Okanda et al., 2018; Islam et al., 2018; Uddin et al., 2018
2017	3 (8.0)	Suchi et al., 2017; Ahmed et al., 2017; Akter et al., 2017; Monira et al., 2017; Roy et al., 2017
2016	2 (6.0)	Begum et al., 2016; Akter et al., 2016; Hasan et al., 2016; Ahsan et al., 2016
2015	8 (22.2)	Chowdhury & Parial, 2015; Yasmeen et al., 2015; Haque et al., 2015; Saha et al., 2015; Khanam et al., 2015; Islam and Shamsuzzaman, 2015
Study Design	Laboratory-based	
Types of Infection		
UTI ^b	13 (36.1)	
BSI ^c	9 (25.0)	
II ^d	10 (27.8)	
WI ^e	4 (11.1)	
Locations^f		
Dhaka	24 (66.0)	
Sylhet	2 (5.6)	Lee et al., 2019; Hossain et al., 2020b
Brahmanbaria	1 (3.0)	Tabassum et al., 2020
Chittagong	3 (8.0)	Chowdhury and Parial, 2015; Uddin et al., 2018; Islam et al., 2018
Rajshahi	1 (3.0)	Haque et al., 2015
Jashore	1 (3.0)	Saha et al., 2015
Bogra	1 (3.0)	Dasgupta et al., 2020
Khulna	1 (3.0)	Saha et al., 2015
Mymensingh	1 (3.0)	Zereen et al., 2019
Chandpur	1 (3.0)	Islam et al., 2019
Not mentioned	2 (5.6)	Akter et al., 2016; Hossain et al., 2020a
Source of Data		
In-patient	20 (55.6)	
Out-patient	3 (8.3)	
Both	11 (30.5)	
Unknown	2 (5.6)	
Pathogens		
<i>Escherichia coli</i>	19 (16.1)	
<i>Pseudomonas spp.</i>	12 (10.2)	
<i>Klebsiella spp.</i>	12 (10.2)	
<i>Staphylococcus spp.</i>	15 (12.7)	
<i>Enterobacter spp.</i>	7 (5.9)	
<i>Enterococci spp.</i>	6 (5.1)	
<i>Proteus spp.</i>	6 (5.1)	
<i>Acinetobacter</i>	5 (4.2)	

Table 1. Continue

<i>Citrobacter</i>	2 (1.7)	
<i>Candida</i>	2 (1.7)	
<i>Salmonella</i> Typhi	11 (9.3)	
<i>Salmonella</i> Paratyphi	7 (5.9)	
<i>Vibrio cholerae</i>	5 (4.2)	
<i>Campylobacter</i>	1 (0.9)	
<i>Aeromonas</i>	2 (1.7)	
<i>Shigella</i> spp.	2 (1.7)	
<i>Streptococcus</i> spp.	4 (3.4)	
Susceptibility testing standard		
CLSI ^e	30 (83.4)	
EUCAST ^h	2 (5.6)	Yu et al., 2018; Farzana et al., 2019
Not mentioned	4 (11)	Tabassum et al., 2020; Nazme et al., 2018; Ahmed et al., 2018; Ahsan et al., 2016
Susceptibility testing method ⁱ		
Disc diffusion	30 (83.4)	
Agar dilution	3 (8.3)	Suchi et al., 2017; Farzana et al., 2019; Hasan et al., 2016
Not mentioned	3 (8.3)	Nazme et al., 2018; Yu et al., 2018; Ahmed et al., 2018

a= percentage, b= Urinary Tract Infection, c= Blood Stream Infection, d= Intestinal Infection, e= Wound Infection, f= Multiple-location studies were counted more than once, g= Clinical & Laboratory Standards Institute, h= European Committee on Antimicrobial Susceptibility Testing, and i= Several methods were used in some studies.

General information

In reviewing studies in this systematic analysis, Tables 2 to 5 describe the identification and are showing the enrollment and test response of patients with collected specimens, ages & pathogens responsible as part of a study intervention in four common infections (UTI, BSI, II & WI).

The total number of specimens were collected by the urine sample of UTI patients was 11785. And the rate of urine culture contamination was 34.5% (4065/11785) (males with predominantly (30.03%) and females with (69.97%) positive culture in ratio 1:2.33). In the majority of the cases, the growth was positive for the middle age (20-40 years), though 28% of children and 9% of the pregnant women were also showed UTI positive. A total of 21 pathogens were commonly responsible for causing UTIs among them, (*Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas* spp., *Enterobacter* spp., *Staphylococcus aureus*, *Enterococcus* spp., & *Staphylococcus saprophyticus*) these 7 were most predominant (Table 2). Blood samples were collected from the patients affected by bloodstream infections were 115,096. A total of 20 pathogens were the most common causing BSI and 9 were most predominant (*Salmonella* Typhi, *Salmonella* Paratyphi A, *Klebsiella* spp., *Acinetobacter*, *Pseudomonas* spp., *Enterobacter*

spp., *E. coli*, *Streptococcus pneumoniae*, *Staphylococcus aureus*) among them. In most of the cases, children were affected more and males have also a higher burden than females (Table 3).

A total of 59,885 collected stool/fecal samples were from the suspected intestinal infection patients (including cholera, diarrhea, and other bacterial infections). And in the majority of the cases, the growth was positive for the infants (1-12 months) and the younger age (0-18 years old). There was a total of 5 pathogens (*Vibrio cholerae*, *E. coli*, *Salmonella* Typhi, *Shigella* spp., *Aeromonas*) showing the predominant for an intestinal infection (Table 4).

A total of 445 wound swab samples were collected from the patients with wound infections. There was a total of 6 pathogens (*Staphylococcus aureus*, *Streptococcus pyogenes*, *E. coli*, *Klebsiella* species, *Pseudomonas* species, *Proteus* species) showing the predominant for wound infections (Table 5).

Antibiotic resistance and susceptibility pattern

The resistance and susceptibility patterns were calculated for the 7 most prevalent (Gr+ & Gr-) pathogens against 19 antibiotics. *Escherichia coli* was founded to be the most prevalent microorganism of UTI showed a ~70% prevalence

Table 2. General data and specifications reviewed from articles for the systematic analysis of the Urinary Tract Infection (UTI)

Serial no.	Gender (Age)	Number of specimens	No. of positive specimens (%)	The Prevalence of Pathogens (Percentage)									References
				<i>E. coli</i>	<i>Pseudomonas spp.</i>	<i>Staphylococcus aureus</i>	<i>Klebsiella pneumoniae</i>	<i>Staphylococcus saprophyticus</i>	<i>Enterobacter spp.</i>	<i>Enterococcus spp.</i>	<i>Proteus spp.</i>	<i>Citrobacter</i>	
01	Female (pregnant) <20 weeks gestations	4034	360 (8.9)	38	-	12	12	23	-	-	0.3	-	(Lee et al., 2019)
02	Both sex (Child) (<11 years)	519	218 (42)	74.3	1.4	-	-	-	-	-	1.4	-	(Noman et al., 2020)
03	Both sex (Child) (All ages)	150	50 (33.3)	48	10	10	-	2	18	-	6	6	(Tabassum et al., 2020)
04	Both sex (All ages)	84	80 (95.3)	-	-	-	-	-	-	100	-	-	(Suchi et al., 2017)
05	Both sex (1-65 Years)	1957	507 (26.0)	82.6	1.4	-	14.6	-	0.2	-	-	0.6	(Chowdhury and Parial, 2015)
06	Both sex (child) 0 to <10 years	120	58 (48.3)	62.1	3.4	-	10.2	-	-	19.2	1.7	-	(Nazme et al., 2018)
07	Both sex (All ages)	874	182 (20.8)	85.2	4.4	1.64	1.7	-	1.7	-	-	-	(Yasmeen et al., 2015)
08	Both sex (All ages)	480	81 (16.9)	100	-	-	-	-	-	-	-	-	(Akter et al., 2016)
09	Both sex (All ages)	1663	1663 (100)	100	-	-	-	-	-	-	-	-	(Hossain et al., 2020a)
10	Not mentioned	106	66 (62.3)	100	-	-	-	-	-	-	-	-	(Hossain et al., 2020b)
11	Both sex (All ages)	1255	537 (42.8)	61.6	7.8	5.4	22.5	-	2.6	-	-	-	(Dasgupta et al., 2020)
12	Both sex (All ages)	443	189 (42.6)	59.3	2.01	-	5.5	19.1	1	11.6	1.5	-	(Haque et al., 2015)
13	Both sex (11 to 70 years)	100	74 (74)	69	8.1	17.6	5.4	17.6	-	-	-	-	(Saha et al., 2015)

Table 3. General data and specifications reviewed from articles for the systematic analysis of the Bloodstream Infection (BSI)

Serial no.	Gender (Age)	Number of specimens	No. of positive specimens (%)	The Prevalence of Pathogens (Percentage)									References
				<i>Salmonella Typhi</i>	<i>Salmonella Paratyphi</i>	<i>Klebsiella spp.</i>	<i>Acinetobacter</i>	<i>Pseudomonas spp.</i>	<i>Enterobacter spp.</i>	<i>E. coli</i>	<i>Streptococcus pneumonia</i>	<i>Staphylococcus aureus</i>	
01	6 months- 64 years Male- 59% Female- 41%	1425	661(46.4)	46	-	-	-	-	-	-	-	-	(Yu et al., 2018)
02	Not mentioned	1082	1082 (100)	87	13	-	-	-	-	-	-	-	(Hooda et al., 2019)
03	Children (1-5years) Younger (6-17 years) Adults (18- 59 years)	72	72 (100)	100	-	-	-	-	-	-	-	-	(Khanam et al., 2015)
04	2 months- 16 years	7834	958 (12.2)	87	13	-	-	-	-	-	-	-	(Saha et al., 2018)
05	Neonates (<30 days old) Male- 83.3%	148	36 (24.3)	-	-	24.3	-	-	-	-	-	-	(Farzana et al., 2019)
06	Neonates	78	78 (100)	-	-	18	32	1	8	-	5	-	(Ahmed et al., 2018)
07	Mean age (65.1 ± 9.1) Male- 43.2% Female- 56.7%	696	604 (86.8)	-	-	18.1	29.7	26.5	-	11.7	-	2.1	(Ahsan et al., 2016)
08	Adult (>12 years) Pediatric (up to 12 years)	103679	14015 (13.6 ± 0.7)	37	8.9	2.7	5.2	12.6	1.3	3	2.0	1.6	(Ahmed et al., 2017)
09	Not mentioned	82	24 (29.3)	22	7	-	-	-	-	-	-	-	(Okanda et al., 2018)

Table 4. General data and specifications reviewed from articles for the systematic analysis of the Intestinal Infection (II)

Serial no.	Gender (Age)	Number of specimens	No. of positive specimens (%)	The Prevalence of Pathogens (Percentage)							References
				<i>Vibrio cholerae</i>	<i>Salmonella Typhi</i>	<i>E. coli</i>	<i>Shigella spp.</i>	<i>Campylobacter</i>	<i>Salmonella Paratyphi</i>	<i>Aeromonas</i>	
01	Child- (<18 years) & Adult	47283	7472 (16)	55.7	-	-	-	-	-	-	(Parvin et al., 2020)
02	Child- (0-15 years)	186	55 (29.6)	-	16.4	70.9	12.7	-	-	-	(Akter et al., 2017)
03	Adult, & Child-(<5 years)	25	7 (28)	12	-	-	-	-	-	-	(Zereen et al., 2019)
04	Child- (10-24 months)	15	15 (100)	1	-	55	-	-	-	1	(Monira et al., 2017)
05	Not mentioned	34	34 (100)	57.5	-	-	-	-	-	-	(Baddam et al., 2020)
06	Infant- (1-12 months)	100	82 (82)	-	-	82	-	-	-	-	(Islam et al., 2019)
07	Infant- (1-12 months)	8580	1067 (12.4)	-	-	12	-	-	-	-	(Begum et al., 2016)
08	Not mentioned	3272	737 (24.5)	0.3	0.2	-	20.9	1	-	2.0	(Houpt et al., 2020)
09	Child-(<5 years)	350	15 (4.3)	-	4	-	-	-	-	-	(Uddin et al., 2018)
10	Not mentioned	40	40 (100)	-	82.5	-	-	-	17.5	-	(Ahsan and Rahman, 2019)

Table 5. General data and specifications reviewed from articles for the systematic analysis of the Wound Infection (WI)

Serial no.	Gender (age)	Number of specimens	No. of positive specimens (%)	The Prevalence of Pathogens (Percentage)							References
				<i>S. aureus</i>	<i>Staphylococcus spp.</i>	<i>Streptococcus pyogenes</i>	<i>E. coli</i>	<i>Klebsiella species</i>	<i>Pseudomonas species</i>	<i>Proteus species</i>	
1	Male (37 years)	105	105 (100)	58.5	-	7.6	24.9	3.2	8.6	2.2	Zaman et al., 2017
2	Male (20- 45 years)	40	18 (45)	29	15.1	-	-	-	-	-	Hasan et al., 2016
3	Not mentioned	100	83 (83)	83	-	-	-	-	-	-	Islam et al., 2018
4	Not mentioned	200	136 (68)	68.2	-	-	-	-	-	-	Islam and Shamsuzzaman, 2015

Table 6. Sensitivity & resistance rate to different antibiotics for UTI in selected studies to the systematic analysis

Antibiotics	Gram-negative Bacteria (Gr -)						Gram-positive Bacteria (Gr+)							
	<i>E. coli</i>		<i>Klebsiella pneumoniae</i>		<i>Pseudomonas spp.</i>		<i>Enterobacter spp.</i>		<i>Staphylococcus aureus</i>		<i>Enterococcus spp.</i>		<i>Staphylococcus saprophyticus</i>	
	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity
Cefixime	10	42.3	41.7	58.3	57.5	42.5	78.6	21.4	59.9	40.1	82	18	62.1	37.9
Nitrofurantoin	23.7	76.3	52	48	52.4	47.6	24	76	21	79	56.4	43.6	9	91
Azithromycin	58.8	41.2	53	47	49.3	50.7	64.3	35.7	44.8	55.2	79.4	20.6	18.4	81.6
Co-trimoxazole	65	35	68.3	31.7	74	26	85.7	14.3	61	39	87	13	63.8	36.2
Gentamicin	29	71	35	65	42.7	57.3	38	62	30	70	75.5	24.5	31	69
Nalidixic acid	79.6	20.4	63.3	36.7	84.3	15.7	95.3	47	94	6	97.8	2.2	91.4	8.6
Ceftriaxone	53.5	46.5	42	58	58.2	41.8	66.7	33.3	20.7	79.3	68.3	31.7	24	76
Cephalexin	62.4	37.6	56.5	43.5	100	0	100	0	34	66	78	22	42.3	57.7
Imipenem	4.3	95.7	2	98	4	96	14	86	3	97	28.5	71.5	-	-
Amoxicillin	72.3	27.7	97.4	2.6	96.7	3.3	100	0	100	0	53	47	85.5	14.5
Cefuroxime	76.3	23.7	57.2	42.8	87.4	12.6	57	43	62	38	80.4	19.6	39.5	60.5
Ceftazidime	48	52	37.6	62.4	53	47	85.7	14.3	31	69	100	0	-	-
Ciprofloxacin	53.4	46.6	50.5	43.5	56	44	90.5	9.5	38.7	61.3	80	20	39.3	60.7
Levofloxacin	50	50	46.6	53.4	47	53	85.7	14.3	41.5	58.5	73	27	69.3	30.7
Amikacin	18.3	81.7	30.6	69.4	23.3	76.7	10.7	89.3	7	93	74.4	25.6	7.7	92.3
Meropenem	21	79	30	70	22	78	21.5	78.5	7	93	82	18	-	-
Netilmicin	24	76	40.4	59.6	27	73	10.7	89.3	27.6	72.4	82	18	-	-
Piperacillin	92	8	100	0	100	0	-	-	-	-	42.2	57.8	-	-
Piperacillin-Tazobactam	12	88	-	-	100	0	-	-	-	-	-	-	-	-

Table 7. Sensitivity and resistance rate to different antibiotics for BSI in selected studies to the systematic analysis

Antibiotics	Gram-negative Bacteria (Gr -)														Gram-positive Bacteria (Gr+)			
	<i>Salmonella Typhi</i>		<i>Salmonella Para typhi A</i>		<i>Klebsiella spp.</i>		<i>Acinetobacter</i>		<i>Pseudomonas spp.</i>		<i>Enterobacter spp.</i>		<i>E. coli</i>		<i>Streptococcus pneumonia</i>		<i>Staphylococcus aureus</i>	
	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity
Cotrimoxazole	30.4	69.6	0.2	99.8	77	23	-	-	60	40	67	33	73.6	26.5	65	35	65.2	34.9
Ciprofloxacin	49	51.0	98.7	1.3	42.7	57.3	92.6	7.4	32	68	13.2	86.8	70.6	29.4	31.6	68.5	74	26.1
Chloramphenicol	26.4	73.6	0	100	53.9	46.1	-	-	76.1	23.9	50	50	0	100	0	100	53	47
Ceftriaxone	0	100	0	100	72.9	27.2	90	10	80.8	19.3	41.8	58.3	78.6	21.5	0	100	32.6	67.4
Gentamicin	0	100	0	100	60.4	39.6	96	4	97.9	2.1	83	17	25.2	74.9	75	25	61.4	38.6
Ampicillin	34.8	65.3	0.3	99.8	-	-	-	-	-	-	-	-	89.8	10.2	3.9	96.2	90.4	9.6
Ceftazidime	-	-	-	-	87.7	12.3	82.7	17.3	59.7	40.3	83	17	69.5	30.5	-	-	100	0
Piperacillin - Tazobactam	-	-	-	-	66.8	33.3	76	24	4.3	95.7	50	50	36.4	63.6	-	-	-	-
Netilmicin	-	-	-	-	70.6	29.4	55.7	44.3	76	24.1	-	-	13.5	86.5	-	-	0	100
Cefixime	0.4	99.6	0.2	99.8	82.5	17.5	80	20	100	0	67	33	72.8	27.2	6.4	93.6	-	-
Amikacin	-	-	-	-	64.8	35.2	73.7	26.3	80.9	19.1	67	33	13.7	86.3	-	-	0	100
Vancomycin	-	-	-	-	31	69	-	-	-	-	-	-	-	-	0	100	0.2	99.8
Colistin	-	-	-	-	15.3	84.7	8	92	26.2	73.8	17	83	-	-	-	-	-	-
Cefotaxime	-	-	-	-	81.2	18.8	100	0	75	25	83	17	100	0	-	-	-	-
Azithromycin	9.8	90.3	0.5	99.5	39.5	60.5	-	-	-	-	-	-	-	-	29.2	70.8	-	-
Nalidixic acid	98	2	100	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Levofloxacin	0	100	33.3	66.7	71	29	-	-	100	0	67	33	-	-	-	-	-	-
Cefmetazole	0	100	0	100	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Imipenem	0	100	0	100	58.3	41.7	74.6	25.4	43.5	56.5	-	-	7.4	92.7	-	-	-	-
Meropenem	0	100	0	100	58.8	41.3	-	-	100	0	67	33	-	-	-	-	-	-
Cefepime	-	-	-	-	93	7	92	8	100	0	83	17	-	-	-	-	-	-
Tobramycin	-	-	-	-	100	0	100	0	100	0	100	0	-	-	-	-	-	-
Polymyxin B	-	-	-	-	0	100	0	100	0	100	0	100	-	-	-	-	-	-
Rifampicin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	100	0
Oxacillin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	100	0

Table 8. Sensitivity and resistance rate to different antibiotics for II in selected studies to the systematic analysis

Antibiotics	Gram-negative Bacteria (Gr -)									
	<i>Vibrio cholerae</i>		<i>E. coli</i>		<i>Salmonella Typhi</i>		<i>Shigella spp.</i>		<i>Aeromonas</i>	
	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity
Azithromycin	6.4	93.6	54.3	45.7	60	40	43	57	0	100
Ciprofloxacin	21.6	78.5	29.7	70.3	10	90	83	17	0	100
Erythromycin	45	55	96.5	3.5	87	13	-	-	100	0
Chloramphenicol	20.5	79.5	5	95	7	93	3	97	-	-
Gentamycin	0	100	19.1	80.9	-	-	-	-	0	100
Norfloxacin	7	93	27	73	-	-	-	-	-	-
Streptomycin	73.5	26.5	48	52	-	-	-	-	-	-
Tetracycline	45.2	54.8	47.3	52.7	33	67	61	39	50	50
Cotrimoxazole	83.5	16.5	84.6	15.4	-	-	-	-	-	-
Ceftriaxone	25	75	21	79	0	100	7	93	100	0
Ampicillin	70	30	77.7	22.4	-	-	40	60	0	100
Nalidixic Acid	97	3	75	25	-	-	-	-	-	-
Sulfamethoxazole - Trimethoprim	25	75	35.4	64.6	40	60	49	51	50	50
Cefepime	-	-	50.6	49.4	0	100	14.3	85.7	-	-
Cefixime	25	75	44	56	0	100	-	-	-	-

Table 9. Sensitivity and resistance rate to different antibiotics for WI in selected studies to the systematic analysis

Antibiotics	Gram-positive bacteria (Gr+)				Gram-negative bacteria (Gr -)							
	<i>S. aureus</i>		<i>S. pyogenes</i>		<i>E. coli</i>		<i>Klebsiella species</i>		<i>Pseudomonas species</i>		<i>Proteus species</i>	
	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity
Azithromycin	54.9	45.2	28.5	71.5	65.2	34.8	33.3	66.7	62.5	37.5	0	100
Gentamicin	44.8	55.2	14.3	85.7	17.4	82.6	0	100	50	50	50	50.0
Ciprofloxacin	62.6	37.4	42.9	57.1	78.3	21.7	100	0	62.5	37.5	50	50
Oxacillin	53.4	46.6	-	-	-	-	-	-	-	-	-	-
Vancomycin	22.9	77.1	14.3	85.7	-	-	-	-	-	-	-	-
Tetracycline	62.6	37.4	42.9	57.1	39.1	60.9	100	0	62.5	37.5	50	50.0
Ceftriaxone	24.5	75.5	14.3	85.7	8.7	91.3	66.7	33.3	37.5	62.5	0	100
Cefotaxime	80	20	-	-	13.1	86.9	66.7	33.3	100	0	50	50
Penicillin	67.2	32.8	42.9	57.1	65.2	34.8	100	0	100	0	100	0
Chloramphenicol	67.5	32.5	-	-	-	-	-	-	-	-	-	-
Nitrofurantoin	20	80	-	-	21.7	78.3	66.7	33.3	87.5	12.5	50	50.0
Imipenem	47.8	52.2	14.3	85.7	8.7	91.3	66.7	33.3	50	50.0	0	100
Cefuroxime	40.7	59.3	42.9	57.1	21.7	78.3	100	0	100	0	0	100
Cefixime	25.9	74.1	28.5	71.5	17.4	82.6	66.7	33.3	87.5	12.5	50	50
Cephradine	40.7	59.3	42.9	57.1	56.5	43.5	100	0	100	0	100	0

rate. The pathogens showed the most resistance among *E. coli* isolates to commonly used drugs such as Nalidixic acid (79.6%), Amoxicillin (72.3%), Cefuroxime (76.3%), and Piperacillin (92%). In contrast, *E. coli* showed the most susceptibility to Imipenem (95.7%), Amikacin (81.7%), Meropenem (79%), and Netilmicin (76%) antibiotics respectively. Similar trends were identified for other organisms that cause UTI. The most common Cephalosporin class of antibiotics was ineffective against all isolates (~35-40% sensitive frequency). Resistance to Ciprofloxacin, Azithromycin, and Co-trimoxazole was 53.4%, 58.8%, and 65%, respectively, in *E. coli* and similar to others. Aminoglycoside showed the most effective against (Gr+ & Gr-) (Amikacin sensitive to (93%) of *Staphylococcus aureus*, and 89.3% of *Enterobacter spp.*) respectively. Piperacillin showed the lowest sensitivity against *E. coli* (8%) which was increased along with tazobactam (88%) (Table 6). Gram-negative bacteria: *Salmonella* Typhi, Paratyphi A, *Klebsiella spp.*, *Acinetobacter*, *Pseudomonas spp.*, *Enterobacter*, *E. coli*, *Streptococcus pneumoniae*, and (Gr+) *Staphylococcus aureus* were the most causative microorganisms and demonstrated significant resistance to frequently used antibiotics such as Cotrimoxazole, Ampicillin Gentamicin. Cotrimoxazole showed 99.8% sensitivity to *Salmonella* Paratyphi A and more resistance to *Klebsiella spp.* (77%). Besides, Cefmetazole, Ceftriaxone, Gentamicin, Imipenem, and Meropenem showed 100% sensitivity to both *Salmonella* Typhi and *Salmonella* Paratyphi. Vancomycin shows 99% and 69% susceptibility against (Gr+) and *Klebsiella*. Penicillin derivatives (Ampicillin-90.4%, Ceftazidime-100%), beta-lactam antibiotics (Oxacillin-100%), and macrocyclic antibiotics (Rifampicin-100%) were the most inactive against *Staphylococcus aureus*. *Pseudomonas* was moderately resistant to Meropenem (56.5%) and sensitive to Imipenem. Azithromycin resistance was found in *Salmonella* Typhi, Paratyphi A, *Klebsiella spp.*, and *Streptococcus pneumoniae* (Table 7).

In this study, the patterns of five high prevalent pathogens (*Vibrio cholerae*, *E. coli*, *Salmonella* Typhi, *Shigella spp.*, *Aeromonas*) were evaluated against 15 common antibiotics. *Vibrio cholerae*, the most common causative organism and showed the highest pattern of susceptibility to Azithromycin (93.5%), Ciprofloxacin (78.4%), Chloramphenicol (79.5%), Gentamycin (100%), Norfloxacin (93%), Ceftriaxone (75%), Sulfamethoxazole- Trimethoprim (75%), Cefixime (75%). Another common causative pathogen was *E. coli* showed the highest pattern of susceptibility to Ciprofloxacin (70.3%), Chloramphenicol (95%), Gentamycin (80.9%), Norfloxacin (73%), and Ceftriaxone (79%). Susceptibility to Ceftriaxone, Cefepime, and Cefixime was 100% and Ciprofloxacin, Chloramphenicol was 90% and 93%, respectively in *Salmonella* Typhi. *Shigella spp.* was the highest susceptible and less resistant to Chloramphenicol and Ceftriaxone which were 97%

and 93%. *Aeromonas* was 100% susceptible to Azithromycin, Ciprofloxacin, Gentamycin, and Ampicillin while it showed 100% high resistance to Erythromycin and Ceftriaxone (Table 8).

In this review, we summarize the antimicrobial resistance and susceptibility pattern of various pathogens to frequently used antibiotics in wound infections. In this review, we showed the resistance and susceptibility patterns of the most prevalent pathogens (*S. aureus*, *S. pyogenes*, *E. coli*, *Klebsiella species*, *Pseudomonas species*, *Proteus species*) against 15. The result showed the highest resistance (100%) to Cefuroxime, Cephradine, and Penicillin against *Klebsiella spp.* & *Pseudomonas spp.* Also, the highest sensitivity (100%) to Azithromycin, Ceftriaxone, Imipenem, and Cefuroxime against *Proteus species* were found (Table 9).

Discursion

In the current study, UTI was shown to be several times more common in women than in males (women 69.97% & men 30.03%). Also, the higher incidence was conducted in other parts of the world, including India (George et al., 2015), Pakistan (Kalsoom et al., 2012), and America (Boucher et al., 2009; Kim et al., 2008) “due to anatomical differences between men and women, besides a short urethra and its external opening adjacent to the vagina and anus in women” (Cohen et al., 2012; Kothari and Sagar, 2008).

According to the current study, *E. coli* was the most frequent (~70% frequency) bacteria that causes UTIs; this result has to resemble more research in different parts of the world. The prevalence rate of *E. coli* was reported 50-80% in Asia (70% in India (George et al., 2015), 58% in Saudi Arabia) (Kader et al., 2004), 60.3% in Africa (Abejew et al., 2014), and 75-90% in the USA (Hickerson and Carson, 2006). According to the current and the mentioned article in the context, *E. coli* is considered as the most prevalent pathogen whereas *Staphylococcus* & (Gr+) *Enterococcus* as the second most and *Klebsiella* is the third most prevalent pathogens causing UTIs. The resistance rate of *E. coli*, *Staphylococcus*, *Klebsiella*, and 3 other prevalent pathogens are reported against 19 several antibiotics in our study (Table 6).

Nalidixic acid and Ciprofloxacin (1st & 2nd generation), Quinolone family antibiotics were studied in the present study, and Nalidixic acid showed a resistance rate to *E. coli*, *Klebsiella* & *Staphylococcus* were reported as 79.6%, 63.3% & 94% respectively. And if it was compared with the Amoxicillin (72.3%, 97.4% & 100%), apparently it was revealed that two of these antibiotics showed relatively high resistance. The resistance rate of Amoxicillin for *E. coli* in different parts of the world have been conveyed 72% in India (Aypak et al., 2009), 67.5% in Senegal (Krishna et al., 2013),

and 85% in European countries (48% in Poland & 60% in Belgium) (Magliano et al., 2012) as well as for Nalidixic acid reported as 84.2% in Pakistan (Mbata, 2007). So, a consistent study with several developing countries, these 2 drugs are used as the most inactive and are not recommended UTI treatments. In contrast, the 2nd generation Ciprofloxacin was found as an intermediate resistance against all isolates which was found susceptible to *E. coli* (46.6%), *Klebsiella* (43.5%), & *Staphylococcus* (60.7%). Whereas, somewhat more susceptible were conducted in India, Ethiopia, Senegal & Nigeria about (70-90%) (Abejew et al., 2014; Lee et al., 2013; Yolbas et al., 2013). And that possibly emanated by the overuse of cited drugs, patients with irregular medication usage, whether by prescribed or willfulness in developing countries without exact surveillance.

Aminoglycosides are another cluster of antibiotics have used to treat UTIs. In this review, it has reported that the resistance rate to Amikacin, Gentamicin & Netilmicin in *E. coli* was (18.3%, 29% & 24%), in *Klebsiella* (30.6%, 35% & 40.4%), & in *Staphylococcus* (7%, 30.5% & 27.6%). Amikacin was indicated utmost sensitivity to UPEC (Uropathogenic *Escherichia coli*) (Momeni Mofrad et al., 2013) in most of the studies and equivalent to our study. For instance, *E. coli* exhibited sensitivity to Amikacin in India (Xiao & Hu, 2012) 90.6%, Saudi Arabia (Xiao & Hu, 2012) 93.7%, South Korea (Lee et al., 2013) 99.4%, America (Zhan et al., 2006) 100% and China (Ti et al., 2003) 88.3% respectively and almost same for *Klebsiella* and others. "Gentamicin and Netilmicin are some of the old antibiotics that can be used for the initial treatment of UTIs until the culture result is prepared because of the strong penetrating power into the bacterial cell wall" (Momeni Mofrad et al., 2013). Although the availability and indiscriminate use of inexpensive Gentamicin and Netilmicin; its resistance was higher than Amikacin and the result of this study has shown that Amikacin can be employed in Bangladesh as the first-line therapy for UTI treatments.

Cephalosporin is the common pharmaceutical group recommended to treat infections in our country. In our study, Cephalexin (1st generation) as well as Cefixime, Ceftazidime (3rd generation) was investigated as a rising rate of resistance against isolates studied (60-65%). Though the conducted study in Ethiopia (Abejew et al., 2014), Senegal (Krishna et al., 2013) & Lebanon (Sire et al., 2007) was showing consistency with our study but a conducted study in Europe (Momeni Mofrad et al., 2013) & America (Pape et al., 2004) have been suggested low resistance to 3rd generation Cephalexin was around (1.8-19.2%) frequency. Therefore, caution and intransitive procedure should be used to avoid increasing resistance. Isolated microbes were most susceptible to the expensive IV formulation Carbapenem drugs like Imipenem (1st generation) & Meropenem (2nd

generation) in the present study whereas Imipenem (95.7% in *E. coli*, 98% in *Klebsiella* & 97% in *Staphylococcus*). *E. coli* was reported 100% susceptible to Imipenem in Taiwan (Chen et al., 2014), India (Gales et al., 2002) 98.9%, & (Europe 99.7%, America 99.8%) (Mortazavi-Tabatabaei et al., 2019) respectively and consistent with ours. Therefore, Carbapenem could be the most effective antibiotic to cure UTI patients.

Nitrofurantoin also found 76.3% sensitivity against *E. coli* in our study with moderate sensitivity to other pathogens and compatible with the neighboring country India (George et al., 2015) 77.4% as well as America (Karlowsky et al., 2011) 96% was reported. Finally, based on our review Amikacin, Imipenem, Meropenem & Nitrofurantoin can be efficiently used for the treatment of UTI patients for their positive results in Bangladesh.

S. aureus was resistant to Folic acid antagonists-Cotrimoxazole (65.15%) for BSI treatment in our study, which was equivalent to our neighboring nation India (Dharmapalan et al., 2017). Vancomycin (Glycopeptide) showed around 100% sensitivity against (Gr+) bacteria. It is also recommended for the treatment of the disease in the UK (Gould, 2008). In contrast, *Salmonella* species had resistance to 98% Nalidixic acid. Ampicillin, Ciprofloxacin (2nd generation Fluoroquinolones), and Ceftriaxone (2nd and 3rd generation Cephalosporin) were noted higher resistance rates, and Amikacin, Netilmicin were showed lower resistance rates to *E. coli* both in ours review and Indian review (Rahman & Huda, 2014). Except for Colistin (sensitivity 92%) and Polymyxin B (100% sensitivity), Carbapenem is responsible for multi-drug resistance (>70%) in *Acinetobacter*. *Pseudomonas* had reported 2nd most prevalent organism in BSIs that showed >55% resistance to Cotrimoxazole, Cefotaxime, Chloramphenicol, Netilmicin, and >80% resistance to Ceftriaxone, Gentamicin (2nd generation Aminoglycosides), and Amikacin. Gentamicin is resistant against *Pseudomonas*, according to the Indian systematic study. The sensitive nature of Fosfomycin to *Pseudomonas*, a combination of Gentamicin, Imipenem, Fosfomycin, and Ciprofloxacin has been used to treat *Pseudomonas* (Gould, 2008; Pachori et al., 2019). *Klebsiella* was resistant to Gentamicin and Imipenem (>55%), (beta-lactam antibiotics) Piperacillin-Tazobactam (>65%).

Intestinal infection (Cholera, Diarrhea, and other intestinal diseases) is an infection mostly associated with these (Gr-) bacteria (such as *Vibrio cholerae*, *Salmonella* Typhi, *E. coli*, *Shigella*, and others). This review offers a summary of the most recent five-year scenario for II in Bangladesh (2015-2020). Specially infants are at risk due to inadequate

sanitation and an unsanitary climate, and infant mortality has occurred as a result of antibiotic abuse and overuse. In Bangladesh, this bacterial infection is commonly recognized as a leading cause of child mortality. *Vibrio cholerae*, *E. coli*, *Shigella spp.*, *Salmonella Typhi*, and *Aeromonas* were the commonest agents responsible for this infection. From a conducted study in Tunisia, the prevalence rate of *E. coli*, MDR (Multi-Drug Resistance) was 6.6% in children aged 6 to 12 years (Islam et al., 2019). MDR of *E. coli* was found in 2.9% of healthy children in Sweden, 10% in Senegal, and 2.7% in Portugal. However, the MDR of *E. coli* in children was 47.68% in our sample, which is concerning. Not only *E. coli*, but also other common pathogens (*Vibrio cholerae*, *Shigella spp.*, and *Salmonella Typhi*) showed higher MDR resistance levels in our country than in other developed countries. Furthermore, there were significant differences between *vibrio cholerae* resistance to antibiotics in Sub-Saharan Africa and resistance in our region. Ampicillin resistance was documented to be 43.3% in Sub-Saharan Africa (Mohammed et al., 2018), while resistance was 70% in Bangladesh. Similarly, resistance to Chloramphenicol (43.3%), Nalidixic acid (30%), Streptomycin (30%), and Ceftriaxone (20%) was found in Sub-Saharan Africa, while it was found in Bangladesh at 20.5%, 73.5%, 97%, and 25%. As a result, these medications can be used effectively to treat intestinal infections.

In a separate setting, *E. coli* was the most common pathogen, followed by *Staphylococcus aureus* in wound infection. "According to the Centre for Disease Control & Prevention (CDC), *Staphylococcus aureus* was the most common organism associated with surgical wound infection." A previous study was conducted in Lahore, which was consistent with our findings that *S. aureus* became the major causative organism of surgical wound infection (Roy et al., 2017). In the present study, we found that only *Staphylococcus aureus* isolated was sensitive to Oxacillin & Chloramphenicol. Among 15 antibiotics, isolated *Proteus spp.* were sensitive (100%) to Azithromycin, Imipenem Ceftriaxone, and Cefuroxime. The high susceptibility pattern suggests that Gentamycin might be an effective antibiotic for treating *Klebsiella species*. The present study showed that Azithromycin, Ceftriaxone, Imipenem & Cefuroxime were the most effective (100% sensitivity) antibiotics against (Gr-) bacteria. We evaluated Gentamicin, Tetracycline, Cefotaxime, Penicillin, Cefuroxime, Cephradine antibiotics were the most ineffective (100% resistance).

Conclusion

The development of multidrug-resistant pathogens and the declining efficacy of antibiotics pose a global public health problem. Antibiotic resistance (ABR) has increased dramatically in recent years, posing a serious threat to human health and the global economy. However, developing countries

are mostly suffering because of indiscriminate use of antibiotics, low drug quality, insufficient monitoring, and national poverty, (inadequate healthcare standard, chronic and recurring disease, malnutrition, unaffordability to purchase more effective and expensive medications). Furthermore, since newer medications are scarce, we must confront the resistance before run out of combative alternatives. Bangladesh, a Southeast Asian developing country poses a global and regional threat with a high degree of ABR. Bangladesh's current situation is becoming increasingly upsetting. In Bangladesh, the most significant factors influencing the recent phenomenon are increased usage of antibiotics, unregulated use, and antibiotic abuse. Emerging regulation and efforts should be made to eradicate this problem immediately. In this review article, we attempt to cover an overall scenario of the antibiotic situation in the last five years (2015-2020). It can be concluded that it is now necessary to generate effective policies or actions to make and monitor antibiotic use in an effective way. Finally, the information that has been provided by our efforts will create awareness for generating rational antibiotic prescriptions to minimize antibiotic resistance, and eventually, it will ensure patient safety by using the proper antibiotic.

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