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A PROSPECTIVE OBSERVATIONAL STUDY OF AETIOLOGY AND OUTCOME OF FEVER PATIENT ADMITTED IN D.M.C.H., LAHERIASARAI, DARBHANGA

Medicine

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ABSTRACT

Background: The objective of this study was to describe aetiology and outcome of fever among patients in DMCH, Laheriasarai, Bihar.
Methods: This was an observational, prospective study conducted in DMCH, Laheriasarai, Bihar. Between March 2019 and February 2020, adult patients admitted to the hospital with temperature ≥ 38.0°C were included consecutively and followed during the hospitalisation period. Demographic and clinical data were collected and analysed for each patient. Associations were sought between death and various clinical and demographic variables.
Results: One hundred patients were included, 66 male and 34 female. Mean fever duration was 28.02days. All were having fever of more than 3 days duration and temp. more than 38^0 C and all were more than 18 yrs. of age. Informed consent was taken. Details of the sociodemographic, clinical, pathological, biochemical and radiological parameters were documented and presented as tabular, graphical and statistical means. Statistical analyses were conducted using widely available and - accepted software p value <0.05 was taken to be significant.
Conclusions: The pattern of fever aetiology found in this study would not be representative for the causes of fever in the general population. There are three main limitations explaining this. The selection of patients admitted to a tertiary care hospital in India is biased as a result of factors such as severity of disease, gender and accessibility. In this study only adults were included, while children would have different fever aetiologies due to exposure and immunity. Entomological factors cause seasonal and geographical variations in vector borne diseases in India, and in our study selecting patients during a particular time period in DMCH would not incorporate such variations.

KEYWORDS

Fever, Aetiology, Malaria, Tuberculosis, neonatal infections

INTRODUCTION

William Osler has rightly said –"Humanity has but three great enemies : fever, famine and war, of these by far, the greatest by far, the most terrible, is fever.[1]

Febrile illness is one of the most frequent cause of attendance at emergency departments (EDs) worldwide. Among the most frequently reported specific principal reason for visiting an ED[2]. In the United States in 2005. Fever was the third reported complaint, accounting for 4.4 to 7.5% of all ED consultations and up to 30% in non-surgical patients. About 5% of people who go to an emergency room have a fever.[3] Nevertheless, there are only a limited number of studies from India reporting on the aetiology of fever, and reliable surveillance data are not available.[4]

Infectious diseases are leading causes of morbidity and mortality in tropical countries. The World Health Organization (WHO) reports that each of the main infectious aetiology (pneumonia, diarrhoea, HIV/AIDS, malaria, tuberculosis (TB) and neonatal infections), cause between 0.56 and 2.6 million deaths respectively per year in low income countries.

In resource-limited settings fever may be treated empirically or self-treated due to lack of access to diagnostic tests.[5] However, clinical algorithms in order to differentiate malaria, for instance, from other causes of fever are not specific. Knowledge of local prevalence of infections is critical in order to target clinical work up and treatment.

Local prevalence of individual diseases influence the prioritization of the differential diagnosis of a clinical syndrome of acute undifferentiated febrile illness. This study is conducted in order to delineate the etiology of AFI that present to a tertiary hospital in DMCH, Darbhanga and to describe disease specific clinical profile.

Pyrexial disease are common worldwide and affect all age groups and both sexes. Most febrile conditions are readily diagnosed on the basis of presenting symptoms and a problem focused physical examination. Occasionally simple test such as complete blood count or urine examination is required to make a definitive diagnosis. Viral illness e.g. upper respiratory tract infections account for most of the self limiting cases.

Although the underlying conditions causing the symptom of fever vary considerably, it requires a systematic approach regardless of the underlying condition, concentrating upon a primary division between bacterial infections and other conditions and subsequent risk stratification, often using the same parameters. Despite many efforts, including the implementation of faster and more accurate diagnostic tools, such as biomarkers, polymerase chain reactions (PCR) and radiological tests, the tests lack sufficient speed and reliability to justify clinical decision-making based on test results alone.[6] Hence, both identification of bacterial infection and risk stratification remains very difficult in these patients in the emergency setting.[7] As a result, antibiotics are prescribed too frequently, leading to the worldwide problem of antibiotic resistance. For an adequate risk stratification of febrile patients, a thorough knowledge about local epidemiology is required, and risk factors associated with adverse clinical outcome have to be identified. Moreover, as up to 50% of patients with fever may have a non-infectious aetiology. Better insight into the epidemiology of fever might also lead to a more restrictive use of antibiotics.[8] This is necessary to find out the local prevalence of individual disease so that the aetiology of fever varies according to local prevalence of individual diseases. Adequate investigation can be done according to aetiology and avoiding unnecessary investigations.

Off let problem of antibiotic resistance can be there due to unnecessary use of antibiotic to each and every patients of fever without exploring the aetiology of fever.

AIMS AND OBJECTIVES

Aims of the study

This study is conducted in order to delineate the aetiology of fever patients who presented to DMCH, Laheriasarai, Bihar and to describe disease specific clinical profile and their outcome and to find out the local pattern of individual diseases .

OBJECTIVES OF THE STUDY

1. Aetiology of fever patients admitted in the Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Bihar over a period of one year.
2. Socio-demographic evaluation of fever patients.
3. Analysis of fever cases based on clinical features , bio-chemical

changes and radiological changes reaching to aetiology.
4. Outcome of the patients.

MATERIALS AND METHODS

Present Hospital based prospective observational study was done at Darbhanga Medical College and Hospital, Laheriasarai, Bihar from March 2019 to February 2020.

Total 100 consecutive patients admitted with fever in DMCH, Laheriasarai, Bihar, indoor patient, in the Department of Medicine. All the patients studied on the basis of following variables : Demographic evaluation, Clinical evaluation, Blood parameters, Radiological evaluation and Others.

INCLUSION CRITERIA OF THE SAMPLE

1. Fever of more than three days duration
2. Temperature more than 38^{o}C

EXCLUSION CRITERIA OF THE SAMPLE

1. Age less than eighteen years
2. Female patients with pregnancy

PARMETERS STUDIED

All the cases are studied as per the following
Demographic
Clinical :

- General Examination
  - Physique and Nutrition
  - Pulse, Blood pressure, Temperature, Icterus, Pallor, Clubbing, Cyanosis, Edema, Lympthadenopathy
- Systemic Examination :
  - Respiratory system
  - Cardiovascular system
  - Central Nervous System
  - Gastrointestinal system
  - Musculoskeletal sytem

Bio-chemical
Microbiological
Radiological (X-ray, USG, CT, MRI)
Laboratory investigation done –
Complete hemogram
Optimal MP (Malaria Parasite) Test, Rapid Malaria Antigen Detection Test, RK39 Test
Blood Sugar, Serum urea, Serum creatinine
Routine Urine Examination
LFT (Liver Fuction Test)
Typhidot IgM (Serological Examination for Typhoid)
Widal test
Dengue NS1 Antigen & IgM
ICTC/HIV (Integrated Counselling and Testing Center)
Blood c\s (Blood culture and Sensitivity)
Urine c\s (Urine Culture and Sensitivity)
CSF (Cebrospinal Fluid) Examination
Bone Marrow Aspiration and Examination
FNAC (Fine Needle Aspiration Cytology) for lymphadenopathy and excision biopsy of lymph node.
Other test if necessary for the particular like RA factor, ANA (Antinuclear Antibody), AntiCCP (Anti Cyclic Citrullinated Peptide), Chest Aspiration, Liver Aspiration, Abdominal Paracentesis and body fluid Examination, USG (Ultrasonography) Guided Pericardial Paracentesis and Examination

METHOD OF DATA COLLECTION

Following a written consent, all the cases will be studied as per Structured questionnaire

DEFINITION OF OUTCOME

Cured
Death

PLAN FOR DATA ANALYSIS

Data will be keyed into the computer. We will make double check to avoid any error in data entry. We will use epi info software 2002, downloaded from WHO site, to manage and analyze the data. The data will be carefully described by tabular and graphic means. Such descriptive analysis will be fundamental and will provide crucial information to us. It will serve as the basis for further intensive analysis.

RESULTS

In our study we find various aetiologies among fever patients ranging from infections like dengue, malaria, kala-azar tuberculosis, pneumonia, enteric fever, CNS infections, UTI etc. to noninfectious causes including malignancy, connective tissue disorders and Pancreatitis.

Table -1 showing different etiologies of fever

Diseases	Frequency	Percent
Bacterial meningitis	3	3
cerebellar abscess	4	4
Cerebral malaria,HE	4	4
Unknown	21	21
Enteric fever	6	6
Hodgkins dis(MixedCellType	3	3
Klebsiella pneumonia	2	2
Klebsiella pneumoniaSepsis	3	3
L,R,T,I.WITH copd Sepsis	1	1
L,R,T,I.WITH copd withTB	1	1
L,R,T,I.WITH Sepsis	1	1
Liver abscess	7	7
LRTI,Sepsis with TB	3	3
Pancreatitis	3	3
Pneumonia, COPD	1	1
Pneumonia,COPD withTB	3	3
Kala-azar	3	3
SLE	3	3
TBM	6	6
TBM with IC positive	1	1
Dengue	3	3
UTI,Pyelonephritis	1	1
UTI,Pyelonephritis Sepsis	3	3
UTI, Sepsis, BHP	4	4
Viral encephalitis	6	6
Viral hepatitis	4	4
Total	100	100

Table – 2 Use of diagnostic procedures among 100 patients admitted with fever

Diagnostic Procedure	Patients Tests	Diagnostic yield	
	n	n	(%)
Chest X ray	100	27/100	(27.00)
Abdominal USG	100	46/100	(46.00)
CT	19	11/19	(57.90)
HBsAg	60	5/60	(8.8)
AntiHCV	62	6/62	(9.6)
ICTC	54	8/54	(14.8)
Dengue IgM	25	8/25	(32.00)
MP	100	25/100	(25.00)
Typhidot	9	6/9	(66.66)
Widal	10	6/10	(60.00)
Urine r/e	99	25/99	(25.25)
Blood c/s	5	5/22	(22.72)
Urine c/s	11	2/11	(18.18)
CSF	20	11/20	(55.00)
RK39	10	3	(3)

Table - 3: Showing comparison between alcohol and liver abscess

			Liver abscess		Total
			Present	Absent	
Alcoholic	Present	Count	7	14	21
		% within liver abscess	100.0%	15.1%	21.0%
	Absent	Count	0	79	79
		% within liver abscess	0.0%	84.9%	79.0%
Total		Count	7	93	100
		% within liver abscess	100.0%	100.0%	100.0%

P VALUE <0.001

Table -4 : Showing comparison between smoking and COPD

			COPD		Total
			Present	Absent	
Smoker	Yes	Count	7	27	34
		% within COPD	100.0%	29.0%	34.0%

	No	Count	0	66	66
		% within COPD	0.0%	71.0%	66.0%
Total		Count	7	93	100
		% within COPD	100.0%	100.0%	100.0%

PVALUE <0.001

Table -5 : Correlation of COPD with age, stay days and TC

COPD		Age	Stay Days	TC
Present	Mean	64.00	10.00	16242.86
	Std. Deviation	3.742	.000	7429.863
Absent	Mean	29.08	10.00	11188.17
	Std. Deviation	14.456	3.394	8981.259
	P VALUE	<0.001	0.995	0.150
	SIGNIFICANCE	S	NS	NS

Table - 6: Showing Case Fatality amongst Male & Female

			Sex		Total
			MALE	FEMALE	
Outcome	Survive	Count	62	32	94
		% within sex	93.9%	94.1%	94.0%
	Died	Count	4	2	6
		% within sex	6.1%	5.9%	6.0%
Total		Count	66	34	100
		% within sex	100.0%	100.0%	100.0%

Table - 7: Showing comparison of outcome between septic & non-septic patients.

			Sepsis		Total
			Present	Absent	
Outcome	Survive	Count	17	77	94
		% within sepsis	94.4%	93.9%	94.0%
	Died	Count	1	5	6
		% within sepsis	5.6%	6.1%	6.0%
Total		Count	18	82	100
		% within sepsis	100.0%	100.0%	100.0%

Table - 8: Showing comparison between sex and sepsis

			Sepsis		Total
			Present	Absent	
Sex	MALE	Count	16	50	66
		% within sepsis	88.9%	61.0%	66.0%
	FEMALE	Count	2	32	34
		% within sepsis	11.1%	39.0%	34.0%
Total		Count	18	82	100
		% within sepsis	100.0%	100.0%	100.0%

DISCUSSION

The diagnosis of different aetiologies of fever can be challenging especially in the resource limited setting. Fever is one of the most perplexing clinical sign. It may occur in such diverse conditions as infections, malignancy and drug effect and due to environmental toxicity. Even after intensive search, the etiology of a siazable proportion of fevers remains unclear . In India infectious disease remains the main cause of fever . In our study among a cohort of patients admitted to Medicine Department of DMCH, Laheriasarai, Bihar with fever, bacterial infections (44%) and TB (14%) were the most common aetiological diagnosis. Mean fever duration was high (28.02days), and therefore the relatively high prevalence of TB is not surprising and is consistent with other hospital based studies reporting aetiology of prolonged fever in India .

One study of 100 patients with fever of unknown origin (PUO) in Calcutta reported that TB (53%), neoplasms (17%) and connecting tissue disorders (11%) were the dominant causes[18]. A similar pattern was found in two studies of PUO in North India, where infectious causes were diagnosed in approximately half of all cases, and TB was the most common infectious aetiology[8,1]. In one study of PUO from the South of Turkey, the most important infectious causes were included TB (17%), endocarditis (7%), intra-abdominal abscess (7%), brucellosis (6%), and UTI (6%)[4]. Bacterial infections and sepsis were associated with all the deaths recorded in this cohort, except for one patient who died due to malignancy. Not surprisingly among patients with severe bacterial infections, old age was a significant risk factor for death. In general, bacterial sepsis is probably undertreated in tropical countries for several reasons, including nonspecific diagnosis of fever, high prevalence of multi-resistant microbes, lack of blood culture facilities, and widespread use of counterfeit drugs. This may explain the high case fatality reported in African patients with fever incorrectly treated as malaria[11]. In India, a retrospective study from Mumbai among 160 patients who died from acute febrile illness reported malaria in 23%, leptospirosis in 22% and dengue fever in 2%, while up to 54% died due to unexplained fever, a proportion of which is likely to have been caused by bacterial infections[12]. However, in our study, as many as 22 among 100 patients were tested with blood culture, and 17 patients with AUF and PUO had negative blood cultures suggesting that bacteraemia may not have been under-diagnosed in this cohort. Antimicrobial resistance patterns were not recorded in all patients in this study, but it is possible that antimicrobial resistance has had an impact on case fatality. Antimicrobial resistance is a well-described predictor of increased fatality rate in sepsis[13]. Malaria is known to be largely underreported in India[14,6], and overtreatment of malaria, at the cost of other potentially severe infections, had also been reported[6]. Malaria prevalence in South India has been reported to be low compared with states in North-East India[16]. Among hospitalized cases in Vellore, Tamil Nadu in 1998, a predominance of P. vivax infections (n = 97) compared with P. falciparum (n = 70) was reported[17]. In our study 25% of fever cases were due to malaria, four of which involved P. falciparum infections. This difference of malaria cases in our study may be due to seasonal variation and low incidence of malaria at that time. A malaria prevalence of 17% among patients hospitalised with acute undifferentiated fever was reported from Vellore, India in 2010, and, among these, 57% were due to P. falciparum[7]. A similar increasing trend of P. falciparum predominance has been reported from Central India[19,20].

In our study we have also found a strong relation between alcohol intake and liver abscess.

We also found that smoking was a risk factor for developing COPD.

WHO has set a target to eliminate kala-azar in India by 2020. The elimination target is defined as achieving less than 1 case per 10,000. Although India has made susbstantial progress in elimination of kala-azar, but remains a stable public health problem in four middle-eastern states including Bihar.

Bihar contributes greater than 61% of total Indian cases annually, and a few district of the state have reported more than 600 cases annually. In our study 10 patients were investigated for kala-azar, in which found 3 patients(3%) as kala-azar.

CONCLUSION

A high number of bacterial and Tubercular infection were found in a cohort of adult patients admitted to a tertiary care hospital with fever in DMCH, Laheriasarai, Bihar and there was a relatively high case fatality rate from sepsis. This underlines the importance of establishment of relevant microbiological diagnosis and targeted antimicrobial treatment in the management of fever. P. falciparum was identified in all malaria cases, and this rapidly fatal infection should be considered in all patients with acute undifferentiated fever in India. A number of kala-azar and extra pulmonary tuberculosis patients were found to be infected HIV in DMCH, Laheriasarai, Bihar. This underlines the importance of HIV in every patients with pyrexia of unknown origin.

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