Communicable Diseases Intelligence

2026 Volume 5

cdc.gov.au/cdi • Electronic publication date: 24.03.2026 • doi.org/10.33321/cdi.2026.50.026

Shigellosis: antibiotics should be strictly reserved for severe disease and cases at very high risk of onward transmission

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Australian Centre for Disease Control

Communicable Diseases Intelligence

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ISSN: 2209-6051 Online

This journal is indexed by Index Medicus and Medline.

Original article

Abstract

Increasing rates of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Shigella* have been detected worldwide. This retrospective review of shigellosis notifications in Southeast Queensland found that XDR *Shigella* accounted for 48% of notifications. Antimicrobial treatment should be reserved for individuals with severe disease, immunocompromise or high risk of onward transmission.

Keywords: antimicrobial resistance; public health; shigellosis

Introduction

Shigella species cause diarrhoeal illness that is usually self-limiting but may be life-threatening, particularly in children aged five years and under; in malnourished people; and in immunocompromised people.[1] Shigellosis may be foodborne or sexually acquired. Specific *Shigella* clones have emerged as an important cause of sexually transmitted infections circulating in communities of men who have sex with men (MSM) in Australia and elsewhere.[1] Antimicrobial treatment reduces symptom duration by two days and is indicated for individuals with severe diarrhoea or immunocompromise. Treatment may also be used to reduce onward transmission. Groups considered at higher risk of transmitting *Shigella* include MSM; children younger than six years; food handlers; healthcare workers; childcare workers; and people living in or working in residential care facilities.[2,3] Among MSM, shigellosis is associated with having dense sexual networks; living with human immunodeficiency virus (HIV); using HIV pre-exposure prophylaxis; use of mobile phone applications to meet sexual partners; visiting sex on premises venues; chemsex (sex between men that occurs under the influence of drugs taken immediately before or during sex); and oral-anal sexual contact.[3,4]

Globally, indiscriminate antimicrobial use has driven the emergence of *Shigella* isolates that are multidrug-resistant (MDR) and extensively drug-resistant (XDR).[1] MDR *Shigella* are resistant to three or more of the following antibiotic classes: azithromycin; fluoroquinolones; third generation cephalosporins; co-trimoxazole; and ampicillin.[5] XDR *Shigella* are phenotypically resistant to third generation cephalosporins or have genotypic detection of an extended spectrum beta-lactamase (ESBL) gene.[i] Our study aimed to describe the epidemiology, including antimicrobial resistance patterns, of shigellosis in Southeast Queensland in 2022 and 2023 to help inform future public health management.

i R. Wright, Australian Government Department of Health, Disability and Ageing; email communication, March 2022.

Methods

We conducted a retrospective review of cases of shigellosis notified to the Gold Coast, Metro North and Metro South Public Health Units from 1 January 2022 to 31 December 2023. Cases were included if they met the Communicable Diseases Network Australia (CDNA) definition for confirmed shigellosis.[6]

Demographic, epidemiological, laboratory and clinical data were abstracted from Public Health Unit records and from Queensland Health's Notifiable Conditions System (NoCS). Public and private pathology laboratories provided phenotypic antimicrobial resistance data to NoCS. Genotypic antimicrobial resistance data were obtained from the Public and Environmental Health Reference Laboratory (PEHRL). Whole genome sequencing was performed using accredited methods. ResFinder and PointFinder were used to detect acquired and chromosomal mutations.[7]

Data were analysed using Microsoft Excel's descriptive statistics tools. Ethics approval was obtained from Metro South Health Human Research Ethics Committee (HREC/2024/QMS/105419).

Results

Of 98 cases of shigellosis notified to participating Public Health Units, 67 were male. Case ranged in age from 1 to 87 years (median 35 years; Table 1). Of notified cases, 56% were overseas acquired and 37% were in men who have sex with men. Groups traditionally considered at high risk for transmitting *Shigella*, including childcare attendees and workers, food handlers and healthcare workers, accounted for 13% of cases. Eighteen percent of cases were hospitalised.

Of notified cases, 95 were analysed for markers of genotypic resistance. Of these, 48.4% were XDR; 5.4% were MDR but sensitive to third generation cephalosporins; and 21.1% were resistant to all of ampicillin, ciprofloxacin, co-trimoxazole, ceftriaxone and azithromycin. XDR *Shigella* was more common in MSM cases than in overseas acquired cases. Eight cases identified as MSM and acquired *Shigella* infection overseas. No carbapenem resistance was detected. Sixty-one percent of cases were treated with antibiotics; 71.9% received appropriate antibiotics.

Table 1: Characteristics and treatment of cases of shigellosis notified to three Public Health Units in Southeast Queensland, 1 January 2022 – 31 December 2023

Characteristic	Category	N[a]	Cases	
			n	%
Age in years	—	98	35[b]	1–87[c]
Sex	male	98	67	68.4%
Species	*Shigella sonnei*	98	63	64.3%
	Shigella flexneri	98	31	31.6%
Overseas acquired	—	95	53	55.8%
Men who have sex with men (MSM)	—	97	36	37.1%
Case is in groups traditionally listed as high-risk[d]	—	98	13	13.3%
Hospitalisation[e]	—	98	18	18.4%
Phenotypic antimicrobial resistance results	Ampicillin resistant	79	52	65.8%
	Ciprofloxacin resistant	76	41	53.9%
	Co-trimoxazole resistant	80	60	75.0%
	Ceftriaxone resistant	48	15	31.3%
	Azithromycin resistant	52	33	63.5%
Genotypic antimicrobial resistance results	Ampicillin resistant	95	62	65.3%
	Ciprofloxacin resistant	95	48	50.5%
	Co-trimoxazole resistant	95	67	70.5%
	Ceftriaxone resistant	95	46	48.4%
	Azithromycin resistant	95	42	44.2%
Extended spectrum beta-lactamase (ESBL) gene detected	—	84	32	38.1%
Summary of antimicrobial resistance[f]	XDR[g]	95	46	48.4%
	MDR[h] but not XDR	95	5	5.4%
Antimicrobial resistance in MSM	XDR	35	28	80.0%
	MDR but not XDR	35	4	11.4%

Characteristic	Category	N[a]	Cases	
			n	%
Antimicrobial resistance in overseas acquired cases	XDR	51	17	33.3%
	MDR but not XDR	51	2	3.9%
Treated with antibiotics	—	72	44	61.1%
	Treated with a suitable antibiotic, based on phenotypic resistance patterns	32	23	71.9%

a Total number of cases for which data on the category (or, where 'category' is blank, the characteristic) is available.

b Median age in years, from 98 cases.

c Range of ages in years, from 98 cases.

d Groups traditionally considered at high risk of transmitting *Shigella* include childcare attendees, childcare workers, healthcare workers and food handlers.

e Median duration of hospitalisation was 4 days, with a range of 1–9 days, from 18 hospitalised cases.

f Summary is based on genotypic antimicrobial resistance and ESBL gene detection.

g XDR (extensively drug resistant): isolate that is phenotypically resistant to any third generation cephalosporin (e.g. ceftriaxone/cefotaxime/ceftazidime) or with genotypic detection of an ESBL gene.

h MDR (multidrug resistant): isolate that is resistant to three or more of the following antibiotic classes: ampicillin; fluoroquinolones; co-trimoxazole; third generation cephalosporin; azithromycin.

Discussion and conclusions

Our study found high levels of antimicrobial resistance, with XDR *Shigella* accounting for nearly 50% of all cases of shigellosis and 80% of MSM cases. Where drug susceptibility testing results were available and antibiotics were administered, 72% of cases received an appropriate antibiotic as assessed by susceptibility testing results.

Our findings are consistent with other reports of shigellosis showing high rates of antimicrobial resistance in Australia, particularly among MSM.[8,9] To our knowledge, this is the first Australian study to assess appropriateness of antibiotics administered, based on drug susceptibility testing. Clinical guidelines should be updated to recommend antimicrobial treatment is reserved for cases with severe illness, immunocompromise, or following a case-by-case risk assessment of onward transmission. All cases should be provided with education to prevent transmission, including hand hygiene and abstinence from sexual contact until no longer infectious. Cases in high-risk groups (including food handlers) should be excluded from higher-risk work duties until they have microbiological evidence of clearance, defined as one negative stool culture or PCR, collected at least 48 hours after diarrhoea has ceased and no sooner than 48 hours after finishing antibiotics.[10] If provided, treatment should preferably be based on antibiotic susceptibility. Where empiric treatment is required, carbapenems may be the only effective option.

Among MSM populations, health promotion is required to prevent sexually transmitted shigellosis. Messaging should be integrated into pre-exposure prophylaxis (PrEP) for HIV prevention and routine HIV care.[11] Potential harm reduction strategies should be considered, including washing hands, sex toys, genitals and anus before and after sexual contact.[12]

This study has potential limitations. Not all cases receive a microbiological diagnosis due to the self-limiting nature of the illness. Some cases of *Shigella* may have been excluded because they were PCR positive but not culture positive. Genotypic data were not available for three of the 98 cases and some data were missing from Public Health Unit records, particularly regarding antibiotic use. Data about antibiotic use were missing for 26/98 cases.

Shigella spp. that are resistant to almost all antimicrobial classes are increasing.[1] A nationally coordinated approach across expert groups (laboratories, foodborne disease epidemiologists, STI experts) is required to manage the public health risks associated with XDR *Shigella*.[13] Currently, case-level data submitted to the National Notifiable Disease Surveillance System (NNDSS) do not include antimicrobial resistance data. Phenotypic antimicrobial susceptibility testing data submitted to the Critical Antimicrobial Resistance Alert System (CARAlert) should be connected to case-level data in NNDSS to identify risk factors for XDR *Shigella*.[13] A national genomic surveillance program may enhance our ability to respond to the threat of XDR *Shigella*.[13]

Our findings contribute to the understanding of drug-resistant *Shigella* in Southeast Queensland. A multifaceted approach is required to respond to the public health threats of MDR and XDR *Shigella*, including improved national surveillance of antimicrobial-resistant shigellosis, judicious use of antibiotics and integrating harm reduction messaging into PrEP.

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