

A Study Related to Undiagnosed Fever in a Known Population: An Cross-Sectional Study

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ABSTRACT

Background: Fever remains the most enigmatic clinical symptom to treat. The differential diagnosis of Fever of unknown origin is the most wide-ranging in medicine. Hence; the present study was conducted for assessing the patients with Undiagnosed Fever in a Known Population.

Materials & Methods: A total of 85 patients with undiagnosed fever were enrolled in the present study. Thorough clinical examination of all the patients was carried out. Blood samples were obtained from all the patients and routine investigations were carried out. Patients remaining undiagnosed after that were referred to higher centers. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software. Chi- square test was used to assess the level of significance.

Results: In all these patients, final diagnosis was established based on haematological and clinical examination. Final diagnosis was found to be infectious in 49.41 percent of the cases, while it was found to be inflammatory (non-infectious) in 16.47 percent of the cases. Haematological pathology was found to be present in 12.94 percent of the cases. Undiagnosed cases were found to be 5 in number.

Conclusion: Undiagnosed fever might occur in such variable pathologies as infections, malignancy and drug effect and due to environmental toxicity. Even after intensive search, the etiology of a sizeable proportion of fevers remains unclear.

Key words: Fever, Infectious, Unknown.


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Article History:

Received: 04-11-2019, Revised: 01-12-2019, Accepted: 29-12-2019

Access this article online

Website: www.ijmrp.com	Quick Response code 
DOI: 10.21276/ijmrp.2020.6.1.034	

INTRODUCTION

Fever remains the most enigmatic clinical symptom to treat. Although in a developing country infectious disease remains the most important cause of fever, the noncommunicable causes, like malignancy, are also becoming important. Preliminary investigations fail to find the etiology in many cases. This comprises a large group called "fever of unknown origin".¹⁻³ The reason may be that with the improvements in the quality of medical care and diagnostic tools, such as the popularization of advanced imaging technology, improvement in pathogen culture technology, newly developed serological detection projects, and application of polymerase chain reaction (PCR) technology, diagnosis rates of common diseases are improved. However, cases that meet the classic definition of FUO are becoming increasingly complex.⁴⁻⁶

The differential diagnosis of FUO is the most wide-ranging in medicine, since more than 200 conditions have been identified as

the cause of FUO. Infectious diseases (ID), neoplasms and non-infectious inflammatory diseases (NIID) are the main categories of diseases causing FUO. However, despite recent advances in medicine, about a quarter of FUO remains undiagnosed.^{7,8} Hence; the present study was conducted for assessing the patients with Undiagnosed Fever in a Known Population.

MATERIALS & METHODS

The present study was conducted in the department of Medicine, Government Medical College, Bharatpur, Rajasthan and it included assessment of patients with undiagnosed fever in a known population. Ethical approval was obtained from institutional ethical committee and written consent was obtained from all the patients after explaining in detail the entire research protocol. A total of 85 patients with undiagnosed fever were enrolled in the present study.

Inclusion Criteria

- Patients with fever of atleast 3 weeks,
- Patients who fulfilled the definition of fever of unknown origin as given in the past literature⁶
- Patients in which no final diagnosis could be reached

Thorough clinical examination of all the patients was carried out. Blood samples were obtained from all the patients and routine investigations were carried out. Patients remaining undiagnosed after that were referred to higher centers. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software. Chi- square test was used for assessment of level of significance.

RESULTS

In the present study, a total of 85 patients with undiagnosed fever were enrolled. Mean age of the patients was found to be 43.7 years. 44.71 percent of the patients belonged to the age group of 30 to 50 years. 56.47 percent of the patients were males while remaining 43.53 percent were females. In all these patients, final diagnosis was established based on haematological and clinical examination. Final diagnosis was found to be infectious in 49.41 percent of the cases, while it was found to be inflammatory (non-infectious) in 16.47 percent of the cases. Haematological pathology was found to be present in 12.94 percent of the cases. Undiagnosed cases were found to be 5 in number.

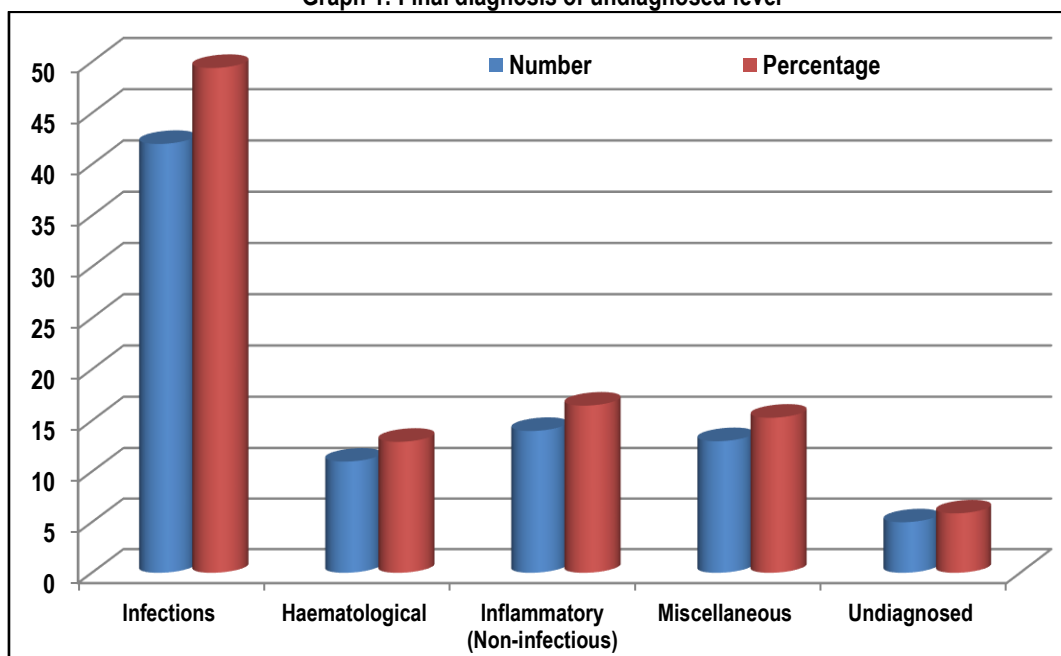
Table 1: Age-wise and gender-wise distribution

Parameter		Number	Percentage
Age group (years)	Less than 30	22	25.88
	30 to 50	38	44.71
	More than 50	25	29.41
Gender	Males	48	56.47
	Females	37	43.53

Table 2: Final diagnosis of undiagnosed fever

Final diagnosis	Number	Percentage
Infections	42	49.41
Haematological	11	12.94
Inflammatory (Non-infectious)	14	16.47
Miscellaneous	13	15.29
Undiagnosed	5	5.88

Graph 1: Final diagnosis of undiagnosed fever



DISCUSSION

Fever is one of the common presenting symptom in clinical practice. Most of the time fever is either self-limiting or with a definite underlying etiology. If fever remains persistent and undiagnosed, it is termed as fever of unknown origin (FUO). Classically FUO was defined by Petersdorf and Beeson's as a temperature above 38.3°C (101°F) on several occasions over a period of more than 3 weeks, for which no diagnosis has been reached despite 1 week of inpatient investigation.⁶⁻⁸

Bandyopadhyay D et al assessed the cause of FUO in a tertiary care hospital of eastern India. This was a prospective study of inpatients, with regard to both clinical signs and investigations. The main diagnosis in the end was tuberculosis, closely followed by hematological malignancy. A substantial number of cases remained undiagnosed despite all investigations. The provisional diagnosis matched with the final in around two thirds of the cases. While for younger patients leukemia was a significant diagnosis,

for older ones, extra-pulmonary tuberculosis was a main concern. In India, infectious disease still remains the most important cause of fever. Thus the initial investigations should always include tests for that purpose in a case of FUO. Geographic variations and local infection profiles should always be considered when investigating a case of FUO.⁶

In the present study, a total of 85 patients with undiagnosed fever were enrolled. Mean age of the patients was found to be 43.7 years. 44.71 percent of the patients belonged to the age group of 30 to 50 years. 56.47 percent of the patients were males while remaining 43.53 percent were females. In all these patients, final diagnosis was established based on haematological and clinical examination. Mir T et al evaluated the etiology of FUO in patients attending SKIMS, a tertiary care teaching hospital, at Srinagar, Kashmir, India. This study was done to examine the profile of patients with FUO. The classic FUO was defined as three outpatient visits or three days in the hospital without elucidation of cause of fever. Infectious agents, collagen vascular diseases and hematological malignancies as well as other etiologies were investigated when appropriate. The data were collected and analyzed. A total of 91 cases (62 males and 29 females), with age ranging from 16 to 80 years were investigated. The mean duration of fever before hospitalization was 26±4 days. The etiology of FUO was delineated in (66%) of cases, whereas, (25%) remained undiagnosed. Most common group of FUO was that of infectious diseases (44%) followed by collagen vascular diseases and malignancies (12 % each). Amongst the infection group, brucellosis and salmonellosis comprised the majority of cases (25% each). Infections are the most common cause of FUO followed by collagen vascular diseases in their region.⁸

In the present study, final diagnosis was found to be infectious in 49.41 percent of the cases, while it was found to be inflammatory (non-infectious) in 16.47 percent of the cases. Haematological pathology was found to be present in 12.94 percent of the cases. Undiagnosed cases were found to be 5 in number. In recent years, some authors proposed to change the quantitative criterion (diagnosis uncertain after 1 week or 3 days of investigation) with the qualitative requirement that fever remained undiagnosed after a minimal diagnostic work-up had been performed; however, investigations that should be included in the work-up remain a matter of debate.⁸⁻¹¹ Chin C et al assessed patients with fever of unknown origin. All patients fulfilling the modified criteria for FUO, either admitted, referred or consulted in a medical center in southern Taiwan, were enrolled for analysis. A total of 94 cases met the criteria of FUO. The final diagnoses of FUO consisted of 54 infectious diseases (57.4%), 8 hematologic/neoplastic (8.5%), 7 noninfectious inflammatory (7.4%), 8 miscellaneous (8.5%) and 17 undiagnosed (18.1%) cases. The single most common cause of FUO was tuberculosis. Some infectious diseases, such as rickettsiosis and melioidosis, were rarely reported in western countries. Three patients with hemophagocytotic syndrome without ascertainable etiologies were present with FUO in this study. Between the patients with and those without a final diagnosis, the short-term survival (3 months) was compared by the Kaplan-Meier analysis, which revealed no difference. Mycobacteriosis is still the leading cause of FUO in Taiwan and it is important to identify this treatable disease from all causes of FUO.¹

CONCLUSION

From the above results, the authors concluded that fever is one of the most confusing clinical manifestation. It might occur in such variable pathologies as infections, malignancy and drug effect and due to environmental toxicity. Even after intensive search, the etiology of a sizeable proportion of fevers remains unclear. However; further studies are recommended.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

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Cite this article as: Gajendra Singh, Kailash Sharma, Ummed Singh. A Study Related to Undiagnosed Fever in a Known Population: An Cross-Sectional Study. *Int J Med Res Prof*. 2020 Jan; 6(1): 137-39. DOI:10.21276/ijmrp.2020.6.1.034