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Evaluation of Fever Management Practices in Rural India

Research Article

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Abstract

Background: Precision regarding treatment of fever is reportedly low among the rural regions of India, leading to its irrational management. This study evaluates fever management practices followed by physicians at primary health centre and correlate this with standard fever management guidelines.

Methods: One hundred and forty patients admitted to hospital with fever were enrolled in the study. Patient's demographic profile and presenting symptoms were precisely studied along with their vital parameters. Patients were divided into two groups (A&B), with and without treated as per standard guidelines. Duration of illness, treatment with various drugs and clinical investigation of patients with fever were analysed statistically as outcome analysis.

Results: Majority of patients (47.86 %) belonged to age of 18-30 years. Symptoms related to Upper respiratory tract infection (URTI), such as cough and rhinorrhoea, were the most common symptoms (104 patients, 74.28%). Most common clinical diagnosis was viral URTI in both the groups followed by enteric fever, acute gastroenteritis etc. No statistical significance observed in duration of illness in both groups. All the patients of group A were advised laboratory investigations to confirm the diagnosis as per the standard management protocol. Most frequently ordered investigations were complete blood count and peripheral smear for malarial parasite. Average number of drugs prescribed was 2.94 and 4.03 in group A and B (p value 0.001). 8.33% and 18.75% were belonged to category of more than 5 drugs per prescription (polypharmacy) in group A and B respectively. Amoxicillin and Azithromycin were the most preferentially prescribed antibiotics. 90% and 20% of antibiotics were prescribed appropriately (P=0.01) as per guidelines in group A and B respectively. Co-prescription of famotidine, pantoprazole etc was significantly high in group B ($p<0.05$).

Conclusion: A large number of patients were prescribed with antibiotics without accurate confirmation of bacterial infections which was contradictory to standard guidelines of fever management practice. Hence increased awareness for rational fever management is desirable among clinical practitioners in rural India.

Keywords: Fever; Management Principles; Symptomatology; Clinical Examination; Laboratory Investigations for Fever; Antibiotics Usage.

Introduction

Fever is considered as one of the most common clinical reasons for physicians, accounting for about one-third of all presenting conditions in adult population [1, 2]. Fever, an elevation in core body temperature above the daily range (98.6°f) for an individual, is a characteristic feature of most infections but is also found in a number of non-infectious diseases such as autoimmune and carcinoma.

Fever is a physiological mechanism with beneficial effects in fighting infection and it is usually not associated with long-term neurologic complications. The only purpose for treating fever must be to relieve the discomfort [3]. Concerns of patients about serious causes of fever (ie, severe bacterial infections) and misconceptions about fever as a sufficient trigger of brain damage have led to the spreading of 'fever-phobia'. Several studies have reported a high percentage of adult population consuming antipyretics and antibiotics even when there is minimal or no fever, with wrong dosages or with insufficient intervals between the doses [3, 4].

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The inappropriate management of fever with irrational use of antipyretics or antibiotics may delay the diagnosis and increase the risk of overdose or significantly contributing to antibiotic resistance. Moreover, other factors may increase drug toxicity such as the alternate/combined use of two antipyretics or combination of antibiotics, the use of other formulations with other medicaments, and the administration of these drugs in the presence of contraindicated underlying diseases. Finally, overtreatment may have a significant economic impact in low-middle income and high income countries. Antipyretics and antibiotics are most preferred self-method of managing fever and there has been an increase in this preference over the past two decades from 67% to more than 90% (91% to 95%) [4].

Fever can pose diagnostic and therapeutic challenge to the health workers, particularly in limited resource settings. A number of viruses, bacteria, protozoa and rickettsia can cause fever [5, 6]. The non-specificity of symptoms and signs and lack of availability of accurate diagnostics not only test the clinical mettle of even astute physicians but often leads to irrational use of antibiotics and antimalarials. Some fever syndromes have a more clear localization to skin and soft tissue (abscess or cellulitis), meninges or neural tissue (headache, neck-stiffness, altered sensorium with or without focal neurological signs), respiratory tract (cough, breathlessness), or urinary tract (dysuria, haematuria). These syndromes have better developed guidelines for their management. On the other hand, acute unidentified fever syndromes (suchas fever-rash, fever-myalgia, fever-arthralgia, fever-hemorrhageand fever jaundice) haveoverlapping etiologies, which makes their diagnosis and management even more challenging [7, 8].

In order to rationalise and standardise the symptomatic management of fever in adult population, national health agencies, WHO and scientific societies have produced and disseminated clinical guidelines. It has been demonstrated that patients do not fully comply with these recommendations of use of prescription drugs, as they used to employ traditional physical means and administer antipyretics and antibiotics with inappropriate indications and posology. Moreover, important discrepancies have been reported between the practices of healthcare professionals and the recommendations of guidelines [4]. Considering the above-mentioned parameters in treatment of fever, this study has been designed with aim of evaluating management practices for fever in rural India.

Methodology

This was a cross sectional observational study conducted in two primary health care centres of the western India to know the management principles of fever being followed at rural level. The study protocol was approved by the institutional ethics committee and written informed consent was obtained from all patients before enrolling them for the study.

Study Participants

All the patients presented to the primary health care centre of ≥ 18 years and of any gender, having chief compliant of fever for at least one day with any other associated symptoms were enrolled for the study. Patients with delirium, serious patients requiring referral to higher centrefacility immediately and those requiring intensive care unit admissions were excluded from the study.

Sample size

Considering the prevalence of fever of unidentified origin in Indian populations around 80% [9, 10], sample size is 126 at 7% precision and 95% confidence interval for this study. Few patients may drop out or lost to follow up (10%) in the entire duration of the study, so 140 patients were enrolled for the study. Considering the dropout total 140 patients were enrolled for the defined time duration of 6 months (November-April 2019).

Study procedure/method of data collection

All the patients fulfilling inclusion-exclusion criteria were interviewed by the principle investigator. Demographic details, clinical examination, history of past and family illnesses, drug therapy and any complications were recorded in a structured case record form using case papers of the patients and interview. All the laboratory investigations carried out for the patients and change in drug therapy after investigations was also recorded. Disease related details like temperature measurement method and physical treatment, patient characteristics (age, gender and main symptoms, including maximal temperature), medication taken with or without prescription, antibiotics consumed or not and medication advice followed or not. Physicians were also asked to give information about temperature measurement during the consultation and the final diagnosis (like upper/lower respiratory infection, enteric fever, malaria, sore throat, isolated fever, gastroenteritis, rash, influenza or other).

Fever management protocol

All the patients' treatment protocol was compared with the standard treatment guidelines issued by the WHO for fever management and local standard treatment guidelines of the state.

As per all the guidelines for management of fever following steps are important:

o Take detail history of fever (temp. reading, type of fever, shivering/perspiration present or not) and associated symptoms.
o With help of symptoms of the system involved each to clinical diagnosis like respiratory tract illness, GI infection, Urinary tract infection, malaria etc (provision/clinical diagnosis).
o Confirm the diagnosis with relevant laboratory tests (like CBC, S. widal test, blood smear examination, stool or urine examination etc) – confirmed diagnosis.
o Give treatment both definitive and symptomatic as per the confirmed diagnosis.
o If started with the empirical treatment, before laboratory investigations, change to definitive treatment.

All case sheets were reviewed for following of these steps and divided in to two groups (A & B). Group A included the patients who were treated as per the guidelines and group B included the patients who were not treated as per the standard guidelines. For ease of data analysis, those patients advised any laboratory investigations for confirmation of diagnosis and treatment were grouped as A and those who were not advised laboratory investigations were grouped as B.

Outcome Analysis

Use of antipyretics, antibiotics and other supportive medicines as well as outcome of fever was compared of the patients given treatment as per standard guidelines with those not treated as per guidelines.

Ethical Considerations

The study protocol was approved by the institutional ethics committee and written informed consent was obtained from all patients before enrolling them for the study. Participants did not receive compensation for their participation in this study. All the patients were given assurance about protecting data confidentiality and anonymity. Copies of the consent forms were given to participants and they had the right to refuse participation or withdraw from the study at any stage without hampering their medical treatment.

Statistical Analysis

Data analysis was done using Microsoft excel 2010. All the data are presented as actual frequencies, percentages, mean and standard deviation. Chi square test was used for comparison of qualitative data and students't test was used for quantitative data. P value less than 0.05 was considered significant.

Results

Total 140 patients having fever were enrolled for the study and their fever management protocol were evaluated. Out of these 140 patients, 60 patients were managed as per standard treatment guidelines (group A) and 80 patients were not managed as per the guidelines (group B). Age and gender wise distribution of patients of both groups is shown in table 1. Majority of patients (47.86 %) belonged to age of 18-30 years and 30-60 years (47.14 %) while only 5% patients belonged to > 60 years of age. 52.14 % patient were male and 47.86 % were females. No statistically significant difference was found among demographic parameters (p>0.05) in both groups.

Presenting symptoms of the patients and their body system wise distribution is shown in table 2. Symptoms related to Upper respiratory tract infection (URTS), such as cough and rhinorrhoea, were the most common symptoms (104 patients, 74.28%) as per body system wise distribution. Symptoms related to gastrointestinal system and urinary system were less frequently observed. There was no significant difference between presenting symptoms among both the groups (p>0.05)

All the patients were subjected to detailed history and clinical examination. Patient's vital parameters are shown in table 3. Mean temperature of patients was 99.45 and 99.42 in group A and group B respectively. Mean heart rate was 87.39 and 87.45 in group A and B respectively. The mean systolic and diastolic blood pressure in group Apatients was found to be 115.37 mmHg and 78.29 mmHg respectively and in group B it was found to be 115.37 mmHg and 78.29 mmHg respectively, with no statistically significant difference among the groups.

Clinical diagnosis was arrived in all the patients and most common disease was URTI in both the groups followed by enteric fever, acute gastroenteritis and urinary tract infection as shown in figure 1. There was no statistically significant difference was found among provisional diagnosis of the patients (p>0.05). Even there was no statistical significance observed in duration of illness of patients enrolled in both the groups for treatment purpose (table 4).

All the patients of group A were advised some or other laboratory investigations to confirm the diagnosis as per the standard management protocol. Most frequently ordered investigations were complete blood count and peripheral smear for malarial parasite. Other laboratory parameters evaluated were liver function test, urine examination, stool examination, blood and sputum culture etc as shown in figure 2. Due to lack of confirmatory tests in group B patients, no definitive diagnosis was reached and thy were treated based on clinical judgement only.

Drug treatment given for the fever patients was compared among both groups. Average number of drugs prescribed was 2.94 and 4.03 in group A and B (p value 0.001). Out of total 140 patients, 56.25% and 43.75% belonged to category of 1-3 drugs prescribed in group Aand Brespectively while 16.66% and 37.5% were belonged to category of 4-5 drugs per prescription and 8.33% and 18.75% were belonged to category of more than 5 drugs per prescription in group A and B respectively (Table 5). There was significantly higher number of drugs prescribed per prescription in group B. (p=0.001).

Table 1. Demographic Profile of study Patients.

Parameter	Group A n(%)	Group B n(%)	P value*
Age in years			
18-30	25 (41.6)	42 (52.5)	0.428
31-60	32 (53.33)	34 (42.5)	
>60	3 (5)	4 (5)	
Gender			
Male	30 (50)	43 (53.75)	0.66
Female	30 (50)	37 (46.25)	

Group A =Patients treated as per the standard guidelines of fever management; Group B = Patients not treated as per the standard guidelines of fever management, *chi-square test

Table 2. Presenting Symptoms of Patients.

Body system affected	Group A n(%)	Group B n(%)	P value*
Fever	60	80	
Respiratory symptoms			0.550
Cough	47 (78.33)	57 (71.25)	
Rhinorrhoea	13 (21.66)	12 (15)	
Lacrimation	7 (11.66)	12 (15)	
Sore Throat	21 (35)	35 (43.75)	
Breathlessness	1 (1.66)	1 (1.25)	
Gastrointestinal Tract			0.67
Vomiting	7 (11.66)	5 (6.25)	
Diarrhoea	3 (5)	2 (2.5)	
Nausea	1 (1.66)	4 (5)	
Constipation	1 (1.66)	1 (1.25)	
Anorexia	3 (5)	3 (3.75)	
Urinary Tract			>0.05
Urinary hesitancy	0	1 (1.25)	
Haematuria	0	1 (1.25)	
Burning pain during micturition	4 (6.66)	4 (5)	
Musculoskeletal System			0.37
Headache	21 (35)	24 (30)	
Generalized Body ache	22 (36.66)	18 (22.5)	
Abdominal Pain	7 (11.66)	5 (6.25)	
Joint Pain	5 (8.33)	1 (1.25)	
Skin			>0.05
Furuncle (BOIL)	0	1 (1.25)	
Tinea	2 (3.33)	1 (1.25)	
Icterus	2 (3.33)	2 (2.5)	
CNS			0.71
Giddiness	8 (13.33)	6 (7.5)	

Group A =Patients treated as per the standard guidelines of fever management; Group B = Patients not treated as per the standard guidelines of fever management, *chi-square test

Table 3. Vital Parameters of Patients.

Parameter	Group A n(%)	Group B n(%)	P value*
Temperature (			
98.6-99	22 (36.66)	32 (40)	0.361
99.1-100	34 (56.66)	38 (47.5)	
100.1-101	3 (5)	6 (7.5)	
101.1-102	0	2 (2.5)	
102.1-103	0	2 (2.5)	
103.1-104	1 (1.66)	0	
Heart Rate			0.35
60-70	1 (1.66)	1 (1.25)	
71-80	2 (3.33)	1 (1.25)	
81-90	37 (61.66)	45 (56.25)	
91-100	10 (16.66)	21 (26.25)	
>100	10 (16.66)	12 (15)	
Blood Pressure (mmHg)			>0.05
Systolic Blood Pressure	117.17	115.37	
Diastolic Blood Pressure	78.51	78.29	

Group A =Patients treated as per the standard guidelines of fever management; Group B = Patients not treated as per the standard guidelines of fever management, *unpaired t test, chi-square test as appropriate

Figure 1. Clinical diagnosis of Patients.

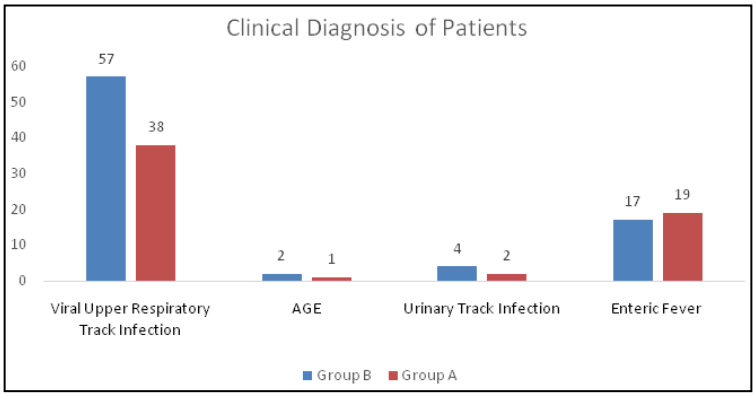

Table 4. Duration of Illness of Patients.

Duration of illness	Group A; n (%)	Group B; n (%)	P value
1-3 days	38 (63.33)	64 (80)	0.075 (NS)
4-6 days	10 (16.66)	11 (13.75)	
7-10 days	9 (15)	4 (5)	
11-15 days	3 (5)	1(1.25)	

Group A =Patients treated as per the standard guidelines of fever management; Group B = Patients not treated as per the standard guidelines of fever management

Figure 2. Clinical diagnosis of Patients.

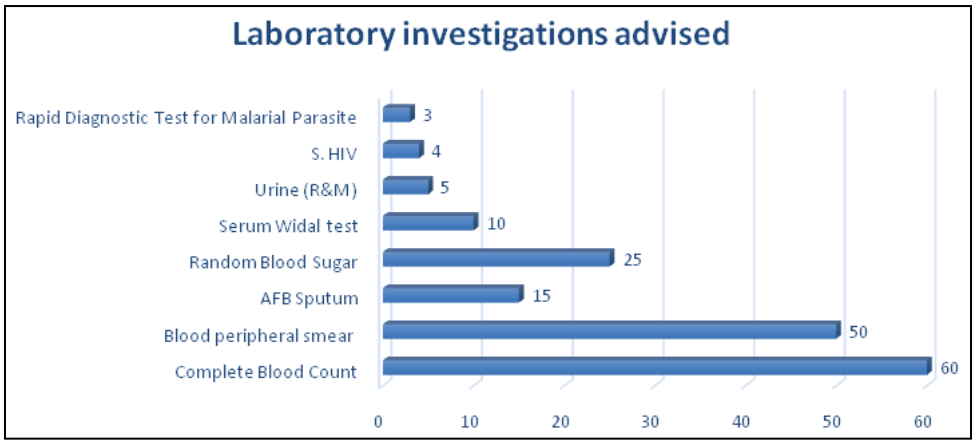

Table 5. Total No. of drugs prescribed to Patients.

Number of Drugs Prescribed	Group A; n (%)	Group B; n (%)	P value
1-3	45 (56.25)	35 (43.75)	0.00107 (significant)
4-5	10 (16.66)	30 (37.5)	
More than 5	5 (8.33)	15 (18.75)	

Group A =Patients treated as per the standard guidelines of fever management; Group B = Patients not treated as per the standard guidelines of fever management

Analysis of drug therapy among both the group patients is shown in table 6. All the patients were prescribed antipyretic, i.e. paracetamol with few patients requiring additional ibuprofen for control of fever. Antibiotics were prescribed to 50% and 100% of patients in group A and B respectively with statistically significant difference (p=0.03). It was found that Amoxicillin and Azithromycin were the most preferentially prescribed antibiotics by the physicians to patients with symptoms of fever.On comparing the use of antimicrobials with the standard treatment guidelines, it was found that 90% and 20% of antibiotics were prescribed appropriately (P=0.01). Prescribing antihistaminic drugs by physicians as an adjuvant therapy to patients suffering from symptoms of fever were reportedly found to be non-significant in both the groups respectively (p>0.05) while drugs acting on GIT like famotidine, pantoprazole etc were prescribed significantly high in group B (p<0.05).

Table 6. Type of drugs prescribed to Patients.

Sr No.	Type of Drug	Group A; n (%)	Group B; n (%)	P value*
		N=60	N=80	
1.	**Antipyretic**			
	Paracetamol	60 (100)	80 (100)	>0.05
	Ibuprofen	5 (8.33)	8 (10)	
2	**Antibiotic**			
	Amoxicillin	12(20)	10 (12.5)	0.032
	Azithromycin	12 (20)	40 (50)	
	Norfloxacin	2(3.33)	10 (12.5)	
	Levofloxacin	1(1.67)	12 (15)	
	Doxycycline	1 (1.67)	4 (5)	
	Ciprofloxacin	2(3.33)	8 (10)	
	No antibiotic	30 (50)	0	
	Antibiotic usage appropriateness*	54 (90%)	16 (20%)	0.01
3.	**Antihistaminic Drugs**			
	Levocetrizine	5 (8.33)	10 (12.5)	
	Chlorpheniramine Maleate	40 (66.66)	65 (81.25)	0.134
	Nil	15 (25)	5 (15)	
4.	**Drugs acting on GIT**			
	famotidine=1	10 (16.66)	68 (18.75)	0.05
	omeprazole=2	2(3.33)	2(2.5)	
	pantoprazole=3	0	10 (12.5)	
	ORS	6(10)	8 (10)	
	Nil	42 (70)	0	

Group A =Patients treated as per the standard guidelines of fever management; Group B = Patients not treated as per the standard guidelines of fever management, *unpaired t test, chi-square test as appropriate

Discussion

This cross-sectional study is the first of its kind investigating the clinical profile of diverse group of patients suffering from a common clinical symptom of fever and its management in rural areas of western India. Our sample was drawn from patients of different ages came for treatment of fever to primary health care centres in Gujarat and analysed for its management comparison with standard treatment guidelines issued by WHO or state government.

Evidences pertaining to Upper respiratory tract infections (URTIs) are the most commonly encountered diseases for visiting the doctor, in all groups of patients. URTIs are the major causes of morbidity and mortality with a worldwide disease burden estimated at 112 900 000 and 3.5 million deaths, respectively which was also coinciding with the results of this study that reveals URTIs as most prevalent cause of fever in majority of patients followed by Acute gastric enteritis, UTI and enteric fever [11].

Our study found that 28.5% of patients reported using antibiotics without undergoing laboratory tests to confirm the diagnosis for bacterial aetiology. Comparatively, a similar study was conducted by Y. Lui et al., 1999, found a slightly lower prevalence of use of antibiotics (25.1%) amongst 203 out-patients in Taiwan without undergoing laboratory examination [1]. Another study conducted in Northern Uganda showed a much higher prevalence of reported antibiotic use of 62.2% without performing lab tests contributing a prevalence of 30.4%. This considerable difference in reported use could likely be as a result of the high prevalence of non-prescription use of antimicrobials in Northern Uganda (75.7%) [2]. Again, another study at two hospitals in Ghana found a higher prevalence of antibiotics in urine (64%) [3].

The significant pervasiveness of prior antibiotic use found in this study could be attributed to the proliferation of antibiotic sources, lax drug regulatory legislation and insidious exposure to antibiotics used in clinical practice and this kind of increased and inappropriate use of antibiotics has serious implications since it contributes to selective pressure, favouring the development antibiotic resistance [4, 12, 13]. Earlier studies reveals that, ceftriaxone and cefixime seemed to be the first line of antibiotic treatment for enteric fever however despite of susceptibility, clinical non-response was seen in around 10 per cent of the patients who needed combinations of antibiotics with penicillin's and macrolides as choice of agents in treatment of fever [14, 15].

Interestingly, more than 25% of patients among the 'fever symptom group with no pathological' were prescribed antibiotics at primary health care centres. In accordance with treatment guidelines and recommendations, only patients who have a confirmed infectious diagnosis are expected to be given an antibiotic pre-

scription [13, 16, 17]. Nonetheless, empirical or presumptive antibiotic therapy is also accepted when the clinical diagnosis, based on the presence of a strong clinical suspicion of bacterial infection, is substantiated by relevant medical history and clinical findings [13].

According to the WHO and the Indian National Treatment Guidelines for Antimicrobial Use, presumptive therapy is typically a one-time treatment given for clinically presumed infection while waiting for the laboratoryinvestigations [16, 17]. According to the WHO and the Indian National Treatment Guidelines for Antimicrobial Use, presumptive therapy is typically a one-time treatment given for clinically presumed infection while waiting for the pathological report [18]. It was distinctly observed that the average duration of treatment was lower in group of patients undergone pathological examination resulting in lower number of drugs prescribed which needs to be encouraged. There may be an increase in compliance, lower cost of therapy and decreased risk of drug interactions with reduced duration of treatment supported by earlier studies investigating fever of unknown origin justified that duration of illness and treatment extends in case of lack of pathological examination [19, 20].

The practice of prescribing antibiotics to patient groups with no registered bacterial infection in the absence of laboratory confirmation could not be considered to be rational. Among the patients with COPD and RHD, the aetiology of the current episode of hospitalisation could potentially be expected to be non-bacterial (e.g, viral infection). However, this could not be confirmed owing to the absence of laboratory investigations. It is worth mentioning here that prolonged empirical antibiotic treatment without a clear evidence of infection is one of the causes of the development of antibiotic resistance. A higher incidence of prescribing macrolides, cephalosporinsand fluoroquinolone classes is further supported by Van Boeckel et al., who observed a significant increase in the consumption of fluoroquinolones and cephalosporins globally over the past decade. This increase was mainly attributed to the increased rates in India and China [21].

In this study both the duration of treatment and the duration of antibiotic treatment were longer in patients without undergoing laboratory examination, possibly because of random use of drug combination without proper justified etiological examination. This association of longer duration of illness and antibiotic treatment in patients without laboratory investigations has also been found in previous studies as well [22, 23].

Irrational use of antibiotics contributes towards difficulties faced in trying to diagnose specific diseases without the access to diagnostic tools at health facilities. Various other barriers substantiating reason for irrational use of antibiotics are the lack of funds for further diagnostic tests, the shortage of specialists at referral facilities, deficiencies of the laboratory services (unreliable and poorly equipped), the limited access to communications and lack of institutional support and opportunities for training.

A large number of patients were screened over a year period; this obviates seasonal variations in infectious aetiology, which would affect antibiotic prescribing strategy with collaboration of pathological analysis. The same form was used for the data collection and the process was supervised and monitored by same person at all hospitals to improve the reliability of the data. The method of collection of data used in the study is robust and reliable. In accordance with one of the WHO goals of the 'Global Action Plan' and in view of limited knowledge of antibiotic use and resistance patterns, our study suggests that there is a need to conduct similar long-term surveillance studies globally.

Conclusion

A larger number of patients suffering from fever with their prescribing occasions were recorded for the study. It was evidently observed that fever was a factor leading to antibiotic prescription at health care facility. Large number of patients without any laboratory investigations and without confirmation of bacterial infections were prescribed with antibiotics, which could not be justified. Broad-spectrum antibiotics with irrational combinations of antibiotics with other adjuvant therapeutics agents were commonly prescribed in the study for non-indicated conditions may contribute to elevated duration of treatment. If microbiology reports could have confirmed the aetiology, some of these might have been categorised in the non-bacterial group and antibiotic misuse can be minimised. However, this was not possible to study in depth owing to the absence of confirmed aetiology and the nature of the study design (observational). Educational interventions and continuous learning programs can be implemented for all practitioners for rational use of drugs specially antimicrobials.

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