Relating knowledge, attitude and practice of antibiotic use to extended-spectrum beta-lactamase-producing Enterobacteriaceae carriage: results of a cross-sectional community survey

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ABSTRACT

Objectives To study the correlation between knowledge, attitude and practices (KAP) of antibiotic consumption with epidemiology and molecular characteristics of extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE) carriage, in order to identify modifiable factors and public health interventions to reduce prevalence of multidrug-resistant organism colonisation in the community.

Design Cross-sectional questionnaire of KAP towards antibiotic use and collection of stool samples or rectal swabs. ESBL-PE isolates obtained underwent whole genome sequencing to identify resistance genes.

Setting A densely populated community in Singapore.

Participants There were 693 healthy community-dwelling questionnaire respondents. Out of which, 305 provided stool samples or rectal swabs.

Results The overall knowledge of antibiotic use was poor (mean score 4.6/10, IQR 3.0–6.0). 80 participants (80/305, 26.2%) carried at least one ESBL-PE isolate. The most common ESBL-PE was *Escherichia coli* sequence type 131 carrying CTX-M type beta-lactamases (11/71, 15.5%). Living overseas for >1 year (OR 3.3, 95% CI 1.6 to 6.9) but not short-term travel, recent hospitalisation or antibiotic intake was associated with ESBL-PE carriage. Interestingly, higher knowledge scores (OR 2.0, 95% CI 1.03 to 3.9) and having no leftover antibiotics (OR 2.4, 95% CI 1.2 to 4.9) were independent factors associated with ESBL-PE carriage in the multivariate logistic regression model.

Conclusions While the role of trans-border transmission of antimicrobial resistance is well known, we may have to examine the current recommendation that all antibiotics courses have to be completed. Clinical trials to determine the optimum duration of treatment for common infections are critically important.

Strengths and limitations of this study

► Based on individual-level data, we adopted a novel approach of correlating knowledge, attitude and practice of antibiotic use with asymptomatic carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae to identify modifiable factors to mitigate antimicrobial resistance in the community.

► We randomly sampled a large number of households in the community representative of the Singaporean general public in terms of demographics and socio-economic status.

► Extended-spectrum beta-lactamase-producing Enterobacteriaceae were confirmed with both phenotypic antibiotic susceptibilities and whole genome sequencing.

► We minimised recall and interviewer biases by designing specific questions that are carefully constructed to maximise accuracy and completeness, and all interviewers were trained to adhere to the question and answer format strictly.

► Correlations found in the study cannot be viewed as causal given the complexities in the emergence and transmission of antimicrobial resistance.

all-cause mortality, transmissibility and burden.[1] Resistance in Enterobacteriaceae is most commonly mediated via the production of extended-spectrum beta-lactamases (ESBL) and carbapenemases.[2] MDRE infections are difficult to treat with few effective antimicrobials on the horizon.[1] Healthy members of the community are increasingly identified as a reservoir of antimicrobial resistance (AMR), especially in the case of ESBL-producing Enterobacteriaceae (ESBL-PE).[3] Asymptomatic carriage of ESBL-PE has been associated with more infections, longer

INTRODUCTION

Multidrug-resistant Enterobacteriaceae (MDRE) have been identified as 'critical priority' resistant organisms by WHO in 2017, and are associated with a high overall

hospitalisations, earlier time to death and higher hospital costs.[4 5]

South East Asian (SEA) countries are known to be a hot spot for AMR.[6] However, the region is heterogeneous with varying healthcare standards and antimicrobial stewardship and utilisation policies.[7] To aid in designing effective public health policies and engage the community in the campaign against AMR, it is crucial to understand the local knowledge, attitude and practices of antibiotic use. This study aims to correlate the epidemiological and behavioural risk factors of ESBL-PE carriage in Singapore, a high-income country in SEA, as well as delineate the genetic mechanisms associated with these resistant organisms.

METHODOLOGY
Study population
The study was carried out in Clementi Township, a densely populated residential area in the west of Singapore. It comprises 27142 households with 91630 residents who are sociodemographically comparable to the general Singapore population in terms of age, gender, ethnicity and housing distribution.[8] The study team returned to non-responding households for up to three times on separate days to maximise the response rate. The first adult aged above 21 years in each household who responded to the study team was invited to participate in this cross-sectional study; all consenting individuals undertook a questionnaire, while some additionally consented to provide a rectal swab or stool sample. To calculate the number of samples required to estimate the prevalence of ESBL-PE in the community, we used one-sample Z-test with an estimated prevalence of 50%, a CI of 95% and maximum tolerable error of 10%. This yielded about 100 stool samples.

Questionnaire on knowledge, attitudes and practices on antibiotic intake and health-seeking behaviour
We conducted a questionnaire study to assess the knowledge, attitude and practices (KAP) of participants towards antibiotic use. A 40-item questionnaire was developed after performing a thorough literature review of comparable studies.[9–14] This was then validated by a pilot study involving 75 community-dwelling volunteers to ensure fluency and accuracy in question design and language. A team of 33 investigators was trained to administer the survey face-to-face, in languages that the participants are fluent in with standardised explanations, to ensure consistency.

The questionnaire comprised four main sections. The first covered sociodemographic data and recent antibiotic intake. The second was an assessment of antibiotic consumption practices, in which two hypothetical scenarios of diarrhoea and upper respiratory tract symptoms were presented, and participants were asked if they would visit the doctor should they experience these symptoms for <1 week, if they would expect or insist on

an antibiotic prescription from the doctor's visit, and if they would seek a second opinion if antibiotics were not prescribed. The third component assessed participants' attitudes and trust towards primary care healthcare providers, and was adapted from a validated questionnaire from Hall et al.[15] The last component examined participants' knowledge on AMR. The full questionnaire and grading system can be found in online supplementary table S1.

Bacterial isolation and antibiotic susceptibility testing
The study team requested fresh stool samples or rectal swabs from all study participants. The samples of those who consented were collected from the participants within 24 hours of production and stored centrally at 0°C–4°C prior to microbiological processing. All sample processing was carried out in the Singapore General Hospital Diagnostic Bacteriology Laboratory. Samples were inoculated onto *CHROMagar ESBL* and *CHROMID CARBA SMART (bioMerieux)* media to detect cephalosporin-resistant and carbapenem-resistant Gram-negative bacteria, respectively. After 24 hours of incubation, growing colonies were subcultured onto sheep blood agar and used for subsequent species identification and antibiotic susceptibility testing. Species identification was done by matrix-assisted laser desorption/ionisation-time of flight mass spectrometry (MALDI-TOF MS) (Bruker) and the Vitek-2 *(bioMerieux)* system.

Antibiotic susceptibilities to ampicillin, cefazolin, ceftriaxone, cefoxitin, cefepime, amoxicillin-clavulanic acid, piperacillin-tazobactam, aztreonam, amikacin, nitrofurantoin, sulfamethoxazole-trimethoprim, gentamicin, ciprofloxacin, fosfomycin, ertapenem and meropenem were assessed by the disc diffusion method and interpreted according to the Clinical Laboratory Standards Institute criteria.[16] Enterobacteriaceae isolates that were not susceptible to third-generation/fourth-generation cephalosporins were identified as potential ESBL producers, while those not susceptible to any carbapenem were identified as potential carbapenemase producers. Potential carbapenemase producers were tested phenotypically for carbapenemase production by modified Hodge test and KPC/MBL and OXA-48 Confirm Kit (ROSCO). All potential carbapenemase producers were also subjected to the Xpert Carba-R test (Cepheid) targeting KPC, NDM, OXA-48 like, IMP and VIM carbapenemase gene sequences.

Whole genome sequencing of ESBL-producing Enterobacteriaceae
DNA extraction was performed for all Enterobacteriaceae isolates that are potentially ESBL or carbapenemase producers, with sequencing libraries for each isolate prepared as per manufacturer's recommendation to be multiplexed sequenced on the Illumina HiSEQ platform generating paired-end sequence reads of 2×150 basepairs, having a data throughput of 1 GB per isolate. De novo assembly of the Illumina reads was performed

using the SPAdes Genome Assembler.[17] Bacterial species were identified using Kraken,[18] comparing with phenotypic results. Multilocus sequence types were determined by a customised script using BLAST search for identification of genotypes at each loci.[19] Genotypic prediction of antimicrobial resistance owing to the existence of specific gene sequences were performed using SRST2.[20]

Statistical analysis

Univariate descriptive analyses are presented for sociodemographics, ESBL-PE or C-PE carriage status and presence of specific resistance genes. Dichotomous variables are expressed in frequencies and percentages, while continuous variables are in means with SD. Categorical variables are compared with χ^2 and Fisher's exact tests and continuous variables with unpaired, two-tailed t-tests or non-parametric Wilcoxon rank sum tests as appropriate. Linear and logistic regressions are used in multivariate analyses to identify statistically significant factors that influence and determine KAP and ESBL-PE carriage. Covariates that were found to be statistically significant in the univariate analyses were included in the multivariate models. All tests of significance are performed at α=5%. Statistical analysis was carried out using R V.1.1.383.[21]

Patient and public involvement

A group of 75 community dwellers partnered with us for the design and validation of the study questionnaire to ensure clarity and accuracy, production of informational material to support recruitment and evaluation of the burden of the sample collection from the patient's perspective. Because there was no clear preference for the sample collection methodology, the study team decided to offer both options of rectal swab and stool collection to the study participants.

RESULTS

From June 2016 to April 2017, we randomly selected 2200 households in Clementi for home visits. Out of these 2200 households, 693 (31.5%) agreed to participate, of whom 305 (44.0%) also provided stool samples or rectal swabs (online supplementary figure S1). Participant demographics are presented in table 1. The median age of participants was 53 (IQR 38–66). A slight majority were women (393/693, 56.7%). The ethnic distribution of the participants was similar to the wider Singapore population, with 513 (74.0%) Chinese, 78 (11.3%) Malay and 83 (12.0%) Indian. The majority had received at least secondary school education (534/693, 77.0%), and stayed in public housing apartments (661/693, 95.4%). The median number of occupants per household was 3 (IQR 2–4) persons. A quarter (25.3%, 175/693) reported having taken antibiotics in the past 6 months, and 102 (14.7%) had recently been hospitalised in the past 1 year.

The survey revealed widespread misinformation about antibiotics, with a mean knowledge score of only 4.6 (IQR 3.0–6.0) out of 10 (online supplementary table S2).

Table 1 Demographics, medical background and antibiotic use of study participants

Characteristic	N (%) Total n=693
Age (median, IQR)	53.0 (38.0–66.0)
Females	393 (56.7)
Race	
Chinese	513 (74.0)
Malay	78 (11.3)
Indian	83 (12.0)
Other ethnicities	19 (2.7)
Education level	
Graduate	88 (12.7)
Diploma	251 (36.2)
Secondary	195 (28.1)
Primary	122 (17.6)
No formal education	37 (5.3)
Housing type	
One-room, two-room or three-room public housing	334 (48.2)
Four-room or five-room public housing	327 (47.2)
Private landed property	32 (4.6)
Number of occupants in the household	
Overall (median, IQR)	3 (2–4)
≤3 persons	369 (53.2)
4–5 persons	257 (37.1)
≥6 persons	67 (9.7)
Comorbidities	
Any chronic illnesses	239 (34.5)
Hypertension	105 (15.2)
Hyperlipidemia	76 (11.0)
Diabetes mellitus	67 (9.7)
Recent hospitalisation in the past 1 year	102 (14.7)
Antibiotic consumption	
Within past 6 months	175 (25.3)
>6 months ago	441 (63.6)
Never taken antibiotics	77 (11.1)

Although the majority of participants knew that viruses are the most common cause of upper respiratory tract infections, a significant proportion (335/693, 48.3%) believed that antibiotics could be used for viral infections and 385 (385/693, 55.6%) thought that the most common cause of diarrhoea was bacteria. The questionnaire also explored participants' compliance to the widely accepted view of completing antibiotic courses. The majority (554/693, 79.9%) said they would complete the course of antibiotics prescribed, while 13.7% (95/693) would stop taking antibiotics when they start to feel better, and 6.3% (44/693) preferred to seek the doctor's opinion before

stopping the course. Most participants (564/693, 81.4%) were aware that antibiotics are prescription-only drugs in Singapore, but were unable to correctly answer questions related to AMR, with 82.5% (572/693) not knowing what causes AMR, and 63.2% (438/693) believing AMR was not present in Singapore. Level of education (p<0.001) and staying in larger housing (p=0.037)—the usual proxies for socioeconomic status in Singapore—were independent factors associated with higher total knowledge scores. However, higher knowledge scores were not strongly related to participants' trust in primary care physicians (OR 1.08, 95% CI 0.97 to 1.20) or the expectation of an antibiotic prescription for common viral infections (OR 0.98, 95% CI 0.96 to 1.0).

A large majority of the community continued to place trust in their primary care doctors (online supplementary table S3). Most strikingly, 627 participants (627/693, 90.6%) trusted healthcare professionals as their primary source of medical information, over the internet, media and family and friends. There were no significant associations between demographic factors and attitude scores in contrast to the differences seen in knowledge scores.

In the two scenarios (of having an upper respiratory tract infection or diarrhoea and vomiting), although about half of the participants (294/693, 42.4% for cough and runny nose, 414/693, 59.7% for diarrhoea and vomiting) envisioned visiting the doctor for common complaints lasting <1 week, only 18.5% (average 128/693) expected an antibiotic prescription (online supplementary table S4). Were antibiotics not prescribed during the initial visit, very few (average 39/693, 5.6%) reported they would insist on antibiotic prescription or seek a second opinion. The only independent factor associated with the expectation of an antibiotic prescription was younger age (OR 0.98, 95% CI 0.97 to 0.99) in multivariate logistic analysis. In dealing with leftover antibiotics, the majority (476/693, 68.7%) declared that they do not have leftovers antibiotics; others reported keeping them for future use (60/693, 8.7%) or disposing with solid waste (130/693, 18.8%) or down the drain (8/693, 1.2%). Only 3.3% (23/693) admitted to having previously shared antibiotics with family members and 5.5% (38/693) to having taken leftover antibiotics from a previous illness.

Asymptomatic carriage of ESBL-PE

Three hundred and five participants (305/693, 44.0%) provided rectal swabs or stool samples for microbiology cultures. The participants who provided stool samples were not significantly different from those who did not, in terms of age, gender and education level. Eighty participants (80/305, 26.2%, 95% CI 21.5% to 31.6%) were found to carry at least one ceftriaxone non-susceptible Enterobacteriaceae isolate. One hundred and fifteen isolates were detected on the ESBL screening media, of which 93 were ceftriaxone resistant or intermediate Enterobacteriaceae. Six bacterial isolates were detected on the CRE screening media, none of which were confirmed to be carbapenemase-producing Enterobacteriaceae. The

factors associated with ESBL-PE carriage from multivariate logistic regression analysis were residency overseas for >1 year (OR 3.3, 95% CI 1.6 to 6.9), with the most common location being other parts of Asia, scoring higher than 6 on the knowledge component in the questionnaire (OR 2.0 95% CI 1.03 to 3.9) and having no leftover antibiotics (OR 2.4, 95% CI 1.24 to 4.9). Interestingly, recent hospitalisation and reported antibiotic intake were not associated with ESBL-PE carriage (table 2).

Out of the 93 ceftriaxone-resistant isolates, 17 were cefoxitin resistant, suggestive of AmpC β-lactamase production. Only one *Enterobacter cloacae* complex isolate was resistant to ertapenem and was of intermediate susceptibility to meropenem (table 3). This *E. cloacae* complex isolate was not a carbapenemase-producer based on phenotypic and genotypic tests. Eighty-three (83/93, 89.2%) of these ESBL-PE isolates were *Escherichia coli*. The majority of ESBL-PE remained susceptible to aminoglycosides including gentamicin (80/93, 86.0%) and amikacin (91/93, 97.8%) as well as nitrofurantoin (76/93, 81.7%), while ciprofloxacin (53/93, 57.0%) and sulfamethoxazole-trimethoprim (32/93, 34.4%) resistance were more common.

Molecular classification of ESBL-PE

Eighty (80/93, 85%) ESBL-PE isolates from unique participants underwent whole genome sequencing. When two or more isolates grew from a single subject's sample, *E. coli*, the most common species observed, was selected to facilitate comparisons. Genotypic species determination from the sequence reads correlated completely with the results by MALDI-TOF MS or the Vitek-2 system. Seventy-one (71/80, 88.8%) isolates were *E. coli*, of which the most common molecular type was sequence type (ST) 131 (11/71, 15.5%) (online supplementary table S5). The most frequently observed ESBL gene was CTX-M (62/80, 77.5%), especially CTX-M-15 (21/71, 29.6%) and CTX-M-27 (16/71, 22.5%). *E coli* ST131 were more resistant to fluoroquinolones than non-ST131 isolates (p=0.041). The only significant factor from the questionnaire associated with ESBL-producing *E. coli* ST131 carriage was having more children in the household, but the difference was marginal (mean 0.3±0.7 vs 0.8±1.1, p=0.034).

DISCUSSION

We found a significant burden of ESBL-PE carriage (80/305, 26.2%) among healthy community dwellers in Singapore, twice the rate found in an earlier study in 2014 of patients at an emergency department.[22] Similar rises have been observed globally.[3] Although these figures are lower than the reported prevalence of over 40% faecal carriage with ESBL-PE elsewhere in South and South East Asia, they are much higher than the 1.5%–3% observed in the USA and UK.[3] Singapore has a tightly regulated antibiotic prescription system similar to Europe and the USA where only registered medical practitioners are allowed

Table 2 Univariate analysis of demographic characteristics associated with carriage of ceftriaxone-resistant Enterobacteriaceae

Factors	Total n=305	Carriers n=80	Non-carriers n=225	P values
Age (median, IQR*)	54.0 (41.0–65.0)	56.0 (38.8–66.0)	54.0 (41.0–65.0)	0.79
Females (%)	169 (55.4)	46 (57.5)	123 (54.7)	0.76
Ethnicity (%)				
Chinese	237 (77.7)	67 (83.8)	170 (75.6)	0.24
Malay	28 (9.2)	3 (3.8)	25 (11.1)	
Indian	30 (9.8)	7 (8.8)	23 (10.2)	
Others	10 (3.3)	3 (3.8)	7 (3.1)	
Education (%)				
No formal education	11 (3.6)	4 (5.0)	7 (3.1)	0.45
Primary	57 (18.7)	12 (15.0)	45 (20.0)	
Secondary	93 (30.5)	21 (26.2)	72 (32.0)	
Tertiary	110 (36.1)	31 (38.8)	79 (35.1)	
Graduate	34 (11.1)	12 (15.0)	22 (9.8)	
Housing (%)				
HDB one-room and two-room	23 (7.5)	5 (6.2)	18 (8.0)	0.75
HDB three-room	115 (37.7)	32 (40.0)	83 (36.9)	
HDB four-room	98 (32.1)	24 (30.0)	74 (32.9)	
HDB five-room and executive apartment	47 (15.4)	11 (13.8)	36 (16.0)	
Landed property	22 (7.2)	8 (10.0)	14 (6.2)	
Pets (%)	33 (10.8)	7 (8.8)	26 (11.6)	0.75
Number of occupants in the household (mean, SD)	3.6 (1.6)	3.6 (1.6)	3.6 (1.6)	0.71
Stayed overseas for >1 year (%)	57 (18.7)	26 (32.5)	31 (13.8)	<0.001
Stayed in South, East or Southeast Asia for >1 year (%)	40 (13.1)	18 (22.5)	22 (9.8)	0.01
Travelled in the past >1 year (%)	178 (58.4)	47 (58.8)	131 (58.2)	1.0
Travelled in South, East or Southeast Asia in the past 1 year (%)	163 (53.4)	43 (53.8)	120 (53.3)	1.0
Any chronic illnesses (%)	127 (41.6)	33 (41.2)	94 (41.8)	1.0
Hospitalisation in the past 1 year (%)	43 (14.1)	14 (17.5)	29 (12.9)	0.41
Previous antibiotics intake (%)	282 (92.5)	76 (95.0)	206 (91.6)	0.45
Antibiotics in the last 6 months (%)	85 (27.9)	23 (28.8)	62 (27.6)	0.61
Knowledge score >6 (%)	89 (29.2)	33 (41.3)	56 (24.9)	0.01
No leftover antibiotics (%)	211 (69.2)	63 (78.8)	148 (65.8)	0.04

to prescribe antibiotics, and they must be purchased from licensed dispensers. We did not find any association between faecal carriage of ESBL-PE and short-term travel, unlike other studies.[23] Singapore is a city-state and overseas travel is very common, making it hard to detect such a relationship when frequent trips to neighbouring countries are made. However, past residency overseas was strongly associated with colonisation, especially those who lived elsewhere in South or South East Asia (OR 3.3, 95% CI 1.6 to 6.9). Distinctions should be made in future studies on overseas travels and AMR carriage in terms of duration and frequency of travel, in addition to destinations. The possibility of substantial acquisition of MDRO colonisation and infection through overseas exposure[24 25] once again highlights the urgent need for a regional, collaborative approach to tackling the problem of AMR.

In addition, we did not find an association between recent antibiotic intake in the past 6 months and ESBL-PE carriage. This is inconsistent with previous reports showing that consumption of certain classes of antibiotics such as beta-lactams and fluoroquinolones are risk factors for predispositions to ESBL-PE carriage.[26 27] The possible reasons could be due to the relatively small number of participants who had recent antibiotic intake (85/305, 27.9%), so we were not able to distinguish the specific classes of antibiotics taken by the participants. It is also

Table 3 Antibiotic susceptibility of the ceftriaxone-resistant isolates

	Escherichia coli (n=83) N (%)	*Klebsiella* (n=6) N (%)	Others* (n=4) N (%)	Total (n=93) N (%)
Piperacillin-tazobactam	73 (88.0)	4 (66.7)	1 (25.0)	78 (83.9)
Cefepime	35 (42.4)	3 (50)	2 (50.0)	40 (43.0)
Aztreonam	39 (47.0)	2 (33.3)	1 (25.0)	42 (45.2)
Amikacin	82 (98.8)	5 (83.3)	4 (100)	91 (97.8)
Gentamicin	75 (90.4)	3 (50)	2 (50.0)	80 (86.0)
Nitrofurantoin	73 (88.0)	2 (33.3)	1 (25.0)	76 (81.7)
Sulfamethoxazole-trimethoprim	32 (38.6)	0 (0)	0 (0)	32 (34.4)
Ciprofloxacin	48 (57.8)	4 (66.7)	1 (25.0)	53 (57.0)
Fosfomycin	63 (75.9)	1 (16.7)	0 (0)	64 (68.8)
Ertapenem	83 (100)	6 (100)	3 (75.0)	92 (98.9)
Meropenem	83 (100)	6 (100)	3 (75.0)	92 (98.9)

*Others include *Enterobacter* species (2), *Proteus mirabillis* (1), *Raoultella ornithinolyitca* (1).

possible that the dominance of a hyperendemic community-associated clone rather than antibiotic selection pressure alone contributed to this finding.

Molecular typing of the ESBL-PE isolates from our cohort showed that *E. coli* ST131 with CTX-M beta-lactamases (11/71, 15.5%) were the most common ESBL mechanism, echoing the global dissemination of this hyperendemic clone, especially in the community.[28] Similar reports showed 11.1% (32/287) in China[29] and 4.1% (8/193) in Thailand[30] have been published. The reason for the rapid worldwide expansion and long-term persistence of *E. coli* ST131 is thought to be due to compensatory mutations within the core genome counterbalancing the fitness cost associated with IncF plasmids, thus sustaining its spread even in the absence of direct antibiotic selection pressure.[31] These *E. coli* ST131 are not just prevalent colonisers but have also associated with invasive bloodstream infections in hospitalised patients in Australia, New Zealand and Singapore.[32] It will be important to better understand the evolutionary ecology and transmission dynamics of this emerging clone.

This study also revealed widespread misconceptions about the utility of antibiotics for viral infections, consistent with the findings of a global survey conducted by WHO in 2015.[33] We also found that, the public continues to place trust in their primary care doctors and their recommendations. This dependence on physicians is in contrast to doctors' perceptions of patient expectations for antibiotic prescriptions.[34] This discordance has been previously described and is thought to be due to the lack of empowerment of the patient and the erroneous attribution of patient satisfaction to antibiotic prescription rather than a focus on better patient-doctor communication.[35 36]

Engaging and educating both the prescribers and the public may reduce inappropriate antibiotic use,[37 38] and has been identified as a key strategy by WHO and the UK

to tackle AMR.[39 40] One of the most striking findings of this study is that having both the knowledge that antibiotic courses should be completed and not having leftover antibiotics is independently associated with the carriage of ESBL-PE. Although these relationships cannot be viewed as causal given the complexities in the emergence and transmission of AMR, there is emerging evidence supporting short course antibiotic therapies, even for severe infections such as bacteraemia, given the collateral damage that antibiotics have on host microbiome.[41] The current WHO recommendation remains that full courses of antibiotics should be completed to prevent the onset of resistance.[33] Similar messages are advocated in national campaigns launched in Australia,[42] the USA[43] and Europe.[44] Given that the minimum effective treatment durations have not been determined for many infections and that a significant proportion of antibiotic prescriptions are inappropriate, the emphasis on completing the course of antibiotics to prevent resistance may have to be re-examined.

To our knowledge, this is the first study that explored antibiotic consumption behaviour with the acquisition of MDRO at a community level. This novel approach has the potential to guide clinicians and policy makers in identifying directly actionable interventions for the population. The main weakness of our study is that the questionnaire data is self-reported and subjected to recall and interviewer biases. We minimised these errors by designing specific questions that are carefully constructed to maximise accuracy and completeness, and all interviewers were trained to adhere to the question and answer format strictly. Further research using antibiotic prescription databases can potentially overcome some of the intrinsic biases arising from cross-sectional questionnaires.

CONCLUSION

There is a significant burden of asymptomatic ESBL-PE colonisation in Singapore, especially with *E. coli* ST131 carrying CTX-M. This is correlated with KAP of antibiotic use, especially with the practice of finishing full courses of antibiotics, and prolonged residency in other parts of Asia. Innovative approaches to control AMR that take into account transboundary transmission of resistance and clinical trials to determine the appropriate duration of antimicrobial therapy will be critical to control the emergence of these resistant clones, which have contributed significantly to the current global antibiotic resistance crisis.

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