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Study of antibiotics prescribing pattern in infants: Retrospective study: The study of drug utilization pattern in pediatric patients

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Abstract
Antibiotics one of most commonly prescribed medications in pediatric group, Infants are most susceptible to diseases due to incomplete of immune system. Antimicrobial especially antibiotics has become a routine use in infant illness may that cause many problems. The rising numbers of antibiotics resistance lead us to judicious the use of antibiotics. In this study, we aim to Evaluation of prescribing pattern of antibiotics in infants group guided by WHO guidelines. Descriptive research conducted at Maternity and Children hospital in Mecca, Saudi Arabia. Sampling 253 infants. Including all the infants' inpatients, excluding outpatients, ICU emergency patients patients with AIDS. Data collected from the parents and medical records. In Conclusion**,** Antibiotics are mostly prescribed drugs. Parenteral route mostly use than oral route, in our present study antibiotic prescription pattern show there are polypharmacy. The average numbers of antibiotic per prescription were markedly higher than which recommended by WHO. Overuse and inappropriate use of antibiotics, excessive parenteral use of antibiotics administration. As the resistance of antibiotics is increasing, so we have to be selected based on culture report and limited use of antibiotics should be done in patients especially infants. Lastly, we recommend further and larger scope prospective study as this is an important issue to emphasize on to ensure rational use of antibiotics and hence fighting against the distressingly increasing antimicrobial resistance. Recruiting clinical pharmacists is very vital in order to observe the clinical use of antibiotics and to deal with related factors. The WHO should supply updates and guidelines on the use of antibiotics in hospitals.

Keywords: antibiotics prescription; prescription pattern; prescription in infants

1. Introduction

Antibiotics are the most effective and widely used medication utilized for treatment and prevention of numerous bacterial infections [1]. It is one of most commonly prescribed medications in pediatric group. Infants are representing as a huge part of population in developing countries; they are most susceptible to diseases due to immature immune system.

Acute respiratory infection, acute watery diarrhea, fever are the common infant diseases that lead to seek for medical consultation at hospital [2, 3, 4]. Antimicrobial especially antibiotics has become a routine use in infant illness may that cause many problems [5]. Some diseases such as URTIs are viral origin and not necessary to give antibiotics, but still widely used. [6, 7, 8, 9, 10] Several studies reported that 50% to 85% of children receive antibiotics in developed and developing countries [1]. Prescribing antibiotics is based on a set of protocols, strong evidence and guidelines that depend on local culture sensitivity data in order to avoid antibiotics adverse events [11, 12, 13]. And take in consideration The rising number of antibiotics resistance lead us to judicious the use of antibiotics [14, 15, 20]. The high risk of opportunistic, nosocomial infections and potentially life threatening events due to intensive antibiotic use in prolonged hospitalized and immunocompromised conditions [16, 17, 18]. Prescribing antibiotics in pediatric group requires careful consideration of age, body weight, drug dose and overall health care costs [19]. Pharmacokinetic parameters and pharmacodynamic of a given antibiotic are completely different when implicating it in pediatric groups compared to its use in adult ones [19]. However, the misuse of antimicrobial agents has been recorded to be frequent in various areas of the world, but there have been few studies in developing countries. Thus, a detailed pattern of antibiotic prescribing should be implemented in all pediatric departments. sensitivity to reduce risk of resistance.

2. Materials and Methods

a) Study Setting: The study was conduct at Maternity and Children hospital in Mecca, Saudi Arabia.

b) Study Period: The study was conducted from April 2016 up August 2016.

c) Study Design: A hospital-based retrospective descriptive study.

d) Source of Population: Pediatric population (infants) age up to 12 months.

e) Exclusion criteria: All the in fants outpatients, ICU, emergency patients and patients with AIDS not include in this study.

f) Sample Size: The sample size for the retrospective study was 253.

g) **Data collection Tool:** Primary data collected from the patient chart, lab. Results, prescription orders and medical records of the patients.

h) **Ethical considerations:** The study was carried out after having the ethical permission.

i) **Data Analysis Methods:** Data has been analyzed by using SPSS software statistical program, version7. For categorical variables, percentage has been used. Numeric data has been presented as mean and standard deviation (SD), or as median and range according to the type of distribution of each variable.

3. Results

253 cases of infants were included and data were collected on predesigned questionnaire. The total patients enrolled in the study were under one year of age. Among 253 patients, 139 (54.9%) were male and 114 (45.1%) were female.

Eighty three patients (32%) of the admitted infants were neonates (age less than an one week old), but 68 patients (26.9%) were neonates (age in between one and 4 weeks), and 46 patients (18.2%) were infants (age in between 1 and 3 months old), and 18 patients (7.1%) were infants (age in between 3 and 6 months old), while 38 patients (15.0%) were infants (age in between 6 and 12 month old). Figure1

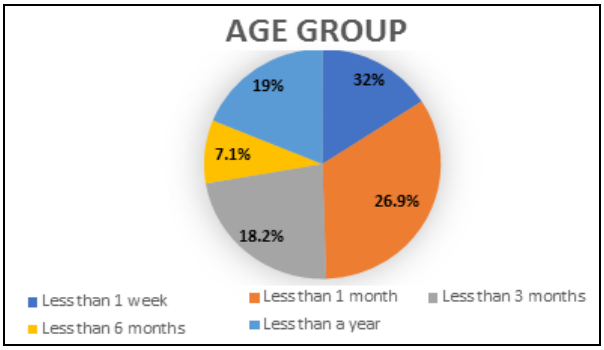

Fig 1

Average hospital stay was 13.35 days. Most of patients stayed as inpatient for 2 days.

The study showed that the most of drugs were indicated for respiratory diseases 131 patients (51.8%), other infectious diseases 53 patients (20.9%), 26 patients (10.3%) for fever, 21 patients (8.3%) with GIT disease, 17 patients (6.7%) with cardiovascular disease, 23 patients (9.1%) with seizure disorder while 59 patients (23%) were preterm. Figure 2, 3

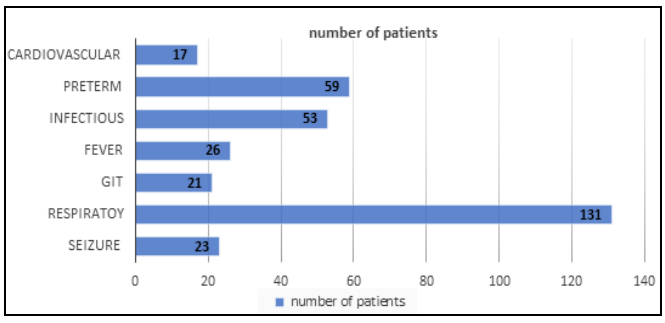

Fig 2

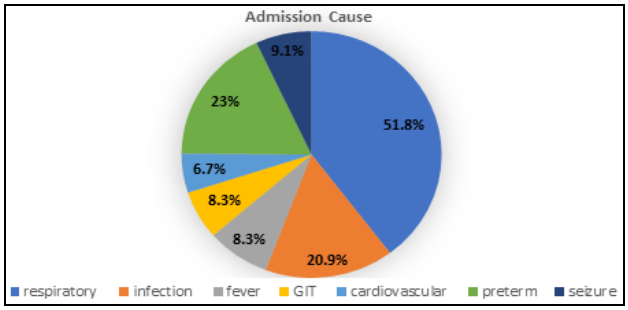

Fig 3

Antibiotics or antimicrobials were frequently prescribed in combination with others drugs in 62 patients (24.5%) with more than 3 drugs, in 37 patients (14.6%) 3 drugs were prescribed, in 60 patients (23.7) 2 drugs were prescribed, 54 (21.3%) one drug was prescribed while in 11 patients (4.3%) antibiotics were prescribed only. Figure 4

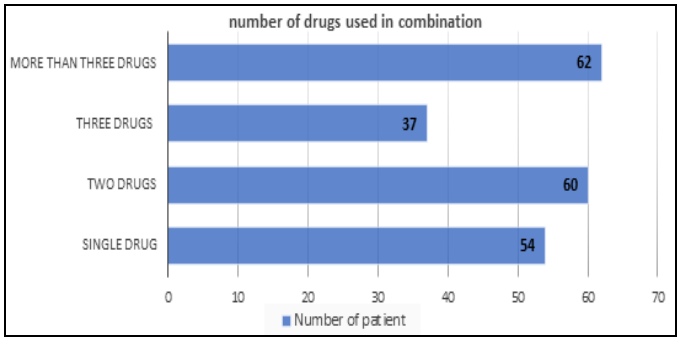

Fig 4

Anti-infective agents were used with IV fluids in 157 out of 253 patients (62%). They prescribed in 49 patients (19.4%) with respiratory agent, 25 patients (9.9%) with CNS medications, 23 patients (9.1%) with anti-inflammatory medications, 10 patients (4%) with GIT medications, 9 patients (3.3%) with cardiovascular medications, and in 7 patients (2.8%) with nutritional supplements. Figure 5

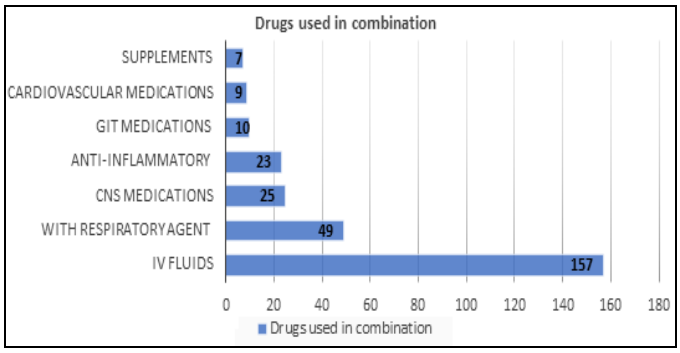

Fig 5

Antibiotics were prescribed in 139 patients (54.9%) as a combination of two antibiotics, in 76 patients (30%) used as a single agent, in 26 (10.3%) three antibiotics used while 10 patients (4%) used more than three antibiotics per prescription. Figure 6

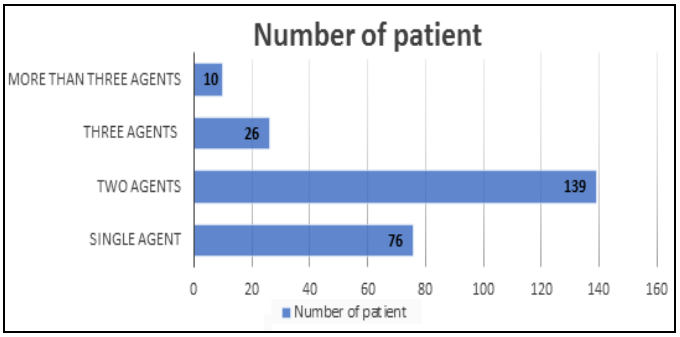

Fig 6

The most frequently used anti-infective groups were beta-lactam in 223 patients (88.1%), aminoglycoside antibiotics were used in 114 patients (45.1%), glycopeptides "vancomycin" were prescribed in 61 patients (24%), macrolides were prescribed in 8 patients (3.2%), antifungal were prescribed in 17 patients (6.7%). Figure 7

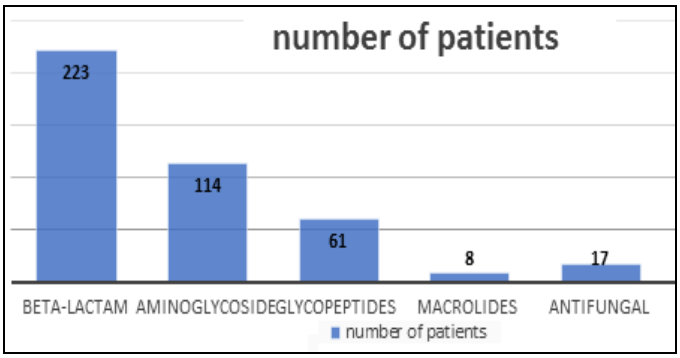

Fig 7

Most of patients were given the antibiotics by injections in 240 patients (94.9%), 8 patients were given orally and only one patient was given by both routes. Most of cases are taking the antibiotics in less than 7 days in 193 patients (76.3%) while 36 patients (14.2%) were using it for more than 7 days. figure 8

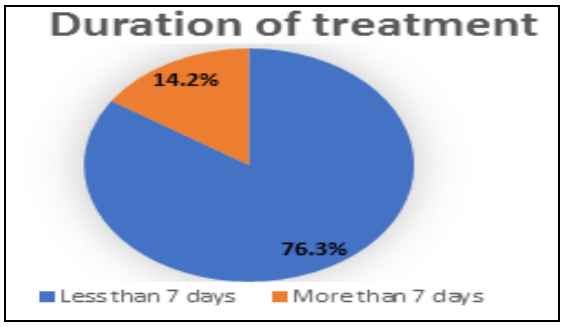

Fig 8

Patients with seizures disorders 22 patient out of 23 were managed with beta-lactam antibiotic. 3rd generation cephalosporin was used in 9 patients (40.90%). 7 patients managed with vancomycin, 4 patients managed with aminoglycoside antibiotics and anti-viral only used in 2 patients. Most of patients managed with 3 drugs (43.48%) and 11 patients were using 2 antibiotics. In 22 (95.65%) patients managed by injectable route. Only 1 patient managed for more than a week.

Respiratory diseases were the most common cause for antibiotics prescription in 131 patients out of 253. 119 patients were managed with B-lactam and most commonly with 3rd generation penicillin in 64 patients (53.78%). 69 patients (27.2%) were managed with aminoglycoside antibiotic and 28 patients (11%) with vancomycin. Two antibiotics were used in 88 patients (67.69%). In 123 patients (96.09%) were managed by injectable route. In 20 patients the duration of treatment was more than a week. Table 1

Table 1

Cause of admissions	Number of patients	Number of antibiotics	Most common antibiotic	Rote of administration	Number of patient stay in hospital less than weak	Number of patient stay in hospital less than weak
Respiratory	131	3	B-lactam (3rd generation penicillin)	Injectable in 123 patient.	111	20
seizure	23	3	beta-lactam (3rd generation cephalosporin)	Injectable in 22 patient.	22	1

B-lactams group of antibiotics were used in 223 out of 253 patients (88.1%). Penicillin derivatives in 93 case (41.70% of B-lactams), carbepenum used in 70 patients (31.39%) and 3rd generation cephalosporin used in 60 patients (26.91%). B-lactams used alone in 10 patients while used in combination of two antibiotic in 129 patients, most commonly with aminoglycoside in 97 patient (43.50% of B-lactams managed patients) and in 50 patients (22.42%) with vancomycin. Most of patients managed with injectable route and with 7 patients with oral route while duration of treatment is less than a week in 177 patients. Aminoglycoside antibiotics used in 114 out of 253 patients (45.1%), most commonly used in combination of two drugs in 77 patients (68.1%) and also used in combination of two antibiotics in 77 patients (68.1%) with Blactams in 97 patients (85.1%) and with vancomycin in 19 patients (16.7%). Route of administration is injectable in 110 patients (98.2), while duration of treatment extended for more than a week in 16 patients (15.1%).

Vancomycin used in 61 out of 253 patients (24.1%), most commonly used in combination of more than four drugs in 23 patients (45.1%) and also used in combination of two antibiotics in 36 patients (61.0%) with Blactams in 50 patients (82.0%) and with aminoglycosides in 19 patients (31.1%). Route of administration is injectable in all patients, while duration of treatment extended for more than a week in 8 patients (15.7%). Table 2

Table 2

Class of antibiotic	Number of patient	Number of drugs	Number of antibiotic	Rote of administration	Number of patient stay in hospital less than weak	Number of patient stay in hospital less than weak
B-lactams	223	4	2	Injectable in 216 patients.	177	7
aminoglycosides	114	2	2	Injectable in 104 patients.	98	16
vancomycin	61	4	2	Injectable in all patients.	53	8

4. Discussion

Antibiotics are a one of the most frequently used medications.

Antibiotics are extensively prescribed in neonates and infants as infections are common and linked with a highly hazard of morbidity and mortality. (Jayakar *et al*, 2011, FDA, 2012) The irrational use of antibiotics leads to a numerous of consequences in term of cost, drug interactions, hospital stay and bacterial resistance.

The present study aimed to evaluate prescribing pattern of antibiotics and antimicrobials in infants group of patients guided by WHO guidelines. It well known that prescribing pattern suggests revision periodically to improve prescribing practice, to make rational medical care and cost effectiveness. Infancy is considered a critical period for growth and development, also, represent a big section of population in developing countries.

The present study was carried out in 253 patients less than 1 year of age. Study data was collected from Maternity and Children Hospital, Makkah, Saudi Arabia in the period from 1ST August 2016 to 1st of November the prescriptions of patients were analyzed. It was found that 139(54.9%) were male and 114 (45.1%) were female. The same finding were seeing in other studies (21). The more numbers of patients are belong to age group less than a week old Eighty-three (32%) were 68 (26.9%) were older than a week and less than month old. 46 (18.2%) were older and less than 3 months old, 18 (7.1%) were older and less than 6 months old. 38(15.0%) were older and less than a year old. This indicates that the higher incidence of infections increased among younger age groups.

The common diseases responsible for hospital admissions in the neonatal and infancy age are infectious in etiology. This may have accounted for a higher usage of antibiotics. This study showed that most of the drugs were used for conditions like acute respiratory disease which is most common complaint with 131 patients (51.8%) of total, 53 patient (20.9%) admitted for infectious cause, 26 patient (10.3%) admitted for fever, while 21 patients (8.3%) with gastrointestinal disease. The rest conditions distributed between 59 patients (23%) were preterm, 23 patients (9.1%) with seizure disorder, 17 patients (6.7%) with cardiovascular disease and 26 patients (10.28%) with other causes. These indicate that the most of patients were suffering from infectious etiology.

The data from the present study were compatible to the study done in USA which revealed that community acquired pneumonia was an important cause to recommend antibiotics in hospitalized children [26].

However, the study done by Rajeswari *et al* on assessment of antibiotic use in pediatric patients put pneumonia at the bottom of the proportion of disorders for which antibiotics were prescribed and gastroenteritis the most commonly occurred disorder [25] Similar studies conducted by Jonathan A Finkelstein in 2001 reported that otitis media accounted for the majority of antibiotic courses dispensed [27]. This dissimilarity might be due to the variation in the time of the conduction of these studies as there is seasonal variation regarding the incidence of some diseases. The average number of drugs prescribed per encounter included the antibiotic were in 62 patients (24.5%) with more than 3 drugs, in 37 patients (14.6%) prescribed with 3 drugs, in 60 patients (23.7) prescribed with 2 drugs, 54 (21.3%) prescribed with one drug and in 11 patients (4.3%) antibiotic was prescribed alone. This prescribing behaviour may be related to the physician`s and patient`s attitude towards patient management. The average number of drugs prescribed per encounter was high as reported in some studies were conducted in other developed countries. The mean ± SD number of drugs prescribed per prescription was 4.8 ±2.4. (Murali *et al*., 2013).

The mean number of drugs prescribed per-prescription was lower in compare with studies done in Nepal (Palikhe, 2004; Kumar *et al*., 2010) and reliable with the WHO commendations (WHO, 1993; WHO, 2001).

The mean number of antibiotics prescribed per-prescription was lower than a study conducted in Ethiopia (Abula *et al*., 2004) and is consistent with the WHO recommendation (WHO, 1993). The mean number of injection prescribed per-prescription in the study confirmed the load of injectable prescription on pediatrics compared to the mean of antibiotics prescription in the same groups. The WHO recommends that the average number of drugs per encounter should be less than two. In our present study 62 patients (24.5%) with more than 3 drugs, this number is more than two, so it indicates polypharmacy. So number of drugs per prescription should be as low as possible to prevent polypharmacy outcomes such as increased risk of drug - drug interactions, high cost, resistance and non-compliance (21). All patients were using anti-infective agents and its most commonly used with intravenous fluids in 157 patients (62.1%). While, in 49 patients (19.4%) anti-infective agent is prescribed with respiratory agent, 25 patients (9.9%) with CNS medication, 23 patients (9.1%) with anti-inflammatory medication, 10 patients (4%) with gastrointestinal medications, 9 patients (3.3%) with cardiovascular medications, and in 7 patients (2.8%) using nutritional supplements. In the present study antibiotics were used in 76 patients (30%) as a single agent, while combination of two antibiotics was present in 139 patients (54.9%), 26 (10.3%) with three antibiotics while 10 patients (4%) were using more than three antibiotics. So in our present study more than

(70%) use multiple antibiotics in contrast to study of (23) which showed more number of patients have received single antibiotics. These absolute numbers of anti-infective agents are in consistence with the data available from another hospital study conducted in Germany by Gortner *et al*., where the exposure to antibiotics in neonates was 98.8% [28]. Similar high exposure numbers for antibiotics are reported from the

USA & Italy [28, 29]. The high rate of antibiotic exposure in our study is similar to prior studies carried out in India as well as other countries and is probably due to the standard practice of prescribing antibiotics or until bacterial culture sensitivity test results in sick neonates or infants and is not a true reflection of the incidence of bacterial infection [37-38]. A study by Fonseca *et al*., revealed that the highest use of anti-infective agents was in small for date neonates and 92% of them received antibiotics within the first 48 hours after birth [39]. These findings may be explained by high susceptibility of neonates to bacterial infections, especially for very preterm neonates, who need mechanical aids for ventilation. Clinical presentation and laboratory tests are not highly sensitive and specific during the early period after birth [40] which also accounts for the high rate of antibiotics treatment of neonates. As harmful infections often become manifest without obvious clinical and laboratory signs, antibiotic treatment is indicated in ill neonates or infants even if the clinical signs are only minimal.

The most frequently used antibiotic group was beta-lactam in 223 patients (88.1%), most common prescribed drug is third generation of penicillin in 93 patients (36.8%), and second most common is third generation of cephalosporin in 60 patients (23.7%), carbapenem was used in 70 patients (27.7%). We found that patients with seizures disorders 22 patients out of 23 were managed with beta-lactam antibiotic with 3rd generation cephalosporin 9 patients (40.90%) Respiratory diseases were the most common cause for antibiotics prescription with 131 patients out of 253, 119 patients were managed with B-lactam with third generation penicillin in 64 patients (53.78%). (22) showed same findings with contrast in using of third generation penicillin predominantly they found that cephalosporin is most commonly used.

In the present study, the authors found that beta-lactam antibiotics were most commonly prescribed also accounted for large percentage of injectable same as (22). Among anti-infective agents, Amikacin, Cefotaxime and Levofloxacin were the drugs most often prescribed. Amikacin and Cefotaxime were prescribed more to full term infants whereas Levofloxacin, Piperacillin-tazobactum and Meropenem were prescribed more to preterm neonates. The use of Levofloxacin, Vancomycin, Fluconazole, Metronidazole and Colistin was mainly more in extreme preterm and very preterm babies. Amikacin, cefotaxime were most frequently used antimicrobials in previous Indian studies [30, 34].

However, looking at individual drugs a great variation with regard to which drugs are used most frequently is apparent [24, 28].

This heterogeneity indicates that empiric antibiotic treatment varies among different countries and in NICUs of the same country. This is because currently no standard guidelines regarding the choice of empiric antibiotics exist. This finding is not surprising as; Cochrane review comparing the antibiotic regimens for infection in infants concluded that there is inadequate evidence from randomized trials in favor of any particular antibiotic regimen for the treatment of suspected infected neonates and infants [36]. The choices of antibiotic depends upon information regarding known flora prevalence in a unit, individual experience of pediatricians and bacterial culture sensitivity test reports rather than being guided by comparative clinical studies.

Therefore, use of individual antibiotics could not be compared with other studies, as its use in respect to gestational age groups & outborninborn groups was not mentioned [28, 34, 35]. Decisions about how to prevent neonatal sepsis, who and how long to treat, and which antibiotics to use remain important clinical problems [31, 32]. So, early sepsis evaluations and empiric antibiotic treatment is required [33].

The present study revealed that injectable use in pediatric patient situations were the most common drugs prescribed as injectable. Amon the antibiotics, Beta-lactam group of antibiotics were prescribed most commonly. However, there is a need to emphasize the need to switch over to other routes of administration as soon as possible. As systematic review concluded that oral therapy appears to be an effective and safe alternative to parenteral antibiotics in hospitalized children with severe pneumonia who do not have any serious sign or symptoms [28]. It need to be investigated if the practice of switching from parenteral to oral drug administration when the clinical condition permits would reduce the cost associated with the drug therapy.

It is important to clear the limitation of the present study. The study samples were collected from only one specialized hospital in MAKKAH district, drug history mainly antibiotics received by these neonates before admission could not be collected, reliance on one time analysis of prescription and inability to assess the rational use of antibiotic in various settings. Some data, also, were missed from the patient`s medical records.

5. Conclusion and Recommendations

In this study we aimed to evaluate prescribing pattern of antibiotics in infants group guided by WHO guidelines. Antibiotics are mostly prescribed drugs for infant patients. Antibiotic prescription pattern showed that there are polypharmacy and excessive parenteral use of antibiotics administration. The average numbers of antibiotic per prescription were markedly higher than which recommended by WHO.

As the resistance of bacteria to antibiotics is increasing, so we have to be selected based on culture report and limited use of antibiotics should be done in patients especially infants. Lastly, we recommend further and larger scope prospective study as this is an important issue to emphasize on to ensure rational use of antibiotics and hence fighting against the distressingly increasing antimicrobial resistance. Recruiting clinica pharmacists is very vital in order to observe the clinical use of antibiotics and to deal with related factors. The WHO should supply updates and guidelines on the use of antibiotics in hospitals.

5. Acknowledgments

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