



## ETIOLOGICAL PROFILE OF 50 CASES OF PROLONGED FEVER IN GOVERNMENT GENERAL HOSPITAL VIJAYAWADA

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### ABSTRACT

**Background and Objectives of Study:** Fever has been recognised as a cardinal manifestation of disease. Fever was well known to ancients as an important manifestation of illness, but it remained for modern medical science to provide a better understanding of the significance of body temperature variations in health and diseases. Most cases of prolonged fever are instances of well known diseases manifesting themselves atypically.

Prolonged fevers are likely to be source of perplexity and frustration to the physicians and for the patients. This study intends to know the various etiological factors responsible for prolonged fever.

**Methods :** In 50 patients who met with inclusion criteria and exclusion criteria are subjected to detail clinical examination and investigations. Depending upon data obtained results are evaluated, tabulated and the percentage of diseases causing prolonged fever is calculated.

**Results:** At the end of the study infectious diseases (76%) constitutes commonest cause for prolonged fever, followed by neoplastic diseases (18%), connective tissue disorders (4%) and miscellaneous (2%).

Among the infectious diseases tuberculosis was the commonest cause for prolonged fever (34%).

**Conclusion:** Among 50 cases of prolonged fever infectious disease was most common cause followed by neoplastic diseases. Usually routine simple diagnostic procedure will clinch the diagnosis in most of the cases. Evaluation of occult infection and neoplasm should not be missed while diagnosing cause for prolonged fever.

**KEYWORDS :** Prolonged fever, diagnostic procedure, neoplasm, infection, tuberculosis

### INTRODUCTION

Fever has been recognized as a cardinal manifestation of disease since ancient times as recorded by ancient scholars like Hippocrates. Fever was well known to the ancients as an important manifestation of illness. Seen first as a disease but later recognized as an accompaniment to a variety of disease entities. Fever is an easily noted and reliable marker of illness.

Prolonged fever was defined as "A rectal (or its equivalent) temperature higher than 38.5degree centigrade on more than four occasions for at least two weeks period". Prolonged fevers are likely to be source of perplexity and frustration to the physicians and for the patients. The discomfort of illness is elevated by the anxiety of uncertainty. These victims tend to seek additional medical opinions and may wander from hospital to hospital repeatedly enduring the same laboratory tests.

Prolonged fever may be due to Infections, Neoplasms, Connective tissue diseases, Granulomatous diseases and Metabolic and Inherited diseases, Thermoregulatory diseases, Psychogenic Fevers and some miscellaneous causes.

### METHODS

This study comprises 50 cases of Prolonged Fever admitted to Government General Hospital, Vijayawada, Krishna District, Andhra Pradesh between July 2018 to July 2019. Case selection was random with respect to age, sex and type of fever.

### Inclusion Criteria

1. The study comprises patients present with fever for more than 2 weeks at Government General Hospital, Vijayawada.

### Exclusion Criteria

1. Patients present with fever for less than 2 weeks.
2. Patients aged less than 12 years.
3. Patients with pregnancy.

All cases with oral temperature higher than 37.7degree centigrade or rectal temperature higher than 38.5 degree centigrade on more than four occasions for at least 2 weeks period were selected for the study.

A detailed history was taken and physical examination was done as per the planned pro forma. Temperature was recorded 4<sup>th</sup> hourly.

All patients were investigated routinely for Hb%, WBC TC, DC and ESR and Screening of chest/ chest X-ray, urine for Albumin, Sugar, Microscopy and stool for Microscopy and occult blood. Further investigations were done based on provisional diagnosis and the physical finding pointing to a particular disease.

Special investigations such as blood culture, urine culture, X-ray abdomen, X-ray skull including paranasal air sinuses, Liver Function Tests, ultrasonography, pus for culture and sensitivity, serological tests like widal test, VDRL, LE cell phenomenon, ANA test, ELISA test for HIV infection, RA factor, ASO titre etc., were done.

Biopsy of lymph node, liver, pleura, peritoneum, bone marrow aspiration and biopsy of thyroid gland was done wherever it was required. Barium studies like barium swallow, barium meal, barium enema and CT scan and MRI were carried out in selected patients.

During their stay in the hospital, repeated clinical examination was done to look for new signs that may give a clue to the diagnosis.

### RESULTS

50 cases of prolonged fever were included in the study. Among 50 cases males outnumbered females (male 36 and female 14) with male to female ratio being 2.6 : 1.

The study includes age group from 16 years to 70 year, among this majority are in the age group of 16 to 30 years 23 (46%) followed by age group above 50 years 11 (22%).

Among males, majority were below 40 years and among females majority were below 30 years.

### Symptomatology

Fever was the presenting symptom in all cases. The duration of fever varied from 18 days to 10 months. Along with fever there are many associated symptoms. Among associated symptoms loss of appetite and loss of weight was the commonest symptom in 43 (86%) cases. Second commonest associated symptom was Chills+/-Rigors 30 cases (60%) followed by third common associated symptom was Cough with expectoration 21 cases (42%).

Other associated symptoms are:  
Breathlessness-17 cases (34%),

Abdominal pain-14 cases (28%),  
Head ache-12 cases (24%),  
Vomiting-6 cases (12%),  
Loose stools -6 cases (12%),  
Abdominal distension-6 cases (12%),  
Chest pain/Palpitations-7 cases (14%),  
Joint pain-2 cases (4%),  
Jaundice-2 cases (4%).

### Clinical Signs

Rise of temperature above 98.9 degrees Fahrenheit was common clinical sign in all the cases. There are many associated clinical signs along with rise of temperature.

Among the associated clinical signs pallor was the commonest clinical sign present in 46 cases (92%) followed by second common clinical sign was respiratory rate more than 20 in 36 cases (72%). Third common associated clinical sign was per abdomen finding in 24 cases (48%) other associated clinical signs are as follows- pulse rate more than 100 in 19 cases (38%), respiratory system finding 17 (34%), toxic look 15 (30%), lymphadenopathy 13 (26%), clubbing 8 (16%), icterus 4 (8%), CVS finding 4 (8%) and CNS finding 1(2%).

### Methods of diagnosis

All patients had Hb% less than 12 gm% (100%) and 35 patients had less than 10 gm% (70%). Total leucocyte count was more than 12000 cells/cum in 5 (10%) cases and less than 4000 in only two cases. Differential count was not much helpful for the diagnosis in this study. ESR was raised in all the 50 cases. In 13 (26%) cases, ESR was above 100 mm/hour and in the remaining cases it was between 40 and 100 mm/hour. Urinary abnormalities were found in 6 (12%) cases, of which 3 (6%) were culture positive. Blood culture was positive in 5 (10%) cases, of which 3 were positive for S-typhi. Out of these 3 (6%) cases 2 were sensitive to Quinolones and 1 case was sensitive to Cotrimoxazole. In remaining 2 cases of blood culture positive cases 1 showed Staphylococcus aureus and other showed Streptococcus viridans which was sensitive to ciprofloxacin and cephalosporin. Sputum examination was diagnostic in 9 cases in which 8 were AFB positive and 1 case showed gram negative bacilli, Klebsiella.

Chest X-ray was used for diagnosis in 17 (34%) cases, majority of them had pulmonary tuberculosis. Pleural effusion was present in 3 cases of which 2 cases were of tubercular aetiology and remaining one case was empyema. Lung abscess was observed in 2 cases. FNAC study was diagnostic in 7 cases. Majority of them were tubercular lymphadenitis (50%). Other lesion included Hodgkins lymphoma, non Hodgkins lymphoma, nonspecific lymphadenitis, lymphocytic thyroiditis. Excision biopsy was diagnostic in one case.

Ultrasound guided percutaneous needle aspiration was done in one case of amoebic liver abscess. Percutaneous liver biopsy and peritoneal biopsy were diagnostic in 2 cases of cirrhosis of liver with suspected tubercular peritonitis.

Ultrasound examination was diagnostic in 3 cases, of which 2 cases had paraaortic lymphadenopathy. Peripheral blood smear examination was diagnostic in 5 cases, of which 3 were positive for malaria and 2 revealed CLL and CML. Bone marrow aspiration study confirmed the diagnosis. ELISA test for HIV infection was positive in 8 cases. CT thorax done in one case shows Mediastinal lymphnode enlargement secondary to Hodgkins lymphoma.

### Diagnostic Categories

	Categories	No. of cases
<b>1. INFECTIONS</b>		
<b>A. Tuberculosis (14)</b>		
1.	Pulmonary TB	7
2.	TB lymphadenitis	4
3.	Ileocecal TB	1
4.	Pleural TB	1
5.	TB Peritoneum	1
<b>B. HIV Infection (8)</b>		
1.	HIV+TB (3)	
a.	HIV+TB Lymphadenitis	1
b.	HIV+ Miliary TB+TB Meningitis	1

c.	HIV+ Pulmonary TB	1
2.	HIV Infection Alone	5
<b>C. Enteric fever</b>		3
<b>D. Malaria</b>		3
<b>E. UTI</b>		3
<b>F. Lung Abscess</b>		2
<b>G. Viral Hepatitis</b>		1
<b>H. Liver Abscess</b>		1
<b>I. Empyemathoracis</b>		1
<b>J. Non Specific Lymphadenitis</b>		1
<b>K. Sub Acute Bacterial Endocarditis</b>		1
<b>2. NEOPLASTIC DISEASE (9)</b>		
1.	Hodgkins Lymphoma	2
2.	Non-Hodgkins Lymphoma	1
3.	Carcinoma Stomach	1
4.	Hepatoma	1
5.	CML	1
6.	CLL	1
7.	Carcinoma Lung	1
8.	Secondaries pleura	1
<b>3. CONNECTIVE TISSUE DISORDERS (2)</b>		
1.	Rheumatic Fever	1
2.	Systemic Lupus Erythematosis	1
<b>4. MISCELLANEOUS, LYMPHOCYTIC THYROIDITIS</b>		1
<b>TOTAL</b>		50

### DISCUSSION

50 cases of prolonged fever were included in this study. Males were more affected than females. Male to female ratio is 2.6:1. In males, majority were below the age group of 40 years and in females majority were below the age group of 30 years. Out of 50 cases, 38 (76%) cases were due to infections, representing the frequent occurrence of infections.

### Infectious diseases

Out of 50 cases, 38 were due to infections (76%) alone. This is probably due to the increased incidence of tuberculosis and HIV infection which accounts for 22 cases (44%).

**Tuberculosis:** Out of 17 cases of tuberculosis, 14 were tuberculosis without HIV and 3 were TB with HIV. In tuberculosis without HIV, 4 had tubercular lymphadenitis, 7 had pulmonary tuberculosis, 1 ileocecal TB, 1 pleural effusion and 1 tubercular peritonitis. In HIV with TB combined group, there were 3 cases, 1 case was TB lymphadenitis, paraaortic tubercular lymphadenitis, 1 case was pulmonary tuberculosis and 1 case was miliary tuberculosis with TB meningitis. Right sided pleuropulmonary tuberculosis constitutes 6 cases, Left sided pleuropulmonary tuberculosis was noted in only 2 cases and in 2 cases bilateral pulmonary tuberculosis was noted. In all the patients who were having pulmonary tuberculosis without HIV infection, sputum was positive for AFB. All the cases responded well to anti tubercular treatment (RNTCP-CAT 1) both symptomatically and radiologically except one case with HIV miliary TB and TB meningitis. Most of the tuberculosis cases were diagnosed by simple tests like sputum examination for AFB, chest X-ray and FNAC in case of TB lymphadenitis.

In one of Ileocecal TB ultra sound abdomen showed mass in right iliac fossa, which responded well to anti tubercular drugs.

**HIV infection:** HIV infection was the second leading cause of prolonged fever among infection group. In the present study, there were 8 cases of HIV infection, out of which 3 cases were associated with tubercular infection and rest were HIV infection alone without evidence of any other infections. All the 8 cases were reactive for HIV 1 and 2 by ELISA method on two different occasions at two different laboratories.

**Enteric Fever:** 3 cases of enteric fever were recorded, 2 cases presented with high degree, remittent fever, whereas one presented with intermittent fever with evening rise of temperature. All the patients were diagnosed by blood culture which shows growth of Salmonella typhi. Widal test was positive in 2 cases and negative in 1 case, 2 cases were sensitive to ciprofloxacin and 1 was sensitive to

cotrimoxazole.

**Malaria:** There were 3 cases of malaria. All the 3 cases presented with chills and rigors 2 cases had splenomegaly and 1 case had hepatosplenomegaly. Peripheral blood smear was positive for Plasmodium Falciparum in 2 cases, of which in 1 case showed ring form and in another case gametocyte were seen.

The remaining 1 case was positive for Plasmodium Vivax ring forms in the smear. All patients responded well to chloroquine and pyrimethamine followed by primaquine in Plasmodium Vivax.

**Urinary Tract Infection:** Of the 3 cases of UTI, 2 cases presented with chills and rigors, another case presented with only mild degree of fever. Urine culture was positive in all 3 cases, of which in one case culture yields Klebsiella with significant bacteriuria, which was sensitive to quinolone group of drugs. In another case, culture was positive for E.Coli which was resistant to all antibiotics. However patient responded to 3<sup>rd</sup> generation cephalosporins. In the remaining one case urine culture was positive for pseudomonas, which was sensitive to gentamycin and quinolone. Urine microscopy in 2 cases revealed no pus cells and 1 case showed 20 to 30 pus cells. Hence urine microscopy may not be sufficient to rule out the possibility of urinary tract infection.

**Other infectious causes:** One case of amoebic liver disease was encountered during the study, the case had multiple amoebic abscesses in the right lobe of the liver. Ultrasound guided needle aspiration of the abscess was done and the aspiration was anchovy sauce coloured. The patient was responded well to metronidazole remarkably.

Lung abscess, empyema thoracis, viral hepatitis, nonspecific lymphadenitis, sub acute bacterial endocarditis constituted 1 case each. All responded well to an appropriate therapy.

**Neoplastic Disease:** Fever may be manifestation of any kind of tumour, whether benign or malignant. It is more common in neoplasms of lymphoid tissue, liver and kidney. Other neoplastic disorders in which persistent fever may be the sole feature were carcinoma of stomach, leukemias, carcinoma of colon, bronchogenic carcinoma. In the present study, neoplastic disease group was the second commonest 9 cases (18%) cause of prolonged fever. 2 cases had Hodgkins lymphoma. Non hodgkins lymphoma, hepatoma, carcinoma stomach, bronchogenic carcinoma, secondaries in pleura, CML, CLL constituted 1 each.

**Connective Tissue Disorders:** 2 cases of connective tissue disorders (4%) were noted in this study. One case was rheumatic fever and another was systemic lupus erythmatosis. In the present study, rheumatic fever was diagnosed on the basis of elevated ASO titres and associated cardiovascular findings. SLE was diagnosed on the basis of positive LE cell phenomena, positive ANA( antinuclear antibody) test. Rheumatic fever case responded well to Aspirin tablet and SLE responded to oral prednisolone.

**Miscellaneous Group:** One case was diagnosed as lymphocytic thyroiditis, presenting with mild fever with throat pain, slight enlargement of thyroid gland and the diagnosis was confirmed by FNAC of thyroid gland. Patient responded to corticosteroids.

No case remained undiagnosed after investigations in the present study.

## CONCLUSION

Among 50 cases of prolonged fever infectious disease was most frequent cause, followed by neoplastic disease. Among the infectious diseases tuberculosis was most common followed by HIV infection.

Usually the simple diagnostic procedure will clinch the diagnosis in most of the cases. However evaluation of occult infection and neoplasm should not be missed while diagnosing the cause of prolonged fever.

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