Study Of Etiological Incidence Of Pyrexia Of Unknown Origin.(P.U.O) In OPD Mayo Hospital, Lahore

A P KHAN M HASAN
Correspondence to: A P Khan Department of Medicine, King Edward Medical College & Mayo Hospital, Lahore.

P.U.O has been a dilemma for a long time for doctors as well as patients, as fever is no doubt a marker of disease and not a disease itself and when this marker is not linked with other markers i.e. clinical symptoms and investigation reports, the alone marker is re-named as P.U.O. P.U.O has been defined as fever which persists for more than 2 weeks and remains undiagnosed despite work-up with other clinical findings and relevant investigations. P.U.O is annoying to the patient as well as the doctor as it may result in diseases with complications beyond treatment strategy or the disease itself in its worst form when it is ultimately diagnosed. The objective of this study is to highlight P.U.O cases in our O.P.D. department, which reflects the number of patients who could not be either assessed fully or diagnosed and we further re-evaluated these cases with an effort to diagnose and treat these patients. 32 patients in O.P.D, Mayo Hospital were included in this study which is still going on till December 1998. Every patient was assessed by a performa which was filled in and was investigated and followed up accordingly. We were successful in diagnosing 78%of the cases and 22% were still left undiagnosed.

Pyrexia of unknown origin, F.U.O i.e. fever of unknown origin has been a challenging experience ever since for doctors and a dilemma for patients, as pyrexia is a marker of illness, but not a disease in itself and at times may not be an indicator for a diagnosis as it may not be accompanied with the associated signs and symptoms, which makes a doctor think of a possible diagnosis.

With the passage of time, and better diagnostic facilities, P.U.O cases are decreasing round the globe but still has not become extinct, as smoldering cases are seen from time to time especially in areas where the advanced diagnostic tools are inaccessible due to various reasons i.e. poverty, lack of health facilities in BHU'S, health policies inadequate staff and other similar factors.

The best definition of P.U.O or pyrexia of unknown origin was given by Petersdorf and Beeson[1] in the United States in 1961 in a paper where they described 100 patients with P.U.O as temperature of 38.3°c or more which persists for more than 3 weeks, intermittent or continuous and remains undiagnosed despite basic investigations which include 7 days hospitalization.

While this definition has stood for 30 years, recently, it has been revised[2] and the definition proposed by Durack and Street is based on a new classification of P.U.O or F.U.O. These are:

1. Classical F.U.O:- It is modified only with regard to duration. It includes duration of three days in the hospital or three OPD visits and a fever of 2 weeks duration.
2. Nosocomial F.U.O:- It occurs in hospitalized patient receiving acute care and infection was not present on admission in these patients. Three days of investigation including atleast two days of incubation of cultures is the minimum duration for this diagnosis. Occult nosocomial infection infected IV lines recurrent pulmonary embolism, transfusion related viral infection and drug fever are possible diagnosis.
3. Neutropenic F.U.O:- Defined as fever of 38.3°C or more seen on several occasion in a patient with less than 500 neutrophils/cmm^3. Candida and Aspegillas infections, herpes simplex or CMV infections are included in this group.
4. HIV associated F.U.O:- Defined as fever of 38.3°C or more on several occasions over a period of more than 4 weeks for outpatients or more than 3 days duration in the hospital with HIV infection.

The diagnosis is invoked if 3 days of appropriate investigation, including 2 days of incubation of cultures reveals no source[4].In this group HIV infection alone may be a cause. M.avium intracellular, toxoplasmosis, CMV, tuberculosis, pneumocystis carinii, salmonellosis, cryptococcosis, histoplasmosis, non-Hodgkin's lymphoma and importantly drug fever or all possible causes. Adaptation of these categories of FUO on a wide scale in the literature allows a more rational approach.

Material & Methods:

32 patients from OPD Mayo Hospital was selected over a six months period starting from July 1997. Patients were randomly selected. All patients above the age of 14 years was included and both male and female group were studies.

Primary criteria for study included.

1. Patients who had never been labeled with a possible diagnosis.
2. 2.Patients who have been from one doctor to another and reached OPD Mayo Hospital with a hope for diagnosis and management.
3. Patients who were labeled with a probable diagnosis but did not show any beneficial response after the trial therapy period was over and patient remained symptomatic.

Exclusion Criteria

1. Already patient is suffering from a disease diagnosed earlier and fever was the outcome of an added complication i.e. known malignancy SLE and related disease. Rheumatoid arthritis on steroids etc.
2. Patient on drug trial therapy with a possible diagnosis established by another physician.

3. Patient presenting as P.U.O but the cause of fever was evident on gross clinical examination (e.g. in a diabetic patient with a carbuncle or cellulitis.)

The primary objective was to know the causatives factors of PUO in our community and to compare it with international studies, and also to help and treat these patients if possible.

The standard criteria as per written in the textbooks of medicine was followed and a performa was prepared and filled in by the patient.

Results

Our result indicate predominantly infective causes as the main etiology in P U O , these were tuberculosis (8 males and 4 females), typhoid fever (6 males and 2 females) and other 4 (table I). Only one case of SLE was seen. A significant majority i.e.,7 (2 males and five females) remained undiagnosed.

Table I Results:

Diagnosis	Male Patients	Female Patients
Tuberculosis	8	4
Typhoid Fever	6	2
Brucellosis	1	1
Liver Abscess	2	0
S.L.E	0	1
Undiagnosed	2	5

Discussion:

In various series of fever of unknown origin[5] infections is found to be the cause in 30-40%, neoplasia in 30%, drugs and connective tissue disease in 15%, miscellaneous causes in 15% which include factitious fever in 5% and in 10% the aetiology remains unknown. The majority of patients do not have a rare disease, but rather a relatively common disease presenting in a unusual way.

Common causes of pyrexia[6] of unknown origin as written in textbook of medicine is listed below:

Infection 40% which includes Pyogenic abscesses e.g. liver abscess, Tuberculosis, Urinary tract infection, Biliary infection, Subacute infective endocarditis, EBV infection,CMV infection, Q fever, Toxoplasmosis & Brucellosis.

Cancer 30% which includes Lymphomas, Leukaemias,Solid tumours e.g. Renal carcinoma, Hepatocellular carcinoma[7,8], Pancreatic carcinoma.

Immunogenic (20%)which includes Drugs, Connective tissue and autoimmune diseases e.g Rheumatoid disease, Systemic lupus erythematosis, Polyarteritis nodosa. Polymyalgias /cranial arteritis, Sarcoidosis & Factitious[9] (15%)which includes Switching thermometers, Injection of pyrogenic material etc.

Remain unknown (5-9%)

We have been successful in diagnosing 78% of cases but still 22% remained undiagnosed. The undiagnosed cases were advised regular check ups every fortnightly or to report if any new symptom/symptoms or sign/signs come up, so that probable/possible working diagnosis could be made and evaluated. Our results are comparable with the causes of P.U.O quoted in the literature but the ratio of infection is much higher than in the literature, although the infective causes have predominated the picture, we do not yet the outcome of undiagnosed cases, and the number of patients is rather too small for proper evaluation.

Conclusion:

Thus, an aggressive approach to the diagnosis of PUO is justified since there is a good chance that determination of a specific diagnosis will influence management and may result in curative treatment.

References:

1. Petersdorf RG, Beeson PB: Fever of unexplained origin. Medicine 40:1. 1961.
2. Durack DT, Street AC: Fever of unknown origin-reexamined and redifined, in Current Clinical Topics in Infectious Diseases, JS Remington. MN Swartz(eds). Cambridge, MA, Blackwell, 1991.
3. Dinarello CA, Wolff SM: Fever of unknown origin, in Principles and Practice of Infectious Diseases, 3rd ed, GL Mandell et al (eds). New York. Wiley. 1990. pp. 468-479.
4. Aduan R et al: Prolonged fever of unknown origin. Clin Research 26:558A, 1978.
5. Howard P JR et al: Fever of unknown origin: A prospective study of 100 patients. Tex Med 73:56. 1977.
6. Jacoby GA, Swartz MN: Fever of undertermined origin. N Engl J Med 289:1407. 1973.
7. Simon HB, Wolf SM: Granulomatous hepatitis and prolonged fever of unknown origin: A study of 13 patients. Medicine 52:1, 1973.
8. Smith JW: Southwestern internal medicine conference. Fever of undermined origin: Not what it used to be. Am J Med Sci 292:56, 1986.
9. Weinsten L: Clinically benign fever of unknown origin. A personal retrospective. ev Infect Dis 7:692. 1985.