Title/ A multicentre point prevalence survey of hospital antibiotic prescribing and quality indices in the Kurdistan Regional Government of Northern Iraq: The need for urgent action

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Abstract

Background

Rationale antibiotic use is crucial to address antimicrobial resistance (AMR) threats. No study has been undertaken in the Kurdistan Regional Government (KRG) using validated methodologies to document current antibiotic use and areas for improvement given high AMR rates.

Research design and methods

Point prevalence survey (PPS), using the Global PPS methodology, was conducted among the three major public hospitals in KRG/northern Iraq from September-December 2019. Prevalence and quality of antibiotic use were assessed using agreed indicators.

Results

Prevalence of antibiotic use was high (93.7%;n=192/205); with third generation cephalosporins the most commonly prescribed antibiotics (52.6%;n=140/266). Reasons for treatment was recorded for only 61.7% (n=164/266) of antibiotics and high use (89.9%) of parenteral therapy was observed. All therapy was empirical, no stop/review dates were recorded and no treatment guidelines were available. The majority of the prescribed antibiotics (62%; n=165/266) were from the WHO Watch list.

Conclusion

Prevalence of antibiotic use was high not only versus other hospitals in the region but globally including Africa, coupled with significant evidence of sub-optimal prescribing. Swift action is needed to improve future prescribing to reduce AMR. One or two areas should initially be targeted for quality improvement including development of local guidelines, documentation of antibiotic indications and/or stop/review dates.

Keywords

Antimicrobial resistance; Antibiotic utilisation patterns; Iraq; Kurdistan Regional Government; Point prevalence survey; quality improvement programmes

Highlights box

- Published data surrounding antibiotic prescribing in the Kurdistan Region of Iraq, an ethnically distinct and semi-autonomous region, are scarce.
- This study, for the first time, measured and assessed the pattern and quality of antibiotic use in adult inpatients among hospitals in the largest city in Kurdistan Region Government in Northern Iraq using the validated Global PPS methodology, an internationally recognised approach, to identify target areas for quality improvement to support rationale use of antibiotics.
- Our study findings revealed a very high prevalence of antibiotic prescribing, a predominance of intravenous and broad-spectrum antibiotic use, lack of antibiotic prescribing guidance and poor documentation of both indication and planned review of treatment.
- These findings, therefore, indicate the need to develop local and national antimicrobial stewardship programmes (ASPs) to improve the future rational use of antibiotics in order to optimise individual patient care and minimise risk of AMR in Iraq and worldwide.
- Key target areas for ASPs include development of treatment guidelines and targeting 1-2 areas for quality improvement interventions such as documenting reasons for indications and stop/review dates to facilitate IV to oral switching, when appropriate.

1. Introduction

Antimicrobial resistance (AMR) is a serious global public health threat increasing morbidity, mortality and costs, with inappropriate antimicrobial prescribing a key modifiable driver [1-4]. Addressing this requires Global, Regional and National action plans to improve future antibiotic prescribing [5,6]. A key first step is the development of programmes to monitor antibiotic use [3,7], building on recommendations by the World Health Organization (WHO) as part of national action plans (NAP) to reduce AMR [8]. In hospitals, this can be achieved through regular monitoring of antibiotic utilisation against agreed quality indicators including adherence to guidelines using Point Prevalence Surveys (PPS) [1,3,7]. In addition, PPS studies can identify areas for quality improvement with the objective of enhancing future appropriate antibiotic prescribing [7,9].

In Iraq, there are already high rates of multi-drug resistant (MDR) bacteria including MDR *Escherichia coli, Pseudomonas aeruginosa, Klebsiella, and Staphylococcus aureus.* Studies also suggest that over 80% E. coli and other Gram-negative organisms are resistant to third and fourth generation cephalosporins as well as fluoroquinolones [10-13]. Despite evidence of high rates of AMR, data on antimicrobial utilisation patterns in secondary healthcare settings in Iraq are scarce and where available a standardised, validated methodology has not been applied [14-16]. We are aware that eight hospitals from Iraq were included in the Global PPS study incorporating secondary and tertiary care hospitals [7,17]. However, data was not presented at country level but combined within the West and Central Asia region making analysis difficult. Furthermore, we are unaware of any published data on antimicrobial prescribing in the Kurdistan Region of Iraq, an ethnically distinct and semi-autonomous region with its separate established Ministry of Health (MoH) [18]. This is important given the commitment of the Government in Iraq to develop a National Action Plan (NAP) to reduce AMR [19], the desire of the Government of KRG to improve healthcare in the Region, as well as need to prescribe medicines wisely given the continued shortages of medicines in Iraq [20,21]. Consequently, this study aimed to address some of these concerns by assessing current antibiotic prescribing patterns in the Kurdistan region using the Global PPS methodology. Subsequently, identify targets for quality improvement to reduce AMR as well as conserve antibiotic use.

2. Patients and methods

2.1. Study design and setting

This was a multicentre, cross-sectional point prevalence survey (PPS) of antibiotic prescribing patterns using the validated Global PPS methodology [3,7]. Data were collected between September and December 2019 in the three main government/public general hospitals in Sulaymaniyah (the largest city in the Kurdistan Region): Shar Hospital (400 beds), Shorsh Teaching/Military Hospital (88 beds) and Shahid Hemin Hospital (76 beds), thereafter referred to as hospital 1, 2, and 3 respectively. Sulaymaniyah accounts for 41% (2.1 million) of the total Kurdistan Regional Government (KRG) population and is the third largest city in Iraq. Consequently, the findings may also help provide an insight into Iraq as a whole. Both hospitals 1 and 2 consisted of adult medical wards (AMW), adult surgical wards (ASW) and intensive care units (ICU); whereas hospital 3 consisted of AMWs only. Although the public sector is the main source of care in Iraq, some of the population, especially the wealthy, are more likely to use private health care facilities which have not been evaluated here.

In hospital 1, out of a total 400 beds, only 292 beds were adult beds. Consequently, eligible for screening and inclusion in the study, with the remaining 108 beds non-eligible as they were for paediatric and dialysis, as well as day-cases beds. Published studies suggest the average bed occupancy rate in Iraq is 50% [22]. A brief overview of the Iraqi healthcare system structure and service delivery is described in Appendix 1.

2.2. Study participants

All adult inpatients who stayed overnight and were on the ward at 8 am on the survey day(s) were included in the study. Data were collected only from patients who were receiving at least one antibiotic on the day(s) of the survey. Patients were excluded if they were admitted for a short stay without an overnight stay (day case), discharged before 8 am or admitted after 8 am on the day of the survey, or admitted to out-patients or accidental and emergency departments.

2.3. Data collection

Data were collected using the standard and validated PPS tools, which has been explained in detail in the Global PPS protocol [7], via a team of four pharmacists and four nurses who received prior training on how to utilise, fill and apply the PPS methodology and data collection forms and tools. In summary, data were collected using the two PPS forms: the ward form to collect ward level data including the total number of inpatients at 8am on the day of the survey (the denominator), and the patient form to record the number of patients on antibiotics (the numerator) and their details, with each ward completed in one day. The patient form included patient demographics (age, gender) and information about any prescribed antibiotic including any diagnosis, indications, and dosage regimen. For the indications, two major categories were used: treatment (defined as antibiotic l prescribing to treat both community-acquired and healthcare-associated infections [infections that become symptomatic more than 48 hours after admission]) and prophylaxis (antibiotic prescribed for medical or surgical prophylaxis) [7]. Paper-based systems are currently essential given the current lack of functional informatic systems within hospitals in Iraq [23].

Quality indicators were also collected to assess current antibiotic prescribing. This included documentation of the indication for prescribing in the patients' notes at the start of the treatment, whether the choice of any antibiotic prescribed complies with any local treatment guidelines if available especially with the development of the Iraq NAP to reduce AMR in 2017 [19], documentation of a stop/review date for the antibiotic prescribed in the patients' notes, and whether treatment was empirical or targeted based on any microbiological data from a relevant clinical sample [3,7,24]. However, we are aware that typically culture/sensitivity (C/S) testing is not routinely undertaken in these hospitals despite the presence of microbiology laboratory facility at each of the three studied hospitals.

2.4. Study outcome and output measures

The main study outcome measures were estimating the prevalence and quality of current antibiotic prescribing. The prevalence was estimated by dividing the number of patients receiving antibiotics (numerator) by the total number of admitted patients (denominator), stratified by the three hospitals, ward types (medical, surgical, ICU), and antibiotic classified according to the WHO ATC classification [25]. Only antibiotics for systematic use were included (ATC code J01) as these are the principal antibiotics prescribed and consequently a good starting point for developing any pertinent quality improvement programmes among hospitals in the KRG Region of Iraq and wider. For metronidazole, we only included parenteral metronidazole (J01XD01) which is indicted for anaerobic bacteria.

The quality indicators used were based on previous PPS studies, and included the availability of local treatment guidelines, frequency of parenteral versus oral antibiotic prescribing, whether therapy was targeted based on culture and sensitivity (CST) findings, documentation of the antibiotic indication and dose as well as documentation of a stop/review date [3,4,7,24]. Finally, antibiotics prescribed were summarised as per the WHO's recent AWaRe (**A**ccess, **Wa**tch, **Re**serve) 2019 classification [26].

2.5. Data analysis

Descriptive statistics were used to summarise the study variables; continuous variables were summarised using mean (±SD), median (IQR) as appropriate; whereas categorical variables were summarised using frequencies and percentages. Differences/variations and comparability of the individual study outcome measures in relation to the study variables, such as types of wards, indications, and diagnosis, were assessed using Chi-square test, as appropriate. The study outcome measures and outputs were stratified by hospitals, ward types and indications. Data were entered into Excel, then double checked for accuracy and completeness before exporting it into STATA 12 for data management and analysis.

In order to compare the study outcome and output measures with the neighbouring countries, the study measures, where possible, were compared with the West and Central Asia region where Iraq is located including the eight hospitals in Iraq [7]. In addition, where possible and pertinent the Global PPs findings (53 countries) [7], as well as those from other countries in the locality who have undertaken multicentre PPS studies. These include India (16 tertiary hospitals) [3], Pakistan (13 hospitals across Punjab) [27], Saudi Arabia (26 hospitals) [4], and Turkey (14 hospitals) [28]. We are aware that the study in Turkey based utilisation data on defined daily doses (DDDs) rather than prescription prevalence; however, we will refer to pertinent findings where relevant.

2.6. Ethical considerations

No unique patient identifiers were recorded and all study data were completely anonymised. The study did not involve any direct contact with patients; consequently, patient consent was not required. The study protocol was approved by the Research and Ethic Committee of Sulaymaniyah General Health Directorate.

3. Results

3.1. Patients' demographics

Of the 205 admitted adult inpatients on the days of the survey from the three hospitals, 266 antibiotics were prescribed to 192 patients. In hospital 1, out of the 292 adult beds only 98 were occupied at the time of the survey giving a bed occupancy of 33.6% (n=98/292), with an overall bed occupancy of 45% (n=205/456) among the three hospitals. The mean age of the patients was 53.3 (±19.4) years and 99 (51.6%) were female. There was no significant difference in the ages between the three hospitals; however, gender distribution was significantly different with female patients comprising 31% (n=32/96), 73.5% (n=50/68), and 64.3% (n=18/28) in hospitals 1, 2 and 3 respectively (p<0.001).

3.2. Prevalence of antibiotic use

93.7% (n=192) were prescribed antibiotics (Table 1), with a significant difference between the hospitals (p<0.001). Overall, 10 antibiotics accounted for all the 266 antibiotic prescriptions prescribed. The types of antibiotic prescribed varied significantly among the three hospitals (p<0.001), with Table 2 containing the details. Prescribed antibiotic classes among the different ward types were comparable in hospital 1 and 2 but varied significantly in hospital 3 (p=0.026) (Table 2).

There was significant variation in the indication for the prescribed antibiotics between the three hospitals (p<0.001) (Table 3). There was no indication recorded for 41.4% (n=110/266) of the antibiotics prescribed, of which 90% (n=100/110) also had no known diagnosis. Community-acquired infections (CAIs) were the second most common recorded indication (38.7%, n=130/266). Hospital acquired infections (HAIs) were recorded in only one of the hospitals and in 5.2% of patients. Of the 166 prescriptions where a diagnosis was recorded, respiratory tract infections (RTIs) (44%, n=73/166) were the most common diagnosis followed by gastrointestinal tract infections (GIT) (21.1%, n=35/166), majority of which were for intra-abdominal sepsis (55%, n=19/35) (Table 3). The site of the infection varied both between hospitals as well as with the Global PPS (Appendix 2). Most of the recorded diagnosis were treated by third generation cephalosporins ranging from 45% (n=33/73) for RTIs to 100% for CNS infections. GIT infections were most frequently treated with parenteral metronidazole (42.9%, n=15/35) (Table 4). For the top three recorded diagnoses (RTIs, GIT, urinary tract infections - UTIs), the second and third most commonly used antibiotics were macrolides and the carbapenems for

RTIs (20.6%, 15/73 and 12.3%, n=9/73), third generation cephalosporins and carbapenems for GIT (40%, n=14/35 and 12.3%, n=5/35), as well as carbapenems and parenteral metronidazole for UTIs (26.1%, n=6/23 and 17.4%, n=4/23) (Table 4).

There was variation, albeit non-statistically significant (p=0.056), among the types of antibiotic classes used in the treatment of the various indications (Table 5). For Community Acquired Infections (CAIs), third generation cephalosporins were the most commonly prescribed antibiotic (43.7%, n=45/103) followed by macrolides (15.6%), n=16/103) and carbapenems (13.6%, n=14/103) (Table 5). Similarly, for HAIs, third generation cephalosporins were the most commonly prescribed antibiotic (57%, n=4/7) followed by carbapenems (28.6%, n=2/7) and macrolides (14.3%, n=1/7). Third generation cephalosporins were principally prescribed for medical and surgical prophylaxis (55.6%, n=5/9 vs. 64.9%, n=24/37) as well as when no indication was recorded (56.4%, n=62/110).

3.3. Quality indicators of antibiotic use

Antibiotic dosage regimens were documented for all prescribed antibiotics in line with Global PPS guidelines, and the majority were administered parenterally (89.9%, n=239/266) regardless of ward type (Table 6, Table 7). The indications for antibiotic use were only recorded in 61.7% (n=164/266) of patients' notes; however, this varied significantly according to the type of hospital ward (Table 7). The stop/review date for antibiotic treatment, use of targeted treatments based on C/S testing results and prescribing according to local treatment guidelines were almost completely lacking. Approximately one third of adult inpatients (35.9%, n=69/192, range 29.4%-46.4%) received a combination of antibiotics, with variation by ward type, highest in the ICU (58.8%, n=10/29). The majority of the prescribed antibiotics were from the "Watch" antibiotics group, with the frequency comparable between medical and surgical wards although lower in the ICU (Table 7) reflecting the high use of ceftriaxone in the hospitals. Overall, the AWaRe classes varied across the three hospitals (p=0.022), driven mainly by the high B-lactams prescribing prevalence in hospital 3 (Table 6) but not across the ward types (Table 7).

4. Discussion

We believe this is the first time Iraqi Global-PPS hospital antibiotic consumption data have been examined and published in detail, building on the findings of the eight Iraq hospitals included in the

Global PPS [17]. The survey findings revealed a very high prevalence of antibiotic prescribing, a predominance of intravenous and broad-spectrum antibiotic use, lack of antibiotic prescribing guidance or any planned review of treatment and a very high prevalence of antibiotic prescribing for which both the indication and diagnosis was not available or not known. This may well reflect a lack of diagnostic capacity or diagnostic requests, enhanced if there are currently no guidance for antibiotic prescribing in the hospital. This is a concern with the results suggestive of a lack of any local antimicrobial stewardship infrastructure and initiatives to control AMR in the hospitals despite the introduction of a NAP to reduce AMR in Iraq [19,29].

4.1. Prevalence of antibiotic use and indications

The extremely high prevalence of antibiotic prescribing (93.7%), albeit with significant differences among the participating hospitals (86% to 100%), is appreciably higher than the average seen in the Global PPS at 34.4% [7], hospitals in the West and Central Asian region averaging 43.8% [7], African countries at 37.7% - 82.0% despite a high prevalence of infectious diseases including HIV, TB and malaria [7,24,30,31], India at 57.4% [3], Pakistan at 77.6% [27], and Saudi Arabia at 46.9% [4] (Appendix 2). However, similar to the 88.5% prevalence reported in one hospital in the south of Iraq, although not using the Global PPS methodology [14]. Variation in prescribing prevalence between the various hospitals could be due to multiple factors. These include local epidemiology, confidence with the diagnosis, prescribers' knowledge, attitudes and perception regarding antibiotic prescribing, patterns of microbiology resistance data and standard treatment guidelines (STGs), level of infection control and prevention measures within the hospital, as well as the extent of antimicrobial stewardship programme (ASPs) [1,24,29,32]. Our findings suggest a fundamental lack of guidance, and a lack of utilising existing microbiological diagnostics facilities, leading to unregulated empirical prescribing; the lack of utilisation of the available microbiology laboratory facilities in the three studied hospital may be due to multiple factors including delays in processing C/S testing from the point of ordering it until results' availabilities (7-10 days) (AK personal communication). Consequently, it is perhaps not surprising that physicians typically prescribed broad-spectrum antibiotics, i.e. third generation cephalosporins (56.4%, n=62/110), to cover the likely causative microorganisms, especially when they are unsure about the diagnosis. This indicates physicians' prescribing behaviour of reserving C/S testing for refractory patients who did not respond to repeated courses of antibiotics, similar to other studies in Iraq [14]. However, this needs further investigating before we can make any definitive statements.

Antibiotic use was higher in surgical wards compared with medical wards similar to the findings from others [14,33], with prescribing often higher when antibiotics are initiated for prophylaxis and continued post-operatively to reduce surgical site infections (SSIs) [31,34]. There was also greater use of antibiotics to address community acquired infections alongside surgical prophylaxis (38.7% and 13.9%, respectively), similar to the West and central Asia region in the Global PPS (44.8% and 23.2%, respectively) and Saudi Arabia (31.3% and 23.4% respectively) [4,7]. Similar to the Global PPS and West and central Asia region [7], the most frequent indication for antibiotics in our study was RTIs followed by GIT and UTIs (Appendix 2). High use of antimicrobials for RTIs was also seen in India and Saudi Arabia but not Pakistan (Appendix 2).

Third generation cephalosporins, mainly ceftriaxone, were the most commonly prescribed antibiotic, similar to the West and central Asia region and the Global PPS although at much lower prevalence (52.6% vs. 26.6%), Pakistan (ceftriaxone 35%) and Saudi Arabia (3rd generation 17.2%), but different to India and Turkey (Appendix 2) [3,4,7,27,28]. The appreciable prescribing of broad-spectrum antibiotics in our study suggests a proportion could be inappropriate [7], potentially reflecting a lack of confidence in diagnosis, lack of utilising microbiology laboratory facilities enhanced by delays in receiving the results, and a lack of STGs (Tables 6 and Table 7). All of which are factors to hinder prescribers' diagnostic capacity and capability leading to high prescribing of broad-spectrum antibiotics [14,35].in view of the high prevalence (60.9%-85.5%) of third generation cephalosporin resistance in E. coli in Iraq [10,36]. High prevalence of third generation cephalosporin prescribing may be also partly explained by a lack of availability of ciprofloxacin (not observed during this PPS) likely due to its high drug acquisition costs even though ciprofloxacin is on the Iraqi national Essential Medicine list [37], as well as shortages of other antibiotics [21]. However, these need to be investigated further. There was also a high use of carbapenems (9.4%), which is comparable to the West and central Asia region (8.5%), potentially reflecting an appreciable prevalence of extended-spectrum β-lactamase producing Gram negative bacteria.

4.2. Quality of antibiotic prescribing

Documenting the reasons for prescribing antibiotics was lower in our study compared with the Global PPS (61.7% vs. 76.9%) and the combined West and central Asia region (72.8%) [7]; however, higher than seen in Pakistan (23.8%) [27], India (37.9% to 45.5%) [3], and Saudi Arabia (48.9%) [4] (Appendix 2). The lack of documented stop/review dates was also a concern, and it is recommended that a review of patients should be performed 48 hrs after the start of antibiotics when more diagnostic information becomes available and de-escalation may be possible to reduce unnecessary antibiotic use especially IV antibiotics [24,38]. Stop/review dates are particularly important when antibiotics are started empirically, as typically seen in Iraq, along with a restricted list of antibiotics for empiric use as well as suggested replacements when shortages [39].

There was higher use of IV antibiotics (89.9%) compared with the Global PPS (71.4%). However, similar to the West and Central Asia region (85.2) [7] and Saudi Arabia (80.6%) [4] although lower than reported in another Iraqi study (96.6%) [14], and in Pakistan (91.5%) [27]. This probably reflects the high use of third generation cephalosporins Ideally, the method of administration should be determined by the severity of the infection, availability of an oral route and the susceptibility of the infecting organism [27]. Nevertheless, many clinicians view parenteral route as more effective which is a concern [27]. Appropriate and timely IV to oral switch programmes are a well-recognised to reduce costs, duration of stay and catheter-related complications with similar outcomes [7,24].

Whilst quinolones were not available to treat ARIs, other suitable oral antimicrobials were available including amoxicillin and doxycycline. However, there are concerns with the lack of guidelines within the studied hospitals in Iraq to guide prescribing since adherence to guidelines is seen as crucial to improving the quality of antibiotic prescribing [1,7,24]. The complete lack of STGs though is also seen among hospitals in Pakistan [27], and among 19.2% of hospitals in the Global PPS; however, STGs were more frequently available in the West and Central Asia region (40.5% overall) [7].

We observed that most of the prescribed antibiotics (62%) in our study were from the Watch group of the WHO AWaRe list [26], which are the highest priority and possess the greatest risk of bacterial resistance. This though is not surprising given the high usage of ceftriaxone; however, needs to be looked at further alongside the use of the Reserve group antibiotics (9.8%), especially in Hospital 3 (21.4%), to assess their appropriateness.

4.3. Implications for policy makers and practice in Iraq and beyond

There is an urgent need to instigate ASPs in Iraq including the development of guidelines treating the most common infections. Guidelines should reflect local antimicrobial susceptibility and resistance patterns [7,29,32], and be readily available at the point of prescribing. The extent of adherence/compliance to these guidelines should subsequently be monitored as part ASPs to improve patient outcomes [7,29]. This will necessarily include documentation of the reason(s) for prescribing alongside initiatives to promote stop and review dates. One approach could be to instigate an antimicrobial prescribing chart with suggested stop/review dates, usually every 48 hrs or the third day, marked with red outlined boxes that prescribers need to review and sign [40].

Additional targets for ASPs include early intravenous-to-oral switching initiatives as well as encouraging greater use of CST and with it the instigation of antibiograms within the hospitals to better target initial empiric use [7,27,31]. However, this will require the timely availability of C/S tests findings.

Whilst several important areas have been identified as potential targets for ASP interventions among the three hospitals, we believe it is essential to implement only one to two tailored interventions at a time to avoid overloading healthcare professionals. The first step is the development of a multidisciplinary ASP with its 7 core elements [41], which includes leadership commitment, accountability, and drug expertise that needs engagement of all key stakeholder groups. Once established, the ASP team can take: “Action” to implement key target areas, “Track” subsequent antibiotic use, “Report” back, and “Educate”. Neighbouring countries and the global community, including the WHO, can provide guidance [29,42].

4.4. Strengths and limitations

We believe this is the first study to estimate antibiotic use and assess the quality of prescribing in the KGR region of Northern Iraq using a validated and standardised Global PPS methodology. However, we do acknowledge a number of limitations. Firstly, the study was conducted among all the major hospitals in only one city (Sulaymaniyah) in the KRG region; consequently, the results might not be generalisable to Iraq as a whole. However, Sulaymaniyah is the largest city in the KRG accounting for about 41% of KRG's population, and the third largest city in Iraq. Secondly, the presented prevalences are averages and were not controlled for patient case mix, disease incidence, infections' prevalence, variations in resistance patterns and institutional factors among the three hospitals, all of which might have influenced variations in antibiotic use patterns among the three hospitals. For instance, hospital 3 seems to have a different antibiotic prescribing pattern with less prescriptions for unknown indications and far more reserve antibiotic prescribing. This could be related to a variation in services provided such as its limitation to medical wards only, with the majority of patients having a diagnosis code for a RTI (78.5%, 33/42), and fewer prescribers in this hospital (2-3 prescribes). Consequently, the observed antibiotic prescribing patterns could possibly reflect and be dominated by the prescribing behaviours/practice of one prescriber; this is unlikely to happen, although not impossible, in bigger hospitals with several prescribing staff. Thirdly, we acknowledge that the applied statistical significance of the associations was univariable and suffer from multiple testing; hence, these statistical associations should not be emphasised and interpreted with cation especially as our study did not aim primarily to assess differences in antibiotic prescribing patterns across the three hospitals. Whilst this study did not assess the complexity or severity of infection in the patients surveyed, it was notable that these were general hospitals and not ones focussed on or specialising in the management of infectious diseases.

4.5. Conclusions

There was a very high prevalence of antibiotic prescribing in patients in the KRG region in Iraq with evidence of sub-optimal prescribing. Swift, collective action is needed to develop ASPs in hospitals to improve future prescribing. Key target areas include the development of STGs and targeting 1-2 areas for quality improvement interventions, which can include routinely documenting the rationale for antibiotics prescribed and stop/review dates to facilitate IV to oral switching when appropriate. Guidance can come from other countries who have successfully implemented ASPs including Scotland [https://www.sapg.scot/about-us/].

5. Authors contribution

Study conception and design: all authors; data collection and management: AH, KB, and ZR; data analysis and interpretation: AK, BG, RAS, JS; manuscript writing and drafting: AK, BG; manuscript reviewing and revising as well as providing constrictive criticism and final approval: all authors

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8. Conflicts of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

9. References

'*' – of interest, of "**" – of considerable interest

1. Saleem Z, Hassali MA, Godman B, et al. Point Prevalence Surveys Of Antimicrobial Use: A Systematic Review And The Implications. Expert review of anti-infective therapy. 2020. * of interest as systematic review of PPS studies
2. Hofer U. The cost of antimicrobial resistance. Nature reviews Microbiology. 2019;17(1):3.
3. Singh SK, Sengupta S, Antony R, Bhattacharya S, Mukhopadhyay C, Ramasubramanian V, et al. Variations in antibiotic use across India: multi-centre study through Global Point Prevalence survey. J Hosp Infect. 2019;103(3):280-3.
4. Al Matar M, Enani M, Binsaleh G et al. Point prevalence survey of antibiotic use in 26 Saudi hospitals in 2016. Journal of infection and public health. 2019;12(1):77-82.
5. Boucher HW, Bakken JS, Murray BE. The United Nations and the Urgent Need for Coordinated Global Action in the Fight Against Antimicrobial Resistance. Annals of internal medicine. 2016;165(11):812-3.
6. World Health Organisation. Antimicrobial resistance. 2018. Available at URL: http://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance (Accessed 23 September, 2020)
7. Versporten A, Zarb P, Caniaux I et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. The Lancet Global health. 2018;6(6):e619-e29. ** of considerable interest as the global PPS including the 8 hospitals from Iraq
8. WHO. GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE. 2015. Available at URL: https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1. (accessed 24 September, 2020)
9. Plachouras D, Karki T, Hansen S et al. Antimicrobial use in European acute care hospitals: results from the second point prevalence survey (PPS) of healthcare-associated infections and antimicrobial use, 2016 to 2017. Euro surveillance. 2018;23(46).

10. . ABDULLAH IM. Multiple drugs resistance among urinary tract infection patients in Duhok city–Kurdistan Region–Iraq. Duhok Medical Journal. 2019;13(1):22-31.
11. Moghnieh RA, Kanafani ZA, Tabaja HZ, Sharara SL, Awad LS, Kanj SS. Epidemiology of common resistant bacterial pathogens in the countries of the Arab League. The Lancet Infectious diseases. 2018;18(12):e379-e94.
12. Al-Charrakh AH, Al-Awadi SJ, Mohammed AS. Detection of Metallo-β-Lactamase Producing Pseudomonas aeruginosa Isolated from Public and Private Hospitals in Baghdad, Iraq. Acta medica Iranica. 2016;54(2):107-13.
13. Hussein NH. Emergence of NDM-1 among carbapenem-resistant Klebsiella pneumoniae in Iraqi hospitals. Acta microbiologica et immunologica Hungarica. 2018;65(2):211-27.
14. Nassr OA, Alridha AMA, Naser RA, Abbas RS. Antibiotic Prescribing in the Acute Care in Iraq. Hernia. 2018;13:16.9. * of interest as one of the earlier studies in Iraq
15. Obaid AA-R. Prescribing pattern of antibiotics in AL-Elwia Pediatric Teaching Hospital, Baghdad, 2016. Al-Kindy College Medical Journal. 2017;13(2):117-26.
16. Sabeeh DQ, Abdulrahman NM, Abass ZA-R. Magnitude of prescribed antibiotics in pediatric emergency department in Basra hospital for maternity and children. Global Journal of Public Health Medicine. 2020;2(1):125-31.
17. The Lancet Global Health Supplementary appendix to Versporten A, Zarb P, Caniaux I, et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. Available at URL: https://www.global-pps.com/wp-content/uploads/2018/05/1-2-LANGH-2015_Global-PPS_results-on-adults_Appendix_Versporten_April2018.pdf (accessed 24 September, 2020)
18. Al Hilfi TK, Lafta R, Burnham G. Health services in Iraq. The Lancet. 2013;381(9870):939-48.
19. WHO EMRO. Iraq develops national action plan to address antimicrobial resistance. 2017. Available from: http://www.emro.who.int/irq/iraq-news/moh-in-collaboration-with-who-develops-national-action-plan-tackling-antimicrobial-resistance-in-iraq.html (Accessed 23 Septemebr 2020)
20. Antony CR. Moore M, Hilborne LH et al. Strengthening Health Care in the Kurdistan Region of Iraq. 2017. Available at URL: https://www.rand.org/pubs/research_briefs/RB9990.html (Accessed 24 September 2020)
21. Aboulenein A, Levinson R. Iraq's healthcare has fallen far. 2020. Available at URL: https://www.reuters.com/article/us-iraq-health-drugs-idUSKBN20P1RP (Accessed 24 September 2020)
22. Al Hilfi TK, Lafta R, Burnham G. Health services in Iraq. Lancet. 2013;381(9870):939-48.
23. WHO - Regional Office for the Eastern Mediterranean Comprehensive assessment of Iraq’s health information system 2019. 2019. Available at URL: https://applications.emro.who.int/docs/9789290223160-eng.pdf (Accessed 24 September 2020)
24. AFRIYIE DK, SEFAH IA, SNEDDON J et al. Antimicrobial Point Prevalence Surveys in two Ghanaian hospitals: opportunities for antimicrobial stewardship. JAC Antimicrob Resist. 2020: 1-9.
25. WHO Collaborating Centre for Drug Statistics Methodology. Anatomical Therapeutic Chemical (ATC) classification system: guidelines for ATC classification and DDD assignment 2020. Available from: https://www.whocc.no/atc_ddd_index/. (Accessed 24 September 2020)
26. Sharland M, Pulcini C, Harbarth S, Zeng M, Gandra S, Mathur S, et al. Classifying antibiotics in the WHO Essential Medicines List for optimal use—be AWaRe. The Lancet Infectious Diseases. 2018;18(1):18-20 - ** of considerable interest as discussing the AWaRe system
27. Saleem Z, Hassali MA, Versporten A et al. A multicenter point prevalence survey of antibiotic use in Punjab, Pakistan: findings and implications. Expert review of anti-infective therapy. 2019;17(4):285-93.
28. Guclu E, Ogutlu A, Karabay O et al. Antibiotic consumption in Turkish hospitals; a multi-centre point prevalence study. Journal of chemotherapy. 2017;29(1):19-24.
29. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review. Antimicrob Resist Infect Control. 2019;8:35. ** - of considerable interest as a key paper discussing ASPs
30. Momanyi L, Opanga S, Nyamu D, Oluka M, Kurdi A, Godman B. Antibiotic Prescribing Patterns at a Leading Referral Hospital in Kenya: A Point Prevalence Survey. J Res Pharm Pract. 2019;8(3):149-54.
31. Anand Paramadhas BD, Tiroyakgosi C, Mpinda-Joseph P et al. Point prevalence study of antimicrobial use among hospitals across Botswana; findings and implications. Expert review of anti-infective therapy. 2019;17(7):535-46.

32. Md Rezal RS, Hassali MA, Alrasheedy AA, Saleem F, Md Yusof FA, Godman B. Physicians' knowledge, perceptions and behaviour towards antibiotic prescribing: a systematic review of the literature. Expert review of anti-infective therapy. 2015;13(5):665-80.

33. Charani E, Tarrant C, Moorthy K, Sevdalis N, Brennan L, Holmes A. Understanding antibiotic decision making in surgery—a qualitative analysis. Clinical Microbiology and Infection. 2017;23(10):752-60.

34. Mwita JC, Souda S, Magafu M, Massele A, Godman B, Mwandri M. Prophylactic antibiotics to prevent surgical site infections in Botswana: findings and implications. Hospital practice. 2018;46(3):97-102.

35. Jumaa KM, Hussien SAR, Jaffer AM, Alaziz ASA, Latif RAA: Antibiotic prescription style in surgery department in Baquba Teaching Hospital. Diyala Journal for Pure Science 2010, 6(3):152-166.

36. Mohammed S, Ahmed M, Karem K. Incidence of Multi-Drug Resistant Escherichia Coli Isolates from Blood and Urine in Kerbala, Iraq. journal of kerbala university. 2014;12(4):222-7.

37. WHO. Iraq - National Medicines List/Formulary/Standard Treatment Guidelines. COMPACT ESSENTIAL DRUGS LIST 2010. Available at URL: https://www.who.int/selection_medicines/country_lists/IRQ_NML_10.pdf?ua=1. (Accessed 24 September 2020)

38. Pollack LA, Plachouras D, Sinkowitz-Cochran R, Gruhler H, Monnet DL, Weber JT. A concise set of structure and process indicators to assess and compare antimicrobial stewardship programs among EU and US hospitals: results from a multinational expert panel. infection control & hospital epidemiology. 2016;37(10):1201-11.

39. Chigome AK, Matlala M, Godman B, Meyer JC. Availability and Use of Therapeutic Interchange Policies in Managing Antimicrobial Shortages among South African Public Sector Hospitals; Findings and Implications. Antibiotics. 2019;9(1). *of interest to address antibiotic shortages

40. Liaskou M, Duggan C, Joynes R, Rosado H. Pharmacy's role in antimicrobial resistance and stewardship. Clinical Pharmacy. 2018. Available at URL; https://www.pharmaceutical-journal.com/research/review-article/pharmacys-role-in-antimicrobial-resistance-and-stewardship/20204885.article?firstPass=false (Accessed 24 September 2020)

41. Pollack LA, Srinivasan A. Core elements of hospital antibiotic stewardship programs from the Centers for Disease Control and Prevention. Clin Infect Dis. 2014;59(suppl_3):S97-S100.

42. World Health Organization. ANTIMICROBIAL STEWARDSHIP PROGRAMMES in health-care facilities in low- and middle-income countries. A WHO PRACTICAL TOOLKIT. 2019. Available at URL: https://apps.who.int/iris/bitstream/handle/10665/329404/9789241515481-eng.pdf. (Accessed 24 September 2020)

Tables

Table 1. Prevalence of antibiotic use in adults' inpatients admitted to the three main hospitals in Sulaymaniyah in the Kurdistan Regional Government in northern Iraq stratified by ward types in comparison with West and Central Asia

	Total		Medical		Surgical		Intensive Care Unit	
	Admitted	Antibiotic use, N (%)	Admitted	Antibiotic use, N (%)	Admitted	Antibiotic use, N (%)	Admitted	Antibiotic use, N (%)
Hospital 1	98	96 (98%)	67	67 (100%)	24	23 (96%)	7	6 (86%)
Hospital 2	79	68 (86%)	42	33 (79%)	24	24 (100%)	13	11 (85%)
Hospital 3	28	28 (100%)	28	28 (100%)	0	0	0	0
Total	205	192 (93.7%)	137	128 (93.4%)	48	47 (97.9%)	20	17 (85%)
West and Central Asia*	3,677	1,610 (43.8%)	1,873	787 (42.0%)	1,249	558 (44.7%)	396	189 (47.7%)

(Notes) Data extracted from the Global PPS [7]

Table 2. Types of antibiotic classes prescribed to the 192 adults' inpatients admitted to the three main hospitals in Sulaymaniyah in the Kurdistan Regional Government in northern Iraq stratified by wards types

Class	Total (n= 266)	Hospital 1 (n=136, 51.1%)				Hospital 2 (n=88, 33.1%))				Hospital 3 (n=42, 15.8%)	
		AMW (n=93)	ASW (n=32)	ICU (n=11)	Total (n=136)	AMW (n=40)	ASW (n=30)	ICU (n=18)	Total (n=88)	AMW (n=42)	Total (n=42)
Cephalosporins, 3rd Generation (J01DD)	140 (52.6%)	48 (51.6%)	18 (56.3%)	3 (27.3%)	69 (50.7%)	29 (72.5%)	22 (73.3%)	9 (50.0%)	60 (68.2%)	11 (26.2%)	11 (26.2%)
Imidazole derivatives (J01XD)	45 (16.9%)	15 (16.3%)	7 (21.9%)	2 (18.2%)	24 (17.7%)	5 (12.5%)	6 (20.0%)	4 (22.2%)	15 (17.1%)	6 (14.3%)	6 (14.3%)
Beta-lactam, Penicillins (J01C)	28 (10.5%)	9 (9.7%)	3 (9.4%)	4 (36.4%)	16 (11.8%)	0 (0%)	0 (0%)	4 (22.2%)	4 (4.6%)	8 (19.1%)	8 (19.1%)
Carbapenems (J01DH)	25 (9.4%)	7 (7.5%)	2 (6.3%)	1 (9.1%)	10 (7.4%)	4 (10.0%)	2 (6.7%)	1 (5.6%)	7 (8.0%)	8 (19.1%)	8 (19.1%)
Macrolides (J01FA)	23 (8.7%)	11 (11.8%)	2 (6.3%)	0 (0%)	13 (9.6%)	1 (2.5%)	0 (0%)	0 (0%)	1 (1.1%)	9 (21.4%)	9 (21.4%)
Aminoglycoside (J01GB)	4 (1.5%)	2 (2.1%)	0 (0%)	1 (9.1%)	3 (2.2%)	1 (2.5%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Glycopeptide (J01XA)	1 (0.4%)	1 (1.1%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

(Notes) AMW: Adult medical wards; ASW: Adult surgical wards; ICU: Intensive care unit

Table 3. Indications for the 266 antibiotic prescriptions in 192 adults' inpatients admitted to the three main hospitals in Sulaymaniyah in the Kurdistan Regional Government in northern Iraq

	Number of antibiotic prescriptions	CAI	HAI	Prophylaxis		Unknown
				Medical	Surgical	
Hospital 1	136	39 (28.7%)	7 (5.2%)	9 (6.6%)	20 (14.7%)	61 (44.9%)
Hospital 2	88	26 (29.6%)	0 (0%)	0 (0%)	17 (19.3%)	45 (51.1%)
Hospital 3	42	38 (90.5%)	0 (0%)	0 (0%)	0 (0%)	4 (9.5%)
Total	266	103 (38.7%)	7 (2.6%)	9 (3.4%)	37 (13.9%)	110 (41.4%)
West and Central Asia*	2,084	934 (44.8%)	436 (20.9%)	161 (7.7%)	498 (23.2%)	70 (3.4%)

(Notes) Data extracted from the Global PPS [7]; CAI: community acquired infections; HAI: healthcare associated infections

Table 4. Types of antibiotic classes prescribed to the 192 adults' inpatients admitted to the three main hospitals in Sulaymaniyah in the Kurdistan Regional Government in northern Iraq stratified by recorded diagnosis where the indication was known

Antibiotic Class	RTI	GIT	UTI	ENT	Gynaecology	SSTI	PUO	CNS	EYE
Cephalosporins, 3rd Generation (J01DD)	33 (45.2%)	14 (40%)	11 (47.8%)	7 (70%)	7 (87.5%)	5 (71.4%)	3 (50%)	3 (100%)	1 (100%)
Imidazole derivatives (J01XD)	5 (6.9%)	15 (42.9%)	4 (17.4%)	2 (20%)	0 (0%)	1 (14.3%)	2 (33.3%)	0 (0%)	0 (0%)
Beta-lactam, Penicillins (J01C)	9 (12.3%)	0 (0%)	1 (4.4%)	1 (10%)	0 (0%)	1 (14.3%)	1 (16.7%)	0 (0%)	0 (0%)
Carbapenems (J01DH)	9 (12.3%)	5 (12.3%)	6 (26.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Macrolides (J01FA)	15 (20.6%)	1 (2.9%)	1 (4.4%)	0 (0%)	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Aminoglycoside (J01GB)	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Glycopeptide (J01XA)	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total (n=166)	73 (100%)	35 (100%)	23 (100%)	10 (100%)	8 (100%)	7 (100%)	6 (100%)	3 (100%)	1 (100%)

(Notes) RTI: respiratory tract infections; GIT: gastrointestinal tract; UTI: urinary tract infections; ENT: ear, nose and throat; SSTI: skin and soft tissue infections; PUO: pyrexia of unknown origin; CNS: central nervous system;

Table 5. Types of antibiotic classes prescribed to the 192 adults' inpatients admitted to the three main hospitals in Sulaymaniyah in the Kurdistan Regional Government in northern Iraq stratified by types of indications

	Number of antibiotic prescriptions	Prophylaxis				
		CAI	HAI	Medical	Surgical	Unknown
Cephalosporins, 3rd Generation (J01DD)	140 (52.6%)	45 (43.7%)	4 (57.1%)	5 (55.6%)	24 (64.9%)	62 (56.4%)
Imidazole derivatives (J01XD)	45 (16.9%)	15 (14.6%)	0 (0%)	4 (44.4%)	8 (21.6%)	18 (16.4%)
Beta-lactam, Penicillins (J01C)	28 (10.5%)	11 (10.7%)	0 (0%)	0 (0%)	1 (2.7%)	16 (14.6%)
Carbapenems (J01DH)	25 (9.4%)	14 (13.6%)	2 (28.6%)	0 (0%)	3 (8.1%)	6 (5.45)
Macrolides (J01FA)	23 (8.7%)	16 (15.6)	1 (14.3%)	0 (0%)	1 (2.75)	5 (4.6%)
Aminoglycoside (J01GB)	4 (1.5%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	3 (2.7%)
Glycopeptide (J01XA)	1 (0.4%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	266 (100%)	103 (100%)	7 (100%)	9 (100%)	37 (100%)	110 (100%)

(Notes) CAI: community acquired infections; HAI: healthcare associated infections

Table 6. Quality indicators of total antibiotics use in the 192 adults' inpatients admitted to the three main hospitals in Sulaymaniyah in the Kurdistan Regional Government in northern Iraq

Quality indicators	Total (n= 266)	Hospital 1 (n=136, 51.1%)	Hospital 2 (n=88, 33.1%))	Hospital 3 (n=42, 15.8%)	West and Central Asia*
Indication recorded in notes (Yes)**	164 (61.7%)	76 (55.9%)	48 (54.6%)	40 (95.2%)	72.8%
Dose documented (Yes)	266 (100%)	136 (100%)	88 (100%)	42 (100%)	Not relevant
Parenteral administration of antibiotics	239 (89.9%)	123 (90.4%)	79 (89.8%)	37 (88.1%)	85.2%
Stop/Review date documented (Yes)	1 (0.4%)	1 (0.7%)	0 (0%)	0 (0%)	19.8%
Guideline missing (Yes)	266 (100%)	136 (100%)	88 (100%)	42 (100%)	40.5%
Targeted therapy	2 (0.8%)	0 (0%)	2 (2.3%)	0 (0%)	14.6%
Number of patients on antibiotic combination therapies (N=192)	69 (35.9%)	36 (37.5%)	20 (29.4%)	13 (46.4%)	NA
WHO AWaRe classification**					NA
Access	75 (28.2%)	43 (31.6%)	19 (21.6%)	13 (31%)	NA
Watch	165 (62%)	83 (61%)	62 (70.4%)	20 (47.6%)	NA
Reserve	26 (9.8%)	10 (7.4%)	7 (8%)	9 (21.4%)	NA

(Notes) *Data extracted from the Global PPS [7]; **p<0.001; NA: Not available

Table 7. Quality indicators of total antibiotics use in the 192 adults' inpatients admitted to the three main hospitals in Sulaymaniyah in the Kurdistan Regional Government in northern Iraq stratified by types of hospital wards

Quality indicators	Medical (n=175)				Surgical (n=62)			ICU (n=29)		
	Hospital 1(n=93)	**Hospital 2 (n=40)**	**Hospital 3 (n=42)**	**Total (%)**	**Hospital 1(n=32)**	**Hospital 2 (n=30)**	**Total (%)**	**Hospital 1 (n=11)**	**Hospital 2 (n=18)**	**Total (%)**
Antibiotic indication recorded in notes (Yes)	53 (60%)	16 (40%)	40 (95.2%)	109 (62.3%)*	22 (68.8%)	19 (63.3%)	41 (66.1%)	1 (9.1%)	13 (72.2%)	14 (48.3%)*
Dose documented (Yes)	93 (100%)	40 (100%)	42 (100%)	175 (100%)	32 (100%)	30 (100%)	62 (100%)	11 (100%)	18 (100%)	29 (100%)
Parenteral administration of antibiotics	80 (86%)	35 (87.5%)	37 (88.1%)	152 (86.9%)	32 (100%)	30 (100%)	62 (100%)	11 (100%)	14 (77.8%)	25 (86.2%)
Stop/Review date documented (Yes)	1 (1.1%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Guideline missing (Yes)	93 (100%)	40 (100%)	42 (100%)	175 (100%)	32 (100%)	30 (100%)	62 (100%)	11 (100%)	18 (100%)	29 (100%)
Targeted therapy	0 (0%)	2 (5%)	0 (0%)	2 (1.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
WHO AWaRe classification*										
Access	25 (26.9%)	6 (10%)	13 (31%)	44 (25.2%)*	11 (34.4%)	6 (20%)	17 (27.4%)	7 (63.5%)	7 (38.9%)	14 (48.3%)
Watch	61 (65.6%)	30 (75%)	20 (47.6%)	111 (63.4%)*	19 (59.4%)	22 (73.3%)	41 (66.1%)	3 (27.3%)	10 (55.6%)	13 (44.8%)
Reserve	7 (7.5%)	4 (10%)	9 (21.4%)	20 (11.4%)*	2 (6.3%)	2 (6.7%)	4 (6.5%)	1 (9.1%)	1 (5.6%)	2 (6.9%)
	Hospital 1 (n=67)	**Hospital 2 (n=33)**	**Hospital 3 (n=28)**	**Total n=128 (%)**	**Hospital 1 (n=23)**	**Hospital 2 (n=24)**	**Total (n=47) (%)**	**Hospital 1 (n=6)**	**Hospital 2 (n=11)**	**Total (n=17) (%)**
Number of patients on antibiotic combination therapies (N=192)	25 (37.3%)	7 (21.2%)	13 (46.4%)	45 (35.2%)	8 (34.8%)	6 (25%)	14 (29.8%)	3 (50%)	7 (63.6%)	10 (58.8%)

(Notes) *p<0.001;