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Short Communication

A point prevalence survey to assess antibiotic prescribing in patients hospitalized with confirmed and suspected coronavirus disease 2019 (COVID-19)

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ABSTRACT

Background: Earlier studies have reported high antibiotic use in patients hospitalised for coronavirus disease 2019 (COVID-19), resulting in concerns of increasing antimicrobial resistance with increase antibiotic use in this pandemic. Point prevalence survey (PPS) can be a quick tool to provide antibiotic prescribing information to aid antimicrobial stewardship (AMS) activities.
Objectives: To describe antibiotic utilization and evaluate antibiotic appropriateness in COVID-19 patients using PPS.
Methods: Adapting Global-PPS on antimicrobial use, the survey was conducted in COVID-19 wards at 2 centres in Singapore on 22 April 2020 at 0800h. Patients on systemic antibiotics were included and evaluated for antibiotic appropriateness.
Results: Five hundred and seventy-seven patients were screened. Thirty-six (6.2%) patients were on antibiotics and which were started at median of 7 days (inter-quartile rate (IQR), 4, 11) from symptom onset. Fifty-one antibiotics were prescribed in these patients. Overall, co-amoxiclav (26/51, 51.0%) was the most often prescribed antibiotic. Thirty-one out of 51 (60.8%) antibiotic prescriptions were appropriate. Among 20 inappropriate prescriptions, 18 (90.0%) were initiated in patients with low likelihood of bacterial infections. Antibiotic prescriptions were more appropriate when reviewed by infectious diseases physicians (13/31 [41.9%] versus 2/20 [10.0%], $p = 0.015$), and if reasons for use were stated in notes (31/31 [100.0%] versus 16/20 [80.0%], $p = 0.019$).
Conclusions: Despite low prevalence of antibiotic use among confirmed and suspected COVID-19 patients at 2 centres in Singapore, there was significant proportion of inappropriate antibiotics use where bacterial infections were unlikely. AMS teams can tailor stewardship strategies using PPS results.

The global response to severe acute respiratory syndrome coronavirus 2 has focused on controlling the spread of infection and development of treatment and vaccines [1]. In a review of common bacterial or fungal co-infections in patients with coronavirus infections, 8% (62/806) of patients with coronavirus disease 2019 (COVID-19) were reported to have such co-infections, while 72% (1450/2010) received antibiotics [2]. Point prevalence surveys (PPS) provide rapid ways to understand the quantity and quality of antimicrobial prescribing, which aids design of antimicrobial stewardship (AMS) strategies [3].

We describe a PPS of antibiotic use conducted on 22 April 2020, at 08:00 h in patients with suspected and confirmed COVID-19 at the National Centre for Infectious Diseases and Tan Tock Seng Hospital. The definition of a suspected case was based on the presence of respiratory symptoms and relevant exposure history. The diagnosis is confirmed with a positive test for SARS-CoV-2, using laboratory-based polymerase chain reaction or serologic

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assays [4]. The objectives were to describe antibiotic use and evaluate antibiotic appropriateness. Trained AMS pharmacists collected antibiotic and clinical data in patients receiving at least one systemic antibiotic at 08:00 h. For each antibiotic, appropriateness was determined by considering the treating physician's diagnosis and adjudicated by the AMS pharmacists and an AMS physician according to in-house and international guidelines. Quality indicators such as the reason for antibiotic prescription and indication of stop/review date were evaluated. Antivirals, antifungals and tuberculosis treatment were excluded.

There were 554 confirmed and 23 suspected COVID-19 patients. Eleven patients (1.9%) were in intensive care units (ICU). Overall, 6% (36/577) of the patients were on antibiotics and these were started at median of 7 days (inter-quartile rate (IQR) 4, 11) from symptom onset. Overall, co-amoxiclav (26/51, 51%) was the most commonly prescribed antibiotic, and oral co-amoxiclav prescribing was often inappropriate (Table 1). Antibiotics were appropriate in 61% (31/51) of prescriptions. The majority of the inappropriate prescriptions (18/20, 90%) were started for conditions deemed to be unrelated to bacterial infections. This resulted in 59 days of inappropriate antibiotic use.

Patients with appropriate antibiotic use had higher age-adjusted Charlson's co-morbidity scores (1 [IQR 1, 4] vs 0 [IQR 0, 0.5], $P = 0.007$) and procalcitonin (0.29 μg/L [IQR 0.13, 1.21] vs 0.07 μg/L [IQR 0.04, 0.12], $P = 0.033$). They were more likely to have severe respiratory illness (10/21 [48%] vs 2/15 [13%], $P = 0.031$) and to need ICU admission (6/21 [29%] vs $n = 0/15$ [0%], $P = 0.030$). Antibiotic prescribing was more appropriate when patients had been reviewed by infectious diseases (ID) physicians (13/31 [42%] vs 2/20 [10%], $P = 0.015$), and if reasons for use were stated in notes (31/31 [100%] vs 16/20 [80%], $P = 0.019$). Other variables are shown in Table 1.

Suspected cases (9/23, 39%) were started on antibiotics more often than confirmed cases (27/554, 5%). Suspected cases were started on antibiotics earlier from symptom onset than confirmed cases (day 4 [IQR 1, 4] vs day 9 [IQR 5.5, 12], $P \leq 0.001$), had higher white blood cell count (11.9×10^9/L [IQR 9.2, 18.83] vs 5.95×10^9/L [IQR 4.98, 7.65], $P = 0.005$), and were more likely admitted to the ICU (3/9 [33%] vs 3/27 [11%], $P = 0.151$). In suspected cases, antibiotics were mainly started for respiratory infections (13/16 [81%] vs 14/35 [40%], $P = 0.006$) and community-onset infections (15/16 [94%] vs 16/35 [46%], $P = 0.001$), and were more often

Table 1
Patient characteristics and antibiotic use in patients.

Unique patients	Overall *N* = 36 (%)	Appropriate use *N* = 21 (%)	Inappropriate use *N* = 15 (%)	*P* value
Patients with confirmed COVID-19 infections	27 (75)	14 (67)	13 (87)	0.252
Patients with suspected COVID-19 infections	9 (25)	7 (33)	2 (13.)	0.252
Age, median, (IQR)	45.5 (36.3, 65.0)	57 (44, 69)	39 (32.5, 45.5)	0.050
Males	27 (75.0)	13 (61.9)	14 (93.3)	0.051
Age-adjusted Charlson's co-morbidity score, median, (IQR)	1 (0, 3.25)	1 (1, 4)	0 (0, 0.5)	**0.007**
Admitted in ICU	6 (17)	6 (29)	0 (0)	**0.030**
qSOFA score, median, (IQR)	1 (0, 1)	1 (0, 2)	1 (0, 1)	0.421
Days from symptom onset to antibiotic initiation, median, (IQR)	7 (4, 11)	7 (4, 11)	7 (4, 11)	0.809
Severe respiratory illness at time of antibiotic initiation[a]	12 (33)	10 (48)	2 (13)	**0.031**
LDH (units/L), median, (IQR)	570 (397, 697.5)	578 (401, 760)	567 (400.5, 648.25)	0.495
WBC ($\times 10^9$/L), median, (IQR)	6.8 (5, 9.25)	7.6 (5.08, 11.28)	5.95 (4.93, 7.63)	0.227
C-reactive protein (mg/L), median, (IQR)	46.1 (11.28, 128.23)	68.5 (10.55, 132.15)	28.4 (15.1, 69.1)	0.409
Procalcitonin (μg/L), median, (IQR)	0.14 (0.07, 0.9)	0.29 (0.13, 1.21)	0.07 (0.04, 0.12)	**0.033**
Unique antibiotic prescriptions	*N* = 51 (%)	*N* = 31 (%)	*N* = 20 (%)	
PO co-amoxiclav	17 (33)	7 (23)	10 (50)	**0.043**
IV co-amoxiclav	9 (18)	6 (19)	3 (15)	>0.999
PO clarithromycin	8 (16)	4 (13)	4 (20)	0.696
IV piperacillin-tazobactam	5 (10)	4 (13)	1 (5)	0.636
PO ciprofloxacin	2 (4)	2 (7)	0 (0)	0.514
PO doxycycline	2 (4)	1 (3)	1 (5)	>0.999
Other antibiotics[b]	8 (16)	7 (23)	1 (5)	0.127
Empiric use	50 (98)	30 (97)	20 (100)	>0.999
Community onset	31 (61)	19 (61)	12 (60)	>0.999
Nosocomial onset	20 (39)	12 (39)	8 (40)	>0.999
Source of infection that each antibiotic was started for				
Unlikely bacterial infection[c]	18 (35)	0 (0)	18 (90)	<**0.001**
Source of likely bacterial infection	33 (65)	31 (100)	2 (10)	<**0.001**
Respiratory	27 (53)	26 (84)	1 (5)	<**0.001**
Ear, nose, throat	2 (4)	2 (7)	0 (0)	0.514
Hepatobiliary	2 (4)	1 (3)	1 (5)	>0.999
Skin and soft tissue	1 (2)	1 (3)	0 (0)	>0.999
Unknown	1 (2)	1 (3)	0 (0)	>0.999
Changes in chest X-radiography	37 (73)	25 (81)	12 (60)	0.107
Signs and symptoms consistent with pneumonia	33 (65)	26 (84)	7 (35)	<**0.001**
Reviewed by infectious diseases physician	15 (29)	13 (42)	2 (10)	**0.015**
Reason for antibiotic was stated in case notes	47 (92)	31 (100)	16 (80)	**0.019**
Stop/review date was stated in case notes	26 (51)	14 (45)	12 (60)	0.301

IQR = interquartile range; ICU = intensive care unit; qSOFA = quick Sequential Organ Failure Assessment; LDH = lactate dehydrogenase; WBC = white blood cell count; PO = per oral; IV = intravenous.
P <0.05 was statistically significant.
[a] See reference [6].
[b] PO amoxicillin, $n = 1$; IV azithromycin, $n = 1$; IV benzylpenicillin, $n = 1$; IV ceftazidime, $n = 1$; IV ceftriaxone, $n = 1$; IV ertapenem, $n = 1$; IV meropenem, $n = 1$; IV metronidazole, $n = 1$.
[c] Patients with unlikely bacterial infection reported median WBC count = 5.9×10^9/L (IQR 4.85, 6.65), median C-reactive protein = 21.4 mg/L (IQR 11.5, 47.2), median procalcitonin = 0.07 μg/L (IQR 0.04, 0.1).

appropriate compared to confirmed patients (13/16 [81%] vs 18/35 [51%], $P = 0.043$).

The low antibiotic prevalence was likely to be a result of fewer severely ill cases, with only 1.9% admitted to ICU. Antibiotics were typically started in the second week of illness during the hyperinflammatory phase, making the differentiation between viral and secondary bacterial infection challenging [5]. Patients with appropriate antibiotic use had more co-morbidities and illness severity in line with the World Health Organization COVID-19 clinical management guidelines [6]. Nonetheless, inappropriate use was significant, often without clinical suggestion of bacterial infections and especially in confirmed cases. Judicious use of oral co-amoxiclav is warranted. Stewardship efforts and consultation with ID physician are recommended, especially when antibiotics are prescribed to confirmed cases and those with mild diseases. Stop/review dates for the antibiotics were only indicated half the time in case notes, and more emphasis should be placed on this to encourage timely review. The evaluation was limited to appropriateness of antibiotic initiation. Only days of inappropriate antibiotic use were collected to illustrate the burden of unnecessary use. Clinical outcomes of patients were not evaluated. Adapting from Global PPS methodology, patients who were not on antibiotics were not assessed and patients' outcomes with and without antibiotics could not be compared [3].

Results from PPS may inform AMS strategies in tailoring educational efforts and targeting interventions to improve quality of antibiotic prescribing.

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Conflict of interest

None declared.

Ethical approval

The study was approved by the institutional review board (DSRB reference: 2020/00677).

Authors' contribution

(1) Conception and design of the study: SH Tan, TM Ng, TH Lee, CB Teng; (2) Acquisition of data: SH Tan, TM Ng, HL Tay, MY Yap, ST Heng, AYX Loo, CB Teng; (3) Analysis of data: SH Tan; (4) Drafting and revision of manuscript: SH Tan, TM Ng, TH Lee.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jgar.2020.11.025.

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