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Clinical Profile and Etiology of Prolonged Pyrexia in Adults Attending a Tertiary Care Hospital in Bangladesh

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Abstract **Original Research Article**

Background: Prolonged Pyrexia or Fever of Unknown Origin (FUO) represents a significant diagnostic challenge due to its prevalence in tropical countries like Bangladesh. ***Objective:*** The study evaluates the medical characteristics alongside causes of prolonged fever among adult patients seeking treatment at a tertiary medical facility. ***Methodology:*** A Prospective observational study was conducted at BIRDEM General Hospital in Dhaka from July 2021 to June 2023. The research included 80 adult patients (40 to 75 years old) who had sustained high temperatures for at least 14 consecutive days. Data collection included clinical factors alongside demographic statistics and laboratory results, which were analyzed through SPSS 25.0. ***Result:*** The study found a male-to-female ratio of 1.86:1; this is a male-dominant study with 65% of male participants. The mean age of study participants was 43.47 ± 14.78 years, where the majority of the patients belongs to the 50-59 years of age group. Most patients came from rural parts (72.5%), and 27.5% of patients came from urban Bangladesh. A total of 66.3% of patients had infectious causes, while tuberculosis remained the most prevalent infection at 29 patients. The study documented 13.8% of cases due to autoimmune conditions and 12.5% due to malignancies. Still's diseases (6 patients) and Vacuities (5 patients) are most prominent in autoimmune disease condition. The patients needed an average of 22 days to receive a correct diagnosis, while those with neoplasm required 28 days for diagnosis. Patients diagnosed with neoplasm presented with severe morbidity at 70% frequency among neoplasm groups ($p<0.001$). The researchers identified hypoalbuminemia below 2.8 g/dL with an odds ratio of 42.0 as well as CRP levels exceeding 90 mg/L with an odds ratio of 19.8 as primary predictors. The clinical condition of 17.5% of patients deteriorated to a severe level that demanded intensive care, yet no case of mortality was recorded in the study. ***Conclusion:*** Infectious diseases and tuberculosis are responsible for most cases of prolonged fever throughout Bangladesh. The main cause of prolonged fever in patients emerges from autoimmune diseases together with cancers. A reduction in morbidity requires complete early diagnosis as the first step.

Keywords: Prolonged pyrexia, fever of unknown origin, tuberculosis, autoimmune diseases, neoplastic.

INTRODUCTION

Fever persisting for two weeks or more after initial diagnosis poses an intimidating clinical dilemma in tropical regions where infections and non-communicable diseases are concurring and prevalent. Prolonged pyrexia or a fever of unknown origin (FUO) can be caused by various factors, including infections, autoimmune disease conditions, and even malignancies [1]. A fever may be described as prolonged when the temperature lies between 101°F (38.3°C) or beyond and persists for two to three weeks [2]. Some contemporary studies claimed that non-communicable disease (NCDs) accounts for death rates up to 40% in developed countries [3]. Comprehensive analysis of etiologies and detailed clinical history becomes necessary for the management of prolonged fever but South Asian data remains predominantly and potentially skewed by diagnostic limitations [4]. The etiological spectrum varies by geographic region, socioeconomic factors, and availability of diagnostic tools, making context-specific studies in case of prolonged fever. WHO reported that NCDs killed 43 million people globally in 2021 [5]. Infection-related conditions, including tuberculosis (TB), enteric fever, and rickettsia infections, stand as the major causes of elevated body temperature in Bangladesh alongside other low- and middle-income countries (LMICs) [6]. Clinicians now recognize that autoimmune disorders such as adult-onset Still's disease

and vasculatures and malignancies, including lymphoma, now comprise substantial proportions of non-infectious arthritis [7]. The clinical implications of prolonged pyrexia are profound. Delayed diagnosis causes prolonged hospital stays and higher morbidity and mortality [8]. The burden of fever of unknown origins worsened due to late hospital presentation, empirical antibiotic use, and lack of standard diagnostic approaches and treatment protocols in Bangladesh [9]. Existing research on South Asian patterns of prolonged pyrexia relies predominantly on retrospective data, and there is a shortage of prospective observational investigations that use modern diagnostic approaches [10]. However, prior studies mostly focus on the young population, thus, prospective analysis became an immediate necessity in Bangladesh as the aging populace presents an increasing challenge from non-communicable diseases, which need refined diagnostic methods and treatment plans. This study aims to identify the clinical and laboratory profile of prolonged pyrexia by assessing the etiological categories.

METHODOLOGY

This is a prospective observational study conducted in the Department of Medicine BIRDEM General Hospital, Dhaka, Bangladesh in from July 2021 to June 2023. This study was conducted with ethical standards and enrolled patients with study-specific inclusion and exclusion criteria.

Inclusion criteria

- Patient aged 40-75 years.
- ≥38°C fever duration for ≥14 consecutive days.
- Willingness to provide written informed consent.

Exclusion criteria

- Immune-compromised Status (HIV/AIDS).
- Case of known pregnancy.
- Fever with an established etiology before enrollment (e.g., culture-positive UTI).
- Unable to provide consent.

Researchers generated case report forms (CRFs) to collect demographic details, clinical presentation, and laboratory findings data. All patients underwent some general testing, including Complete Blood Count (CBC), S. Albumin and CRP testing to understand the disease profile and maintain the uniformity of the data. Continuous variables were analyzed using t-tests and categorical variables with chi-square tests. Statistical significance was set at $p<0.05$. MS Excel and SPSS version 25.0 were the main data analysis tools.

RESULTS

This prospective observational study enrolled 80 participants, 52 males and 28 females. This is a male-dominant dominant where the male-to-female ratio is 1.86:1.

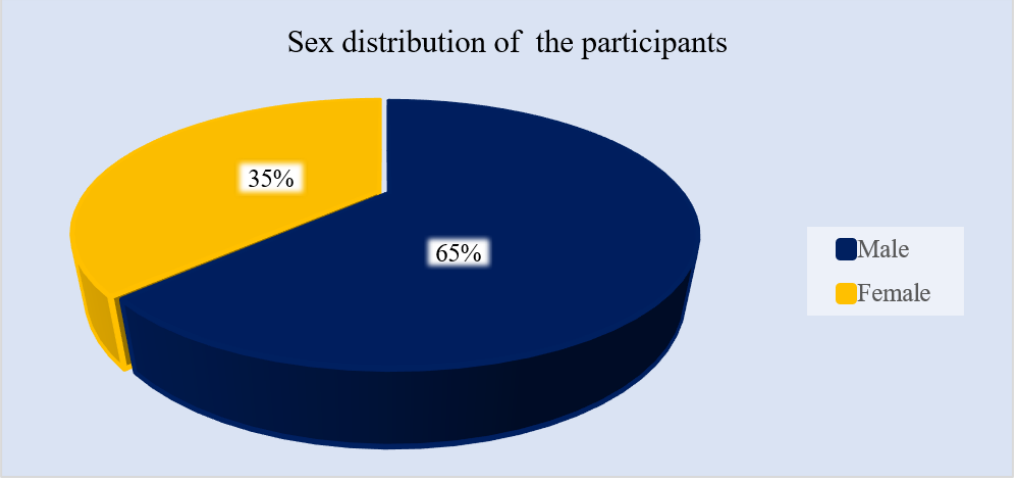

Figure 1: Pie chart showed demographic distribution of patients, sex (N=80)

This study included participants aged from 40 to 75 years. The mean age calculated for this study is 43.47 ± 14.78 years, with a minimum age of 40 and maximum of 75 years.

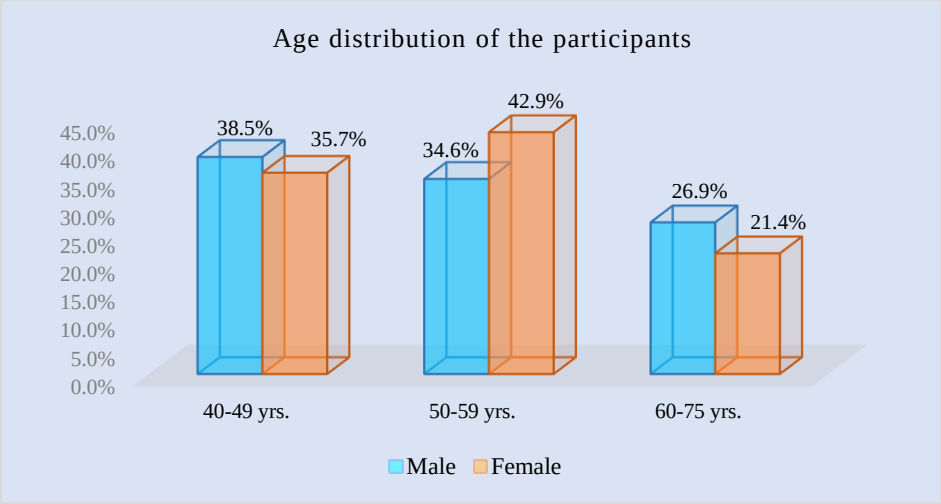

Figure 2: Column chart showed demographic distribution of patients, age (N=80)

Figure 02 shows that the study enrolled the maximum male patients from the 40-49 years of age group and the maximum female patients from the 50-59 years of age group. Both male-female enrolment was low in the 60-75 years group. The mean age calculated for male patients was 43.8 ± 10.1 years and for female 47.6 ± 8.9 years.

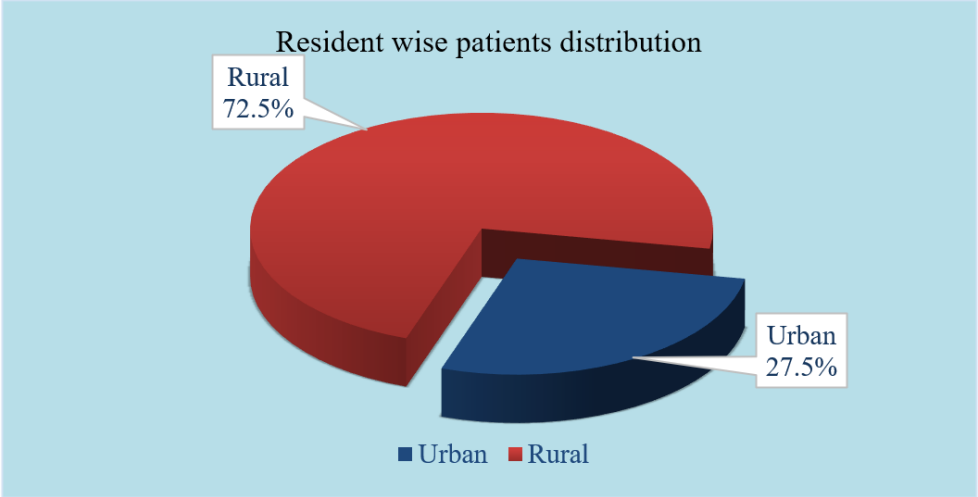

Figure 3: Pie chart showed Pie chart showed demographic distribution of patients, resident (N=80)

Figure 03 figured out that the rate of prolonged fever is almost two times higher in rural regions with 58 rural residents and 22 urban residents. In the rural area, males are again dominating with 72.5% of the population.

Table I: Demographic and Clinical profiles of patients (N=80)

Parameter	**Total (N=80)**
Demographics	
- Age (years)	55.2 ± 9.8
- Rural residence	58 (72.5%)
Clinical Presentation	
- Fever duration (days)	4.47 ± 1.55 [17–29]
- Weight loss (>5% body mass)	55 (68.8%)
- Night sweats	41 (51.3%)

Table I denotes that the patients have a history of an average 22 days of fever (17-29); a total of 55 patients (68.8%) lost weight in this phenomenon, and 41 patients had a history of night sweats, which is 51.3% of the total population.

Table II: Etiological distribution of patients (N=80)

Category	N (%)	Specific Diagnoses	Confirmatory Method
Infectious (n=53, 66.3%)			
- Bacterial	38 (47.5%)	Tuberculosis (29), Enteric fever (9)	GeneXpert (24), Culture (5), Serology
- Rickettsial	7 (8.8%)	Scrub typhus (5), Leptospirosis (2)	IgM ELISA
Non-infectious (n=17, 21.2%)			
- Autoimmune	11 (13.8%)	Still's disease (6), Vasculitis (5)	ACR/Yamaguchi criteria
Neoplastic (n=10, 12.5%)			
- Hematological	6 (7.5%)	Lymphoma (6)	Lymph node biopsy
- Solid tumors	4 (5.0%)	Renal cell carcinoma (2), HCC (2)	CT-guided biopsy

Table II reveals that most of the participants diagnosed with infectious prolonged fever (66.3%) where bacterial infection is the most prominent (47.5%), more specifically TB; 13.8% patients had autoimmune fever and 12.5% fever caused by neoplastic, among them 7.5% are lymphoma and 2.5% renal cell carcinoma.

Table III: Diagnostic process and mortality rate (N=80)

Parameter	Infectious (n=53)	Non-infectious (n=17)	Neoplastic (n=10)	Total (N=80)
Time to diagnosis (days), median [IQR]	18 [14–23]	25 [19–32]	28 [21–38]	22 [17–29]
Required invasive testing	5 (9.4%)	5 (29.4%)	7 (70.0%)	17 (21.2%)
Severe morbidity	5 (9.4%)	2 (11.8%)	7 (70.0%)	14 (17.5%)
Mortality	0	0	0	0

Table III shows that it took an average of 22 days to diagnose the cause of prolonged fever; among them, neoplasm took the most time (avg. 28 days) to assess. Severe morbidity refers to patients who required ventilation support due to prolonged fever. A total of 14% of patients were taken to the Intensive Care Unit for infection (9.4%), Non-infection (11.8%), and neoplastic (70%). No case of mortality was found in this study.

Table IV: Statistical analysis and predictors of severity

Parameter	Non-Severe (n=66)	Severe (n=14)	Mean Difference (95% CI)	p-value	Clinical Threshold
Age (years)	53.1 ± 8.9	62.4 ± 7.8*	+9.3 (4.1 to 14.5)	0.001*	≥60 years
Fever duration (days)	20.4 ± 6.8	27.6 ± 8.3*	+7.2 (3.1 to 11.3)	0.002*	≥25 days
Hemoglobin (g/dL)	10.4 ± 1.7	8.3 ± 1.4*	-2.1 (-2.9 to -1.3)	<0.001*	<9 g/dL
Albumin (g/dL)	3.3 ± 0.4	2.5 ± 0.3*	-0.8 (-1.1 to -0.5)	<0.001*	<2.8 g/dL
CRP (mg/L)	58 ± 25	104 ± 32*	+46 (28 to 64)	<0.001*	≥90 mg/L
Platelets (×10³/μL)	192 ± 70	118 ± 55*	-74 (-112 to -36)	<0.001*	<120 ×10³/μL

Table IV describes details of clinical parameters and the cause of severities in prolonged pyrexia patients. P-value<0.05 denotes statistical significance among severe and non-severe groups. Severity was mostly observed among the aged population (P=0.0001). The severe group exerts a history of more prolonged fever (P=0.002); a drastic reduction of hemoglobin was also found in severe groups (p<0.0001). S. albumin also reduced in severe groups in comparison to survivors (p<0.001). Significantly high CRP (p<0.001) and low platelet counts (p<0.001) were also found in the laboratory findings of patients switched to mechanical ventilation (severe cases).

DISCUSSION

Pyrexia or fever is a physiological response of the human body to infectious or non-infectious causes such as inflammation, malignancy, or autoimmune processes [11]. The current study discusses the clinical profile and etiology of prolonged pyrexia among adult populations of Bangladesh. The study was conducted with 80 participants of 52 male and 28 female. The male-female ratio was 1.86:1, and the duration of the fever recorded was 17-29 days in this study. A similar study conducted earlier showed that males are more prone to pyrexia (65%) [12], which replicates recent findings (65%) as well. Another Bangladeshi study found the male dominance of prolonged fever based study with a duration of 20±12 days [9]. Seguin P. *et al.*, 2012 counted the mean age of the participants as 58 ± 18 years [12], which partially allies with the current study with 43.47 ± 14.78 years of mean age. A Sri Lankan study also agrees with these findings, with 55% of male patients of 49.65±15.55 years of mean age and 45% of female patients with 46.87±16.19 years of mean age [13]. The current study found the mean age of the male population to be 43.8 ± 10.1 years and among the female population 47.6 ± 8.9 years. According to recent data, almost one-fourth (72.5%) of the population presents to tertiary care hospitals from rural areas. A Bhutanese study showcased that 81.7% of hospital admissions due to prolonged pyrexia were from rural regions [14]. A Bangladeshi

study on children recorded a dengue-related fever outbreak where they found that in the 2019 outbreak, 33.9% of patients and in the 2022 outbreak, 30.0% of patients came from rural areas in Chattogram [15]. The current study found that bacterial infection (47.5%) is the prime cause of the majority of hospital admissions; Tuberculosis is the main culprit (29 patients). A 1996 study in Bangladesh shows indistinguishable data with 63.21% of cases of prolonged pyrexia due to microbial infection, 12.74% of neoplasm, and 10.85% of connective tissue or autoimmune disorders; Tuberculosis accounts for 24.53% of prolonged fever [16]. Rahim M. A. *et al*., 2016 reported that 60.6% of infection-related fever patients and 27.3% malignancy; extra-pulmonary tuberculosis (25%) was the most common cause of infectious prolonged fever [17]. Likewise, Bhuiyan M. E. *et al.* 2024 also showed that 48% of prolonged fever is caused by infectious diseases, 24% by connective tissue or autoimmune diseases, 16% related to malignancy, and 12% of miscellaneous causes [9]. The zero mortality rate of this study relates to other studies on prolonged pyrexia [9] [17] [16]. Apart from this, a total of 14 patients required ventilation support due to prolonged fever in this study. A 2015 Indian study displays that a total of 34.5% of patients required mechanical ventilation and 3.91% of patients required prolonged ventilation [18]. The prime reasons for morbidity assessed by this study are aging (+9.3 years), unusual prolongation of fever (+7.2 days), reduced hemoglobin (-2.1 g/dL), reduced albumin (-0.8 g/dL), elevated CRP (+46 mg/L), and reduction of platelet count (-74×10^3/μL).

LIMITATION

Single-centered studies always limit the scope of enrolling varieties of patients. Advanced molecular or imaging techniques insert more accuracy of the study, and long-term follow-up might express the appropriate patient outcome.

CONCLUSION

Prolonged pyrexia in adult patients of a tertiary care hospital in Bangladesh shows primarily infectious and autoimmune, and neoplastic causes with particular clinical manifestations. Tuberculosis stands as the foremost infectious cause of prolonged fever, which is followed by autoimmune diseases and cancers. The study demonstrates prolonged fever combined with older age, low hemoglobin values, hypoalbuminemia and elevated CRP results, and thrombocytopenia as important risk factors for severe disease progression. Certain patients needed to be hospitalized in intensive care settings but no one passed away from the condition. There is a paramount need to identify patients early and undertake specific diagnostic methods to enhance patient success rates.

Author Contribution

MSH planned the research, collected data, analyzed data, and drafted the manuscript. R Chakrabarty, MT Islam, MRR Rahman, and JU Ahmed participated in the critical review of the manuscript and overall supervision. All authors read and approved the final manuscript for submission.

Abbreviations

FUO: Fever of Unknown Origin
NCDs: Non-communicable diseases
TB: Tuberculosis
UTI: Urinary Tract Infection
HIV: Human Immunodeficiency Virus
AIDS: Acquired immunodeficiency syndrome
CBC: Complete Blood Count
CRP Testing: C-reactive protein testing
WHO: World Health Organization
LMICs: Low- and Middle-Income Countries
CRFs: Case Report Forms

Conflicts of Interest: The authors declare no conflicts of interest.

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