



A Prospective Study of Etiology of Classical Puo in a Tertiary Care Hospital Located in Northern Andhra

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Abstract

Background: *Pyrexia of unknown origin (PUO) is a diagnostic dilemma in clinical practice. Despite the proper accessibility of different investigations, still diagnosis cannot be reached. The aim of the study was to determine the causes of PUO in a tertiary care hospital located in Northern Andhra.*

Materials and Methods: *This study was a prospective observational study done in the department of General Medicine in tertiary care Hospital over period of 10 months from November 2019 to August 2020. All patients who satisfied the inclusion criteria and exclusion criteria were taken into the study.*

Results: *out of 100 patients 65 were male and 35 were female. Infectious causes found to be the most common cause out of which Tuberculosis was most common; followed by neoplasms and then connective tissue disorders.*

Conclusion: *The most common cause of PUO in this study was infectious causes (Tuberculosis). Undiagnosed cases are still problematic condition that needs exhaustive investigations.*

Keywords: *PUO- pyrexia of unknown origin, Tuberculosis, Neoplasms, Connective tissue disorders.*

Introduction

Fever is a common presenting symptom in clinical practice. PUO is defined as an illness of >3 weeks duration with fever $\geq 38.3^{\circ}\text{C}$ ($\geq 101^{\circ}\text{F}$) on two occasions and an uncertain diagnosis despite 1 week of inpatient evaluation. Most of the fevers were readily diagnosed based on history and symptom directed physical examination. Additionally, Routine blood investigations such as complete blood counts, complete urine examination, Qbc for malarial parasite, are necessary to establish a definitive diagnosis.

The causes of PUO can be divided into four categories: infective, neoplastic, connective tissue

disorders and miscellaneous. The relative importance of each cause has changed over time, with an increasing fraction of patients who remain undiagnosed, which can be up to 51% of cases. However, in many cases the cause for failure of diagnosis is lack of a proper protocol for investigation. If the investigation is based on the clinical findings, most of the cases can be easily diagnosed. The causes of fever change with the geographical distribution as also with time. Durack and Street classified PUO into Classical, Nosocomial, Neutropenic, HIV PUO.

Table 1 : Durack and Street classification of PUO (1991) modified*

Category	Classic PUO	Nosocomial PUO	Neutropenic PUO	HIV PUO
Definition	> 3 wks or > 2 OPD visits or > 3 days of indoor investigation	> 3 days, not present or incubation on admission	> 3 days, absolute neutropenia (< 500 / ml)	3 wks of outpatients or 3 days indoor
Leading causes	Infections, collagen vascular disorders, Cancers	LRTI (lower respiratory tract infection), UTI, catheter sepsis, post operative complications	Infections but can be found in only 50%	Typical or atypical mycobacteria, CMV (cytomegalo virus), toxoplasma
Time course of disease	Months	Weeks	Days	Weeks to months
Tempo of investigations	Weeks	Days	Hours	Days to weeks

(*All required temperature of > 38° C and blood culture negative at 48 hrs.)

Aims and Objectives

To determine the causes of classical PUO in a tertiary care hospital located in northern Andhra.

Materials and Methods

The present prospective study was done for a period of 10 months from November 2019 to August 2020 in the department of general medicine at a tertiary care Hospital in North Andhra. All patients satisfying the inclusion criteria and exclusion criteria are taken into study. A total of 100 patients were included after taking the informed consent.

After taking a detailed history all patients were examined for lymphadenopathy, any skin lesions, any lesions in oral mucosa any nodules, any hepatomegalay, splenomegaly. Every patient in our study were subjected to preliminary investigations

like complete blood counts, renal function tests, liver function tests, complete urine analysis, blood sugar levels, blood and urine cultures, CRP, QBC for malarial parasite, Screening for HIV, HBSAG, HCV, Widal test and a chest Xray, Mantoux test, Erythrocyte sedimentation ratio. All investigations were sent before starting of antibiotics. However if fever persisted after three days of antibiotics

repeat cultures were sent. The decision to obtain further diagnostic studies was based on abnormalities found in the initial laboratory work-up. Abdominal sonography, pelvic sonography, or CT scanning was performed early in the diagnostic process to rule out some common causes of FUO as intra-abdominal abscess or malignancy, depending on the primary evaluation. Invasive procedures like lumbar puncture bone marrow aspiration and bone marrow biopsy, lymph node FNAC and biopsy depending upon the clinical scenario if they are indicated. . All the collected data was arranged using Microsoft excel sheet.

Inclusion Criteria

All patients aged >13 years satisfying the criteria of Classical PUO

Criteria of Classical PUO:

1. Fever $\geq 38.3^{\circ}\text{C}$ ($\geq 101^{\circ}\text{F}$) on two occasions
2. Duration of fever >3 weeks
3. Uncertain diagnosis despite >2 OPD visits or >3 days of inpatient investigation.

Exclusion Criteria

- Patients with Known malignancy
- Patients on steroids

- Patients with HIV infection
- Women in mid menstrual cycle
- Patients taking antitubercular therapy
- Patients with neutropenia

Results

out of 100 patients 65 were males and 35 were females. Male to female ratio is 1.85:1.

Sex	Number of patients	percentage
Male	65	65%
Female	35	35%
Total	100	100%

Out of 100 patients, 86 were diagnosed, whereas 14 were discharged without definite diagnosis. Out of 86 cases most common cause was infectious causes (53) followed by neoplasms (18%) and then connective tissue disorders (12%) and then Miscellaneous causes (3); the most common infection being Tuberculosis (24) followed by abscesses(7).

Diagnostic category	Number of cases
INFECTIONS	53
Tuberculosis	27
Abscesses	10
Bacterial endocarditis	7
Enteric fever	5
Urinary tract infection	4
NEOPLASMS	
Non Hodgkins lymphoma	8
Hodgkins lymphoma	4
Acute myeloid leukemia	2
Chronic myeloid leukemia	1
Multiple myeloma	1
Colonic cancer	1
Bronchogenic carcinoma	1
CONNECTIVE TISSUE DISORDERS	11
Systemic lupus erythematosus	6
Mixed connective tissue disorders	4
Takayasu arteritis	1
MISCELLANEOUS	3
HLH Syndrome	1
Atrial myxoma	1
Autoimmune Hepatitis	1
UNDIAGNOSED	14
Self limiting	11
Persistent	3

Laboratory procedures utilized for the final diagnosis

Diagnostic methods	No. of cases	Percent
NON INVASIVE	58	67.5%
Diagnostic blood tests	15	17.4%
Culture	12	14%
Radiology or Imaging	9	10.5%
Bone marrow aspirate/FNAC	6	7%
Theurapeutic Trial	5	5.8%
Clinical course	11	12.8%
INVASIVE	28	32.5%
Biopsy	26	30.2%
Arteriography	2	2.3%

Discussion

Fevers of unknown origin remain one of the most difficult diagnostic challenges in medicine. PUO is caused by different etiologies despite different investigations, diagnosis could not be reached in some cases. This study aim is to find the causes of classical form of PUO around the studied patients. In our study total number of cases studied were 100. This sample size was similar to previous studies. 91 patients in Mir et al study, Petersdorf and Beeson studied 100 patients, Kejariwal et al. studied 100 patients, Bandyopadhyaya et al studied 164 patients.

In our study, definitive diagnosis was established in 86 (86%) patients, whereas 14 (14%) patients were discharged without establishing a definite diagnosis. The number of the undiagnosed cases in previous studies range from 7 to 30% in the study by Petersdorf and Beeson, 7–12% in Bandyopadhyaya et al, 14% in Kejariwal et al, 29% in Montasser et al.

In this study, infectious causes were the most common cause of PUO comprising 53%. out of which Tuberculosis was the single most common infection (27%). Bandyopadhyay D et al study conducted in Kolkata, Tuberculosis accounted for 28% of the cause of PUO out of which 72% were found to be extra pulmonary tuberculosis. In the series by Kejariwal et al, tuberculosis was again the commonest diagnosis.

In our study second most common infectious cause was Abscesses (10%) followed by

endocarditis (7%), enteric fever(5%), urinary tract infection(4%).

In our study, hematological malignancies in the form of non-Hodgkin lymphoma was diagnosed in eight (8%) patients, Hodgkin lymphoma in four (4%) patients, acute myeloid leukemia in two (2%)patients, and chronic myeloid leukemia was diagnosed in one (1%) patient and multiple myeloma in one patient (1%) and colonic cancer in one patient (1%) and bronchogenic carcinoma in one patient (1%).

Connective tissue disorders such as systemic lupus erythematosus were diagnosed in six(6%) patients and mixed connective tissue disorders in four patients(4%), takayasu arteritis in one (1%) patient.

Miscellaneous causes include Haemophagocytic lymphohistiocytosis in one patient (1%), atrial myxoma (1%), autoimmune hepatitis(1%).

In Mir et al study 91 patients with classical PUO were selected. A definite diagnosis was established in 77% cases. Out of which infections accounted for 44% cases of PUO, followed by malignancies 12% of cases, and connective tissue disorders for 12%of the cases.

Montasser et al study showed that infections were main cause of PUO (66.3%), followed by neoplasms (7.2%), connective tissue disorders (7.2%), 11.4% cases were diagnosed as miscellaneous (inflammatory bowel disease, Behcet disease, drug fever, familial mediterranean fever).

Barbado et al study showed that infectious diseases accounted for 31% of cases of PUO followed by neoplasms (8.27%). out of 4.5%cases were Hodgkin's disease and (3.75%) cases were non-Hodgkin's disease.

Conclusion

Infection especially tuberculosis was the most important cause of PUO in India, despite the decreasing importance of infections in western literature. The incidence of neoplasm was also high in this study when compared to previous studies from northern India. This trend needs further confirmation. The diagnosis was

established by non invasive methods in more than two third of cases.

Limitations

The study is done in limited number of subjects in one region. Results may vary in a large number of subjects and various regions.

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Conflicts of Interest: None

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