Surgical Antimicrobial Prophylaxis Among Pediatric Patients in South Africa Comparing Two Healthcare Settings

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Background: Appropriate use of surgical antimicrobial prophylaxis (SAP) is a concern in view of its impact on morbidity, mortality and costs. Little is currently known about SAP in South Africa.

Objective: To assess compliance to SAP guidelines for pediatric patients undergoing surgery in 1 of 4 surgical subspecialties among hospitals in South Africa.

Methods: An eight-month retrospective chart review in both a teaching hospital and a private hospital between February and August 2015. Prescriptions of antimicrobials as SAP were compared with current SAP Guidelines, consolidated from a literature review, regarding 5 criteria—appropriate antimicrobial selection, dosing, timing of administration, redosing and duration of treatment.

Results: We reviewed 224 charts, 112 from each hospital type. The majority ($P = 1.000$) of patients received SAP when indicated (77.3% and 100.0%, respectively, from the teaching and private hospitals). A noteworthy 21.1% and 45.9% of patients received antimicrobials without an indication, respectively, from teaching and private hospitals. Compliance to all 5 of the criteria was not met by either hospital type. Overall, the teaching hospital met the most criteria (3 out of 5) in 58.8% of situations.

Conclusions: Current SAP practices in South Africa's teaching and private hospitals diverge from current SAP Guidelines. Inappropriate overuse of SAP occurs in both hospital sectors, while underuse was found in the teaching hospital. Full compliance to the 5 criteria was not met by either hospital. Noncompliance was largely attributed to inappropriate selection and dosing. Quality improvement interventions, continued surveillance and local standardized evidence-based SAP Guidelines are needed to improve care. This is already happening.

Key Words: surgical antimicrobial prophylaxis, pediatrics, South African healthcare, compliance, guidelines

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Antimicrobials are one of the most commonly prescribed medications especially amongst pediatricians.[1] However, because of increasing antimicrobial resistance (AMR) rates, there is increasing morbidity, mortality and costs.[2] Consequently, there is a need to improve their utilization, which includes appropriate surgical antimicrobial prophylaxis (SAP).[3] This includes assessing how appropriately antimicrobials are being utilized during pediatric surgery.[4] The goal for SAP is to prevent surgical site infections (SSIs), ideally by administering antimicrobials that are safe, cost-effective and with a relevant spectrum of activity.[5] Although half of SSIs are preventable, they remain one of the most common complications of pediatric surgery associated with significant morbidity and mortality,[6,7] which can be reduced with appropriate use of SAP.[6]

Globally, there is substantial variability in the use of SAP, with prophylaxis among children accounting for 64.3% of all prophylactic antimicrobial prescribing. However, current recommendations on SAP pertain mostly to adults.[7] Although children undergoing surgery are commonly prescribed SAP, the details of SAP use in them are poorly understood.[7] In Africa, currently more than 80% of the pediatric population undergoing surgery receive prophylactic antimicrobials[8]; however, there are limited data on the appropriateness.

To date, limited research, studies and guidelines have been conducted and developed on SAP use in South Africa,[9] with no comparable studies on SAP use in South Africa's pediatric surgical population. Consequently, this article aims to describe current compliance to SAP guidelines for pediatric patients undergoing surgery in 1 of 4 surgical subspecialties after national initiatives to improve antibiotic use[10] and use the findings to guide future activities in South Africa to improve SAP in children.

METHODS

A dual approach was used including a systematic review and a retrospective review of current usage.

Systematic Review

A systematic review of studies pertaining to SAP use in children undergoing surgery in 1 of 4 surgical subspecialties—urology, ear, nose and throat (ENT), maxillofacial or general surgery—was performed, with studies published between January 2010 and December 2016 being included. The primary outcomes had to relate to either compliance to SAP use, specific recommendations pertaining to SAP choice, timing, dosing, reducing and discontinuation or current practices of SAP use in pediatrics. The following search terms were used: pediatric, pediatric surgical antibiotic, antimicrobial prophylaxis, guidelines, compliance, usage, practices, patters, recommendations, urology surgery, ENT surgery, general surgery, maxillofacial surgery, with studies limited to English language. Review articles as well as those specific to the adult population (18 years of age or older) were excluded. The principal researcher (N.v.d.S.) read the articles and along with the research team developed the final list of relevant papers (Fig. 1).

Specialty-specific SAP guidelines and consensus statements were cross-referenced with key guidelines[11–15] to define the most appropriate recommendations for SAP use, including dosing and type of surgical procedures (Table 1).

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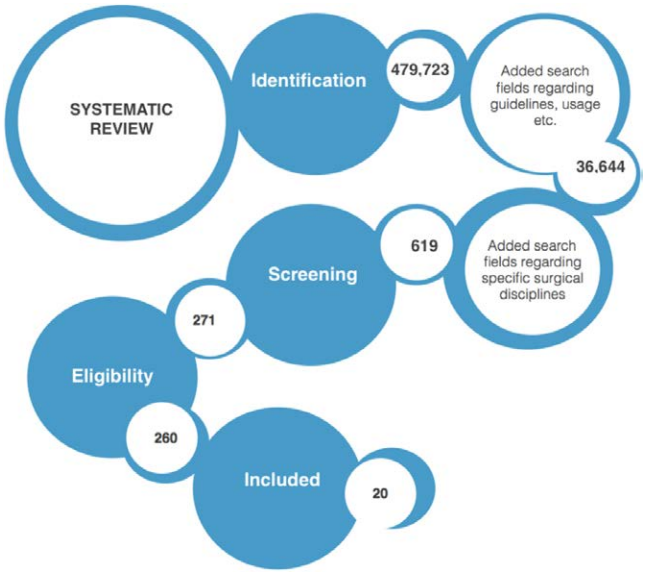

FIGURE 1. Outcome of the systematic review. full color online

Study Design, Setting and Study Period

A retrospective chart review was conducted over an 8-month period between January and August 2015 by studying the prescribing patterns in discharged patients who had surgery in the 4 surgical subspeciality units. Surgical procedures were analyzed as they are the most frequently encountered in pediatrics in both teaching and private hospitals. In addition, these were the 4 designated subspecialties in the pediatric surgical ward in the teaching hospital at the time of the study.

The chosen teaching hospital is a 1650-bed hospital with 28 clinical departments, 20 approved ICU beds, 60 high-care beds and 17 surgical theatres, providing services to an estimated 1.7 million people from the surrounding area. It is the second largest hospital in South Africa. During the study period, the teaching hospital's pediatric surgical ward consisted of the 4 designated cubicles with a total of 40 beds.

The private hospital, reflecting the dual healthcare system in South Africa,[10] has 358 beds and 17 wards, 2 ICUs, 2 high-care facilities and 4 surgical theatres. During the study period, this hospital did not have a dedicated pediatric surgical ward, and children were allocated to wards based on the type of surgery that they underwent.

Study Population and Sample

During the 8-month study period, 701 charts were reviewed: 164 from the teaching hospital and 537 from the private hospital. Thereafter 224 charts, 112 from each hospital, were sampled.

Compliance to the Guidelines

SAP appropriateness was evaluated with regards to indication, administration and compliance to SAP guidelines in line with previous studies after the literature review (Table 2).[5,11–15,17] Compliance was defined as appropriate selection of SAP, dose, timing of administration, redosing and duration of use. All 5 of the criteria had to be met for SAP to be deemed compliant in this study, that is, SAP selected based on recommendations, appropriate doses based on body weight, SAP administered 60 minutes before incision apart from fluoroquinolones and vancomycin, where administration over 1 to 2 hours was recommended, potential redosing and SAP administered within 24 hours postsurgery.

Data Collection and Analysis

The data collection form was developed and compiled based on previously published studies following the systematic literature review,[4,6,7,17,18] with slight modifications to meet the objectives of the study. It included key information such as the type of surgery, if SAP was administered, dosage, route, time and date of administration of antibiotics.

All statistical analyses were performed on SAS (SAS Institute Inc, Carey, NC). Fisher exact test (*f*) was used for comparisons of percentages, and the Student *t* test (*t*) for comparisons of mean values. All tests were 2-sided, and *P* values ≤0.05 were considered significant.

Ethical Considerations

Data collection commenced after ethical approval from Sefako Makgatho Health Sciences University Research Ethics

TABLE 1. Suggested Antimicrobial Prophylaxis Among Patients Based on Current Guidelines

Type of Surgery	SAP Recommendation
Ear, nose and throat (ENT) surgery	
Tympanostomy (Grommets)	A single dose of topical SAP is recommended. Single dose of Gentisone ear drops at surgeon's discretion.[13] Or a single dose of ciproflaxcain[16]
Tonsillectomy	SAP is not recommended
Adenoidectomy	SAP is not recommended
General surgery	
Appendectomy	SAP is highly recommended
	Cefoxitin or ampicillin/sulbactam or cefazolin plus metronidazole. If major reaction to β-lactams; clindamycin plus gentamycin
	Cefoxitin, cefotetan, cefazolin plus metronidazole
	Clindamycin plus aminoglycosides or aztreonam or fluoroquinolones
Colorectal surgery	SAP is highly recommended
	Gentamycin plus metronidazole
Hernia-repair groin (inguinal/femoral with or without mesh)	SAP is not recommended
Hernia-repair groin (laparoscopic with or without mesh)	SAP is not recommended
Hernia repair (incisional with or without mesh)	SAP is not recommended
Obstructed hernia repair (hernioplasty and herniorrhaphy)	Cefazolin, clindamycin, vancomycin
Urology surgery	
Circumcision	SAP is not recommended
Maxillofacial	
Extractions	SAP is not routinely recommended in healthy patients

SAP indicates surgical antimicrobial prophylaxis.

TABLE 2. Antimicrobials Used for SAP in Both Hospitals

ATC Code	Class	ATC Code	INN	Teaching *n* (%)	Private *n* (%)	*P**
J	Anti-infectives for systemic use					
J01	Antibacterials for systemic use					
J01C	β-Lactam antibacterials					
J01CR	Combo of penicillins, including β-lactamase inhibitors	J01CR02	Amoxicillin–clavulanic acid	3 (8.33)	47 (88.68)	<0.0001†
J01D	Other β-lactam antibacterials					
J01DB	First-generation cephalosporin	J01DB04	Cefazolin	32 (88.88)	0 (0)	<0.0001†
J01DC	Second-generation cephalosporin	J01DC02	Cefuroxime	1 (2.77)	1 (1.89)	1.0000
J01DD	Third-generation cephalosporin	J01DD04	Ceftriaxone	0 (0)	2 (3.77)	0.5128
J01F	Macrolides, lincosamides and streptogramins					
J01FA	Macrolides	J01FA10	Azithromycin	0 (0)	1 (1.89)	1.0000
J01FF	Lincosamides	J01FF01	Clindamycin	0 (0)	1 (1.89)	1.0000
J01X	Other antibacterials					
J01XD	Imidazole derivate	J01XD01	Metronidazole	0 (0)	1 (1.89)	1.0000
Total				36 (100)	53 (100)	

*Fisher exact test.
†Highly statistically significant difference.
ATC indicates Anatomical Therapeutic Chemical classification (https://www.whocc.no/atc_ddd_index/); INN, International nonproprietary name.

Committee (SMUREC) (SMUREC/H/185/2015: PG), as well as from the Research Operations Committee of the private hospital used (UNIV-2016-0013). Confidentiality and anonymity of patient information was maintained throughout the study, by means of allocating study numbers.

RESULTS

Systematic Review

A total of 479,723 papers were identified through database searches, refined down to 619 through adding additional search terms (Fig. 1)

After reviewing for eligibility, a total of 20 final papers remained for review.

Retrospective Chart Review

Demographics

Both groups were similar in terms of weight and gender ($P < 0.963$ and $P < 0.591$, respectively). However, there was a statistically significant difference in terms of age ($P < 0.005$), with younger patients in the private hospital. The mean age (standard deviation, interquartile range) for patients in the teaching hospital was 5.45 years (±3.1, ±3.00–7.5) compared with that in the private hospital at 4.32 years (±2.7, ±2.0–6.0).

Surgical Procedures Performed

In both hospitals, the majority of patients who underwent ENT surgery were diagnosed with chronic adenotonsillitis (30, 54.6%; 90, 92.8%; for the teaching and private hospitals, respectively; $P < 0.0001$).

In the teaching hospital in urology, the majority were diagnosed with undescended testicles (12 out of 33, 36.4%) compared with redundant, prepuce phimosis and paraphimosis in the private hospital (7, 87.5%; $P < 0.0001$). In both hospitals, all maxillofacial surgical patients (13, 100.0%; 4, 100.0% for the teaching and private hospitals, respectively) presented with dental caries ($P = 0.0408$). Acute appendicitis (5, 45.5%; 2, 66.7%) was the main diagnosis for those who underwent general surgery, respectively, for both the teaching and the private hospitals ($P = 0.0498$*). Overall, there were statistically significant differences in the total number of surgeries performed per surgical discipline between the 2 study populations ($P < 0.0001$).

Surgical Antimicrobial Prophylaxis Use

Antimicrobials Used for Surgical Antimicrobial Prophylaxis

A statistically significant difference was seen in the antimicrobial selection for the 2 hospitals ($P < 0.0001$; Table 2). The vast majority of patients from the teaching hospital received cefazolin, appropriately selected in one third of cases, however, underdosed in 60.0%. Further to this, 8.3% of patients received amoxicillin–clavulanic acid and 1 patient received cefuroxime (2.8%). This is different to the private hospital where the vast majority of patients received amoxicillin-clavulanic acid (Table 2).

A statistically significant difference ($P = 0.0399$; $P = 0.0130$) was noted between the 2 hospitals, for both patients who did not receive any antimicrobials as SAP and those who received 1 antimicrobial as SAP, respectively. The majority (67.7%) of patients from the teaching hospital, and 52.7% from the private hospital, did not receive any antimicrobials as SAP. Despite being construed to a small population, more antimicrobial combination use was seen in the teaching hospital.

Assessment of Surgical Antimicrobial Prophylaxis Use

In the teaching hospital, SAP was indicated in 19.6%, however, administered in 17.8%. This was compared with limited numbers in the private hospital, with a statistically significant difference seen where SAP was not indicated nor administrated (Table 3).

Compliance to Surgical Antimicrobial Prophylaxis

Overall compliance to all 5 of the criteria (antimicrobial selection, dosing, timing of administration, redosing and duration) was not achieved in either hospital sector. Overall 58.8% of the patients treated at the teaching hospital met 3 of the 5 criteria (Table 4).

Comparative results between the teaching and private hospitals were demonstrated for selection and dosing. Compliance in terms of timing was only met in 8 patients at the teaching hospital. Full compliance to redosing and duration of treatment was achieved by both hospitals (Table 4).

DISCUSSION

Statistically significant differences were seen in the patient characteristics between the 2 hospitals in terms of age, primary diagnosis and the total number of surgeries performed. More elective ENT surgeries, specific to chronic adenotonsillitis, were performed in the

TABLE 3. Assessment of Surgical Antimicrobial Prophylaxis Use

Hospital	SAP Indicated, n = 112 (100%)	Administered n (%)	*P**
Teaching	22 (19.64)	17 (77.27)	1.000
Private	3 (2.67)	3 (100)	
Hospital	SAP Not Indicated, n = 112 (100%)	Not Administered n (%)	*P**
Teaching	90 (80.36)	71 (78.89)	0.0003
Private	109 (97.32)	59 (54.12)	
Total compliance	88 (78.57)	62 (55.36)	0.0003†

*Fisher exact test.
†Highly significant.
SAP indicates surgical antimicrobial prophylaxis.

TABLE 4. Compliance to the 5 Criteria

Criteria		Teaching n = 17 (100)	Private n = 3 (100)	*P**
1	Drug selection	5 (29.41)	0 (0)	0.5395
2	Dose	1 (5.88)	0 (0)	1.0000
3	Timing	8 (47.06)	0 (0)	0.2421
4	Redosing	17 (100)	3 (100)	NA
5	Discontinuation	17 (100)	3 (100)	NA

*Fisher exact test.
NA indicates not applicable.

private hospital, reflecting more limited access to health and specialist care in the public system, which is now being addressed.[10] As a result, adeno-/tonsillectomy has been typically reserved for patients with severe sleep disordered breathing in the public system.[19] Additionally, the burden of acute tonsillitis disease is higher compared with that in developed countries in view of current unemployment and poverty issues in South Africa as this is more commonly seen in pediatric patients of lower socioeconomic status.[19] As the teaching hospital is located in a rural area of Gauteng, other factors that may result in the variation of adeno-/tonsillectomy rates seen are the Healthcare Professional (HCPs)-to-population ratio and geographical access barriers. As a result, private health care patients under 7 years of age are more likely to undergo adeno-/tonsillectomies than their public health care counterparts, with HCPs feeling pressurized to accept their demands.[19]

The majority of patients did not receive any antimicrobials as part of SAP, with the overall use of SAP at 32.3% to 47.3% for the teaching and private hospitals, respectively, lower than worldwide practices (64.3%).[17] However, when SAP was indicated, this was administered to 77.3% and 100.0% of patients from the teaching and private hospitals, respectively, higher than the studies conducted in the United States (72.2%).[7] In the 2 categories regarding SAP use, that is, indication and administration and no indication nor administration, the teaching hospital had the highest overall compliance (78.6%) compared with the private hospital (55.4%). These findings are though both lower than in Italy where SAP was administered in 81.0% of cases with an indication[17] and in the United States (93.8%).[7] In addition, despite an indication for SAP, 22.7% of patients in the teaching hospital did not receive SAP. The inappropriate and overuse of SAP without an indication is also a concern and occurred in both hospitals, with a statistically significant difference between them ($P = 0.0003$), which exposes patients to increased risks of SSIs and/or adverse drug reactions, as well as potentially increasing AMR rates.[17] All of these are a cause for concern that needs to be addressed.

Specifically, ENT surgical procedures were performed for the majority of patients in both groups where SAP is not routinely recommended.[11,13,14,16,20]

Compliance to all 5 of the criteria (Table 4) was not met in either hospital sector. However, the teaching hospital complied to most criteria. This though compares well with findings from in Italy where SAP was administered appropriately in only 8.0% of cases,[17] similar to the in Philippines (13.0%).[21]

Of all patients who received SAP with an indication in the private hospital sector, none complied with current SAP guidelines with regards to appropriate antimicrobial selection. In contrast, nearly a third of all patients treated in the teaching hospital received an appropriate selected antimicrobial. These results are though much lower than those in similar studies in New York (97.1%)[22] and Singapore (57.0%),[6] again raising concerns.

An appreciable contributing modifiable driver to AMR is the appropriate selection of antimicrobials.[23] Cefazolin was the SAP of choice in the majority (88.9%) of patients in the teaching hospital in line with current guidelines[11–15]; however, amoxicillin–clavulanic acid was principally used (88.7% of patients) in the private hospital. This is a concern as this may contribute to the emergence of AMR. This may be because amoxicillin–clavulanic acid has been shown to be effective in preventing post-tonsillectomy morbidity[24] but needs this to be addressed. However, there are concerns with underdosing with cefazolin in the teaching hospital that needs addressing along with timing of administration, with results worse than seen in Greece,[25] Singapore[6] and the United States.[17] Encouragingly though, full compliance to both redosing and duration of treatment was found in both hospitals, higher than in Greece.[25]

Limitations

Care should be taken in the generalization of these results across South Africa. We also accept that this study did not investigate possible causes of deviations from current guidelines, including any influence of local/hospital-specific antibiograms. In addition, we did not investigate physician knowledge, attitudes or perception to SAP. Neither did we investigate the impact of nonadherence of guidelines on morbidity, mortality and costs. Additionally, hospital charts were used for data collection with accuracy depending on the accuracy of the hospital files. However, this reflects current practice. Despite these limitations, we believe the findings are robust given the nature of the hospitals taking part and can form the basis for future strategies to improve SAP in hospitals in South Africa in the future.

CONCLUSION

This study found substantial variation in SAP use among the teaching and private hospitals, especially on SAP selection, illustrating that overall compliance to national and international SAP guidelines is suboptimal. One possible explanation for the variation in SAP use is the lack of pediatric-specific SAP guidelines, both internationally and in South Africa.

SAP practices did diverge from current guidelines, with inappropriate overuse of SAP occurring in both sectors, while underuse was limited to the teaching hospital. Full compliance to the 5 agreed criteria was not met though by either hospital, and there were concerns with the high inappropriate use of amoxicillin–clavulanic acid in the private hospital.

The importance of proper use of SAP cannot be overemphasized. Areas for concern have been identified, and quality improvement interventions including potential indicators, continued surveillance and local standardized pediatric SAP guidelines in South Africa are needed.

REFERENCES

1. De Luca M, Donà D, Montagnani C, et al. Antibiotic prescriptions and prophylaxis in Italian children. Is it time to change? Data from the ARPEC Project. *PLoS One*. 2016;11:e0154662.
2. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. 2016. [online] amr.review.org. Available at: https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf
3. Romano JC. Stimulus for change: result of standardization of antimicrobial prophylaxis duration in pediatric cardiac surgery. *J Thorac Cardiovasc Surg*. 2016;152:1121–1122.
4. Sviestina I, Mozgis J, Mozgis D. Analysis of antibiotic surgical prophylaxis in hospitalized children suffering upper and lower extremity injuries. *Int J Clin Pharm*. 2016;38:233–237.
5. Anderson D, Sexton D. Antimicrobial prophylaxis for prevention of surgical site infection in adults 2016. [online] Uptodate.com. Available at: https://www.uptodate.com/contents/antimicrobial-prophylaxis-for-prevention-of-surgical-site-infection-in-adults
6. So JP, Aleem IS, Tsang DS, et al.; SickKids Surgical Site Infection Task Force. Increasing compliance with an antibiotic prophylaxis guideline to prevent pediatric surgical site infection: before and after study. *Ann Surg*. 2015;262:403–408.
7. Sandora TJ, Fung M, Melvin P, et al. National variability and appropriateness of surgical antibiotic prophylaxis in US children's hospitals. *JAMA Pediatr*. 2016;170:570–576.
8. Versporten A, Bielicki J, Drapier N, et al.; ARPEC project group. The Worldwide Antibiotic Resistance and Prescribing in European Children (ARPEC) point prevalence survey: developing hospital-quality indicators of antibiotic prescribing for children. *J Antimicrob Chemother*. 2016;71:1106–1117.
9. Southern African Journal of Epidemiology and Infection. 2016. 5th FIDSSA Congress 2013. [online] Available at: http://dx.doi.org/10.1080/10158782.2013.11441546
10. Meyer JC, Schellack N, Stokes J, et al. Ongoing initiatives to improve the quality and efficiency of medicine use within the public healthcare system in South Africa; a preliminary study. *Front Pharmacol*. 2017;8:751.
11. ASHP. Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery 2013. [online] Available at: http://www.ashp.org/DocLibrary/BestPractices/TGSurgery.aspx
12. Choc Children's. Antibiotic Prophylaxis for Surgery Guideline 2010. [online] Available at: http://www.choc.org/userfiles/AntibioticProphylaxisForSurgeryGuideline.pdf
13. RHSC recommendations for antibiotic prophylaxis in paediatric surgery 2016. [online] Available at: http://www.clinicalguidelines.scot.nhs.uk/media/2105/antibiotic-prophylaxis-paediatric-surgery.pdf
14. SIGN. Antibiotic prophylaxis in surgery 2014. [online] Available at: http://www.sign.ac.uk/pdf/sign104.pdf
15. The National Department of Health. (2013). Standard treatment guidelines and essential medicines list, for SA, Hospital level, Paediatrics. [online] Available at: http://passthrough.fw-notify.net/download/326174/http://www.kznhealth.gov.za/ pharmacy/PaedsSTG2013LR.pdf
16. NHS. Paediatric Antibiotic Surgical Prophylaxis & Perioperative Guideline. [online] Available at: http://www.nhstaysideadtc.scot.nhs.uk/Antibiotic%20site/pdf%20docs/Paeds%20Surgical%20Proph%20final.pdf
17. Ciofi degli Atti M, Spila Alegiani S, Raschetti R, et al.; APACHE Study Group. Surgical antibiotic prophylaxis in children: adherence to indication, choice of agent, timing, and duration. *Eur J Clin Pharmacol*. 2015;71:483–488.
18. Khoshbin A, So JP, Aleem IS, et al.; SickKids Surgical Site Infection Task Force. Antibiotic prophylaxis to prevent surgical site infections in children: a prospective cohort study. *Ann Surg*. 2015;262:397–402.
19. Douglas-Jones P, Fagan JJ. Tonsillectomy rates in the South African private healthcare sector. *S Afr Med J*. 2016;106:1134–1140.
20. ASHP therapeutic guidelines - Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery. Available at URL: https://www.ashp.org/-/media/assets/policy-guidelines/docs/therapeutic-guidelines-antimicrobial-prophylaxis-surgery.pdf
21. Nabor M, Buckley B, Lapitan M. Compliance with international guidelines on antibiotic prophylaxis for elective surgeries at a tertiary-level hospital in the Philippines. *Healthcare infection* 2015;20(3–4):145–151
22. Carmeli I, Feigin E, Freud E, et al. Compliance with surgical antibiotic prophylaxis guidelines in pediatric surgery. *Eur J Ped Surg* 2014;25:199–202.
23. Holmes AH, Moore LS, Sundsfjord A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet*. 2016;387:176–187.
24. Piltcher OB, Scarton FB. Antibiotic use in tonsillectomies: therapeutic or prophylactic? Required or excessive? *Braz J Otorhinolaryngol*. 2005;71:686–690.
25. Dimopoulou A, Kourlaba G, Psarris A, et al. Perioperative antimicrobial prophylaxis in pediatric patients in Greece: Compliance with guidelines and impact of an educational intervention. *J Pediatr Surg*. 2016;51:1307–1311.