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ORIGINAL RESEARCH

A Prospective Study of Cases of Pyrexia of Unknown Origin Admitted At A Tertiary Care Institute With Reference To Their Etiology and Outcome

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ABSTRACT

Background: One of the most common presenting symptoms patient presents to any medicine OPD is fever. This prospective study was conducted to find out the spectrum of diseases causing PUO in A Tertiary Care Hospital (in the eastern part of the country). **Materials &Methods:** This study was conducted at PEERLESS HOSPITAL & B. K. ROY RESEARCH CENTRE, KOLKATA, multi- Speciality state-of-art tertiary care hospital on 80 patients admitted over duration of one and half year duration of January 2013 to November 2014.A thorough history and standardized thorough physical examination followed by routine laboratory investigations such as complete haemogram, urine examination and culture, peripheral blood smear for malarial parasite, sugar, urea & creatinine, blood culture, chest x-ray, ultrasonography abdomen and dengue IgM,NS-1Ag was performed. **Results:** Infections diseases were major category of causes of PUO (48.75%),and was followed by autoimmune diseases (12.5%)and close to that were neoplastic diseases (11.25%).Tuberculosis (n=13,16.25%) dominated, in various forms as the both pulmonary and extra pulmonary, affecting central nervous system and lymph nodes specially. Other Major causes were Brucellosis and enteric fever. HIV is emerging as important cause of PUO.Autoimmune diseases constituted second major category of disease after infectious disease, among which Systemic lupus Erythematous was the most common (n=5,6.25%) followed by other diseases including MCTD, sarcoidosis, etc.Neoplastic Disease were among third more common disease with hematopoietic malignancies being the most common.Miscellaneous diseases found were hepatic abscess in 5 (6.25%), Thyroiditis in 2 (2.50%) and Hashimato's thyroiditis in 1 (1.25%). Total 66 patient (n=66, 82.5%) were diagnosed of total 80 patients. Out of 18 undiagnosed patients 3 patients remained afebrile on follow up for 3 months. Diagnosed patients were either treated or referred to other specialities. **Conclusion:** Infections remain the most important cause of PUO in India, confirming the trends found earlier in other studies. The incidence of Autoimmune diseases and neoplasms is nearly same. Tuberculosis remains most common cause among the all causes of PUO. Meticulous history taking followed by clinical examination is important to gain diagnostic clues and accordingly guiding diagnostic tools, and thereby ensuring judicious use of diagnostic tools in resource limited setting.

Keywords: Pyrexia of Unknown Origin, Autoimmune diseases, neoplasms

INTRODUCTION

One of the most common presenting symptoms patient presents to any medicine OPD is fever. Most episodes of fever in humans are short-lived and do not require diagnostic investigation or specific therapy.[1] Some are manifestations of more serious illnesses, most of which can be readily diagnosed and effectively treated.However,a small but important subgroup of fevers are both persistent and difficult to diagnose.[2] Such puzzling fevers have fascinated and frustrated clinicians since the earliest days of clinical thermometry, resulting in a welter of clinical

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publications.[3] Pyrexia of unknown origin (PUO) was defined by Petersdorf and Beeson in 1961 as (1) temperatures of >38.3°C (>101°F) on several occasions; (2) a duration of fever of >3 weeks; and (3) failure to reach a diagnosis despite 1 week of inpatient investigation. While this classification has stood for more than 30 years.[4]

The spectrum of diseases found in several series examining PUO shows some variation, but overall, infections continue to be the most important cause of PUO, accounting for about 20-40% of cases, followed by neoplastic lesions, collagen vascular disorders and other rare illnesses.[5] Scanty data on PUO from northern India suggests a preponderance of infections as the cause of PUO and infrequency of neoplasms, connective tissue diseases as a causative agent.[6,7] Accordingly, we are conducting this prospective study to find out the spectrum of diseases causing PUO in A Tertiary Care Hospital (in the eastern part of the country).

MATERIALS & METHODS

This study was conducted at PEERLESS HOSPITAL & B. K. ROY RESEARCH CENTRE, KOLKATA, multi- Speciality state-of-art tertiary care hospital on 80 patients admitted over duration of one and half year duration of January 2013 to November 2014.

Inclusion criteria was the fever case with (1) temperatures of >38.3°C (>101°F) on several occasions; (2) a duration of fever of >3 weeks; and (3) failure to reach a diagnosis despite 3 days of inpatient investigation.

Data such as name, age, gender etc. was recorded. A thorough history and standardized thorough physical examination followed by routine laboratory investigations such as complete haemogram, urine examination and culture, peripheral blood smear for malarial parasite, sugar, urea & creatinine, blood culture, chest x-ray, ultrasonography abdomen and dengue IgM,NS-1Ag was performed.Results thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Relative Proportion of Etiologies

Etiologies	Number	Percentage
Infectious	39	48.75%
Autoimmune	10	12.50%
Neoplasm	9	11.25%
Miscellaneous	8	10%
Undiagnosed	14	17.50%

Using various diagnostic tools according potential diagnostic clues, diagnosis were established and patients were found to have Infections diseases as major category of causes of PUO (48.75%),and was followed by autoimmune diseases (12.5%)and close to that were neoplastic diseases (11.25%).

Table II Relative proportion of infectious etiologies

Infectious etiologies	Number	Percentage
Tuberculosis	13	16.25%
Brucellosis	8	10%
Enteric Fever	9	11.25%
scrub Typhus	1	1.25%
Nocordiasis	1	1.25%
EBV	2	2.50%
HSV	1	1.25%
TORCH	1	1.25%
HIV	3	3.75%

When considered as individual disease, Tuberculosis (n=13,16.25%) dominated, in various forms as the both pulmonary and extra pulmonary, affecting central nervous system and lymph nodes specially. Other Major causes were Brucellosis and enteric fever. HIV is emerging as important cause of PUO.

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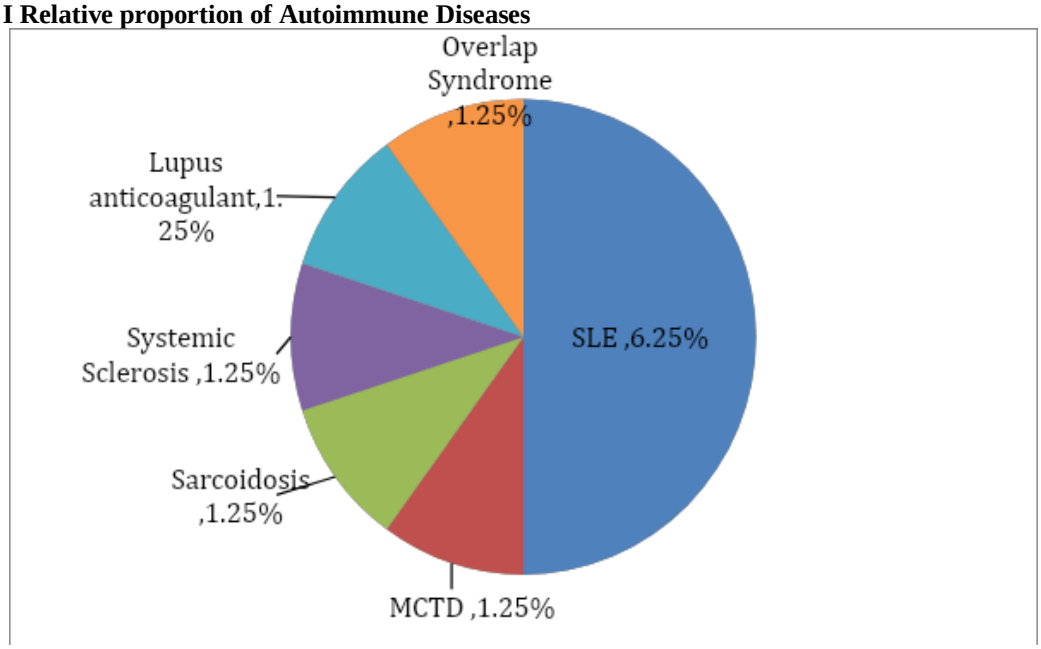
Graph I Relative proportion of Autoimmune Diseases



Autoimmune diseases constituted second major category of disease after infectious disease, among which Systemic lupus Erythematous was the most common (n=5,6.25%) followed by other diseases including MCTD, sarcoidosis, etc.

Table III Relative proportion of the neoplastic diseases

Neoplastic disease	Number	Percentage
Hodgkin's lymphoma	2	2.50%
Non-Hodgkin's	1	1.25%
Acute Myeloid leukaemia	3	3.75%
Multiple Myeloma	1	1.25%
Carcinoma Lung	1	1.25%
MGUS	1	1.25%

Neoplastic Disease were among third more common disease with hematopoietic malignancies being the most common.

Table IV Miscellaneous Diseases

Disease	Number	Percentage
Hepatic Abscess	5	6.25%
Thyroiditis	2	2.50%
Hashimato's thyroiditis	1	1.25%

Miscellaneous diseases found were hepatic abscess in 5 (6.25%), Thyroiditis in 2 (2.50%) and Hashimato's thyroiditis in 1 (1.25%).

Table V Outcome of the fever

Outcomes	N	Percentage
Diagnosed	66	82.50%
Febrile Undiagnosed	1	1.25%
Afebrile Undiagnosed	3	5%
Lost Follow Up	8	10%
Died	2	2.50%

After assessment of patient and complete data collection, we could diagnose total 66 patient (n=66, 82.5%) of total 80 patients. Out of 18 undiagnosed patients 3 patients remained afebrile on follow up for 3 months. Diagnosed patients were either treated or referred to other specialities.

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DISCUSSION

Fever is one of the most perplexing clinical signs. It may occur in such diverse conditions as infections, malignancy and drug effect and due to environmental toxicity.[8,9] Even after intensive search, the etiology of a sizeable proportion of fevers remains unclear. India infectious disease remains the main cause of fever.[10,11] Comparison between series of patients with PUO is difficult because of the large number of possible causes and the influence of numerous factors on the relative proportion of the various diagnostic categories.[12] Geographic factors, referral patterns, time of the study and age of the patient have been shown to influence the distribution of the various diagnostic categories.[13,14] Our study represents the disease spectrum in a tertiary referral centre in Eastern India, and we limit the detailed comparison to other studies from India.

In our study, 48.75% of the fevers had infectious causes. Tuberculosis was at the top of the list, constituting one third that is 33% of infectious diseases and 16.25% of all the causes. This is true for other developing regions of the world.[15,16] Autoimmune diseases occupies a high proportion 12.5% of the causes of fever followed by malignancies 11.25%. However, in our series the malignancies were mostly hematological. Malignancies of other sites were rare.In a similar study from eastern India, the investigators found 58% infectious, 22% malignancies and nearly same proportion of autoimmune diseases.[4]

In our study, we could establish the diagnosis in 88% of the cases. This is similar to a study from eastern India.[4] For diagnosis of tuberculosis, we depended on sputum examinations, chest X-ray and adenosine deaminase (ADA) levels. Tuberculosis polymerase chain reaction (TB-PCR) was used in suspected cases not diagnosed otherwise. Also in some cases, a therapeutic trial with anti-tubercular drugs (ATDs) was used. Thus, the approach to a case of fever in our country should always include infectious causes. With the current upsurge of HIV infection, especially in developing countries, HIV is a major cause of FUO(17). In some studies,[18] lymphoma is found as a more prevalent hematological malignancy; but in our case, we found leukemia equally prevalent. However, like in other regions of Southeast Asia,[19]we also found SLE as the most prevalent autoimmune disease.

CONCLUSION

In India, infectious disease still remains the most important cause of fever. Thus, the initial investigations should always include tests for ruling out or confirming diagnosis of infectious disease. Signs and symptoms can guide us to the final diagnosis in majority of the cases.[22]This study aims to find the trend of various etiologies in eastern part of India getting admitted at tertiary care institute. Infections remain the most important cause of PUO in India, confirming the trends found earlier in other studies. The incidence of Autoimmune diseases and neoplasms is nearly same. Tuberculosis remains most common cause among the all causes of PUO.Meticulous history taking followed by clinical examination is important to gain diagnostic clues and accordingly guiding diagnostic tools, and thereby ensuring judicious use of diagnostic tools in resource limited setting.

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