

Research Article,

Evaluation of the Appropriate Use of Ceftriaxone in Internal Medicine Wards of Wad Medani Teaching Hospital in Sudan

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Abstract:

Background: Antibiotics are one of the commonly prescribed drugs over the world. Overprescribing of antibiotics may result in serious bacterial resistance. The main cause of inappropriate prescription of antibiotics is the absence of guidelines and protocols for its use. The aim of this study was to evaluate the appropriate use of ceftriaxone (broad-spectrum third generation cephalosporin antibiotic) in internal medicine wards of Wad Medani teaching hospital in Sudan, as well as comparing its use with reference to the standard of Sudan treatment guidelines and reliable references like British National Formula (BNF) and Sanford guide.

Methods: Prospective cross –sectional study conducted in the internal medicine department at Wad Medani Teaching hospital by reviewing the files of all in-patients admitted to medical wards, who received ceftriaxone between November and December, 2018 and the appropriateness use of ceftriaxone was evaluated depending on six criteria: indication, dose, frequency, duration of treatment, culture and sensitivity test and drug –drug interaction

Results: A total of 280 admitted patient's treatment chart containing ceftriaxone injection were analyzed. Ceftriaxone was indicated empirically in 91.1% mostly for respiratory tract infection (35%). Ceftriaxone appropriate dose was given in 59% of patients, inappropriate frequency in 68.9% and incorrect duration in 51.1%. Co-administered drugs with major interaction in 3.6% of patients.

Conclusions: This study revealed high inappropriate use of ceftriaxone where it was given without implementing culture and sensitivity test in the majority of patients. This may result in treatment failure so educational programs is recommended to address the irrational use of antibiotic.

Key words: ceftriaxone, appropriate indications, internal medicine.

Introduction:

The concept of rational drug use refers to a prescription of the right drug to the right patient, in the right dose, at the right time intervals and for the right duration (1). Misuse of antibiotics

inappropriately can be in form of prescribing antibiotics for patient who has no bacterial infection or use for prolonged unnecessary period

Or use of broad spectrum antibiotics when not needed (2).

The inappropriate use of antibiotic can be in form of inappropriate doses, incorrect frequency, incorrect duration or continuing antibiotic treatment regimen without doing a culture and sensitivity test or use with drugs that interact with antibiotic inappropriately (3). Studies done in the USA (4), Australia (5) and Turkey (6), disclosed prevalence of inappropriate use of antibiotics. The vital role of antibiotic in treating infectious disease begins to decrease due to the emergence of resistance to antibiotics (7). Overuse and inappropriate use of antibiotics have significant role in the prevalence of multidrug-resistant pathogens (2). Resistant bacteria increases patients suffering because antimicrobial therapy needed to treat resistant pathogen may be less safe and more expensive than previous antibiotic used (8). A study conducted in Spain revealed that the cost of inappropriate antibiotic use was twice as much for patients who were treated appropriately (9). Prevention of irrational use of antibiotic has a major role in decreasing antibiotic resistance (10). Ceftriaxone is a broad-spectrum third generation cephalosporin antibiotic for intravenous or intramuscular administration. It is one of the most commonly used antibiotics due to its high antibacterial potency, wide spectrum of activity and low potential for toxicity (11). It is effective against many aerobic gram-negative bacilli and has good activity against *Streptococcus pneumoniae*, *Neisseria meningitidis* and methicillin-sensitive *Staphylococcus aureus* (MSSA). It lacks activity against *Enterococci* species, methicillin-resistant *Staphylococcus aureus* (MRSA), *Listeria* spp., *Pseudomonas aeruginosa* and *Bacteroid fragilis*. It is susceptible to inactivation by extended spectrum beta lactamases and chromosomal induced cephalosporin's (12). It is widely used in community-acquired pneumonia; hospital-acquire pneumonia; intra-abdominal infections; acute exacerbation of chronic obstructive pulmonary disease; complicated urinary tract infection; complicated skin and soft tissue infection; joint and bone infections; suspected bacterial infection in neutropenic patients; bacterial meningitis; bacterial endocarditis; surgical prophylaxis; uncomplicated gonorrhoea; pelvic inflammatory disease; syphilis; disseminated Lyme borreliosis (early stage 2) and late(stage 3); prevention of secondary case of meningococcal meningitis; prevention of secondary case of *Haemophilus influenzae* type b disease and Acute otitis media

(13). The wide-spread use of expanded spectrum beta-lactam antibiotic, in particular the third generation cephalosporin for nosocomial infection has led to emergence of beta-lactamase (ESBs). ESBs are defined as beta lactamases capable of hydrolyzing oximino cephalosporins (cefuroxime, ceftaxime, ceftriaxone, ceftazidime) and are inhibited by clavulanic acid (14). Ceftriaxone has drug interaction with calcium chloride, heparin, warfarin, and gentamicin (15), as well as interaction with heparin and furosemide (16). In Sudan there was high inappropriate antibiotic prescribing, which result in high bacterial resistance to several antibiotics (17). This study focused on Ceftriaxone because in Sudan most hospitals consume a large amount of cephalosporin, among them Ceftriaxone is one of the most prescribed antibiotics (14). In Sudan there is an over prescription of antibiotics particularly Ceftriaxone and this lead to the emergence of bacterial resistance to ceftriaxone particularly *E. coli* and *Klebsella pneumoniae* (14). Another study done in Khartoum, Sudan demonstrated increase prevalence of ESBs producing *E. coli* which is resistant to ceftriaxone (18). Some studies done in Sudan revealed the inappropriate use of antibiotics. One of these studies, was the study which was conducted in Elobeid, West Sudan and it disclosed high use of antibiotic particularly cephalosporin among them ceftriaxone was the most commonly prescribed antibiotic, also this study revealed that most patients received antibiotics empirically without performing culture and sensitivity test (19). Another study done to audit the use of prophylactic antibiotics for elective surgery at Khartoum Teaching Hospital, Sudan revealed that 25% of cases received inappropriate antibiotic and 70.9% received sub therapeutic dose (20). Continuing overprescription of antibiotics, including ceftriaxone without regulation will result in serious bacterial resistance and at the end there will be loss of very important drug, so the goal of this study was to focus on this problem to alert authority to put strict regulation for antibiotics prescription. So this study aimed to evaluate appropriate use of Ceftriaxone (in terms of indications, dose, frequency and duration of treatment, interactions with other medications and implementation of culture and sensitivity test) in internal medicine wards of Wad Medani teaching hospital in Gezira state, Sudan as well as comparing its use with

reference to the standard of Sudan treatment guidelines and reliable references like BNF and Sanford guide.

Methodology:

Study area setting

This study was conducted in the internal medicine wards at Wad Medani Teaching hospital which is located in Wad Medani city, in Gezira state, central Sudan. The medical bed capacity is 122 beds including different medical specialists. The hospital offered services to approximately 4768 inpatients in 2017.

Study design and population

Prospective cross-sectional study conducted by reviewing all files of the patients of both sexes, who were admitted and received ceftriaxone in internal medicine wards (in the period of November-December 2018) at wad Medani teaching hospital. Ceftriaxone use was evaluated and its appropriateness use was assessed depending on six criteria, namely selection of ceftriaxone, dose, frequency, duration of treatment, culture and sensitivity test and drug-drug interaction. The evaluation depends on Sudan treatment guidelines (21), Sanford guidelines (12) and BNF (13). All patients participated in the study were followed until their treatment with ceftriaxone was completed.

Inclusion criteria:

- Patient age \geq 18 years on ceftriaxone during the study period.
- Files of patients with complete information.

Exclusion criteria:

The file that contains incomplete information in main variable was excluded from this study.

Data collection

Data was collected by the data collection sheet, which was developed based on the world health organization (WHO) criteria for Drug Use Evaluation (22), as well as the drug use evaluation Criteria prepared by the American Society of Health System Pharmacists (23). Data collection format was designed to include data of interesting domains (demographic data: gender, age, date of admission and date of discharge, information regarding Ceftriaxone (indication, dose, frequency of administration and duration of therapy), and implementation of culture and sensitivity test).

Data analysis

The data codes were checked for completeness and entered into the Statistical package for social sciences (SPSS) version 21 for analysis. The WHO drug use evaluation criteria set, namely indication; dose, frequency, duration, drug-drug interaction and culture and sensitivity test were used as major measurements against Sudan national treatment guidelines (STG), BNF and Sanford guide. Appropriateness of indication, dose, frequency and duration of administration of Ceftriaxone in the hospitals was determined by comparing the observed Ceftriaxone prescribing in the chart records to the recommendations in Sudan national treatment guidelines (STG) (Appendix-2), BNF (Appendix-4) and Sanford guide (Appendix-3) where ceftriaxone should be given for the following conditions:

- Aspiration pneumonia 1g once daily use as primary for 7-10 days (Sanford guide)
- Community acquired pneumonia moderate to severe 1-2 g once daily use as an alternative for 7-10 days (STG, BNF)
- Meningitis 2g twice daily use as primary for at least 5 days (STG, BNF)
- SBP 2g once daily use as primary for at least 5 days (Sanford guide)
- Complicated UTI 1-2 g once daily use as primary for 10-14 days (BNF)
- Variceal bleeding 2g once daily use as an alternative for 5-7 days (Sanford guide)
- Cellulitis 2g once per day use as primary for 7-10 days (BNF, Sanford guide)
- Typhoid 2g once daily use as primary for 7-14 days (STG, BNF and Sanford guide)
- Sepsis 2g twice daily use as primary for 10-14 days (Sanford guide)
- Shigellosis 1-2g once daily use as primary for 5 days (Sanford guide)
- Osteomyelitis 2g once daily use as primary for 6-8 weeks (Sanford guide)

The overall appropriateness of ceftriaxone use determines when ceftriaxone was appropriate with respect to each of six criteria.

Finally, descriptive analysis of this data was done.

Ethical consideration

Approval for the study was obtained from the research and ethics committee at the hospital. The study was conducted in accordance with the Declaration of Helsinki, and informed written consent was obtained from all participants in the study.

Results:

Socio-demographic characteristics of patients
A total of 280 admitted patient’s treatment charts containing ceftriaxone injection were analyzed in this study. 114 (40.7%) were females and 166 (59.3%) were males. The mean age of the study population was 52.29 years (SD±20.3 years; range 17 to 102 years). Most of the study participants were in the age group 18-65 years.

Prescription pattern

Ceftriaxone according to Sudan national treatment guidelines and reliable reference BNF and Sanford guide. Table (1).

Table 1: Indication of Ceftriaxone and type of treatment with ceftriaxone for study population

Characteristic	Category	Frequency	Percent	Inappropriate	Appropriate
Indication of ceftriaxone	Alternative	89	31.8 %	45.7%	54.3 %
	Not-indicated	39	13.9 %		
	Primary	152	54.3 %		
Type of treatment with ceftriaxone	Therapeutic	255	91.1 %	91.1%	8.9%
	Empiric	255	91.1 %		
	Specific	0	0.0 %		
	Prophyl	25	8.9 %		

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Indications for ceftriaxone use

The most common reasons for ceftriaxone use was respiratory tract infection (RTI), (35%) followed by gastrointestinal tract (GIT) infection 9.3% and urinary tract infection (UTI) 9.3% based on standard Sudan treatment guideline and reliable reference BNF and Sanford guide. Table (2).

Table 2: Indications for which ceftriaxone was used in the study population

Infection	Frequency	Percent
Aspiration Pneumonia	36	12.9
Community-acquired Pneumonia	64	22.9
Cellulitis	15	5.4
Gastroenteritis	26	9.3
GI bleeding	25	8.9
Meningitis	21	7.5
Osteomyelitis	1	0.4
SBP	18	6.4
Sepsis	3	1.1
Typhoid	6	2.1
UTI	26	9.3
No Indication	39	13.9
Total	280	100

Dosage of administration

The prescribed dose (amount per administration) was 1g or 2g for all types of ceftriaxone indications. The most commonly prescribed dose was found to be 1g in 258 of patients and 2 g in 22 patients. 41% of patients took the dose of ceftriaxone inappropriately and 59% took the dose appropriately as shown in table (3).

Table 3: Dosage of ceftriaxone administration to the study participants

	Inappropriate	Appropriate	Total	P. Value
1 g	112 (43.4%)	146(56.6%)	258	0.004
2 g	3(13.6%)	19(36.4%)	22	
Total	115(41%)	165(59%)	280	

Frequency of ceftriaxone administration

The most common use frequency of administration was twice daily dosing and inappropriate frequency of the administration was found in 68.9% of patients in whom ceftriaxone was given 1 g twice per day, based on standard Sudan treatment guideline and reliable reference BNF and Sanford guide and 50% of cases received ceftriaxone with dose 2g once per day was given inappropriately.

Duration of treatment

212 (75%) Of patients received ceftriaxone for 2-7 days, and 68(24%) for 8-14 days.143 (51.1%) of patients took ceftriaxone with incorrect duration and137 (48.9%) had appropriate duration.

Evaluation appropriateness of ceftriaxone dose with duration of treatment

The dose 1g in duration 2-8 days was common and given inappropriately in 52% of cases.

Concomitant administration of drugs with ceftriaxone

Among the drug co-administered with ceftriaxone, maintenance fluids (46%) were the most commonly used followed by omeprazole (40%) and metronidazole (28.6%).

Concomitant drugs with potential drug-drug interaction

Concomitant drug with major interaction with ceftriaxone was seen with ringer lactate in (3.6%) of cases. Concomitant drug with moderate interaction with ceftriaxone was seen with heparin and warfarin in two cases (0.7%) and also concomitant drug with minor interaction with ceftriaxone were seen with furosemide observed in (12.9%) case and with gentamicin observed in two cases (0.7%). Table (4).

Table 4: Co-administered drugs with potential drug- drug interaction with ceftriaxone in the study population

Co administered drug	Severity of DDI	frequency(n=280)	Percentage
Ringer lactate	Major	10	3.6%
Gentamicin	Minor	2	0.7%
Heparin	Moderate	2	0.7%
Warfarin	Moderate	2	0.7%
Furosemide	Mimor	36	12.9%

Culture and sensitivity test

In this study no culture and sensitivity test was sent to any patient 255 (91.1%) of patients were given ceftriaxone empirically and for 25 (8.9%) Of patients there was no need for culture and sensitivity as shown in table (5).

Table 5: Culture and sensitivity tests in patients prescribed with ceftriaxone in study population

Culture	Frequency	Percent. %
No need for culture	25	8.9
Not done	255	91.1
Done	0	0

Practice of ceftriaxone use versus guidelines

Considering indication, dose, frequency and duration of ceftriaxone used in addition to culture and sensitivity test and drug interaction all cases were found to be inappropriate (100%) based on standard Sudan treatment guideline and reliable reference BNF and Sanford guide. Most inappropriate use of ceftriaxone was attributed to the absence of culture and sensitivity test (91.1%), and inappropriate frequency of administration as shown in fig. (1).

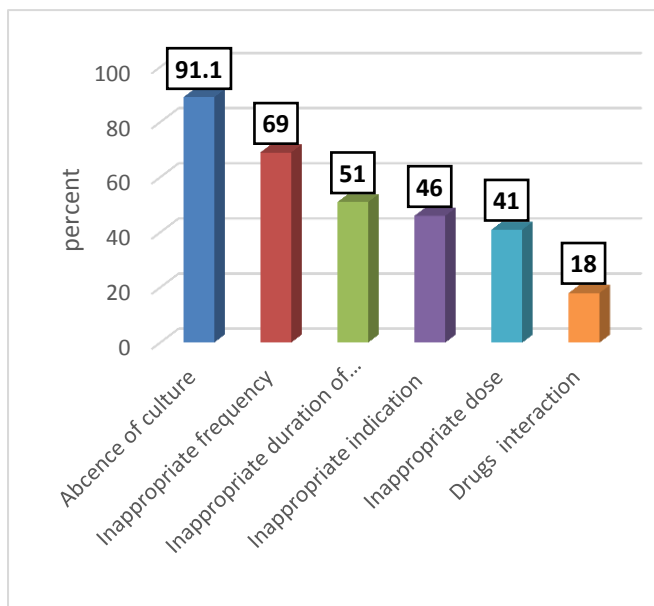


Figure1: Criteria referenced inappropriate use of ceftriaxone in the study population.

Discussion:

In this study a total of 280 admitted patient's treatment chart containing ceftriaxone injection were analyzed. 40.7% were females and 59.3% males. Generally, ceftriaxone was found to be prescribed inappropriately, considering indication, dose, frequency and duration of administration in addition to culture and sensitivity test and drug – drug interaction, this finding was similar to studies done in Tikur Anbessa specialized hospital, Ethiopia (24). This finding was higher than studies done in Ayder referral hospital, Mekelle, Ethiopia (11) and in Flege Hiwot referral hospital, Bahir Dar, North Ethiopia (25) and also higher than study conducted in Korea (26). The difference may be attributed to the availability of DTC and due to the fact that, these studies done in both medical and surgical wards but this study was done only in medical wards. The major cause of inappropriate use of ceftriaxone in this study was found to be, the continuous use of ceftriaxone as empirical therapy in 91% of cases.

Culture and sensitivity test:

In this study (91%) of participant took ceftriaxone empirically. This finding was similar to the studies conducted in: Elobeid, in Western Sudan which revealed that, most patients received antibiotics empirically without performing culture and sensitivity test (19) and in the study carried out in Tikur Anbessa specialized hospital in Ethiopia,

87.3% of patients received ceftriaxone without implementation of culture and sensitivity test (24), and in Medicine and Surgery inpatient Departments of K.S Hegde teaching Hospital, in Mangalore, India (83.5%) (27), Victorian hospitals, Australia (82%) (27) And also in line with the study done in medical and emergency wards of Gondar university referral hospital, Ethiopia (79.5%) (28) But higher than the study done at 10 university hospitals in Korea (33.5%) (26). The explanation for not requesting culture and sensitivity test by physician, could be due to the fact that culture and sensitivity takes time, about three days for laboratory result to be available in addition to the high cost of culture and sensitivity test.

Frequency:

In this study twice daily dosing account for 71% of patients and inappropriate frequency of administration observed in 68.9% of cases. This finding was in line with studies done in medical and emergency wards of Gondar university referral hospital, Ethiopia (78.3%) (28) And in medical and emergency wards of Tikur Anbessa specialized hospital, Ethiopia (80.3%) (24).

Duration:

The mean duration of ceftriaxone in the study was 6.18 which was lower than studies done in Mekelle, Ethiopia 7.2 (11), Korea 10.3 (26), Tikur, Ethiopia 10.39 (24) and India 7 (29). The difference may due to the fact that, most of patients admitted at Wad Medani Teaching Hospital were not terminally ill. The inappropriate duration was found to be in 51 % of cases which was similar to studies done at Tikur, Ethiopia (50%) (24), Gondar, Ethiopia (47%) (28) and Korea (42.8%) (26) And was higher than the study conducted at Bahir Dar, North Ethiopia (18%) (25). The difference may be attributed to the fact that, physician shorten duration of the ceftriaxone therapy and shifted to oral treatment putting in consideration the economic status of patients by decreasing the cost resulting from long stay in the hospital.

Dose:

In this study the most commonly prescribed dose was found to be 1 g account for 92% of cases this finding was similar to the study done at Tikur, Ethiopia (87.9%) (24) and Gondar, Ethiopia (70%) (28) And higher than studies done in Korea (15%) (26) and Mekelle, Ethiopia (20.6%) (11). the

difference may be, because, most prescribers at Wad Medani Teaching Hospital tend to give dose of 1g twice per day. In the present study, 41% of patients took ceftriaxone with incorrect dose this finding was higher than the study done in Bahir Dar, North Ethiopia (14%) (25). Considering dose and frequency together in this study it was found that the dose of 1g twice per day was the most common and the main cause of ceftriaxone inappropriate use, this may be because the prescriber tends to give 2g/day in divided dose. Considering dose and duration together, it was observed that a 1g dose for 2-8 day was the most common and the most leading cause of inappropriate use of ceftriaxone, this may due to the prescriber tend to give low doses for a short time.

Indication:

In this study the most common indication was community acquired pneumonia and aspiration pneumonia (35%) this finding was similar to studies done at Tikur, Ethiopia (35.5%) (24) and Mekelle, Ethiopia (35.1%) (11). In this study inappropriate indication of ceftriaxone was observed in 45.7% of cases this finding is higher than study done in Bahir Dar, North Ethiopia (8%)(25) and in medical and emergency wards of Gondar university referral hospital, Ethiopia (3.5%)(28) the difference may be attributed to the absence of the DTC at Wad Medani Teaching Hospital. In this study, 13.9% of patients took ceftriaxone without indication; this finding was higher than study done in India in which 10.75 % of cases received antibiotic for fever (30). The high proportion of ceftriaxone use without indication may be attributed to the prescriber who might prescribed ceftriaxone as prophylaxis fearing of nosocomial infection.

Concomitant Drugs:

In this study the most common co-administered drug use with ceftriaxone were maintenance intravenous fluids (46%) followed by omeprazole (40%) and metronidazole (28.6%). This finding was similar to study done in medical and emergency wards of Gondar university referral hospital, Ethiopia where fluid was given to 43.8% of cases and metronidazole for 17.5 of the cases (28) . In this study ceftriaxone was co-administered inappropriately with ringer lactate, heparin, warfarin, gentamicin and frusemide. Co-administered ceftriaxone with ringer lactate which

constitute major drug-drug interaction was observed in (3.6%) of cases and this finding was lower than studies done at Tikur Anbesa Specialized Hospital, Addis Ababa 6.7% of cases (24) and lower than study done in Mekelli, Ethiopia(33.1%) case (11). The difference may be because prescriber at Wad Medani teaching hospital were aware about the major interaction between ceftriaxone and calcium chloride which is one of the component of ringer lactate.

Conclusions:

This study revealed very high inappropriate use of ceftriaxone in internal medicine wards of Wad Medani Teaching Hospital. The majority of inappropriate use was resulting from giving the treatment regimen without implementing culture and sensitivity test. This may lead to the emergence of resistant bacteria to ceftriaxone and ultimately result in treatment failure and high cost of eradicating resistant pathogens.

Recommendations

An extensive effort to decrease inappropriate use of antibiotic and to raise of awareness of prescribers via implementing educational programs is recommended. Prescriber should adhere to national protocol and current evidence-base guidelines and should restrict ceftriaxone only for proven infections. Continuous use of ceftriaxone should be done after culture and sensitivity test result whenever it is possible. Decrease of inappropriate use of antibiotic can be done via implementation of the antimicrobial management program which termed antimicrobial stewardship. Clinical pharmacist should be part of health providers team in all hospitals.

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References:

- [1.] Kumar, J; Shaik, M; Kathi, M; Deka, A and Gambhir, S. Prescribing indicators and pattern of use of antibiotics among medical outpatients in a teaching hospital of Central Nepal. Journal of College of Medical Sciences-Nepal6 (2):7-13. 2010.
- [2.] Katzung, B G; Masters, S B and Trevor, A J. Basic & clinical pharmacology.

- McGraw-Hill Companies. United State of America: 789. 2012.
- [3.] Holloway, K; Green, T and Organization, W H. Drug and therapeutics committees: a practical guide. 2003.
- [4.] Fleming-Dutra, K E; Hersh, A L; Shapiro, D J; Bartoces, M; Enns, E A; File, T M; Finkelstein, J A; Gerber, J S; Hyun, D Y and Linder, J A. Prevalence of inappropriate antibiotic. 2016.
- [5.] Ingram, P; Seet, J; Budgeon, C and Murray, R. Point-prevalence study of inappropriate antibiotic use at a tertiary Australian hospital. *Internal medicine journal*42 (6):719-721. 2012.
- [6.] Ceyhan, M; Yildirim, I; Ecevit, C; Aydogan, A; Ornek, A; Salman, N; Somer, A; Hatipoğlu, N; Camcioglu, Y and Alhan, E. Inappropriate antimicrobial use in Turkish pediatric hospitals: a multicenter point prevalence survey. *International Journal of Infectious Diseases*14 (1):e55-e61. 2010.
- [7.] Ndiokubwayo, J B; Yahaya, A A; Dester, A; Ki-Zerbo, G; Asamoah-Odei, E and Keita, B. Antimicrobial resistance in the African Region: Issues, challenges and actions proposed. *African Health Monitor*16:27-30. 2013.
- [8.] Eliopoulos, G M; Cosgrove, S E and Carmeli, Y. The impact of antimicrobial resistance on health and economic outcomes. *Clinical Infectious Diseases*36 (11):1433-1437.2003.
- [9.] Pereira, L M P; Phillips, M; Ramlal, H; Teemul, K and Prabhakar, P. Third generation cephalosporin use in a tertiary hospital in Port of Spain, Trinidad: need for an antibiotic policy. *BMC infectious diseases*4 (1):59.2004.
- [10.] Sintchenko, V; Coiera, E and Gilbert, G L. Decision support systems for antibiotic prescribing. *Current opinion in infectious diseases*21 (6):573-579.2008.
- [11.] Abebe, F A; Berhe, D F; Berhe, A H; Hishe, H Z and Akaleweld, M A. Drug use evaluation of ceftriaxone: the case of Ayder Referral Hospital, Mekelle, Ethiopia. *International Journal of Pharmaceutical Sciences and Research*3 (7):2191.2012.
- [12.] Sanford, J; Gilbert, D; Chambers, H; Eliopoulos, G; Moellering, R and Saag, M. The Sanford guide to antimicrobial therapy 2010–2011. Jeb C. Sanford, Wavre, Belgium.2011.
- [13.] Mehta, D. British national formulary (BNF). London, Pharmaceutical Press. 2018.
- [14.] Kheder, S I. Cephalosporins usage and resistance trend in a Sudanese hospital surgical wards. *Journal of Pharmaceutical and Biomedical Sciences (JPBMS)* 11(11).2011.
- [15.] Committee, P F. BNF for children (BNFC) 2017-2018, Pharmaceutical Press.2017.
- [16.] MedscapeDrugInteractionChecker. Available from <http://www.referencemedscape.com/drug-interactionchecker> [Last accessed on 2018 Dec 20].
- [17.] Awad, A; Eltayeb, I and Baraka, O. Changing antibiotics prescribing practices in health centers of Khartoum State, Sudan. *European journal of clinical pharmacology*62 (2):135.2006. 18.
- [18.] Ibrahim, M E; Bilal, N E; Magzoub, M A and Hamid, M E. Prevalence of extended-spectrum β -lactamases-producing *Escherichia coli* from hospitals in Khartoum State, Sudan. *Oman medical journal*28 (2):116.2013.
- [19.] Elfaki, A. Assessment of Antibiotics prescription in Hospitalized Patients at Elobeid Hospital, Sudan. *Sudan Journal of Medical Sciences*4 (3).2009.
- [20.] Elbur, A I; Yousif, M A E R; ElSayed, A S A and Abdel-Rahman, M E. An audit of prophylactic surgical antibiotic use in a Sudanese Teaching Hospital. *International journal of clinical pharmacy*35 (1):149-153.2013.
- [21.] Almahadi, O Z B a A F. Sudan National Treatment guidelines 2014: 92.2014.
- [22.] Holloway, K; Green, T and Organization, W H. Drug and therapeutics committees: a practical guide.2003.
- [23.] Phillips, M; Gayman, J and Todd, M. ASHP guidelines on medication-use evaluation. American Society of Health-system Pharmacists. *American Journal of*

- Health-System Pharmacy 53 (16):1953-1955.1996.
- [24.] Sileshi, A; Tenna, A; Feyissa, M and Shibeshi, W. Evaluation of ceftriaxone utilization in medical and emergency wards of Tikur Anbessa specialized hospital: a prospective cross-sectional study. BMC Pharmacology and Toxicology 17 (1):7.2016.
- [25.] Bantie, L. Drug use evaluation (DUE) of ceftriaxone injection in the in-patient wards of Felege Hiwot Referral Hospital (FHRH), Bahir Dar, North Ethiopia. Int J Pharm Sci 4:671-676.2014.
- [26.] Lee, H; Jung, D; Yeom, J S; Son, J S; Jung, S-I; Kim, Y-S; Kim, C K; Chang, H-H; Kim, S-W and Ki, H K. Evaluation of ceftriaxone utilization at multicenter study. The Korean journal of internal medicine 24 (4):374.2009.
- [27.] Robertson, M B; Dartnell, J G; Korman, T M; Ioannides-Demos, L L; Kirsa, S W; Lord, J A; Munafa, L and Byrnes, G B . Ceftriaxone and cefotaxime use in Victorian hospitals. Medical Journal of Australia 176 (11):524-529.2002.
- [28.] Ayele, A A; Gebresillassie, B M; Erku, D A; Gebreyohannes, E A; Demssie, D G; Mersha, A G and Tegegn, H G. Prospective evaluation of Ceftriaxone use in medical and emergency wards of Gondar university referral hospital, Ethiopia. Pharmacology research & perspectives 6 (1):e00383.2018.
- [29.] Jyothi, K and Babu, D. Drug utilization evaluation of Cephalosporins in general medicine units of rural tertiary care hospital. Int J Curr Pharm Res 4(2):88-91.2012.
- [30.] Gururaja, M. Cephalosporin utilization evaluation in a University Teaching Hospital: a prospective study. Journal of Drug Delivery and Therapeutics 3 (2).2013.