Prophylactic Antibiotic Use in Abdominal Surgery in Kabul, Afghanistan

Literature Study and Questionnaire

Hamideh Qasemi & Parwana Hussaini

Supervisor: Natkai Safi

Co-Supervisor: Eyrun Florecke Kjetland

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1. Introduction

Antibiotics are substances that are used to combat bacterial infections. They work by either killing the bacteria or slowing down the growth of the bacteria (1). For over the last 80 years, healthcare professionals worldwide have relied on antibiotics as the primary treatment for bacterial infections. In 1928, Alexander Fleming accidently observed that the penicillium fungus could inhibit bacterial growth (Figure 1) (2). However, it wasn't until the 1940s that penicillin's mass production and use as an antibiotic in treating infectious diseases began. This breakthrough led to significant reductions in mortality and morbidity among patients, earning antibiotics the reputation as lifesaving agents. Due to the discovery of a large number of effective antibacterial agents, many predicted that full control of bacterial infections would be achieved (3). However, the predictions never came true. In a short span, some antibiotics began to lose their efficiency as bacteria developed resistance to them. This evolving issue has escalated into a formidable global health challenge, demanding continuous efforts to address antibiotic resistance (Figure 2).

Figure 1: Sir Alexander Fleming, a Scottish researcher, is credited with the discovery of penicillin in 1928. Source: Adobe Stock

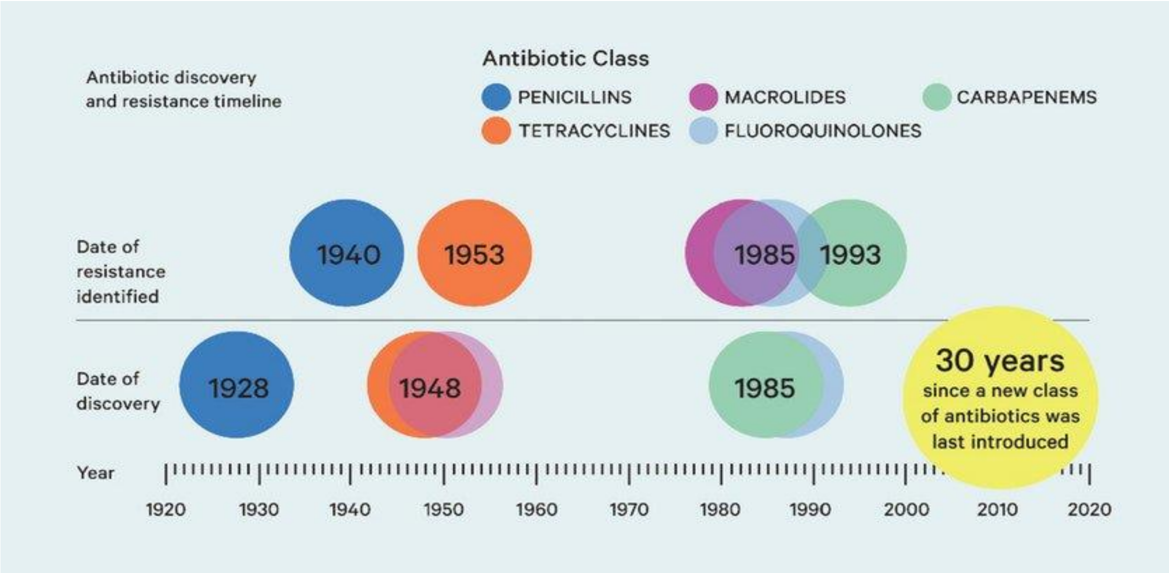


Figure 2: Antibiotic discovery and resistance timeline (https://pbs.twimg.com/media/DEb5bxuWsAAOzcF.jpg)

Antimicrobial resistance is defined as the ability of microorganisms such as bacteria, viruses, fungi, and parasites to defeat the effect of antimicrobial agents aimed to fight them. The consequences of antimicrobial resistance can be observed in several arenas. In clinics, it leads to failure in the treatment of common infectious diseases like flu and respiratory tract infections, extended duration of illness and treatment, potential hospitalization, and even life-threatening consequences. In addition, the lack of inefficient antibiotics can increase the probability of unsuccessful management of immunosuppressive health conditions like organ transplantation, HIV, cancer, and diabetes significantly. Higher healthcare cost is an unavoidable outcome of antibiotic resistance. In the food production industry, poultry, cattle, and animal farms, we are facing the same challenges as those encountered in the clinical settings (4). Therefore, knowledge about the mechanisms of antimicrobial resistance is essential to prevent and control the development of this problem. To get a better understanding of the resistance mechanism it is important to take a look at how different types of antibiotics work.

Antibiotics are either bacteriostatic or bactericide. A bacteriostatic antibiotic inhibits the growth of bacteria without directly causing bacterial death while a bactericidal antibiotic kills bacteria (4, 5). The mechanism of action of antibacterial agents can be classified as following.

1.1. Antibiotic action mechanisms

Inhibition of cell wall synthesis: Bacterial cell walls play an important protective role by shielding against osmotic pressure, with peptidoglycan as a key component. Certain antibiotics disrupt cell wall formation of cell walls by either substituting peptidoglycans e.g., β-lactams, or inhibiting the linkage between peptidoglycans e.g., glycopeptides. These types of antibiotics are therefore bactericidal which means they make bacteria die. A good thing about this class of antibiotics is that they do not affect human cells because these cells do not have cell walls and therefore no peptidoglycan (4, 5).

Inhibition of protein synthesis: Bacteria need to make proteins in order to survive. They use proteins in their structure, as enzymes, or for transport. Some antibiotics inhibit the synthesis of proteins by acting on different subunits of ribosomes which are the protein fabrication unit in cells. Bacterial ribosomes consist of two subunits; 30s and 50s which are different from eucaryote ribosomes. Due to this distinction, they do not interfere with the protein synthesis process in human cells. Different antibiotics target either 30s subunit or 50s subunit of ribosomes. Antibiotics like erythromycin and chloramphenicol inhibit the 30s subunit, whereas tetracycline, streptomycin, and gentamycin inhibit the 50s subunit. As a result, these antibiotics inhibit protein synthesis in bacteria without killing it. Therefore, they are bacteriostatic, meaning they slow down bacterial growth but do not cause immediate death.

Inhibition of DNA and RNA synthesis: A group of antibiotics prevents RNA and DNA from being synthesized by affecting key enzymes like DNA-gyrase (e.g., fluoroquinolones), topoisomerase II or IV (e.g., quinolones) and RNA-polymerase (e.g., rifampicin) (4, 5). This class of antibiotics has bactericidal properties.

Inhibition of folic acid metabolism: Another type of antibiotic inhibits folic acid metabolism. Folic acid is essential for the synthesis of adenine and thymine, two of the four nucleic acids in DNA structure. Bacteria normally use a precursor molecule called para-aminobenzoic acid (PABA) to make folic acid. Sulfonamide and trimethoprim prevent the conversion of PABA to folate and therefore prevent proper DNA synthesis (4).

Disruption of cell membrane function: Cell membrane integrity is vital for cellular homeostasis. The last mechanism by which some antibiotics work is to bind to the cell membrane. This will alter the cell membrane structure, make it more permeable, disrupt the osmotic balance, and cause leakage of cellular molecules. As a consequence, the bacterial cells die. Polymyxin is an example of an antibiotic that targets cell membranes (4).

1.2. Antibiotic resistance mechanisms

In general, in order to use antibiotics as useful medicines they have to have maximum effect on microorganisms and minimum side effects on human cells. Antibiotic resistance disturbs this balance and can be considered a barrier to getting a good effect of antibiotics. Previously, it has been discussed the mechanisms by which antibiotics act on bacteria. But it is much more important to take a closer look at the mechanisms that bacteria use to counteract the effect of antibiotics.

There are two types of bacterial resistance: intrinsic and acquired.

Intrinsic resistance can be basically defined as an inherent ability in some bacterial species that enables them to resist the effect of an antibiotic. This ability is due to the structural and functional differences that exist in those specific bacterial species. The antibiotic has no effect on the pathogen because the pathogen lacks the structural target that antibiotic usually uses to work against. As an example, gram-negative and gram-positive bacteria react differently against penicillin because of their different structures. Since in gram-negative bacteria, the peptidoglycan layer in the cell wall structure is thin and is surrounded by an additional outer membrane layer it will be difficult for penicillin to work. In contrast in gram-positive bacteria, the cell wall is made of a thick layer of peptidoglycan and no further barrier exists, so the penicillin can work effectively (4).

Acquired resistance occurs when a bacteria develops the ability to resist a specific antibiotic to which it was previously sensitive. It is the result of the adaptation of bacteria to antibiotics through genetic mutation or receiving foreign genetic codes from other bacteria (horizontal gene transfer). The movement of genetic information between bacteria can be done by three genetic mechanisms: transformation, transduction, and conjugation.

Transformation means that bacteria take up free DNA from their environment, while in conjugation the genetic material transfers from one bacteria to another by cell-to-cell contact. In transduction, the resistance genes transfer between bacteria by bacteriophages (3)

Another way to classify the mechanisms of resistance against antibiotics is the reduction of intracellular antibiotics concentration, inactivation of antibiotics by enzymatic modification, and changes in target sites of antibiotics.

Reduction of intracellular antibiotics concentration: it occurs by either reducing the permeability of antibiotics into the bacterial cells (influx) or increasing the antibiotics out of bacterial cells (efflux). Porins as outer membrane proteins and entry points for some antibiotics in bacteria can be downregulated, modified in structure, or even be deleted and therefore results in reduced permeability of antibiotics into the bacterial cell. On the other hand, increased efflux of antibiotics by multidrug transporters, which are normally used by bacteria to pump out toxic substances, decreases the accumulation of antibiotics inside the bacteria (4, 6).

Inactivating of antibiotics by enzymatic modification: bacteria inactivate the antibiotics by using the enzymes in two ways; either by adding acetyl, adenyl, and phosphate to antibiotics or by direct hydrolysis of the antibiotics (4, 6).

Changing in target sites of antibiotics: genetic mutation or post-translational modification where the methyl group binds to the target site, modifies the structure of the target site of antibiotics and consequently, the antibiotics lose their function.

As it was mentioned previously, soon after the introduction of antibiotics there was evidence of the correlation between antibiotic use and the development of antibiotic resistance. Some factors contribute to this resistance development. The fact that bacteria try to escape the effect of antibiotics by using their genetic plasticity characteristics is one of these factors. Another factor is the irrational use of antibiotics which means that antibiotics are prescribed when it is not indicated, the antibiotics that are chosen are not the narrowest spectrum agent and their dose and duration are not appropriate (7). The development of the resistant population of bacteria due to the irrational use of antibiotics occurs via a process called "selective pressure". Naturally, the large number of antibiotic-susceptible organisms in the body of a healthy person hold down the small numbers of bacteria that are intrinsically resistant to antibiotics. In the selective pressure process, the use of antibiotics leads to the removal of susceptible organisms to those antibiotics, allowing resistant bacteria to thrive (8).

Unnecessary prescription of antibiotics where they are not indicated e.g., viral or spontaneously resolving bacterial infections, are examples of irrational use of antibiotics. Physicians' prescription of antibiotics can be affected by clinical and non-clinical factors. Antibiotics may be prescribed because of some clinical feature of the disease e.g., purulent secretions or cough for more than three days, or maybe because physicians do not have enough time to inform patients about the uselessness of antibiotics in that specific case. On the other hand, patients want antibiotics to be confirmed that the disease is not serious and is curable. Additionally, they want to get antibiotics to relieve bothersome symptoms.

As noted above, overuse and misuse of antibiotics lead to antibiotic resistance emerging. Surgery is one of the medical areas where antibiotics are widely used to prevent post-operative infection and where the irrational use of antibiotics is reported frequently. An important reason for the excessive use of antibiotics in surgical settings is rooted in the doctor's incorrect antibiotic prescription practice, which can be affected by clinical and non-clinical factors. Not following the international surgical antibiotic prophylaxis guidelines is a crucial clinical factor contributing to the wrong antibiotic prescription. Guidelines are international evidence-based recommendations designed to help clinical professionals and other healthcare workers and are usually updated regularly according to the current medical knowledge and are aimed to increase the patient’s safety. Inadequate attention to standard recommendations for prescribing antibiotics by surgeons and other practitioners leads to the wrong indication, wrong selection of the type of antibiotic, wrong duration, incorrect timing as well as incorrect dosage. The consequence of such a practice would be unnecessary excessive antibiotic utilization, which can increase antimicrobial resistance, morbidity, mortality, and unneeded expenditure on both hospitals and patients.

Particularly, this is a most common problem in developing countries where they either have no idea that there is a guideline to follow or if they are aware of it, they disregard it. Afghanistan as a least-developed country is the focus of our literature study and can be a good example of this issue.

There are several reasons why inappropriate and irrational prescribing, overuse, and misuse of antibiotics are prevalent in war-ravaged countries like Afghanistan. Being a resource-limited country, Afghanistan has suffered long periods of armed conflicts, that have further worsened the already crumbling healthcare system. However, as healthcare professionals, we can take certain steps to reduce the risk of antibiotic resistance by modifying our prescription practices during surgeries and operations performed on Afghan patients.

There are only a few articles published on the utilization of antibiotics in the management of infectious diseases, particularly in primary healthcare settings and trauma surgical care units within military hospitals in Afghanistan (9-13).

However, since there are not enough resources and research available in Afghanistan, we decided to do the literature study on articles from some neighboring countries like Iran and Pakistan which are similar to Afghanistan from several perspectives such as antibiotic resistance profile, antibiotics prescription culture, social, economic, and cultural background.

Furthermore, we also designed a questionnaire in consultation with our supervisor Natkai Safi (N.S) regarding gastrointestinal surgeries and sent it to surgeons in three different hospitals in Kabul, Afghanistan. Gastrointestinal surgeries are the most performed surgery in these three hospitals, and we concentrated specifically on acute appendicitis, acute perforated appendicitis, elective cholecystectomy, small bowel resection without perforation, and elective colon resection without perforation surgeries. Therefore, we are going to write a two-part project thesis. The first part consists of reviews of articles, studies, and research conducted in Iran and Pakistan, on how surgical antibiotic prophylaxis was practiced. The second part is an analysis of questionnaires hand-delivered to surgeons in three different hospitals in Kabul-Afghanistan investigating surgical antibiotics prophylaxis practice.

2. Method

2.1. Literature search

We conducted a systematic electronic search in PubMed and Medline with no time restriction (up to November 2022) using the following keywords: [(surgery OR surgical) AND (prophylaxis OR prophylactic) AND (antibiotic(s) OR antibiotica OR antibacterial agent) AND (overuse OR misuse) AND (preoperative OR perioperative OR postoperative) AND (Iran OR Pakistan)]. We also hand-searched for relevant literature using snowballing, i.e., using suggested similar articles to identify any additional relevant articles. Established guidelines from reputable sources like the World Health Organization (WHO), and the American Society of Hospital Pharmacists (ASHP) were consulted. All titles and abstracts were screened and cross-checked with supervisor N.S. Only articles directly relevant to antibiotic usage in certain surgeries, particularly acute appendicitis, acute perforated appendicitis, elective cholecystectomy, small bowel resection without perforation, and elective colon resection without perforation, were taken into consideration. Although, we did include a few well-crafted publications relevant to our study from other surgical fields. Weak publications were excluded. These potential entries were further evaluated in detail (Table 1).

Table 1: Inclusion and exclusion criteria

Inclusion	Exclusion
▪ Neighboring countries: Iran and Pakistan ▪ Antibiotics prophylaxis during surgical procedures: acute appendicitis, acute perforated appendicitis, elective cholecystectomy, small bowel resection without perforation, and elective colon resection without perforation ▪ Other relevant well-crafted publications about antibiotics prophylaxis during surgery ▪ English language	▪ Other geo-economical different countries ▪ Developing countries ▪ Not prophylactic antibiotics studies ▪ Antibiotics studies not related to any surgical procedures ▪ Weak or inconclusive studies ▪ Other languages than English

2.2. Questionnaires

Under the supervision of N.S and Dr. Nazir Naimy, gastrointestinal surgeon, we designed a questionnaire that specifically focuses on the most common gastrointestinal surgeries performed in 3 hospitals in Kabul. Hospitals that were included were Jamhoryat Hospital (H1), Ibnesina Hospital (H2), and Isteqlal Hospital (H3). The following surgical procedures were included in the questionnaire:

- Acute appendicitis
- Acute perforated appendicitis
- Elective cholecystitis
- Small bowel resection without perforation
- Elective colon resection without perforation

The questionnaires were hand-delivered with the help of Dr. Naimy, to 70 gastrointestinal surgeons and residents in hospitals, as mentioned above. In our questionnaires, we mainly focused on details concerning the antibiotic regimens, such as the type, dosage, duration, timing (pre-, per-, and postoperatively), and administration route (Appendix A). In addition, we included inquiries regarding the doctor's level of education and work experience to assess their impact on their prescribing practices for antibiotics.

3. Result

3.1. Literature search

In our initial search, we identified 90 studies by screening titles (Figure 3). The duplicates were excluded, and 71 articles remained. The remaining articles were carefully reviewed with our supervisor NS and 38 articles based on titles and abstracts were excluded. The remaining 33 full-text articles underwent thorough evaluation. Ultimately, 17 studies met strict inclusion criteria, forming the core of our review (Figure 4) (Table 2).

The selected studies were analyzed to investigate the following outcomes:

- Indication of Prophylactic Antibiotics
- Type of Prophylactic Antibiotics
- Duration of Prophylactic Antibiotics
- Dosage of Prophylactic Antibiotics
- Timing of Prophylactic Antibiotic Initiation
- Route of Administration
- Type of Surgical Procedure
- Age and Gender of Patients
- Knowledge of surgeon/doctor
- Antibiotic Cost and Hospital Stay
- Overall compliance with guideline

3.1.1. Mostly used guidelines

- Infection Disease Society of Amerika (IDS)
- American Society of Health-System Pharmacists (ASHP)
- Surgical Antibiotic Prophylaxis Guidelines
- The Surgical Infection Society (SIS)
- The Society for Healthcare Epidemiology of America (SHEA)
- Global guidelines for the prevention of surgical site infection – WHO

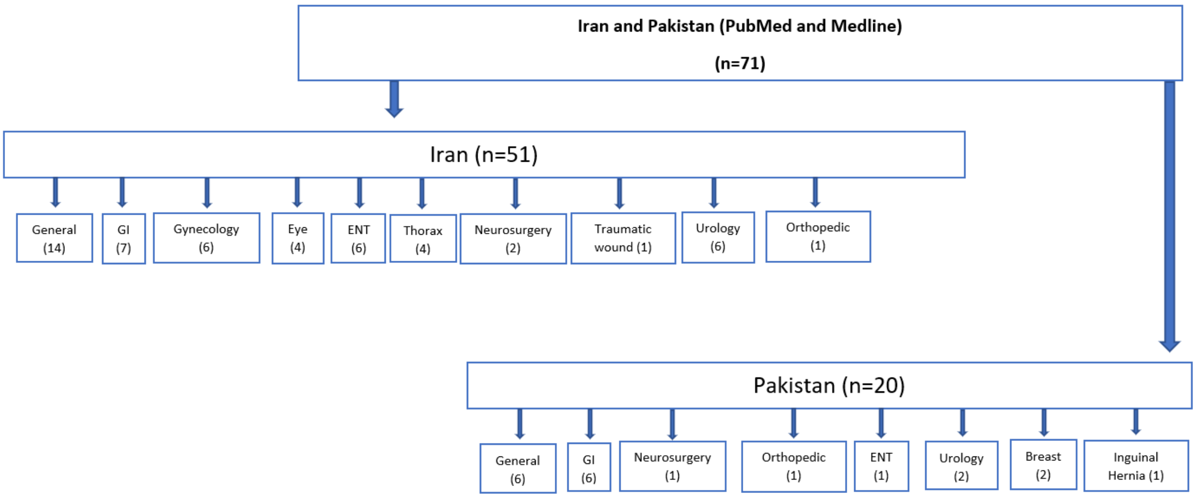


Figure 3: Search results from PubMed and Medline for articles on Antibiotic Usage in specific clinical fields in Iran and Pakistan

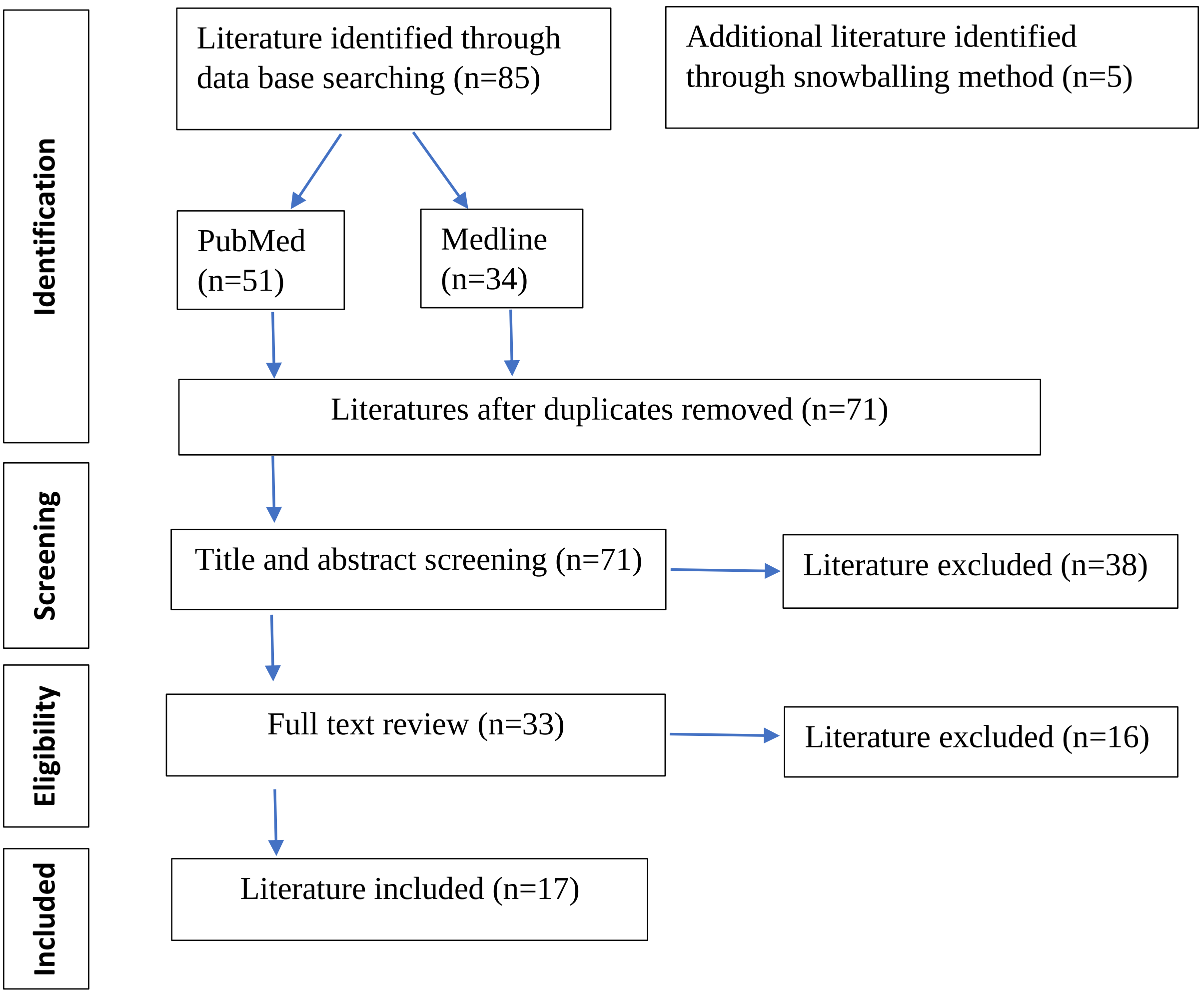


Figure 4: Flow chart illustrates the search strategy by inclusion and exclusion criteria.

Table 2: Main characteristics of studies included in the literature study

No.	Author (year)	Subject	Country	Title	Study Design	Aims	Number of participants	Main results
1.	S. Elyasi et al. (2019)	GI	Iran	Evaluation of antibiotic prophylaxis for gastrointestinal surgeries in a teaching hospital: An interventional pre-post study	Interventional (pre-and post)	To compare the appropriateness of antibiotic prophylaxis in gastrointestinal surgery, before and after an evidence-based guideline implementation.	200 patients	Incorrect usage and duration of antibiotics reduced significantly
2.	L. Mahmoudi et al. (2019)	GI	Iran	Optimizing compliance with surgical antimicrobial prophylaxis guidelines in patients undergoing gastrointestinal surgery at a referral teaching hospital in southern Iran: clinical and economic impact	Interventional (pre-and post)	To assess the impact of (IDSA) guideline implementation on the rational use of prophylactic antibiotics and its cost-saving effect in gastrointestinal surgery by clinical pharmacist intervention.	875 patients	Antibiotic usage practice improved. Cost and length of hospitalizatio n reduced.
3.	S.M. Razavi et al. (2005)	GI	Iran	Abdominal surgical site infections (SSI): incidence and risk factors at an Iranian teaching hospital	Observational	To determine the risk factors affecting abdominal surgical site infections and their incidence at a major referral teaching hospital in Iran with questionnaires.	802 patients	SSI rate higher than in literature. Several factors affect SSI.
4.	H. Abbasian et al. (2019)	General	Iran	Antibiotic Utilization in Iran 2000-2016: Pattern Analysis and Benchmarking with Organization for Economic Co-operation and Development Countries	Descriptive-analytical study	To recognize the patterns, trends, and changes of consumption in Iran and to compare them with those of Organization for Economic Co-operation and Development (OECD) countries.		Consumption of antibiotics has increased drastically

No.	Author (year)	Subject	Country	Title	Study Design	Aims	Number of participants	Main results
5.	M. Askarian et al. (2006)	General	Iran	Adherence to American Society of Health-System (ASHP) Pharmacists Surgical Antibiotic Prophylaxis Guidelines in Iran	Observational	To assess compliance with the American Society of Health-System Pharmacists (ASHP) guidelines of antibiotic prophylaxis for surgical procedures in the 6 teaching hospitals in Shiraz, Iran.	1000 patients	Only 0.3% of procedures complied with all guidelines.
6.	A. Ebrahimzadeh et al. (2021)	General	Iran	The compliance of surgical prophylactic antibiotics with standard protocols in Imam Reza teaching hospital of Birjand, Iran	Descriptive-analytical study	To investigate administration prophylactic antibiotics in surgery ward and its compliance with standard protocol in a teaching hospital in Iran	300 patients	Indication and type of antibiotics were inconsistent with the Guidelines.
7.	B. Foroutan et al. (2014)	General	Iran	Perioperative antibiotic prophylaxis in elective surgeries in Iran	Retrospective study	The aims of the present study are: 1) to analyze the assessment. of prophylactic ab usage prior to surgery, 2) to assess the drug admin. based on antibiograms and 3) to compare the results with the national and international standards.	516 patients	Insignificant differences. in comparison with national and international studies.

No.	Author (year)	Subject	Country	Title	Study Design	Aims	Number of participants	Main results
8.	N. Hatam et al. (2011)	General	Iran	Economic burden of inappropriate antibiotic use for prophylactic purpose in shiraz	cross-sectional study	To measure costs and appropriate use of antibiotics in surgical wards of 6 training hospitals affiliated to Shiraz University of Medical Sciences (SUMS), Iran	1000 patients	Inappropriate use of antibiotic in 98% of cases, leading to a great amount of economic burden.
9.	H. Mahdavizad et al. (2011)	General	Iran	Iranian surgeons' compliance with the American Society of Health-System Pharmacists guidelines: antibiotic prophylaxis in private versus teaching hospitals in Shiraz, Iran	Observational (cross-section)	To assess the compliance with the American Society of Health System Pharmacists (ASHP) guideline of prophylactic antibiotic in private hospitals in Shiraz, Iran.	365 patients	The overall compliance with ASHP guidelines was 10.13%
10.	S. Mousavi et al. (2017)	General	Iran	An Audit (financial inspection) Perioperative Antimicrobial Prophylaxis: Compliance with the International Guidelines	cross-sectional study using prospective data	To evaluate the use of antibiotics in a tertiary care center according to the recommendation of ASHP guideline.	100 patients	Only 22% of procedures followed guideline recommenda tions.
11.	M. Rafati et al. or A. Shiva et al. (2014)	General	Iran	Adherence to American society of health-system pharmacists surgical antibiotic prophylaxis guidelines in a teaching hospital	Observational (retrospective)	To evaluate an antibiotic administration pattern for surgical antibiotic prophylaxis in a teaching hospital against the American Society of Health System Pharmacists (ASHP)	759 patients	About 56.4% of prophylactic antibiotics were in accordance with ASHP

No.	Author (year)	Subject	Country	Title	Study Design	Aims	Number of participants	Main results
12.	A.Vazin et al. (2022)	General	Iran	Compliance with Antibiotics Prophylaxis Guideline in Surgical Patients in ICUs of a Teaching Referral Hospital	Cross-Sectional (prospective)	To assess the compliance of prophylactic antibiotic administration to the Infectious Diseases Society of America **(IDSA)** guideline for in variable surgeries conducted in the intensive care units (ICUs) of a major referral hospital	137 patients	Only 8.75% of antibiotics prophylaxis were appropriate
13.	G. Vessal et al. (2011)	General	Iran	Evaluation of prophylactic antibiotic administration at the surgical ward of a major referral hospital, Islamic Republic of Iran 2011	Observational (prospective-retrospective)	Evaluated the appropriateness of antibiotic prophylaxis administered before surgery at a major referral hospital in Shiraz, against the American Society of Hospital Pharmacists (ASHP) guidelines.	155 patients	Only 1 out of 155 patients received correct antibiotics regimen according to ASHP.
14.	S.M. Alavi et al. (2014)	General	Iran	Antibiotics use patterns for surgical prophylaxis site infection in different surgical wards of a teaching hospital in ahvaz, iran	Descriptive study	To determine the pattern of prophylactic antibiotic use in a teaching hospital affiliated to Jundishapur University of Medical Sciences, Ahvaz, Iran	8586 patients	44% of those who received prophylaxis did not need it.
15.	A. Sadatsharifi et al. (2019)	General	Iran	Economic Burden of Inappropriate Empiric Antibiotic Therapy: A Report from Southern Iran	Observational (prospective)	To evaluate the prescription patterns of empiric antibiotic therapy in relation to treatment guidelines and the economic burden of discordance with guidelines in a major referral Iranian university hospital	229 patients	Overall guideline adherence was 27.8%.

No.	Author (year)	Subject	Country	Title	Study Design	Aims	Number of participants	Main results
16.	S. Baniasadi et al. (2016)	Thorax	Iran	Surgical antibiotic prophylaxis: A descriptive study among Thoracic surgeons	Questionnaire	To evaluate the current use of prophylactic antibiotics in thoracic surgeries in Iran by assessing thoracic surgeons' knowledge, attitude and practice (KAP) about surgical antibiotic prophylaxis (SAP) compared to ASHP guidelines	50 thoracic surgeons	A continuing education program on appropriate antibiotic selection is necessary to improve SAP
17.	M.Z. Satti et al. (2019)	General	Pakistan	Compliance rate of surgical anitimicrobial prophylaxis and its associateion with knowledge of Guidelines among surgical residents in a tertiary care public hospital of developing country.	Observational, cross-sectional+ questionnaire	To compare the practice of SAP in a tertiary health care hospital of a developing country Pakistan, with internationally recommended protocols and evaluate the impact of knowledge of international guidelines on SAP practice.	150 patients + 33 surgical residents	Awareness of guidelines among surgeons is highly significant, ($p<0.000$).

3.1.2. Indication of Prophylactic Antibiotics

Five studies reported low compliance rate with antibiotic prophylaxis guidelines; M. Askarian 2011, S. Mousavi, M. Rafati, S.M. Alavi, G. Vessal, 38.4%, 53.0%, 56.4%, 72.6% and 70.3%, respectively (14-18). In these studies, antibiotics were prescribed unnecessarily in at least 27.4% to 60.0% of the surgical cases when they were not indicated. While in the other two studies, antibiotics were given to under 20% of cases where they were not indicated (8.0-19.4%) (19, 20). Two interventional studies by Elyasi et al. and Mahmoudi et al. compared the appropriateness of antibiotic prophylaxis before and after the implementation of guidelines in gastrointestinal surgery. In both studies, the rate of incorrect use of antibiotics decreased from 55% to 18% and 91.4% to 30.1%, respectively (21, 22).

3.1.3. Type of prophylactic antibiotics

Cefazolin and Metronidazole were the most common antibiotics used in most of the studies (17, 18, 20-25). The most inappropriate use of antibiotics was aminoglycosides (Gentamicin), carbapenems (meropenem), and third generation cephalosporins (Ceftriaxone), where the indication, dosage, and duration were incorrect (18, 19, 26). Two studies showed that in more than 70% of cases, prophylactic antibiotics were given in accordance with the guidelines (11, 20). However, in four other studies, the compliance rates ranged from 25.4% to 67.7% (14, 17, 18, 23). Implementing the protocol in S. Elyasi et al.'s study resulted in a reduction in the inappropriate selection of antibiotics from 55% to 18% (21). Askarian et al. reported that in only 5.9% of the procedures the antibiotics administered were consistent with the guidelines and that in 71.3% of cases, patients received 2 or more antibiotics instead of one (17).

3.1.4. Duration of prophylactic antibiotics

S. Elyasi et al. reported a reduction in the duration of prophylactic antibiotics from 43% to 23% after the reimplementation of guidelines (21). L. Mahmoudi et al. have also studied the duration of prophylactic antibiotic use, but in a different way (22). They have set a limit of 48 hours for the duration (over and under 48 hours) and compared antibiotic usage before and after administering the guidelines. There was an increase in the proportion of patients who received antibiotics for less than 48 hours, whereas the proportion of patients who used antibiotics for more than 48 hours decreased after applying the guideline. In other words, there was a longer duration of antibiotic usage in the pre-intervention group than guideline recommendations (22). Several studies reported accordance with the guidelines between 29.4 - 86% of cases (14, 16-18), and just in one study duration was consistent with guidelines over 90% (90.5%) (15).

Contrary to guideline recommendations, Askarian et al. and Vazin et al. found inconsistent durations of antibiotic prophylaxis at rates of 94.2% and 100%, respectively (20, 27).

3.1.5. Dosage of prophylactic antibiotics

Three studies reported inappropriate dosage in over 40% of cases while S.M. Alavi et al. showed 91.8% dose compliance with guideline recommendations (15). According to S. Elyasi et al. after applying the protocol inappropriate doses diminished but not significantly (8% vs. 5%, $p=0.321$) (21).

3.1.6. Timing of prophylactic antibiotics initiation

In the case of initiation time of administration three studies showed compliance between 42-74% (14, 17, 26) and A.Vazin et al. reported 100% inappropriate timing (27). In contrast A. Ebrahimzadeh et al. and M.Z. Satti et al. found over 90% in accordance with a standard protocol (23).

3.1.7. Route of administration

Three studies reported that the route of administration was in accordance with guidelines (19, 23, 28).

3.1.8. Type of surgical procedure

In the case of the type of surgery, the lowest compliance with guidelines was reported in appendectomy bile duct, liver, and pancreatic surgery. However, gastrointestinal procedures such as cholecystectomy and colon surgery, as well as plastic and orthopedic surgeries, has the least inappropriate use of antibiotics (23, 26). Although, Vazin et al. demonstrated the same level of misuse and overuse of prophylactic antibiotics in different surgical fields (gastroenterology, urology, vascular, orthopedics, and neurosurgery) antibiotics prescription was found to be correct in only 8.75% of cases (27).

3.1.9. Age and gender of patients

Literature has found no significant correlation between sex and incidence of surgical site infection (SSI), whereas the correlation with increasing age was significant at $p < 0.001$ (4, 29). In most of the conducted studies, male participation was greater than that of the female (15, 24, 27). Another study reported that patients in the age range of 20-30 years were the most recipients of antibiotics. Men received more antibiotics in comparison with women, and about 75% of patients received antibiotics as prophylaxis (24).

3.1.10. Knowledge of surgeon/doctor

S. Baniasadi et al. found 70% of surgeons had good knowledge about appropriate SAP (26) while M.Z. Satti et al. reported that 51% of surgical residents were aware of the guidelines (28). In the last-mentioned study, chi-square analysis revealed a highly significant association between the awareness of guidelines and the number of compliant procedures performed by a resident ($p<0.000$). The odds ratio for awareness and correct prophylaxis was 4.064 ($p<0.000$) (28). S. Elyasi et al. showed that adherence of surgeons to all antibiotic prophylaxis guideline parameters was 15% in the pre-intervention phase which increased to 33% after guideline implementation which was not statistically significant (21).

3.1.11. Antibiotic cost and hospital stay

L. Mahmoudi et al. showed a significant reduction in the length of hospital stay (4.2 vs 5.1 days) and cost of antibiotic prophylaxis in the intervention group compared to the baseline group (22). Three other studies evaluated the antibiotic prophylaxis cost in different ways, but they all came to the same conclusion that inappropriate antibiotic prescribing leads to huge unnecessary extra costs (16, 19, 20, 25). M. Askarian et al. estimated the direct cost of the antibiotics used for the 1,000 procedures which was 6 times greater than what it would have cost to administer antibiotic prophylaxis that adhered to the ASHP guideline recommendations (US$9,988 versus US$1,656). This is equivalent to a total extra cost of approximately US$8,332 for the 1,000 procedures (20). G. Vessal et al. estimated that the average extra cost per patient due to misuse of antibiotics was 92 528 (SD 133 650) rials, which is approximately equal to US$ 9. The total extra cost due to misuse of antibiotics during the 15 days was 15 267 170 rials (US$ 1471) (16). A. Sadatsharifi et al. reported that inappropriate antibiotic prescribing resulted in excess costs of $471,319.69 USD (19,795,427,225 IRR), with the total antibiotic usage cost over 6 months being $578,959.39 USD (24,316,294,800 Iranian Rials, IRR). In other means 81.4% of the total cost. The estimated annual excess cost is 942,639.38 USD (39,590,854,450 IRR) (19).

3.1.12. Overall compliance with guideline

According to S. Mousavi, M. Askarian 2011 and M.Z. Satti there was an overall low adherence rate of about 10.0-49.33% with ASHP guidelines (14, 17, 28). Askarian et al. in 2006 assessed compliance with guidelines for prophylactic antibiotic use in 6 teaching hospitals in Iran and reported that only 2 out of 87 surgical procedures received correct antibiotics. The compliance rate with guidelines recommendation was only 0.3 % (20). The same author with Askarian et al in 2011 in the same city of Iran, but in this time in private hospitals, reported 10.13% overall compliance with guidelines (17). In a study conducted by Vessal et al., only 1 out of 155 surgical procedures had all evaluated parameters correct (16). Satti et al in Pakistan reported a compliance rate of 49.3% (28).

3.2. Questionnaires

A total of 70 surgeons answered questionnaires in three hospitals in Kabul, Afghanistan: Jamhoriyat Hospital (Hospital 1), Ibnesina Hospital (Hospital 2), Istiqlal Hospital (Hospital 3). After evaluating the responses, 5 of them did not meet the criteria for further analysis due to ambiguity in their answers. The findings from the remaining 65 questionnaires and responses are as follows:

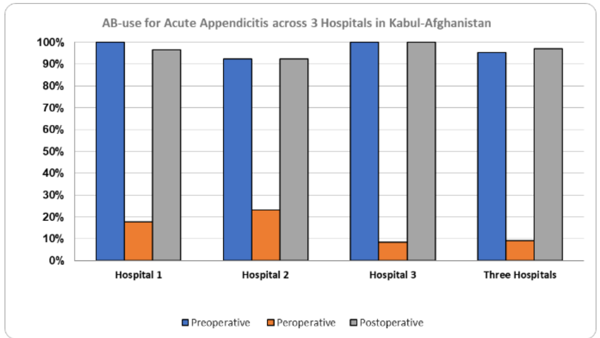
Our study on the timing of antibiotic prescription by surgeons revealed that in five types of surgeries namely appendicitis, acute perforated appendicitis, elective cholecystectomy, small bowel resection without perforation, and colon resection without perforation, antibiotics were prescribed before and after the operation in over 90% of the cases. However, the antibiotics given during the operation were reported to be approximately 10% in all three hospitals (Figure 5), but Ibnesina Hospital (Hospital 2) seemed to have a slightly different practice. They have reported a more limited use of antibiotics preoperatively specifically in elective cholecystectomy and colon resection without perforation (Figure 5c, 5d).

Ceftriaxone, a third-generation cephalosporine, was reported to be the most used antibiotic both pre- and postoperatively. They have been used in combination with other antibiotics, especially metronidazole. This combination has been observed mainly postoperatively (Figure 6).

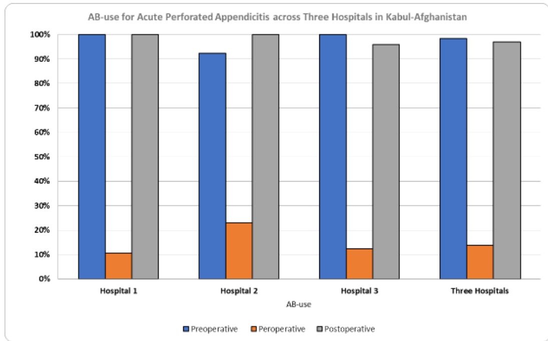
The reported duration of postoperative antibiotic prescription varied widely, from 1 to 14 days, but most surgeons chose to give antibiotics for one week (Figure 7).

In general, prophylactic antibiotics have been administered intravenously but postoperative antibiotics have been given intravenously for the first 24 hours and then continued in oral form for several days.

Surgeons' experience varied from two months to 38 years with an average of 11 years. The use of prophylactic antibiotics was to some extent related to the surgeons' length of experience. There was less tendency to give antibiotics by surgeons who had longer experience. Most experienced surgeons chose to give shorter courses of antibiotics and not in combination.



a



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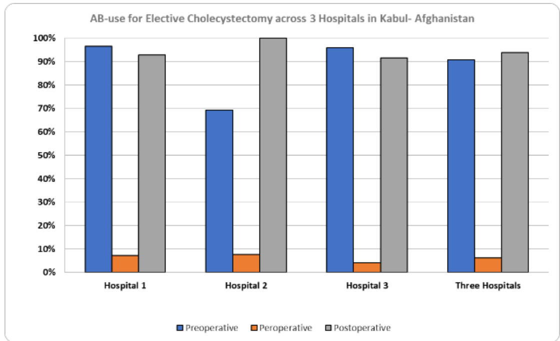

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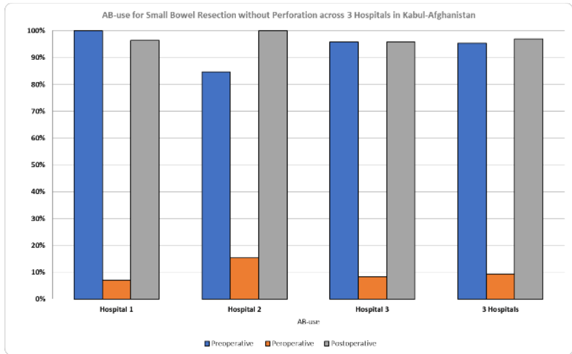

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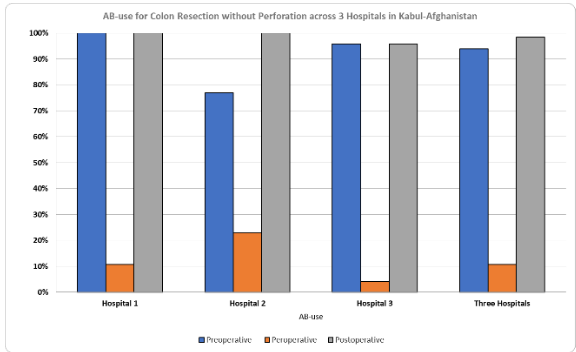

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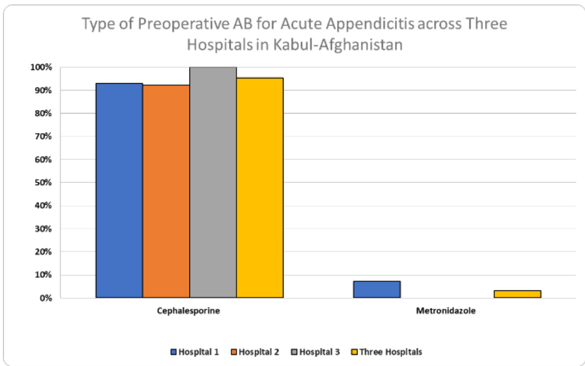
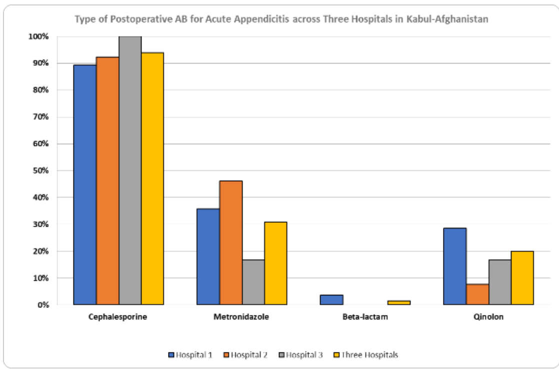
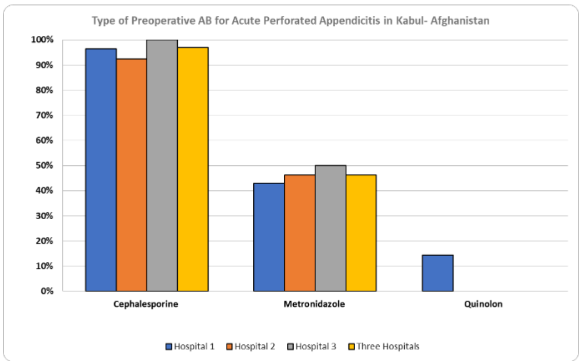
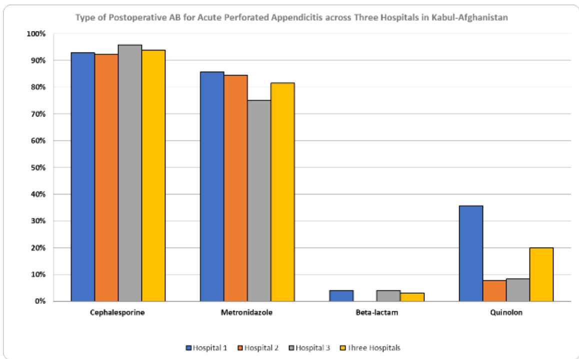
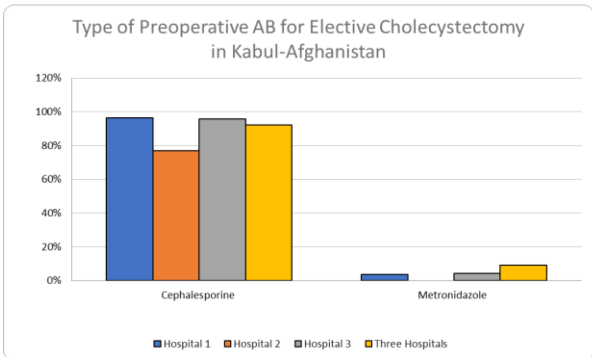
Figure 5: Percentage of surgeons' responses regarding timing of administering of prophylactic antibiotic 5 different surgeries across three different hospitals in Kabul-Afghanistan

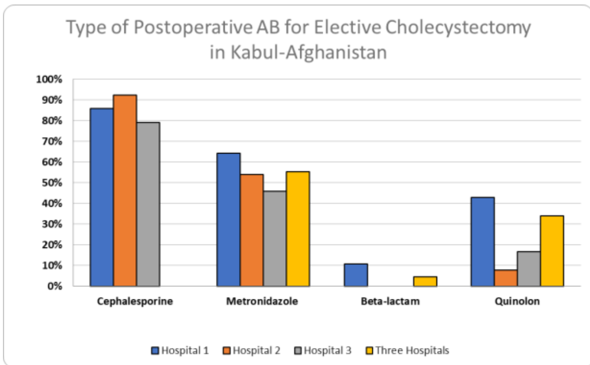

Type of Preoperative AB for Acute Appendicitis across Three Hospitals in Kabul-Afghanistan
Cephalesporine
Metronidazole
Hospital 1
Hospital 2
Hospital 3
Three Hospitals

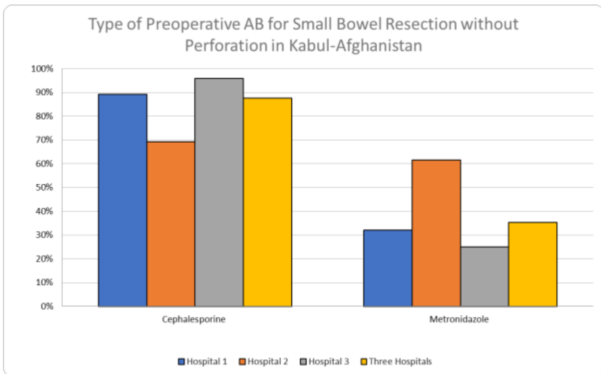

Type of Postoperative AB for Acute Appendicitis across Three Hospitals in Kabul-Afghanistan
Cephalesporine
Metronidazole
Beta-lactam
Qinolon
Hospital 1
Hospital 2
Hospital 3
Three Hospitals

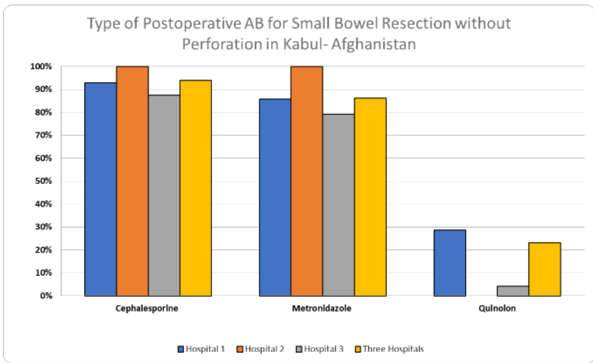

Type of Preoperative AB for Acute Perforated Appendicitis in Kabul- Afghanistan
Cephalesporine
Metronidazole
Quinolon
Hospital 1
Hospital 2
Hospital 3
Three Hospitals


Type of Postoperative AB for Acute Perforated Appendicitis across Three Hospitals in Kabul-Afghanistan
Cephalesporine
Metronidazole
Beta-lactam
Quinolon
Hospital 1
Hospital 2
Hospital 3
Three Hospitals


Type of Preoperative AB for Elective Cholecystectomy in Kabul-Afghanistan
Cephalesporine
Metronidazole
Hospital 1
Hospital 2
Hospital 3
Three Hospitals


Type of Postoperative AB for Elective Cholecystectomy in Kabul-Afghanistan
Cephalesporine
Metronidazole
Beta-lactam
Quinolon
Hospital 1
Hospital 2
Hospital 3
Three Hospitals


Type of Preoperative AB for Small Bowel Resection without Perforation in Kabul-Afghanistan
Cephalesporine
Metronidazole
Hospital 1
Hospital 2
Hospital 3
Three Hospitals


Type of Postoperative AB for Small Bowel Resection without Perforation in Kabul- Afghanistan
Cephalesporine
Metronidazole
Quinolon
Hospital 1
Hospital 2
Hospital 3
Three Hospitals

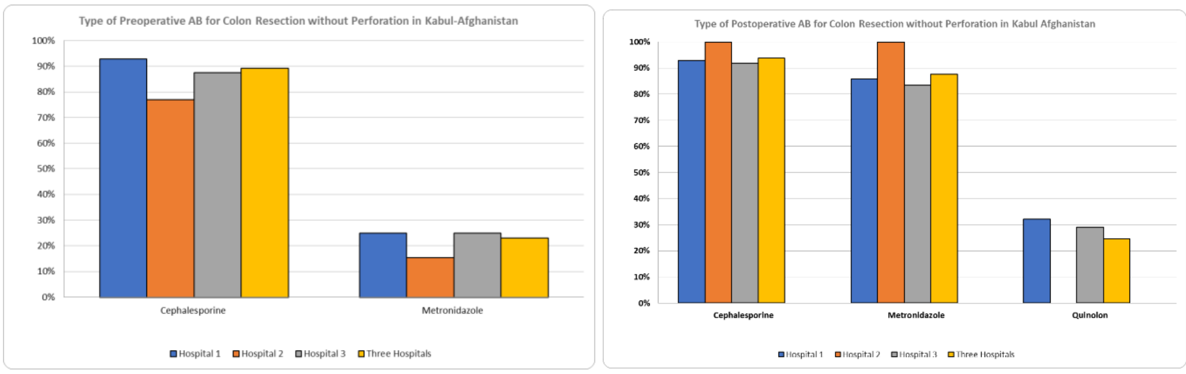


Figure 6: Percentage of surgeons' responses regarding type of pre-and postoperative prophylactic antibiotic in 5 different surgeries across 3 hospitals in Kabul-Afghanistan

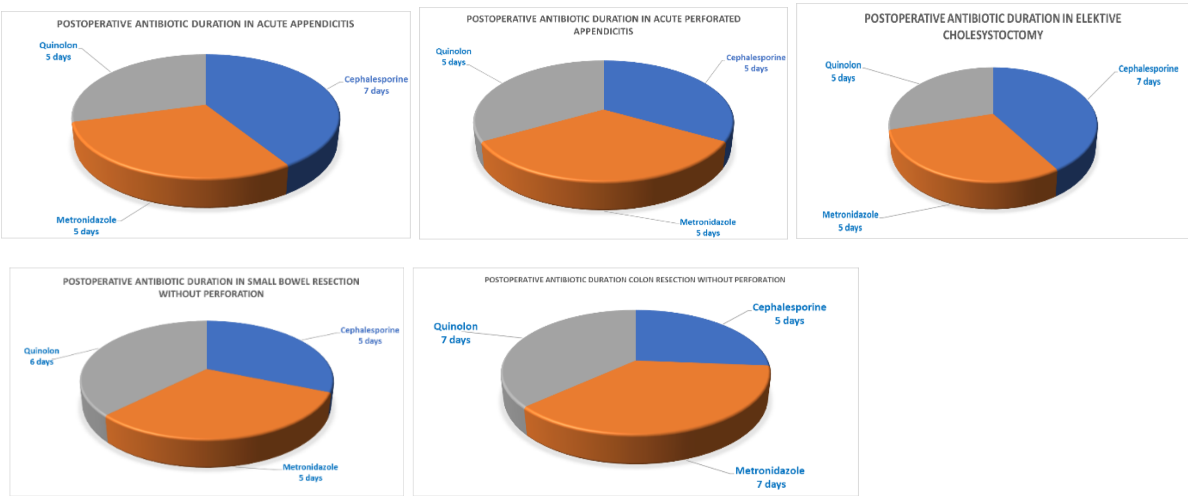


Figure 7: Duration of postoperative prophylactic antibiotics for 5 different surgeries across three hospitals in Kabul-Afghanistan

4. Discussion

This is, to our knowledge, the very first study conducted in Kabul, Afghanistan on prophylactic antibiotics for abdominal surgery. The results show extensive similarity in the incorrect use of prophylactic antibiotics among Afghanistan and its neighboring countries, Iran, and Pakistan. The findings highlight the urgent need for targeted interventions to address improper antibiotic use and this concerning rise of antibiotic resistance.

Nine studies evaluated indications for antibiotic prophylaxis (14-22, 27). Five of them reported low accordance with guidelines while two of them adhered to over 80% of international recommendations (19, 20). Studies have shown that the lack of indication is a common reason for the inappropriate use of antibiotics (19). The most frequent mistake about indication appeared to be excessive use of antibiotics. Overuse and misuse of antibiotics have been reported mostly in developing countries (30-33) as well as Iran, but in contrast, underuse has been reported in a developed country (34). The rate of wrong indication varies between different types of surgeries. For instance, a high rate of incorrect indication has been observed among the general surgery and gynecology disciplines (14, 19). Distinctive surgical systems, complex surgical methods, and higher surgery rates have been argued as possible reasons for a higher rate of incorrect indication in these wards (14). Excessive use of antibiotics can also occur due to differences in the epidemiological status of antimicrobial resistance. Although overuse of antibiotics can reflect the awareness of surgeons about the importance of antibiotics in the prevention of surgical site infection it may cause an increase in cost of treatment as well as bacterial resistance. The implementation of guidelines, as S. Elyasi et al and L. Mahmoudi et al. showed in their studies, resulted in a significant reduction in the incorrect use of antibiotics (21, 22). This emphasizes the necessity of the presence and adherence to guidelines when administering prophylactic antibiotics in developing countries.

According to the guidelines, the recommended prophylactic agent in surgical procedures (except in beta-lactam allergy cases) is a first-generation cephalosporin, cefazolin. Cefazolin has a moderate spectrum of activity targeting only the suspected surgical pathogens, so that the development of antimicrobial resistance can be prevented. In addition, cefazolin is a safe drug with an appropriate duration of action and low cost (26, 28). As it was mentioned in the result, nine studies evaluated the accordance of antibiotic regimens with guidelines. Of these studies, just two of them reported adherence to recommendations over 70% and other studies had even lower compliance with guidelines. S. Elyasi and colleagues showed that applying the prepared protocol resulted in the reduction of inappropriate selection of antibiotics from 55% to 17%. Errors in antibiotic selection included the use of more than one drug without any indication for multidrug prophylaxis, and the use of antibiotics that are not recommended for prophylaxis, such as third-generation cephalosporins and fluoroquinolones (33). Third-generation cephalosporins, aminoglycosides, and fluoroquinolones should not be used for SSI prevention. These groups of antibiotics are less active against staphylococcal infections compared to cefazolin, emerging resistance, and high cost (16). As observed in most studies it was common to use third-generation broad-spectrum cephalosporin, ceftriaxone, alone or in combination with other antibiotics rather than cefazolin (18, 19, 21-23, 27, 28). This finding is consistent with previous studies conducted in Pakistan, India, and Ethiopia which reported the use of ceftriaxone in 57.6%, 60.7%, and 84% of procedures, respectively (35-37). Interestingly, we found the same result from the questionnaires in Afghanistan where the first choice and the dominant prophylactic antibiotic is ceftriaxone in combination with metronidazole and/or quinolones and/or aminoglycosides, especially for postoperative prophylaxis. Despite the presence of a significant discrepancy between guidelines and everyday-practice in Afghanistan, in the case of choosing the type of prophylactic antibiotics, there have been a few surgeons (0.02%) who chose cefazolin as recommended in the guidelines. These results point out a general tendency among physicians in developing countries to prefer broad-spectrum drugs in the surgical setting, which exacerbates the antimicrobial resistance problem mentioned above. The possible explanation for the high use of this group of antibiotics might be physicians' attitude toward broad-spectrum antibiotics as the best option to treat many infections. They decide based on empirical treatment rather than waiting for a laboratory test result (38). Another explanation underlying the incorrect selection of antibiotics is that most of the antibiotics were prescribed by medical residents who are not as fully trained in medication choices as they are in diagnosing diseases and performing procedures (16, 21). The unavailability of a clinical pharmacist to assist physicians in properly selecting medications can be additional argumentation. Another argument arises from the urgency of certain surgeries, like appendectomy and cholecystectomy, causing surgeons to overlook standard guidelines, leading to inappropriate antibiotic prescriptions (16). Lack of medication protocols or not considering it may be another reason for the wrong choice of antibiotics (16). All these explanations are actual in Afghanistan. In addition, poor hygiene of the patients, poor nursing care, long hospital stays, lack of standard and aseptic operation equipment, easy access to antibiotics, possibly developed antibacterial resistance, lack of culturing possibility, high cost for culture, covering both aerobic and anaerobic bacteria, covering both gram-positive and gram-negative bacteria and low quality of medicines are also other factors which were reported in the questionaries.

According to ASHP guidelines, the minimum duration for antimicrobial coverage includes the time from the incision until the closure of that incision and it can be extended up to 24 hours and in some cases up to 48 hours after surgery (38, 39). Thus, postoperative administration is not recommended in guidelines (39). Whereas the majority of surgeons, as reported in some studies, tend to use antimicrobial prophylaxis for longer than the recommended period to cover their patients sufficiently (14). Previous studies from Greece and the Netherlands demonstrated 36.3% and 82% adherence to the guidelines regarding duration, respectively (40, 41). In our analysis, we found that several studies reported a rate of accordance with guidelines between 29.4-86% (14, 16-18), and just in one study the duration was consistent with guidelines over 90% (15). Approximately the same results are reported from other studies performed in different countries (33, 42-45).

Responses from surgeons in Afghanistan indicated above 90% deviation from the recommendation. The length of postoperative antibiotic use was reported from 1-14 days with an average of 7 days. Respondents' explanations underlying the long duration of antibiotic use in Afghanistan were lack of education in the population about how to deal with and take care of patients, poor hygiene of patients, lack of access to healthcare services to control infection, no home access to medical care after surgery, no home nursing care facility, poor nutritional condition, prevent infection, low quality of the drug, longer use when empirical treatment fails, patients do not come for check and do not use drugs regularly.

The result of a meta-analysis showed that there was no additional advantage for postoperative maintenance antibiotics (46). On the contrary, it can increase the risk of colonization with hospital-acquired pathogens with a high rate of resistance to available antibiotics, increase patient morbidity due to the risk of side effects of antibiotics, and develop superinfection (18, 47). In addition, extended use of antibiotics increases the risk of antibiotic resistance and imposes unnecessary costs on patients and hospitals (22). In studies, where they assessed the effect of applying protocols, a reduction in the duration of prophylactic antibiotic use was observed (21, 22).

Regarding the time of administration of prophylactic antibiotics, the guidelines indicate that the optimal timing for the first dose of the prophylactic medication is within 120 minutes before incision (39). This appears more effective than antibiotic administration immediately before surgical incision (26). On the other hand, administering antibiotics before 120 minutes of incision increases the risk of surgical site infections, as the drug concentration in blood and tissues at the time of incision and during the surgical procedure, may fall below the level required for its effects (39, 48, 49). As it was identified in the result three studies pointed out a compliance between 42-74% (14, 17, 26). Approximately the same result was reported by studies conducted in the USA and Netherlands (41). On the other hand, A. Ebrahimzadeh et al. and M.Z. Satti et al. found over 90% adherence to standard protocol (23). A Greek study by Tourmousoglou and colleagues showed almost the same result (100%). On the contrary, A.Vazin et al. reported 100% inappropriate timing (27). Similarly, a study conducted in India reported that timing was not compliant with any guidelines and, in some cases, started several hours before surgery (36). When it comes to the timing av prophylactic antibiotics in Afghanistan above 90% of surgeons chose to give prophylactic antibiotics preoperatively as recommended, but the exact initiation time was not reported. Therefore, it is difficult to conclude whether their practice is consistent with guidelines or not. However, postoperative prophylactic antibiotic practice was not in adherence to recommendations where questionaries' respondents chose to give antibiotics above 90% postoperatively.

The correct route of administration of prophylactic drugs is important to ensure a steady and predictable level of drugs. For this reason, international guidelines recommend the intravenous (IV) administration of prophylactic antibiotics. In our analysis, three studies assessed the proper route of administration, and all of them were reported in accordance with guidelines (19, 23, 28). This finding is consistent with a similar study in the Philippines, which also reports 100% adherence to the recommendations (50). Based on the questionnaires' results from Afghanistan the route of administration for preoperative antibiotics was IV in 100% of cases. Postoperatively antibiotics were given intravenously for the first 24 hours and then continued in oral form for several days.

The type of surgery can also affect the usage of prophylactic antibiotics in surgery. In some studies, the lowest prophylactic antibiotic compliance was found with appendectomy whereas the highest was reported for orthopedic surgery (23). Our findings, in this review, indicate that the lowest compliance was within internal medicine (22), gastrointestinal (1), and appendectomy (23) but plastic surgery (23) and general surgery (19) had the most concordance with guidelines. Surgeries we chose in our questionnaire were among these which are associated with low adherence with guidelines in term of prophylactic antibiotic use. These findings illustrate that type of surgery, urgent or elective plays a role in how much prophylactic antibiotic use can be in accordance with recommendations.

The management of economic resources is an important factor affecting the quality of a healthcare system, especially in developing countries. Wrong and unnecessary antibiotic use are contributing factors leading to the waste of such resources. Studies indicate that widespread utilization of third-generation cephalosporins should not be used due to the emergence of resistance and their high prices compared to first-generation cephalosporins (48, 49). Moreover, wrong prescriptions and unneeded antibiotic combinations are also associated with more antibiotic resistance which complicates the treatment of many infections which again leads to an increase in health-associated medical costs, length of hospital stays, morbidity, and mortality of affected patients (14, 19, 28). Consultation with a clinical pharmacist or infectious diseases consultant, educational courses, and application of the latest version of guidelines are some not-so-complicated actions that might help reduce the excessive cost of prophylactic antibiotics (51-57).

Clinical guidelines are evidence-based recommendations that are designed to guide clinicians and other healthcare practitioners in clinical decision-making, diagnosing and treating different diseases and medical conditions more properly. The purpose of these recommendations is to make sure that patients receive the appropriate treatment and care. Guidelines can be designated either national or international. Two studies from Iran and Pakistan indicated that the awareness of surgeons, surgical residents, and other practitioners of guidelines improves the rational use of surgical antibiotics prophylaxis (26, 28). In the study of M.Z. Satti et al. the odds ratio for awareness of surgical residents and appropriate prophylaxis were 4.064 ($p<0.000$) and this indicated that surgical residents who were aware of international recommendations on surgical antibiotics prophylaxis compared to those who were not, were four times more probably to carry out the proper prophylaxis and achieve a 100% compliance (28).

Although many countries refer to the different international guidelines, they do not fully follow them and the overall compliance rate is low (10-49.33%) (14, 17, 19, 21-23, 25, 27, 28). This is the repeated result in several studies which assessed how much international recommendations were being adhered to. Some possible explanations underlying non-adherence to guidelines can be a lack of a common and standard protocol, lack of clinical pharmacists, easy accessibility to several antibiotics, cultural factors, educational background, training, type of surgery, and surgeons' preference to use excessive amounts of antibiotics for more days to reduce the risk of post-operative infection (20-23, 25, 27). Therefore, prescribing practice is not so simple.

As already noted, two interventional studies conducted in Iran showed that the active application of guidelines improves clinical practice when it comes to surgical antibiotics prophylaxis (21, 22). Another issue that has been focused on in some studies is the use of national guidelines, and they pointed out that the local recommendations improve rational utilization of antibiotics and adherence to these may be easier to attain than adherence to international guidelines (21, 22, 26). Preferably if in developing countries like Iran, Afghanistan, and Pakistan guidelines are specifically adjusted to the local conditions, local microbial detection, local antimicrobial resistance profile, cultural background, available antibiotics, and the most common types of surgeries performed there will be more likely to be followed by surgeons and other healthcare professionals (22). Active collaboration between surgeons and clinical pharmacists to choose the correct and most cost-effective types of antibiotics, automatic stop-order programs, and educational courses are the other initiatives that can improve surgical antimicrobial prophylaxis practice in these countries and therefore increase adherence to the standard protocols and better surgical care will be provided (22).

5. Conclusion

The development of resistance among bacteria due to the overuse and misuse of antibiotics is one of the major public health issues. Surgery is one of the medical areas where antibiotics are widely used to prevent post-operative infection and where the irrational use of antibiotics is reported frequently. Inadequate attention to standard recommendations for prescribing antibiotics by surgeons and other practitioners leads to unnecessary excessive antibiotic utilization, which can increase antimicrobial resistance, morbidity, mortality, and unneeded expenditure on both hospitals and patients. Particularly, this is a most common problem in developing countries where they either have no idea that there is a guideline to follow or if they are aware of it, they disregard it. Afghanistan, one of the least developed countries and the heart of conflict and war in the last four decades, has encountered lots of challenges within cultural, economic, social, political, and healthcare areas. Regime changes, lack of security, lack of infrastructure, a messy healthcare system, corruption, import of counterfeit drugs, geographical challenges for patients, hygienic conditions, and cultural obstacles related to gender are some factors affecting the quality of public health in this country in recent years. One of the major concerns within the healthcare sector in Afghanistan is the irrational use of antibiotics. To get an overview of the situation in the country, initiating studies was a logical starting point, but the situation in Afghanistan prevented us from conducting such studies. Due to the lack of local research in Afghanistan, articles from neighboring countries were collected to analyze. This is because of the similarity between neighboring countries and Afghanistan from several perspectives such as antibiotic resistance profile, antibiotics prescription culture, and social, economic, and cultural background, which were selected to analyze. In addition, designing a questionnaire, in which surgeons in Afghanistan were asked about their daily practice, was a supply to article analysis to show the real situation of prophylactic antibiotic use in this country.

Analysis of 17 articles, that evaluated the appropriateness of surgical antimicrobial prophylaxis, showed an overall low rate of compliance with guidelines in terms of indication, type, timing, and duration. These studies revealed that even though there are several international guidelines available, they are not actively used, and this causes incorrect antibiotic utilization patterns. Guideline implementation led to more proper election, timing of preoperative administration, and especially duration of prophylactic antibiotics. Data from the questionaries in Afghanistan pointed out some of these findings and this means that initiatives should be taken to improve the surgical antibiotic prophylaxis practice. As several factors may have a role in low adherence rate, several initiatives may impact improving surgical antibiotic prophylaxis practice. Active collaboration between surgeons and clinical pharmacists to choose the correct and most cost-effective types of antibiotics, automatic stop-order programs, and educational courses are some initiatives that can improve surgical antimicrobial prophylaxis practice in these countries, including Afghanistan. However, preparing a national protocol adjusted to the local medical condition, antibiotics accessibility, local resistance profile, and cultural background should be prioritized. However, approaching such a guideline in Afghanistan requires better knowledge about the resistance profile of the pathogens in this country. This literature study can be used as a pre-study for further research in this field in the future.

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7. Appendix A

Questionnaire of antibiotic use before, during, and after surgery for appendectomy, cholecystectomy, and bowel resection

1. **Hospital Nr……..**
2. **Department of general surgery.**
3. **Job experience as a doctor, years ________________**
4. **Job experience as resident (trainee), years ______________**
5. **Job experience as consultant (trainer), years _________________**
6. **Use of antibiotic and type.**

1. **Acute appendicitis:**

Before surgery ☐ No ☐ Yes

↓

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

During surgery: ☐ No ☐ Yes

↓

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

After surgery: ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________Oral ☐ Nr of days ....

IV ☐ Nr of days ....

2. **Acute perforated appendicitis:**

Before surgery ☐ No ☐ Yes

Type of AB _____________________________ Oral ☐ IV ☐

Type of AB _____________________________ Oral ☐ IV ☐

Type of AB _____________________________ Oral ☐ IV ☐

During surgery: ☐ No ☐ Yes

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

After surgery: ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

3. **Elective cholecystectomy:**

Before surgery ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

During surgery: ☐ No ☐ Yes

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

After surgery: ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

4. **Small bowel resection without perforation:**

Before surgery ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

During surgery: ☐ No ☐ Yes

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

After surgery: ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

Type of AB ______________________________ Oral ☐ Nr of days ....

IV ☐ Nr of days ....

5. **Small bowel resection without perforation:**

Before surgery ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

Type of AB ______________________________ Oral ☐ IV ☐

During surgery: ☐ No ☐ Yes

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

Type of AB ______________________________ IV ☐

After surgery: ☐ No ☐ Yes

Type of AB ______________________________ Oral ☐ Nr of days ……..

IV ☐ Nr of days ……..

Type of AB ______________________________ Oral ☐ Nr of days ……..

IV ☐ Nr of days ……..

Type of AB ______________________________Oral ☐ Nr of days ……..

IV ☐ Nr of days ……..

Why do you use multiple antibiotics at the same time?

Answer:

Why do you prescribe antibiotics for a long time after the operation?

Answer:

Skriftlig redegjørelse for hvordan arbeidet har vært fordelt i gjennomføringen av prosjektarbeidet og i skrivingen av oppgaven

Prosjektarbeidet vårt består hovedsakelig av 6 deler: litteratursøking og valg av relevante artikler, analyse av utvalgte litteratur, utforming av spørreskjema, analyse av dataene, og skriving av oppgaven.

Søkemaskinene vi tok i bruk er Medline og PubMed. Vi fordelte disse søkemaskinene mellom oss for å finne relevante litteratur. I tillegg hver av oss brukte snowballingsmetode i litteratursøkingen. Vi gjennomgikk omtrent 100 artikler sammen. Noen av disse artiklene er tatt med for å skrive fakta i introduksjon- og bakgrunn delen. Videre satte vi igjen med ca. 70 artikler kandidat til analyse. Ved hjelp av vår veileder valgte vi de mest relevante og lovende artiklene, nemlig 17, til viderearbeid. Analyse av disse artiklene ble gjort sammen.

Etter råd fra veileder laget vi et forslag til spørreskjema, men den endelige formen ble ferdiggjort av vår prosjektveileder og Dr. Nazir Naimy, norsk-afghansk gastrokirurg. Spørreskjemaene ble håndlevert til kirurger i 3 forskjellige sykehus i Kabul, Afghanistan av Dr. Nazir Naimy. Etter tilbakesamling av ca. 70 spørreskjema-svar analyserte vi dataene sammen.

Vi samarbeidet gjennom hele prosjektoppgaveskrivingen. Det var ikke et tydelig skille eller fordeling av oppgaver, men mest som et fellesarbeid har dette blitt fullført.