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Article

Utilization of Antibiotic Prophylaxis in Three Common Abdominal Surgeries, Adherence to Standard Guidelines and Surgeons' Perception in Teaching Hospitals, Islamabad, Pakistan

Zakir Khan [1*], Naveed Ahmed [2], Asim ur Rehman[3], Faiz ullah Khan[4], Hazir Rahman[5]

[1*] Department of Pharmacy Quaid-i-Azam University, Islamabad, 45320, Pakistan; e-mail: zakirkhan300@gmail.com.
[2] Department of Pharmacy Quaid-i-Azam University, Islamabad, 45320, Pakistan; e-mail: natanoli@qau.edu.pk
[3] Department of Pharmacy Quaid-i-Azam University, Islamabad, 45320, Pakistan; e-mail: arehman@qau.edu.pk
[4] Department of Pharmacy Administration and Clinical Pharmacy, School of Pharmacy, Health Science Centre, Xi'an Jiao tong University, China; e-mail: fkhan@bs.qau.edu.pk
[5] Department of Microbiology, Faculty of Chemical and Life Sciences, Abdul Wali Khan University, Mardan, Pakistan; e-mail: hazirrahman@awkum.edu.pk

*Correspondence: Zakir Khan; email: zakirkhan@bs.qau.edu.pk Tel.: 0092-3486062557

Abstract: *Background and objectives:* The appropriate use of antibiotics is the main strategy of Antimicrobial stewardship program. This study was planned to evaluate the quality of antibiotic prescriptions, its adherence with standard guidelines and surgeons' perception regarding antibiotic use in surgeries. *Methods:* A prospective cross-sectional observational and survey-based study comprised of two sections: *Phase 1;* to investigate the antibiotic utilization in three most common abdominal surgical procedures during 9 months (January 2017 to September 2017). The appropriateness of antibiotics was compared with evidence-based guidelines. *Phase 2;* the surgeon's perspectives were evaluated through a self-administered questionnaire (13 items) during the next three months (October 2017 to December 2017). Descriptive statistics, chi-square and Fisher's exact tests analysis were used through SPSS Statistical Package 21.0. *Results:* A total of 866 eligible surgical cases out of 1015 were investigated. An acute appendectomy (n= 418; 48.2%) was most common surgical intervention followed by laparoscopic cholecystectomy (n= 278; 32.1%) and inguinal hernia (n= 170; 19.7%). About 97.5% of patients received antibiotics. Among these, 9.5% adhered according to guidelines with respect to correct choice, 40% for timing, 100% for dose and route (optimal value 100%). The ceftriaxone (J01XD04; n= 503; 59.5%) was most frequently prescribed antibiotic. A 200 participants (response rate 70.6%) filled out a validated questionnaire (internal consistency; $\alpha \geq 0.7$). One hundred and thirty-eight (69%) reported the overuse of antibiotics and most of them (97%) preferred broad-spectrum antibiotics instead of narrow-spectrum. The participants reported that non-availability hospital-based guidelines (n=193; 96.5%), prescribing of antibiotics without guidelines (n=186; 93%), underestimation of infection (n=177; 88.5%), lack of consensus (n=135; 67.5%) and poor awareness about guidelines (n=122; 61%) were the main determinants in their health care settings. *Conclusions:* The compliance of Surgical antibiotic was far below the recommendations of guidelines. The urgent needs of awareness among surgeons and implementation of antimicrobial stewardship program were important recommended interventions for appropriate use antibiotics.

Keywords: audit; utilization; surgery; antibiotics; perception; infections; hospitals

1. Introduction

The development of antimicrobial resistance even to the newer and broad-spectrum agent is a global health threat [1]. The antimicrobial resistance is closely associated with its inappropriate usage [2, 3]. Antimicrobial stewardship (APs) emphasize on the appropriate utilization of therapeutic agents for the improved patients' health outcomes, minimization of resistance, adverse events and infection issues [4]. APs also recommend the educational and research-based program for good prescribing behaviors among healthcare practitioners [5].

It is well documented that, surgical infections are responsible for serious health concern throughout the world [6, 7]. The surgical site infections (SSIs) are the most common cause of hospital-acquired infections. The use of Surgical prophylactic antibiotics (SAP) is an evidence-based practice for the prevention of SSIs [8]. The optimal benefits can be avail through the only appropriate use of antibiotics [3, 8]. However, the excessive or inappropriate antimicrobial use is a root cause for the health-related problems due to emerging resistance, increased the rate of Clostridium difficile infection, toxicity, drug interactions and prolonged hospitalization [3, 9]. There is a need for increased education and awareness about the inappropriate use of antimicrobials amongst the public and healthcare professionals [10].

It is evident that the adherence with evidence-based guidelines is related to improved good prescribing practices and health outcomes for the patients [3, 8, 11, 12]. In spite of the recommendations, administrative regimens of SAP are often inappropriate in surgical procedures and health care settings [3, 13-15]. Antibiotics are the main therapeutic agents and frequently use in surgery [16]. Due to the higher utilization of antimicrobials, the periodic evaluation SAP, adherence with standard protocols, understand the perception, attitude, and practices of surgeons are crucial for the better plan of therapy.

Therefore, considering the importance of antibiotic use in surgery, this study was carried out to evaluate the quality of antibiotic prescription, adherence with standard guidelines and surgeon's perception in teaching hospitals, Islamabad, Pakistan.

2. Materials and Methods

2.1. Observational study phase

2.1.1. Study design and settings

A six-month prospective, observational, medical record-based study from January 1, 2017, to September 30, 2017, was conducted to investigate adherence of SAP practices with treatment guidelines (phase 1). General surgical departments of Pakistan institute of Medical Sciences and Shifa International hospital, Islamabad were selected for this study. These are national level referral hospitals with 600 beds, providing medical facilities to the capital city of Pakistan, Khyber Pakhtunkhwa, Azad Jammu Kashmir, and Punjab areas.

2.1.2. Data collection tool

Medical records of adult's patients underwent the commonest abdominal surgeries, ages greater than 16 years, with no previous infection and surgery, were analyzed during the study period. The desired information was collected from medical records through already design standardized form ***(Supplementary file 1)***. The type of surgery, details of antibiotic prophylaxis (antibiotic agents, administration route, dosage, time), and length of hospital stay were recorded.

2.1.3. Data analysis

The SAPs were judged as has been appropriate if the antibiotic, dose, route and timing were in accordance with international guidelines recommendations [8, 17]. These guidelines have the same

recommendation for administration of SAP regarding choice, dose, route, and timing. These guidelines emphasized on the following aspects; a) use of inexpensive narrow-spectrum antibiotics b) intravenous single dose prophylaxis c) administration of SAP within 1 hour before the first incision d) A Cefazolin is the first drug of choice, however, if there is allergy to beta-lactams then Vancomycin or Clindamycin should be appropriate alternative regime (Metronidazole should be added against anaerobic microorganism activity) f) dose of SAP. The steps for reviewing the prescription of SAP to assess adherence with guidelines are presented in ***figure 1***. World Health Organization Anatomical therapeutic classification (ATC) were also used to report antibiotic utilization [18].

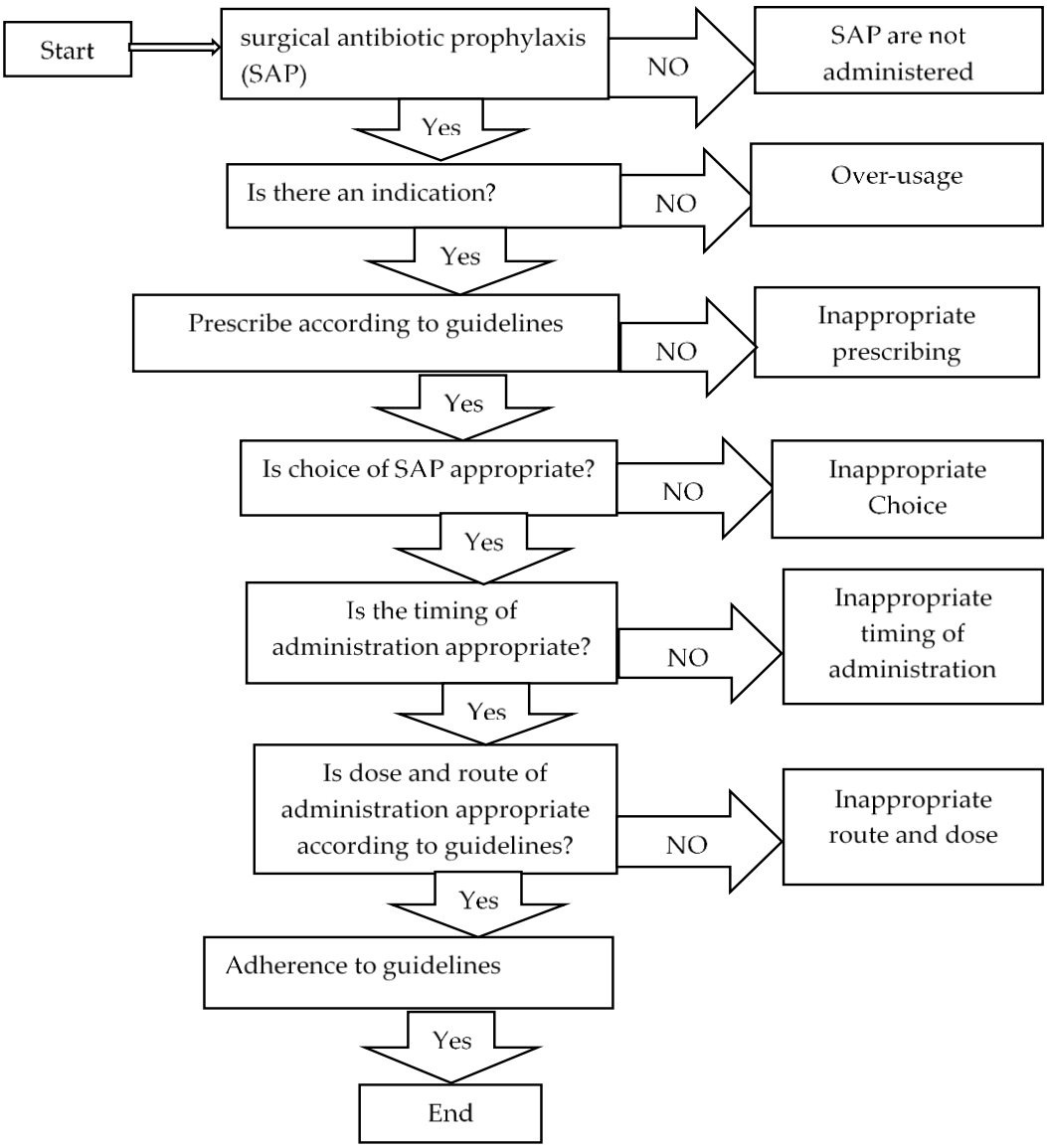

Figure 1. Steps for reviewing the prescription of SAP to assess adherence with guideline

2.2. Phase 2: Questionnaire-based study

2.2.1. Study design and settings

After completion of the first phase of the study, a three-month prospective questionnaire-based survey was carried out to assess surgeons' views regarding antibiotic use and guidelines adherence items.

Surgeons working at surgical units of the selected settings were included in the questionnaire-based study from October 1, 2017, to December 30, 2017. Pharmacists, nurses and paramedical staff working at surgical wards were under exclusion criteria.

2.2.2. Data collection tool

Surgeons were recruited on a daily basis on ward round using a convenient sampling method. A participant has a full choice to accept or reject to participate in the study. A participant information leaflet was provided to all surgeons before the study. Investigators systematically and thoroughly reviewed available literature [19-24] for development of a self-administered questionnaire ***(Supplementary file 2)***. The questionnaire was modified through content and face validity. Content of a questionnaire was further validated by two academic experts. The content modification was done after their views about the importance and content relativity. For further, modification, feasibility, and adjustment, the questionnaire was administered to a small group of 20 prescribers (10 from each hospital). After that, the recommended modifications were included in the questionnaire.

2.2.3. Data analysis

The Cronbach's alpha was used to measure the reliability coefficients and internal consistency of the questionnaire in SPSS version 22.0. The calculation for Cronbach's alpha was set at .76. A questionnaire was divided into two main sections. The demographic history of the participants included in the first section. While the second section contains 13-questions which was further divided into a and b sections. Section "a" contain questions related to an antibiotic used in surgical procedures and section "b" includes details questionnaires items regarding guidelines adherence. The response of participants recorded on the Likert scale (1 to 5) questionnaire.

2.3. Statistical Analysis

The descriptive statistics were used for frequency and percentages. The frequency of each category was compared through chi-square or Fisher's exact tests analysis as appropriate. A p-value of 0.05 or less was defined as statistically significant. Statistical analysis was conducted using SPSS Statistical Package 21.0 (IBM Corporation, Armonk, NY, USA).

2.4. Ethics approval

The study was performed in accordance with the declaration of Helsinki. Ethical approval was obtained from the Bioethics Committee of the university and Institutional review boards of selected hospitals ***(Supplementary file 3)***. The purpose and protocols of the study were explained before participation, and written consents were obtained.

3. Results

3.1. The pattern of surgical procedures

A total of 1015 patients underwent the three common abdominal surgeries in selected settings during the study period. About, of 149 (14.7%) patients were excluded due to the incomplete medical record (62 patients), having previous surgery (34 patients) and age less than 16 years (53 patients). Finally, 866 cases were recruited for the present study. An acute appendectomy 418 (48.2%) was the most commonly performed surgery followed by laparoscopic cholecystectomy 278 (32.1%) and inguinal hernia 170 (19.7%). These were frequently performed abdominal surgeries in selected settings.

3.2. Quality of antibiotic prescription and overall SAPs Practices according to guidelines

3.2.1. Indication

According to protocols, antibiotics were indicated for all surgical procedure however non-use of an antibiotic was observed in this study. A total of 21 patients (2.5%) out of 866 did not receive prophylactic antibiotic: 11 in laparoscopic cholecystectomy and 10 in inguinal hernia (Table 1). The significant difference was observed between antibiotic practices and surgical procedures (P < 0.001) **(Table 1)**.

Table 1. Antimicrobial prophylaxis practices in surgeries (n=866).

SAP Practices	Appendectomy n (%)	Laparoscopic cholecystectomy n (%)	Inguinal hernia n (%)	Total n (%)	Optimal values
Use of antibiotic	418 (100)	267 (96)	160 (94)	845 (97.5)	100%
Non-use of antibiotic	0 (0)	11 (4)	10 (6)	21 (2.5)	0%
Antibiotic correct choice	35 (8.4)	27 (10.1)	18 (11.2)	80 (9.5)	100%
Correct dose	35 (100)	27 (100)	18 (100)	80 (100)	100%
Route					
Intravenous (IV)	418(100)	267 (100)	160 (100)	845 (100)	100%
Timing					
30-60 minutes before *SI*	162 (38.7)	109 (40.8)	67 (41.9)	338 (40)	100%
More than 30-60 min	256 (61.3)	158 (59.2)	93 (58.1)	507 (60)	100%

Abbreviation: *SI*: Surgical incision, *n*: Number, %: Percentage

3.2.2. Selection of antibiotics

Antibiotic was prescribed to 845 patients (97.5%) who underwent surgical procedures. However, appropriate antibiotics according to evidence-based guidelines were given to only 9.5% (n=80) of surgical patients. About, 765 (90.5%) patients received wrong antibiotics with respect to guidelines. The selection of correct choice according to protocols was more in the inguinal hernia (11.2%) as compared to laparoscopic cholecystectomy (10.1%) and acute appendectomy (8.4%); P = 0.001. Seven hundred and sixty-five (90.5%, consisting of 383 in the acute appendectomy, 240 in the laparoscopic cholecystectomy and 142 in the inguinal hernia procedures) received antibiotics differing from the recommended choice according to standard protocols **(Table 1)**.

3.2.3. Dose and route

The patients who did not receive antibiotics according to guidelines were not included in the computation of correct dose. The dose (n=80; 100%) and route (n=845; 100%) of antibiotic adhered with the guidelines in all patients **(Table 1)**.

3.2.4. Timing

The timing of administration within an optimal range (within 30-60 minutes before surgical incision) was noted only in less than half of the patients (40%). The timing was more appropriate in inguinal

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hernia as compared to laparoscopic cholecystectomy and acute appendectomy (41.9%% vs 40.8% and 38.7%; P = 0.001) **(Table 1)**.

3.2.5. Utilization pattern of antimicrobials

The overall commonly prescribed antimicrobials were ceftriaxone (J01XD04: n=503; 59.5%) followed by Amoxicillin plus Clavulanic acid (J01CR02: n=89, 10.5%). The remaining patients were managed with other different types of regimens. The combination use of antibiotics was also in 20.9% (n=177) of the patients **(Table 2)**.

Table 2. Frequency and percentages of various SAP prescribed in selected surgical procedures.

Surgical prophylactic antibiotic (dose)	WHO/ATC code	Acute Appendectomy (%)	Laparoscopic cholecystectomy n (%)	Inguinal hernia n (%)	Total n (%)
Ceftriaxone (2g)	J01XD04	323 (77.2)	143 (53.5)	37 (23.1)	503 (59.5)
Amoxicillin *plus* Clavulaunic acid (1.2 g)	J01CR02	0 (0)	15 (5.6)	74 (46.2)	89 (10.5)
Cefazolin (2g)	J01DB04	7 (1.7)	27 (10.1)	18 (11.2)	52 (6.1)
Cefoperazone *plus* Sulbactam (1g)	J01DD62	47 (11.2)	0 (0)	0 (0)	47 (5.5)
Azithromycin (500 mg)	J01FA10	0 (0)	46 (17.2)	0 (0)	46 (5.4)
Cefuroxime (1.5g)	J01DC02	0 (0)	23 (8.6)	23 (14.3)	46 (5.4)
Ceftriaxone (2g) *plus* metronidazole (500 mg)	J01XD04+ J01XD01	28 (6.7)	0 (0)	0 (0)	28 (3.3)
Amikacin (500 mg)	J01GB06	0 (0)	4 (1.5)	8 (5)	12 (1.4)
Ciprofloxacin (500 mg)	J01MA02	9 (2.1)	0 (0)	0 (0)	9 (1)
Piperacillin *plus* Sulbactam (4.5g)	J01CR05	4 (0.9)	9 (3.3)	0 (0)	13 (1.5)
Non-use of SAP	-	0 (0)	11 (4.1)	10 (6.2)	21 (2.5)
Grand Total		418 (100)	278 (100)	170 (100)	866 (100)

Abbreviations: *WHO/ATC:* World Health Organization/ Anatomical Classification System, *n*: Number, %: Percentage.

3.3. SAPs practices in individual surgical procedures

3.3.1. Acute Appendectomy

Antibiotic was prescribed in all of the 418 (100%) eligible patients undergoing an acute appendectomy. In 81% (n=339) of the cases, only one antibiotic was prescribed. Ceftriaxone was given to 323 (77.2%) patients, Cefoperazone plus Sulbactam to 47 (11.2%) patients, and other antibiotics were prescribed to 48 (11.5%) patients. In 81% of the cases, 2 g of ceftriaxone was used. The route of administration was appropriate in all patients. Only in 8.4% (n=35) of the cases received antibiotic according to the guidelines. About 38.7% of the patients received antibiotic within optimal timing **(Table 1 and 2)**.

3.3.2. Laparoscopic cholecystectomy

A total of 278 of 267 (96%) patients undergoing laparoscopic cholecystectomy received a prophylactic antibiotic. Whereas, only 1 drug was ordered in 91% (n=243) of the patients. Ceftriaxone was prescribed to 143 (53.5%),

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azithromycin for 46 (17.2%), and other drugs were used in 78 (29.2%) cases. The dose of Ceftriaxone, azithromycin, and cefazolin was 2 g, 500 mg, and 2g respectively. The dose and route of administration adhered to guidelines in all patients who received antibiotics. The choice and timing of antibiotics adhered with the guidelines in only 10% (n=27) and 40.8% (n=109) of the cases **(Table 1 and 2)**.

3.3.3. Inguinal hernia

A total 160 of 170 (94%) patients undergoing inguinal hernia received prophylactic antibiotics. Amoxicillin *plus* Clavulanic acid was the most frequently prescribed drug (74 cases). The other patients received ceftriaxone (n=37), Cefuroxime (n=23), or other antibiotics (n=26). The dose of Amoxicillin plus Clavulanic acid was l.2 g (100%). A single antibiotic was prescribed to fifty-four (n=86; 54%) percent of the patients. The drug of choice according to guidelines is Cefazolin, which was only prescribed to 18 (11.2%) of the patients. The timing was appropriate in only 41.9% of the patients **(Table 1 and 2)**.

3.4. Demographic characteristics of Surgeons

A total of 283 surgeons were approached using a convenient sampling method and the questionnaire was completed by 200 prescribers from selected settings with a response rate of 70.6%. Most of the prescribers were male (n=110, 55%) and level of education was associate (n=93, 46.5%). The highest proportion of respondents consisted of the age group of less than 30 years (n=171, 85.5%), 74% had experience of <10 years (n=148). Statistically significant differences were found between age, final academic degree, and experience with respect to perception regarding Evidence-based guidelines (Question-5) (P<0.05) **(Table 3)**.

Table 3. Details of participants (n=200).

Variables	*Frequency (n)*	*Percentage (%)*	*P-value*
Gender			
Male	110	55	
Female	90	45	**.238**
Age			
Age <30 years	171	85.5	
Age >30 years	29	14.5	**.001**
Final academic degree			
Bachelor degree (M.B.B.S)	80	40	
Associate degree (M.S)	93	46.5	**.001**
Post graduate degree (PhD-S/Post.Doc-S)	27	13.5	
Work experience			
<10 years	148	74	
11-20 years	48	24	**.001**
>20 years	4	2	
Hospital setting			
Government	100	100	**.964**
Private	100	100	

Abbreviation: M.B.B.S: Bachelor of Medicine and Bachelor of Surgery, M.S: Master of Surgery, PhD-S: Doctor of Philosophy in surgery, Post-Doc-S: Post Doctorate in surgery, *n*: Number, %: Percentage

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3.5. Perceptions of Participants about antimicrobial use in surgery

Most of the participated surgeons reported (69%; n=138, strongly agreed; 6% n=12 or agreed; 63% n=126) overuse of antibiotic in surgical procedures; only two (1%) disagreed. The overuse of antibiotic was more reported in government-funded hospital (n=72;36%) as compared to private-funded (n=66; 33%); p=.002. Most of them strongly (97%, n=194) preferred broad-spectrum antibiotics instead of low-spectrum. About twenty-seven surgeons underrated this variable. Surgeons having post-graduate degree preferred broad-spectrum agent versus narrow spectrum less than their colleagues who obtained bachelor or associate educational background (13.5%, n=27 versus 38%, n=76 and 45.5%, n=91; p=.013) ***(Supplementary file 4)***. The details about perceptions of surgeons are reported in **Table 4**.

Table 4. Surgeons perception regarding guidelines adherence and other determinants (n=200)

Variables	*Response n (%)*				
	Strongly disagree	*Disagree*	*Uncertain*	*Agree*	*Strongly Agree*
Section a: Antibiotic-related items					
Q1: Antibiotics are overused in surgical procedures?	0 (0)	2 (1)	60 (30)	126 (63)	12 (6)
Q2: Are you preferred broader-spectrum antibiotics instead of low spectrum antibiotic in a surgical procedure?	2 (1)	1 (.5)	3 (1.5)	170 (85)	24 (12)
Q3: Are low availability of antibiotics in the hospital pharmacy affecting the choice of an antibiotic according to guidelines?	1 (.5)	17 (8.5)	64 (32)	109 (54.5)	9 (4.5)
Section b: Guidelines adherence related items					
Q4: Are you agree to prescribed antibiotic prophylaxis with accurate choice, dose, and timing according to guidelines?	1 (.5)	0 (0)	17 (8.5)	171 (85.5)	11 (5.5)
Q5: Evidence-based guidelines should be followed before prescribing antibiotic in surgery?	0 (0)	24 (12)	48 (24)	92 (46)	36 (18)
Q6: Prescribing of antibiotics without evidence-based guidelines is responsible for a high financial burden on patients?	2 (1)	9 (4.5)	3 (1.5)	162 (81)	24 (12)
Q7: Poor awareness about guidelines is a factor of irrational use of antibiotics in surgery?	1 (.5)	29 (14.5)	48 (24)	94 (47)	28 (14)
Q8: Are lack of consensus by the surgeons with the recommendation in	0 (0)	27 (13.5)	38 (19)	107 (53.5)	28 (14)

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the guidelines is a factor for inappropriate use of antibiotics?					
Q9: Disagreement with guidelines is a contributing factor for the inappropriate use of antibiotics?	0 (0)	50 (25)	43 (21.5)	92 (46)	15 (7.5)
Q10: Underestimation of infection rate is a factor for non-adherence with guidelines?	1 (.5)	1 (.5)	21 (10.5)	169 (84.5)	8 (4)
Q11: Are guidelines are good educational tools and also a convenient source of advice According to your opinion?	0 (0)	14 (7)	29 (14.5)	126 (63)	31 (15.5)
Q12: I use the guidelines on a daily or weekly basis?	0 (0)	3 (1.5)	42 (21)	125 (62.5)	30 (15)
Q13: There are no available hospital-based guidelines for antibiotic use in surgery?	1 (.5)	0 (0)	6 (3)	167 (83.5)	26 (13)

Abbreviatoions: n: Number; % Percentage, SSI: Surgical site infection.

3.6. Participants' Perceptions about guidelines

Regarding guidelines adherence, a total of 128 (64%) of surgeons agreed/strongly agreed that "Evidence-based guidelines should be followed before prescribing antibiotic in surgery." About, 186 (93%) surgeons perceived that "Prescribing of antibiotics without evidence-based guidelines are responsible for a high financial burden on patients". Furthermore, 67.5% (n=135) of participants agreed/strongly agreed that "lack of consensus by the surgeons with the recommendation in the guidelines is a factor for inappropriate use of antibiotics. This was highly rated by 46% (n=92) of junior surgeons as compared to seniors; P-value=.004 (11 to 20 years' experience n=39; 19.5% and more than 20 years' experience (n=4; 2%) ***(Supplementary file 4).***

Most of the surgeons perceived (n=157; 78.5%) that guidelines are good educational tools and a convenient source of advice for appropriate antibiotic use. A total of 77.5% (n=155) reported the use of guidelines on a daily or weekly basis, however surgeons having bachelor (28%, n=56) or associate degree (39.5%, n=79) were highly responded as compared to post-graduate degree holders (10%, n=20); P=.012 ***(Supplementary file 4)***. However, the non-availability of local based hospital guidelines was reported by 96.5% (n=193) of participants (13% (n=26) strongly agreed and 83.5%, n=167 agreed). More details are described in **Table 4**.

4. Discussion

We performed a comprehensive assessment of antibiotics used in the most common abdominal surgical procedures in two teaching hospitals. We found a substantial proportion of inappropriate SAP contradictory with evidence-based standard treatment guidelines. Most of the patients (n=845; 97.5%) received SAP in this study. However, the non-use when it is recommended in 2.5% (21 out of 866) cases leads to increase chances of wound development and its consequences related to increasing length of stay, morbidity, and mortality [3, 11]. The SAP was administered in line with standard guidelines recommendations in 9.5% (n=80) of patients. These findings are aligned with other studies conducted in Italy [25] and Brazilian hospital [26] which reported an adherence rate of 5.7% and 3-5.8% respectively. However, the previous studies in Qatar (68%) [27], India 52% [28] and Philippines

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(44%) [29] were reported higher adherence rates as compared to our study. The first step for the appropriate use of SAP is to provide educational training on antibiotic stewardship program and associated SSIs risk. Many previously conducted studies demonstrated the benefits of an educational intervention for antibiotic prophylaxis. The studies conducted in Nigeria [13] and Italy [25] found that compliance with antibiotic prophylaxis guidelines improved with increased awareness among surgeons and other health care team members.

Appropriate timing of administration of SAP was 40% (n=338) in our study. Comparable results also reported by the studies in the Philippines and Australia [30, 31]. Previous studies conducted in, Northern Nigeria (16.5%) [13] and Egypt (5%) [32] reported low adherence rate as compared to our study. Whereas, the higher rate was reported by other studies conducted in Jorden (99%) [15], France (76.6%) [33], and Palestine (60%) [34]. Less protection was received by patients who did not receive the antimicrobial at the optimal time. It is the best evidence that delayed administration of SAP is associated with two times greater risk of SSIs as compared to timely administration [13]. Appropriate time of administration of PPA can also reduce the duration of stay and hospitalization cost [8, 17]. Non-availability of standard guidelines and protocols for antibiotic prophylaxis in these hospitals could be a reason for non-compliance in our study [13, 14]. Lack of knowledge, unavailability of clinical pharmacist and poor collaboration with health care team are another reason for non-compliance in the present study. Further, large scale and multi-centered studies are needed to dig out others contributing factors of non-compliance.

Most commonly prescribe SAP was Ceftriaxone, given to 503 (59.5%) cases. The studies conducted in Ethiopia [3] and Turkey [35] also reported that ceftriaxone was excessively and inappropriately used in their settings. Antibiotics should be cost-effective, non-toxic and of the limited spectrum [8, 34]. Cefazolin is enough to cover pathogens involved in surgical infection. Inappropriate use of antibiotics provides a favorable environment to microbial resistance and also increased the possibility of adverse reactions [8, 17]. However, we observed a very low proportion of cefazolin in our study. Our findings are also supported by the research studies in Iran [36], and Saudi Arabia [37]. These findings revealed that the surgical team is not keeping up-to-date standards of best practice.

The second phase of this study was to evaluate the surgeon's views through a validated questionnaire. A wide range of influencing factors was explored through this research study. Most of the respondents in this study perceived that antibiotic overused, preference of broad-spectrum antibiotics and non-availability of antibiotics are the main problem in surgical wards. Similar findings were also reported by the studies from other settings outside Pakistan [19, 38-40]. Furthermore, similar results were reported in studies carried out in Malaysia [20] and India [28]. They reported that surgeons perceived that broad-spectrum antibiotics with long duration are more effective than narrow-spectrum antibiotics [20, 28]. These findings are important to address because overuse, broad-spectrum antibiotics, and non-availability problems have a potential impact on patient care and infection control activities.

The importance of evidence-based treatment guidelines cannot be denied. Prescribers scored highly to the guideline adherence items in this study which, suggesting a general acceptance of evidence-based guidelines. Guidelines adherence scores were similar to other studies conducted in England [19] and France [41]. This reflects a positive attitude and preference of prescribers towards guidelines. Standard treatment guidelines are crucial for rational use of therapy. Update and evidence-based guidelines should be provided to prescribers which, ultimately enhance effective and quicker route to appropriate antibiotics use [42]. Most of the participants reported that they used guidelines on a daily basis but also reported un-availability of hospital-based local guidelines. Similar results were reported by Philippine study [43]. Although positive attitudes towards guidelines are shown in our study but limited impact on their practice observed. However, reasons behind non-adherence of guidelines in our study may be due to lack of awareness about appropriate guidelines, lack of

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consensus by the surgeons with the guidelines, ineffective distribution system for the latest version of guidelines and lack of regular educational training sessions [20].

4.1. Strengths and Limitations

This study focused on specific three common abdominal surgeries, quality of antibiotic prescription, compliance rate with standard protocols and surgeon's perception in two tertiary care hospitals. As to the best of our knowledge, no previous studies have been focused on antibiotic utilization in selected abdominal procedures and surgeons, in a global or local perspective. The study has a novel concept, to documented the prescribing practices in three common abdominal surgical procedures and compare with International standard guidelines. This study also provides useful information to understand the perception of surgeons. Further, a sample size of 866 prescriptions and 200 surgeons is a huge sample that result in most authentic findings. Data collection from 2 tertiary care teaching hospitals was also a challenging task. The use of International evidence-based guidelines were best steps to strengthen the study. Due to which areas associated with drug use problems were identified and the degree of problems were also measured. Outcomes of present study add to a growing literature, particularly around medicine use and pharmaceutical health systems in developing countries. Some limitations of this study must be acknowledged. First, we used published recommendations of evidence-based international guidelines to measure against the appropriate use of SAPs in selected surgeries. Because there were no local consensus guidelines available in both hospitals. However, the possibility exists that recommendations given by the guidelines were not practicable in our patients or for the situation in Pakistan. Second, the study did not monitor the post-surgical infection rate. Therefore, we do not know if the nonadherence to the guidelines had any clinical consequences. Third, the questionnaire was only distributed at two tertiary care hospitals in the capital city of Pakistan. Thus, these findings cannot be generalized for the whole country.

5. Conclusions

The compliance of Surgical antibiotic was far below the recommendations of guidelines. The inappropriate choice, the timing of administration, overuse of antimicrobials, prescribing of antibiotics without guidelines, poor awareness, underestimation of infection, lack of consensus and non-availability of hospital-based guidelines were the main problems observed in this study. Good prescribing practices are crucial for patient safety and better health outcomes. Although, prescribers still rely on their own personal experiences while prescribing therapeutic agents. Surgeons are at the forefront in treating patients with infections therefore, the direct involvement of surgeons with knowledge in surgical infections can be highly impactful. The urgent needs of awareness among surgeons, continuous educational training, availability of appropriate antibiotics, implementation of local or international treatment guidelines and antimicrobial stewardship program were important recommended interventions for appropriate use antibiotics in surgery.

Supplementary Materials: None

Author Contributions: "conceptualization, Z.K.; methodology, N.A.; software, A.R, F.K; validation, Z.K, H.R. and N.A.; formal analysis, N.A, A.R, H.R; investigation, Z.K.; resources, N.A; data curation, Z.K, HR.; writing—original draft preparation, Z.K ; writing—review and editing, Z.K, N.A, A.R, F.K and H.R; visualization, N.A, AR.; supervision, Z.K. NA.; funding acquisition, not applicable

Funding: This research received no external funding.

Acknowledgments: Special thanks to the staff of selected hospitals for their assistance during data collection.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Supplementary file 1: Data collection form to retrieve data from patient charts.

Supplementary file 2: Questionnaire for perception of surgeons.

Supplementary file 3: Institutional/ Ethical review boards approval letters from University and concerned hospitals

Supplementary file 4: Statistical analysis of some important variables.

Availability of data and material

Further detail data can be provided on a reasonable request to the corresponding author.

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Supplementary Files attached below

Supplementary file 1: Institutional/ Ethical review boards approval letters from University and concerned hospitals

Supplementary file 1: Data collection form to retrieve data from patient charts.

Supplementary file 3: Questionnaire for perception of surgeons.

Supplementary file 4: Statistical analysis of some important variables.

Department of Pharmacy

QUAID-I-AZAM UNIVERSITY,
ISLAMABAD, PAKISTAN

Supplementary file 1

Data Collection form (For Observational study)

This data extraction format is prepared to retrieve data from patient charts on the utilization pattern of antibiotic prophylaxis for surgical site infections at Pakistan institute of Medical Sciences and Shifa international hospital, Islamabad from January,1, 2017 to September 30, 2017.

1. Medical and Surgical history of patients underwent surgery

1.1	Type of surgery	1. clean 2. clean contaminated
1.2	Most common surgical procedure performed for the patient	1.Appedoctomy 2. Incisional Hernia 3.Laparoscopic cholecystectomy
1.3	Co- morbid condition does the patient has?	1.DM 2. HIV-AIDS……... 3.TB 4.Hypertetion 5.Malignancy 6.Other co morbidity_____
1.4	Previous infection and surgery	1. Yes 2. No

2. Surgical Antibiotics Usage

2.1	Type of wound that the patient	1.Clean 2.Clean contaminated 3.Contaminated 4.Dirty
2.2	Antibiotic prescribed or not?	1.Yes 2.No
2.3	If Yes, type of antibiotic given to the patient as prophylaxis	1. Ceftriaxone 2. Cefazolin 3. Cefuroxime 4. Metronidazole

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		5. Others------
2.4	The form of antibiotics	1.single 2.combined
2.5	Duration of treatment (in hours)	----------
2.6	Dose of antibiotics	----------
2.7	Dosage form of antibiotics	----------
2.8	Route of administration	1.intera venous 2.intra muscular 3. intra dermal 4.other ------
3.9	Timing of administration	1.within 30-60 minutes before surgical incision 2. More than 1 hour before surgical incision

3. Adherence with Standard treatment guidelines

3.1	Is choice of SAP appropriate according to guidelines?	1.Yes 2. No
3.2	Appropriate dose?	1.Yes 2. No
3.3	Route of administration?	1.Yes 2. No
3.4	Duration of SAP?	1.Yes 2. No
3.5	Is timing of administration before surgical incision appropriate?	1.Yes 2. No

Department of Pharmacy

QUAID-I-AZAM UNIVERSITY,
ISLAMABAD, PAKISTAN

Supplementary file 2

The finding of current study will be kept confidential and used only for research purposes. The completion of questionnaire only required 5-10 minutes.

Anonymity and confidentiality

The data collected through this study will be strictly confidential by the researchers. Names and confidentiality of participants will not be revealed. Your identification information's will not be released to your organization or anyone

Right of withdrawal

You have fully rights to take participation or withdrawal of study.

FIRST SECTION: Demographic information

1. Please indicate your name (Optional)

2. Please indicate your gender

	Male
	Female

3. Please indicate your age

	Less than 30 years
	More than 30 years

4. Please indicate your final academic degree

	Bachelor degree
	Associate degree
	Postgraduate or above

5. Please indicate your work experience in this hospital

	Less than 10 years
	11-20 years
	More than 20 years

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6. Please indicate your hospital setting

	Government
	Private
	Others

SECOND SECTION: This section contains questions about perception of surgeons and determinants of antibiotic practices.

DIRECTION:

Please indicate to what extent you agree or do not agree with each statement below.

KEY:

Strongly disagree: 1	Disagree: 2
Uncertain: 3	Agree: 4
Strongly Agree: 5	

Section A: Antibiotic use in surgical procedures.

Q-1	Antibiotics are overused in surgical procedures?	1	2	3	4	5
Q-2	Are you preferred broader-spectrum antibiotics instead of low spectrum antibiotic in surgical procedure?	1	2	3	4	5
Q-3	Low availability of antibiotics in the hospital pharmacy affecting the choice of antibiotic according to guidelines?	1	2	3	4	5

Section B: Perception about Standard treatment guidelines.

Q-4	Are you agree to prescribed antibiotic prophylaxis with accurate choice, dose and timing according to guidelines?	1	2	3	4	5
Q-5	Evidence based guidelines should be followed before prescribing antibiotic in surgery?	1	2	3	4	5
Q-6	Prescribing of antibiotics without evidence-based guidelines are responsible for high financial burden on patients?	1	2	3	4	5
Q-7	Poor awareness about guidelines is a factor of irrational use of antibiotics in surgery?	1	2	3	4	5
Q-8	Lack of consensus by the surgeons with the recommendation in the guidelines is a factor for inappropriate use of antibiotics?					
Q-9	Disagreement with guidelines is a contributing factor for inappropriate use of antibiotics?					
Q-10	Underestimation of infection rate is a factor for non-adherence with guidelines?					
Q-11	Guidelines are good educational tools and also a convenient source of advice?					

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Q-12	I use the guidelines on a daily or weekly basis?					
Q-13	There are no available hospital-based guidelines for antibiotic use in surgery?					

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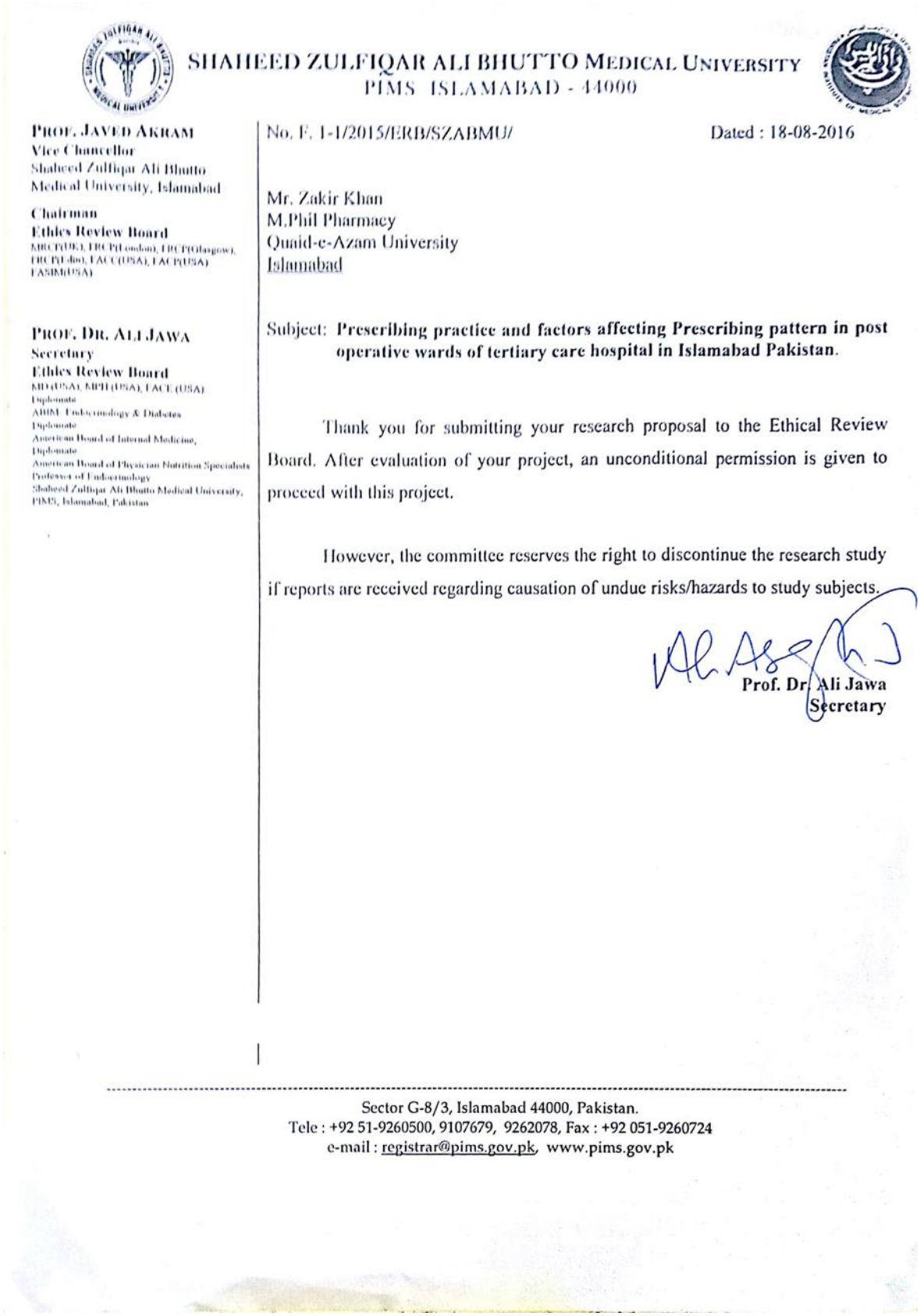

SHAHEED ZULFIQAR ALI BHUTTO MEDICAL UNIVERSITY
PIMS ISLAMABAD - 44000

PROF. JAVED AKRAM
Vice Chancellor
Shaheed Zulfiqar Ali Bhutto
Medical University, Islamabad

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Ethics Review Board
MRCP(UK), FRCP(London), FRCP(Glasgow),
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MD (USA), MPH (USA), FACE (USA)
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ABIM: Endocrinology & Diabetes
Diplomate
American Board of Internal Medicine,
Diplomate
American Board of Physician Nutrition Specialists
Professor of Endocrinology
Shaheed Zulfiqar Ali Bhutto Medical University,
PIMS, Islamabad, Pakistan

No. F. 1-1/2015/ERB/SZABMU/ Dated : 18-08-2016

Mr. Zakir Khan
M.Phil Pharmacy
Quaid-e-Azam University
Islamabad

Subject: **Prescribing practice and factors affecting Prescribing pattern in post operative wards of tertiary care hospital in Islamabad Pakistan.**

Thank you for submitting your research proposal to the Ethical Review Board. After evaluation of your project, an unconditional permission is given to proceed with this project.

However, the committee reserves the right to discontinue the research study if reports are received regarding causation of undue risks/hazards to study subjects.

Prof. Dr. Ali Jawa
Secretary

Sector G-8/3, Islamabad 44000, Pakistan.
Tele : +92 51-9260500, 9107679, 9262078, Fax : +92 051-9260724
e-mail : registrar@pims.gov.pk, www.pims.gov.pk

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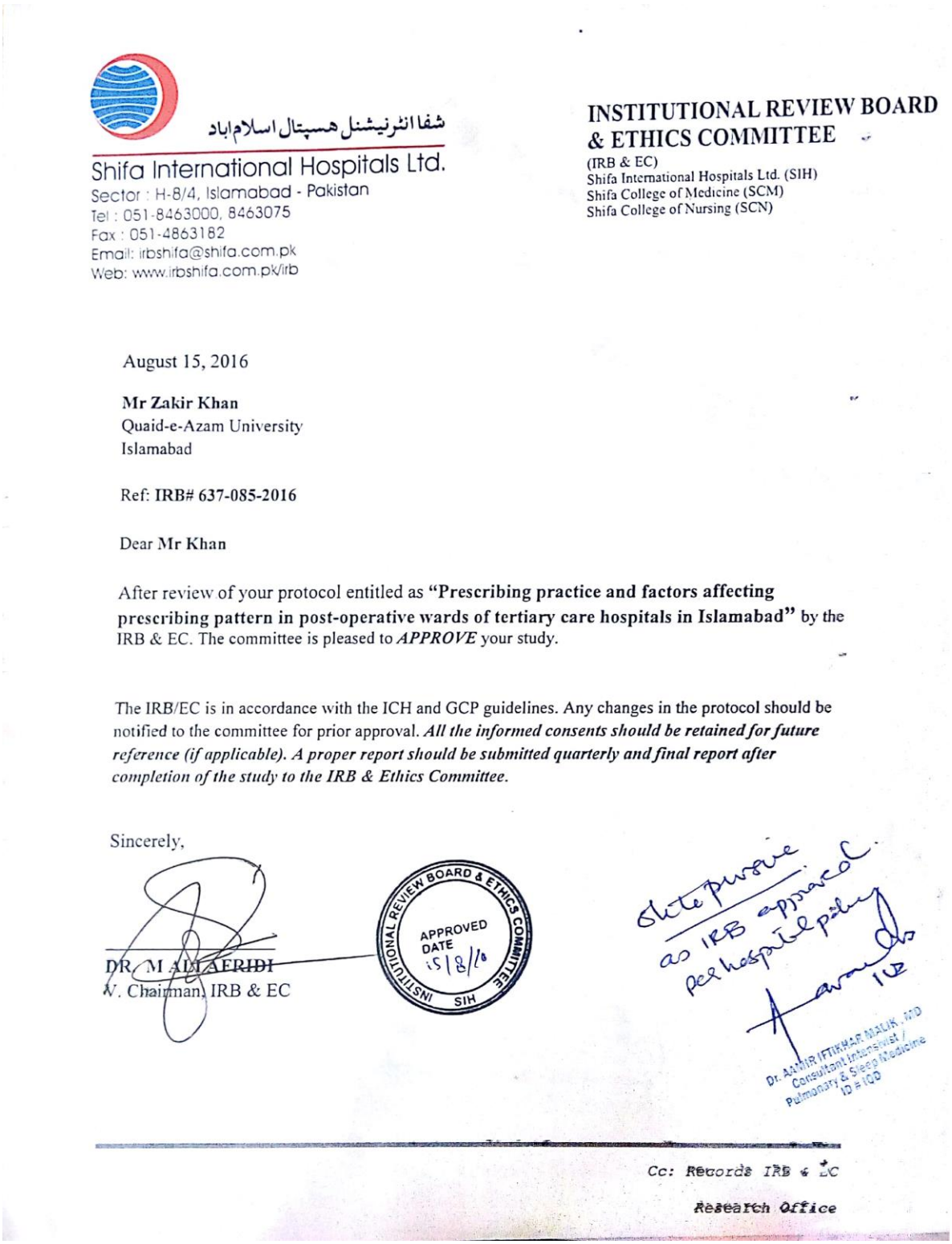

شفا انٹرنیشنل ہسپتال اسلام اباد
Shifa International Hospitals Ltd.
Sector : H-8/4, Islamabad - Pakistan
Tel : 051-8463000, 8463075
Fax : 051-4863182
Email: irbshifa@shifa.com.pk
Web: www.irbshifa.com.pk/irb

INSTITUTIONAL REVIEW BOARD & ETHICS COMMITTEE
(IRB & EC)
Shifa International Hospitals Ltd. (SIH)
Shifa College of Medicine (SCM)
Shifa College of Nursing (SCN)

August 15, 2016

Mr Zakir Khan
Quaid-e-Azam University
Islamabad

Ref: **IRB# 637-085-2016**

Dear **Mr Khan**

After review of your protocol entitled as **"Prescribing practice and factors affecting prescribing pattern in post-operative wards of tertiary care hospitals in Islamabad"** by the IRB & EC. The committee is pleased to ***APPROVE*** your study.

The IRB/EC is in accordance with the ICH and GCP guidelines. Any changes in the protocol should be notified to the committee for prior approval. ***All the informed consents should be retained for future reference (if applicable). A proper report should be submitted quarterly and final report after completion of the study to the IRB & Ethics Committee.***

Sincerely,

DR. M ALI AFRIDI
V. Chairman, IRB & EC

INSTITUTIONAL REVIEW BOARD & ETHICS COMMITTEE
APPROVED
DATE
15/8/16
SIH

Note pursue as IRB approval per hospital policy

Dr. AMIR IFTIKHAR MALIK, MD
Consultant Intensivist / Pulmonary & Sleep Medicine
ID # 1010

Cc: Records IRB & EC
Research Office

QUAID-I-AZAM UNIVERSITY
OFFICE OF THE DEAN FACULTY OF BIOLOGICAL SCIENCES

No.DFBS/2016- 623

Dated: December 22, 2016

Dr. Naveed Ahmed
Assistant Professor
Department of Pharmacy
Quaid-i-Azam University
Islamabad.

SUBJECT: "PRESCRIBING PRACTICE AND FACTORS AFFECTING PRESCRIBING PATTERN IN POST-OPERATIVE WARD IN TERTIARY CARE HOSPITALS, ISLAMABAD PAKISTAN".

Dear Dr. Naveed Ahmed,

We wish to inform you that your subject research study has been reviewed and is hereby granted approval for implementation by Bio-Ethical Committee (BEC) of Quaid-i-Azam University. Your study has been assigned protocol # BEC-FBS-QAU-99.

While the study is in progress, please inform us of any adverse events or new, relevant information about risks associated with the research. In case changes have to be made to the study procedure, the informed consent form and/ or informed consent process, the BEC must review and approve any of these changes prior to implementation.

Sincerely,

22/12/16

Prof. Dr. Wasim Ahmad
Dean Faculty of Biological Sciences
Chairperson, BEC

Prof. Dr. Wasim Ahmad
Dean
Faculty of Biological Sciences
Quaid-e-Azam University, Islamabad

Office of the Dean Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, 45230 Pakistan
Tel No: 92-51-90643073 92-51-90643101 & 92-51-90643003 Fax: 92-51- 90643170

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552 **Supplementary file 4.** Statistical analysis of some important variables

1- Antibiotics are overused in surgical procedures

Hospital setting	*Strongly disagree*	*Disagree*	*Uncertain*	*Agree*	*Strongly Agree*	Total
Government-funded	0	2	26	60	12	100
Private funded	0	0	34	66	0	100
Total	0	2	60	126	12	200

Pearson Chi-Square p value=.002; Fisher's Exact Test p-value=.001; Phi test= .227; Cramer's V test=.227 (p-value=.001)

2- Are you preferred broader-spectrum antibiotics instead of low spectrum antibiotic in surgical procedure?

Final academic degree	*Strongly disagree*	*Disagree*	*Uncertain*	*Agree*	*Strongly Agree*	Total
Bachelor degree (M.B.B.S)	2	1	1	75	1	80
Associate degree (MS)	0	0	2	73	18	93
Post graduate degree (PhD/Post.Doc)	0	0	0	22	5	27
Total	2	1	3	170	24	200

Pearson Chi-Square p value=.013; Fisher's Exact Test p-value=.001; Phi test= .310; Cramer's V test=.220 (p-value=.013)

3- I use the guidelines on a daily or weekly basis?

Final academic degree	*Strongly disagree*	*Disagree*	*Uncertain*	*Agree*	*Strongly Agree*	Total
Bachelor degree (M.B.B.S)	0	1	23	38	18	80
Associate degree (MS)	0	1	13	68	11	93
Post graduate degree (PhD/Post.Doc)	0	1	6	19	1	27
Total	0	3	42	125	30	200

Pearson Chi-Square p value=.012; Fisher's Exact Test p-value=.005; Phi test= .285; Cramer's V test=.202 (p-value=.012)

4- Lack of consensus by the surgeons with the recommendation in the guidelines is a factor for inappropriate use of antibiotics?

Work experience	***Strongly disagree***	***Disagree***	***Uncertain***	***Agree***	***Strongly Agree***	Total
<10 years	0	18	38	71	21	148
11-20 years	0	9	0	32	7	48
>20 years	0	0	0	4	0	4
Total	0	27	38	107	28	200
Pearson Chi-Square p value=.004; Fisher's Exact Test p-value=.001; Phi test= .314; Cramer's V test=.222 (p-value=.003)						

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