Section: Medicine

A Cross-sectional Study of Undiagnosed Fever in a Rural Population at a Tertiary Care Hospital of West Bengal.

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ABSTRACT

Background: Undiagnosed fever has been a predicament to physicians all over the world for decades. This study was undertaken to evaluate the demographic and etiological pattern of a rural population in Eastern India. Objectives. 1. To study the spectrum of etiology of prolonged fever. 2. To evaluate the demographic characteristics of the patients. **Methods:** All patients with undiagnosed fever for more than three weeks attending the Medicine outpatient Department were included in the study. History and clinical examination were recorded in a proforma. All patients under went routine as well as relevant special investigations including RDT for Malaria, IgM ELISA for Leptospira and Chikungunya and Brucella. Blood, urine and other body fluid culture including BACTEC and CB NAAT (as required) were also done. Endoscopies, imaging studies and guided biopsies were performed where needed. Results were recorded and analysed using appropriate descriptive statistical methods using SPSS Software (version 20). **Results:** A total number of 110 patients were included in the study. Of them 52(47.2%) were male and 58 (52.7%) were female. The age of the patients varied from 15 years to 78 years mean age being 33.68±18.77. **Conclusion:** The patients were mainly from rural background, most common districts being Murshidabad (40%) followed by24 Parganas S (20%), Midnapur (14.5%) and Nadia (10.9%). Socioeconomic status of the patients varied from lower (47.2%) lower middle class (39%) to middle class(13.8%). 65.3% of the patients were literate of whom 10.9 % of the people were matriculate while 1.8% were graduates. The commonest etiology of prolonged fever were infections 76(69%) out of which Tuberculosis 44(40%), took the lions' share. Tuberculosis was followed by chronic UTI (8.2%) enteric fever(5.5%) and malaria(4.5%). This was followed by various malignancies 14(12.7%) and inflammatory disorders 12(10.9%) It was notable that while prevalence of infections were comparable in males and females the prevalence of cancers (15.3%vs10.3%) and inflammatory disorders (7.6%vs 13.8%) varied. No diagnosis could be reached in 3.6% cases.

Keywords: Prolonged fever, tuberculosis, rural, literate.

INTRODUCTION

Prolonged fever without diagnosis is an unpleasant situation which neither the patient nor the treating physician would like to be in. However this is the single most baffling problem faced by every physician in their daily practice.

The definition of classic PUO is fever of more than 101^OF on several occasions for greater than three weeks duration with failure to reach a diagnosis by 3 days of OPD visits or indoor admission or one week of invasive and ambulatory investigations.[1]

But in a developing country like ours especially for the rural population it is difficult to adhere to these stringent criteria for all investigations to be complete in this stipulated time. Hence our study included any patient with greater than three weeks of fever who were referred to our tertiary care centre from outside without elucidation of a cause.

Aims and Objectives

1. To study the spectrum of etiology of prolonged fever
2. To evaluate the demographic characteristics of the patients

MATERIALS AND METHODS

This was an observational study conducted in the Department of Medicine of a Tertiary care hospital for a period of one year. All patients with undiagnosed fever for greater than three weeks attending the outpatient department or getting

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admitted were included in the study. Nosocomial infections or known neutropenic or immunocompromised patients with prolonged fever were excluded from the study. Institutional ethical clearance was taken for this study.

After taking informed consent, detailed history and clinical examination were recorded in a revalidated proforma. All patients under went routine as well as relevant special investigations including RDT for Malaria, IgM ELISA for Leptospira and Chikungunya and Brucella. Blood, urine and other body fluid culture included BACTEC and CB NAAT (as required). Endoscopies, imaging studies and guided biopsies were performed where needed.

Results were recorded and analysed using appropriate descriptive statistical methods using SPSS Software (version 20).

RESULTS

Table 1: Weight, Age and Sex

	Weight	Age	Sex
Total no of patients	110	110	M-58 (52.7%) F-52 (47.33%)
Mean	47.30	33.68	
Median	45.50	25.50	
Std. Deviation	15.920	18.772	

Table 2: Distribution of population in different districts

District	Male	Female	Total	percentage
Murshidabad	28	16	44	40%
24 Pargana(S)	06	16	22	20%
Midnapure	06	10	16	14.5%
Nadia	04	08	12	10.9%
24 Parganas(N)	06	02	08	7.4%
Burdwan	00	04	04	3.6%
Howrah	02	02	04	3.6%

Table 3. Distribution of socioeconomic class as per modified BG Prasad scale.

Socioeconomic class	Per capita monthly income in 1961	Per capita monthly income in 2017(January 2017 CPI)	Patients(number)	Percentage
Upper class	>100	>6254	00	00
Upper middle class	50-99	3127-6253	00	00
Middle Class	30-49	1876-3126	15	13.6%
Lower middle class	15-29	938-1875	43	39.1%
Lower class	<15	<938	52	47.3%

A total number of 110 patients were included in the study. Of them 52(47.2%) were male and 58 (52.7%) were female [Table 1]. The age of the patients varied from 15 years to 78 years mean age

being 33.68±18.77 [Table 1]. The maximum number of patients belonged to the age group of 1-20 yrs (43.63%) followed by 21—40 (23.63%) years [Figure 1]. 65.5% of our patients were less than forty years.

The patients hailed from various districts of West Bengal most common being Murshidabad (40%) followed by24 Parganas S (20%), Midnapur (14.5%) and Nadia (10.9%). [Table 2]

Socioeconomic status of the patients were categorized according to the Modified BG Prasad Scale. Most of our patients were from lower 47.2% and lower middle class 39% [Table 3].

73.6% (81of the patients) were Muslims, 24.5% (27of the patients) were Hindus and 1.8% (2 of the patients)were Christians.

Table 4: Aetiology of fever.

Disease	No of patients	Percentage
Infections :Total Subdivisions:	76	69%
a.Tuberculosis	44	40%
b.UTI	9	8.2%
c.Enteric fever	6	5.5%
d.Malaria	5	4.5%
e.Kalaazar	1	0.9%
f.Cholangitis	2	1.8%
g.prostatitis	2	1.8%
h.appendicitis	2	1.8%
i.Atypical pneumonia	2	1.8%
j.Brain Abscess	1	0.9%
k.leptospirosis	2	1.8%
Cancer:	14	12.7%
a. Acute Leukemia	6	5.5%
b. Lymphoma	3	2.7%
c. Carcinoma lung	2	1.8%
d. Carcinoma stomach	2	1.8%
e. Hepatocellular carcinoma	1	0.9%
Inflammatory diseases:	12	10.9%
a. SLE	6	5.5%
b. Adult Still's disease	2	1.8%
c. Rheumatoid Arthritis	2	1.8%
d. Rheumatic fever	2	1.8%
No cause found	4	3.63%
Miscellaneous	4	3.63%
a. Post operative urinoma	1	0.9%
b. Hemophagocytic syndrome	2	1.8%
c. ITP	1	0.9%

The educational levels were documented and 65.3% of the patients were literate (Literate means above 7 years person able to read and write any Indian language.). 10.9 % of the people were matriculate while 1.8% were graduates. [Table 3]

The commonest etiology of prolonged fever were infections 76(69%) out of which Tuberculosis 44(40%), took the lions share [Table 4]. Of the total number of TB patients, miliary TB was found in 36.4%, pulmonary TB in 22.7%, TB lymphadenitis in 18.8%, TB meningitis in 13.6% , followed by tubercular peritonitis and pericarditis [Table 5]. Tuberculosis (40%) was followed by chronic UTI(8.2%) enteric fever(5.5%) and malaria (4.5%).[Table 4]

Table 5: Distribution of different tubercular infections

Disease	No of patients (44)	Percentages
Miliary Tuberculosis	16	36.4%
Pulmonary Tuberculosis	10	22.7%
Tubercular lymphadenitis	08	18.7%
Tubercular meningitis	06	13.6%
Pericardial Tuberculosis	02	4.3%
Tubercular Peritonites	02	4.3%

Table 6: Educational Status of the Patients

| Level of Education(Used by census India 2011)		
Iliterate(Total)	38	34.55%
Literate(Total)	72	65.45%
1.Literate without educational level$	19	17.27%
2.Below Primary	11	10%
3.Primary	09	8.18%
4.Middle	10	9.09%
5.Matriculation/Secondary	12	10.9%
6.HigherSecondary/Pre University	05	4.5%
7.Non technical diploma or certificate not equal to degree	02	1.8%
8.Technical diploma or certificate not equal to degree	02	1.8%
9.Graduate and above	02	1.8%
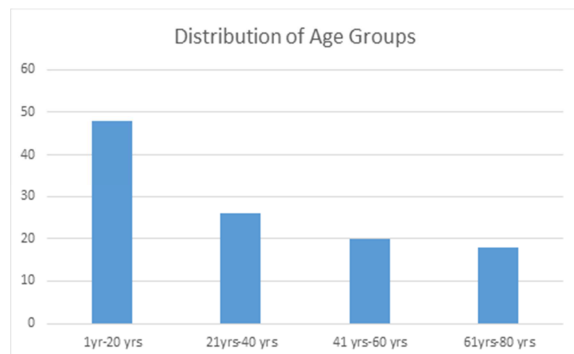
Figure 1: Age Distribution.
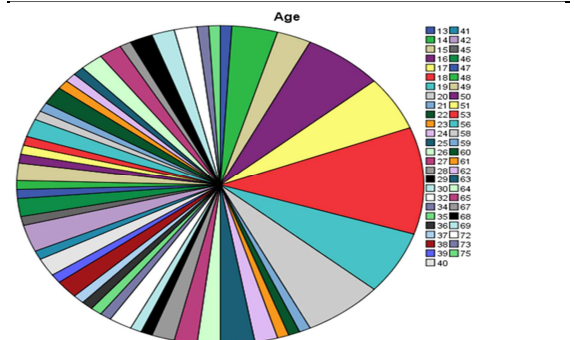
Figure 2: Age Distribution.

This was followed by various malignancies 14(12.7%) including leukemias(5.5%), lymphomas (2.7%), CA lung(1.8%) and gastric CA(1.8%) [Table 4] and inflammatory disorders 12(10.9%) [Table 4]. It was notable that while prevalence of infections were comparable in males and females the prevalence of cancers (15.3%vs10.3%) and inflammatory disorders (7.6%vs 13.8%) varied. No diagnosis could be reached in 3.6% cases. The provisional diagnosis in referral sheets reflected a pattern different from actual diagnosis. The cases were referred as undiagnosed PUO in 36.3%, enteric fever in 14.5%, lower respiratory tract infection in 10.9% and acute encephalitic syndrome (AES) in 7.2%.

DISCUSSION

Studies on prolonged fever dates back to the 1930 but even after so many years this entity still poses problems to physicians.[2] Our observational study was conducted with 110 patients of undiagnosed fever attending the outpatient department, many of whom were referred from rural hospitals and Block Primary Health Centres. The notable feature among the subjects was the preponderance of young subjects (65.45% less than 40 years of age) in the study. This was similar to other studies but the etiology predominant in this age group varied.[3,4] In our study infections especially tuberculosis were the commonest etiology in this young group.

The subjects of our study hailed from the rural areas of Murshidabad, 24 Parganas (S), Nadia, and Midnapur [Table 3]. Their socioeconomic status varied from lower (47.4%) lower middle (39.1%) to middle class (13.3%) depicted in [Table 4]. It has been fairly documented that prolonged fever is often a result of delayed presentation at health care centres.[5] Illiteracy, poverty and longer travel time leads to delay in assessment. This results in longer hospital stay and increased cost of treatment.[6]

The etiological pattern in both Indian and Western studies over the years are more or less similar showing infections as the most common cause. TB was found to be the most common infection causing FUO not only in India but also in studies done in Turkey and Taiwan.[4,7-13] Brucellosis and enteric fever were found to be the commonest infections in a study from Kashmir while brucellosis and infective endocarditis were most frequent in Egypt.[3,14] In a study with critically ill patients Ventilator associated Pneumonia(VAP) was found to be the most common infection.[15] Another study among paediatric population found enteric fever and acute lymphoblastic leukemia as the most frequent causes.[16] As obtained by D.Prabahkumar et al, there has been a fall in the incidence of infections ranging from 16%-57%,in parallel to increase in diagnosis of inflammatory disorders attributed mainly due to increased awareness and advances in diagnostic facilities.[17]

It is to be noted that even after the introduction of ongoing Revised National Tuberculosis Control Program (RNTCP) from 1997, the scourge of Tuberculosis still plagues our rural population. This is a reflection of the effect of socioeconomic background, poor education, overcrowding and

malnutrition in our country. Tuberculosis (40%) followed by UTIs (8.2%), enteric fever (5.5%), and malaria (4.5%) were other predominant infections found.

Comparing among Indian studies malignancies varied from 19%-22% while our studies had shown 12.7% of prevalence, most common being Acute leukaemia.[4,7,8] An interesting observation is the differences in provisional referral diagnosis from rural centres to our tertiary care hospital, commonest being undiagnosed fever of unknown origin (FUO) followed by enteric fever diagnosed on the basis of Widal test and Lower respiratory tract infection based on chest X-ray. Referral to the tertiary care had resulted in the decrease of undiagnosed cases from 36.3% to 3.6%. These 3.6% of cases remained undiagnosed even after culture, imaging and invasive studies. But it is to be remembered that percentage of undiagnosed fever has come down from 75% in 1930(2) to around 10% in 1960s and at our present study to less than 5%.[18]

The need for advanced diagnostic tools in our centres cannot be overstressed. Use of 18 FDG PET and PET CT has been documented in several studies to differentiate various etiologies without resorting to invasive techniques as employed by our centres when the first line investigations fail to give a diagnosis.[19,20] PET CT had contributed to 25%-69% of final diagnosis of FUO especially focal abdominal/ thoracic infections, osteomyelitis, large vessel vasculitis, sarcoidosis and malignancies.[20] Absence of PET CT, electron microscopy and viral marker probes can be considered a limitation of our study.

CONCLUSION

To conclude the cross section of population in our study was predominantly young (<40 years) of low educational and economic status, and hailed from various rural districts. The most common etiology was found to be infections predominantly Tuberculosis followed by malignancies and inflammatory disorders but to a much lesser extent. This upholds the necessity for better health awareness, early transport and presentation along with better diagnostic tools at primary health care facilities. All this will help avoid excessive referrals, delayed diagnosis and increased morbidity.

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