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Original Article

Fever of unknown origin: A 12-year case series in Colombia

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Abstract

Background: Fever of unknown origin (FUO) is a diagnostic challenge with highly heterogeneous causes. Its etiology can change according to the studied regions, and the chance of reaching a diagnosis depends on available resources. The aim of this study is to describe the clinical characteristics, etiology and the usefulness of diagnostic aids in cases of FUO managed over 12 years in a Colombian reference center.

Methodology: Single-institution retrospective case series. All cases of FUO between 2006 and 2017 were identified with the help of an electronic medical record search software. Cases of adults with fever for more than three weeks who remained undiagnosed after three days of hospitalization are described.

Results: Of 1,009 cases evaluated, 112 cases met the inclusion criteria (median age 43 years, 66% men). The etiologies identified were infectious (31.2%), inflammatory (20.5%), neoplastic (14.3%), and miscellaneous (2.7%) diseases. 31.2% remained without etiological diagnosis. The most frequent conditions were tuberculosis (17%), Hodgkin's lymphoma (7.1%), systemic lupus erythematosus (6.3%), disseminated histoplasmosis, and adult Still's disease. Contrast tomography and biopsies were the studies that most frequently supported or confirmed the final diagnosis.

Conclusions: This series of contemporary Latin American cases suggests that the categories of FUO etiologies are similar to those reported in studies from developed countries, with tuberculosis being the most frequent cause in our setting. Our results highlight the importance of tomography-guided invasive studies in the diagnostic approach to FUO.

Key words: Fever; fever of unknown origin; pyrexia; tuberculosis; lymphoma; biopsy.

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Introduction

Fever is one of the most common symptoms in clinical practice. The diagnostic approach depends on accompanying signs and symptoms. Many febrile conditions can be easily diagnosed and treated, but in some cases, fever persists and the underlying cause remains elusive even after extensive investigations [1].

The definition of fever of unknown origin (FUO) has changed in past decades, becoming more relevant after the introduction of the classification by Petersdorf and Beeson in 1961. They defined FUO as a fever of 38.3°C or higher lasting at least 3 weeks and with no obvious cause after appropriate workup [2]. In 1991, Durack and Street classified FUO by categories: HIV-associated, neutropenic, nosocomial, and classical. They also proposed new parameters for the definition, a minimum of three outpatient visits or three days of in-hospital investigation. Such an adjustment considered the time needed for blood cultures and tuberculosis skin tests to show possible positive results [3].

Fever of unknown origin is one of the greatest diagnostic challenges for clinicians. Its differential diagnosis is extensive and includes infectious, autoimmune, neoplastic, and other rare disorders [4]. The proportion of FUO etiologies has evolved over time as new technologies have become available to enhance the diagnostic process. There are variations in etiologies depending on the setting and the countries where FUO is described. For instance, the frequency of infectious diseases is decreasing in developed countries, but in developing countries, they remain the cause [5,6].

In 2014, Hernandez *et al*. published that the distribution of FUO causes in Colombia was similar to that of developing nations. In that study, the majority of FUO causes were infectious (30.5%), followed by autoimmune (19.4%), neoplastic (11.1%), and

miscellaneous (2.7%), with about 36% undiagnosed [7]. The objective of this study is to describe the clinical and demographic characteristics and the usefulness of diagnostic aids in a contemporary series of patients with FUO in a reference hospital in Colombia.

Methodology

This is a single-institution retrospective, consecutive case series study at the Hospital Universitario San Ignacio, a reference hospital in Bogotá D.C., Colombia, conducted from 2006-2017. We included patients older than age 18 who had a body temperature of 38.3°C or higher for at least 3 weeks (4 weeks for HIV patients), and in whom the cause of fever remained unknown after three days of in-hospital studies. The institutional ethics committee approved this study (act FM-CIE-0180-18). The board waived informed consent as allowed by international declarations and local and institutional regulations.

We identified the patients using the specialized engine DISEArch [8] developed by researchers of the Pontificia Universidad Javeriana, Bogotá D.C., Colombia, a proved tool that uses structured and non-structured data to analyze sets of electronic health records (EHR), and identify patients with a specific characteristic or disease. DISEArch proved to reduce considerably the time required to obtain relevant information from EHR, without losing information in comparison with a manual search performed by a trained medical team. We searched unstructured text fields in EHR for key terms in Spanish ("*fiebre de origen desconocido*," "*síndrome febril prolongado*," "*síndrome febril sin causa aparente*," "*fiebre sin foco*," "*fiebre prolongada*"), and for the international classification of diseases (ICD-10) code R501 (persistent fever). The software selected and sorted cases according to the probability of meeting inclusion criteria. The authors also screened each case to determine compliance with inclusion and exclusion criteria. All the authors reviewed the cases, determining their inclusion by consensus.

Two authors collected clinical and demographic data from each EHR, including past medical history, sign or symptom besides fever, tests and images performed and its results, etiologies finally reached of FUO, and vital status at discharge. If the same patient had a new episode of FUO (with a cause other than the patient's first event), it was considered a new episode. Differences in data collected by different reviewers were resolved by consensus.

To define the utility of diagnostic tests, we considered *helpful clinical tests* those that oriented or supported final diagnosis, and *confirmatory diagnostic tests* those that ultimately settled the diagnosis. The data collection and storage processes were conducted using Google Drive, an online software solution.

The study presents frequency and percentages for qualitative data, and central tendency and dispersion measurements for quantitative data. Data analysis used SPSS 24, (IBM, Armonk, USA).

Table 1. Baseline Characteristics.

Characteristic	Total n = 112
Male sex – No (%)	74 (66.1)
Age – years, Median (IQR)	43.0 (29.2 - 59.8)
Fever duration before admission – days, Median (IQR)	30.0 (20.1 - 60.0)
Length of stay – days, Median (IQR)	20.0 (13.2 - 28.8)
Time to diagnosis from admission – days, Median (IQR)	19.5 (10.0 - 30.0)
Comorbidities	**No (%)**
HIV	28 (25.0%)
Hypertension	16 (14.3%)
Ischemic heart disease	1 (0.9%)
Valvular heart disease	2 (1.8%)
Heart failure	1 (0.9%)
Solid cancer	2 (1.8%)
Hematologic cancer	2 (1.8%)
Chronic kidney disease	6 (5.4%)
Diabetes	6 (5.4%)
Systemic autoimmune disease	9 (8.0%)

IQR: interquartile range.

Results

The search engine retrieved 1,009 cases, and after verification of eligibility criteria 112 FUO cases were finally included (66% male, median age 43 years, IQR: 21-80). Table 1 presents basal characteristics of the studied population.

The most frequent etiologies of FUO were infectious diseases (31.2%), followed by inflammatory diseases (20.5%), neoplastic diseases (14.3%), and miscellaneous diseases (2.7%). The most common condition was tuberculosis (TB), followed by Hodgkin's disease, and systemic lupus erythematosus. Table 2 summarizes the etiologies identified of FUO. When we evaluated the final diagnosis according to the years evaluated from 2006 to 2017, the proportion of undiagnosed cases progressively decreased from 50% to 12%, while infectious and inflammatory diseases increased and became the most common causes of FUO (Figure 1).

Tuberculosis was the cause of FUO in 17% of patients. The majority of cases were extrapulmonary TB with lymph node involvement (n = 6). One case was meningeal TB, and 6 cases were disseminated TB (concurrent pulmonary and extrapulmonary disease). The majority of disseminated cases presented with a miliary pattern (n = 3) and the remaining with

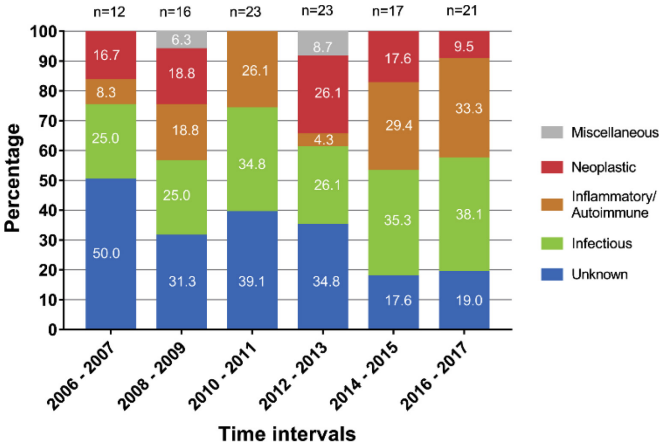
Table 2. Fever of unknown origin: classified by etiology groups.

Fever of unknown origin: classified by etiology groups	No.	%
Unknown	35	31.2
Infectious	35	31.2
Tuberculosis	19	17.0
Extrapulmonary	7	36.8
Pulmonary	7	36.8
Disseminated	6	85.7
Disseminated histoplasmosis	5	4.5
Multiple deep mycoses (*Histoplasma capsulatum, Scedosporium spp.*)	1	0.9
Leptospirosis	1	0.9
Non-tuberculous mycobacteria infection	1	0.9
Malaria	1	0.9
Epstein-Barr virus infection	1	0.9
Infected sub-diaphragmatic hematoma	1	0.9
Disseminated *Candida tropicalis* infection	1	0.9
Infective endocarditis	1	0.9
Disseminated cryptococcosis	1	0.9
Recurring suppurative cholangitis	1	0.9
Brucellosis	1	0.9
Inflammatory	23	20.5
Systemic lupus erythematosus	7	6.3
Adult-onset Still's disease	5	4.5
ANCA-associated vasculitis	3	2.7
Hemophagocytic syndrome	1	0.9
Sjögren's syndrome	1	0.9
Sarcoidosis	1	0.9
Inflammatory myopathy	1	0.9
Mixed connective tissue disease	1	0.9
Bowell inflmmatory disease	1	0.9
Undifferentiated connective tissue disease	1	0.9
Dermatomyositis	1	0.9
Neoplastic	16	14.3
Hodgkin's lymphoma	8	7.1
Non-Hodgkin high grade B cell lymphoma	3	2.7
Myelodysplastic syndrome	1	0.9
Chronic myelomonocytic leukemia	1	0.9
Hairy cell leukemia	1	0.9
Kaposi's Sarcoma	1	0.9
Solid tumor induced fever	1	0.9
Miscellaneous	3	2.7
Drug-induced fever	2	1.8
Hemolytic crisis in hereditary spherocytosis	1	0.9

* The patient had active breast cancer before admission. ANCA: antineutrophil cytoplasmatic antibody.

esophageal, central nervous system (CNS), or lymph node involvement. Sixteen (16) patients (14,3%) had a neoplastic disease causing FUO. Hodgkin's disease (n = 8) was the leading cancer, followed by aggressive non-Hodgkin B lymphoma (n = 3). Autoimmune/inflammatory diseases caused 23 (20.5%) of FUO cases. The most common diseases were

Figure 1. Etiology of FUO by 2-year periods.



systemic lupus erythematosus (7 cases), adult-onset Still's disease (5 cases), and ANCA-associated vasculitides (3 cases) (Table 2).

In 28 HIV infected individuals with FUO, the most common causes were extrapulmonary TB (5 cases), followed by disseminated TB (4 cases), disseminated histoplasmosis (4 cases), pulmonary TB (3 cases), and Hodgkin's lymphoma (3 cases). Kaposi's sarcoma, non-Hodgkin lymphoma, non-tuberculous mycobacterial infection, Epstein-Barr virus infection, and disseminated cryptococcosis accounted for 1 case each, while 4 cases remained undiagnosed.

The most frequent symptoms are summarized in Table 3. In summary, general symptoms such as malaise, chills, and diaphoresis were prevalent and appeared in similar proportions among etiologies. Cough and diarrhea were also common and similar among groups. Enlarged lymph nodes were more common in neoplastic diseases, whereas arthralgia, arthritis, myalgia, and skin lesions were more representative of inflammatory diseases. All patients had at least one concomitant symptom, even in undiagnosed cases.

Chest and abdominal computed tomographies (CT) were the first and second most frequent tests that oriented diagnosis in infectious and neoplastic diseases (helpful clinical tests).

Table 3. Most frequent concomitant symptoms.

	Unknown n = 35 (%)	Infectious n = 35 (%)	Inflammatory n = 23 (%)	Neoplastic n = 16 (%)	Total* n = 112
Cough	13 (37.1)	16 (45.7)	9 (39.1)	6 (37.5)	44 (39.2%)
Arthralgia	8 (22.9)	4 (11.4)	11 (47.8)	1 (6.3)	24 (21.4%)
Weight loss	6 (17.1)	7 (20.0)	3 (13.0)	3 (18.8)	19 (16.9%)
Myalgia	10 (28.6)	2 (5.7)	4 (17.4)	1 (6.3)	17 (15.2%)
Diarrhea	4 (11.4)	6 (17.1)	3 (13)	3 (18.8)	16 (14.2%)
Skin lesions	4 (11.4)	4 (11.4)	7 (30.4)	1 (6.3)	16 (14.0%)
Headache	7 (20.0)	5 (14.3)	1 (4.3)	2 (12.5)	15 (13.4%)
Hyporexia	4 (11.4)	3 (8.6)	3 (13.0)	2 (12.5)	12 (10.7%)

* Only symptoms with a total frequency of 10% or more are shown. Data from miscellaneous etiologies is not shown duo to the small number of cases.

Table 4. Tests that provided diagnostic clues (*helpful clinical tests)* distributed by category of FUO.

Test*	Infectious n = 35 (%)	Inflammatory n = 23 (%)	Neoplastic n = 16 (%)	Other n = 3 (%)
Any	25 (71.4)	15 (65.2)	13 (81.3)	2 (66.7)
Chest CT	15 (42.9)	3 (13,.0)	6 (37.5)	0 (0.0)
Abdominal CT	6 (17.1)	2 (8.7)	6 (37.5)	0 (0.0)
Head CT	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Chest X-Ray	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal ultrasound	1 (2.9)	0 (0.0)	2 (12.5)	0 (0.0)
Complete blood count	2 (5.7)	5 (21.7)	5 (31.3)	1 (33.3)
Bronchoalveolar lavage	0 (0.0)	3 (13.0)	0 (0.0)	0 (0.0)
Echocardiogram	2 (5.7)	1 (4.3)	0 (0.0)	0 (0.0)
Adenosine deaminase	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Brain MRI	2 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)
LDH	0 (0.0)	2 (8.7)	0 (0.0)	0 (0.0)
Auto-antibodies	0 (0.0)	2 (8.7)	0 (0.0)	0 (0.0)
Creatinine	0 (0.0)	2 (8.7)	0 (0.0)	0 (0.0)
Urinalysis	0 (0.0)	3 (13.0)	0 (0.0)	0 (0.0)
Peripheral blood smear	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
Hemolysis profile[+]	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
Histoplasma capsulatum urinary antigen	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Bone marrow biopsy	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
Serum complement	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
Direct Coomb's test	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
Liver function profile	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)

*Sum of diagnostic tests does not equal total number of patients in categories because one patient may have multiple diagnostic tests. [+]Refers to values for reticulocyte count, LDH, bilirubin, and haptoglobin compatible with hemolysis. CT: Computed tomography; MRI: magnetic resonance imaging; LDH: lactate dehydrogenase.

Table 5. Confirmatory diagnostic tests by category of FUO.

Test*	Infectious n = 35 (%)	Inflammatory n = 23 (%)	Neoplastic n = 16 (%)	Miscellaneous n = 3 (%)
Biopsy, any site[+]	20 (57.1)	8 (34.8)	14 (87.5)	0 (0.0)
Lymph node biopsy	11 (31.4)	1 (4.3)	7 (43.8)	0 (0.0)
Skin biopsy	4 (11.4)	0 (0.0)	0 (0.0)	0 (0.0)
Bone marrow biopsy	0 (0.0)	1 (4.3)	6 (37.5)	0 (0.0)
Kidney biopsy	0 (0.0)	3 (13.0)	0 (0.0)	0 (0.0)
Lung biopsy	6 (17.1)	1 (4.3)	0 (0.0)	0 (0.0)
Esophageal biopsy	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Liver biopsy	2 (5.7)	0 (0.0)	1 (6.3)	0 (0.0)
Colonic biopsy	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
Salivary gland biopsy	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
Bacilloscopic	2 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)
Blood cultures[#]	3 (8.6)	0 (0.0)	0 (0.0)	0 (0.0)
TB and rifampin resistance NAAT test	2 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)
Biopsy culture, any site	3 (8.6)	0 (0.0)	0 (0.0)	0 (0.0)
Bone marrow culture	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Autoantibodies	0 (0.0)	13 (56.5)	0 (0.0)	0 (0.0)
Clinical features only	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
Serum *Leptospira* IgM levels	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchoalveolar lavage	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Puncture of subdiaphragmatic collection	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
CSF adenosine deaminase levels	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Bone marrow flow cytometry	0 (0.0)	0 (0.0)	1 (6.3)	0 (0.0)
Osmotic fragility test	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)
Echocardiogram	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Rose Bengal test	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Histoplasma capsulatum urinary antigen	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Thick blood smear	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Necropsy	1 (2.9)	0 (0.0)	1 (6.3)	0 (0.0)
Serum creatinine kinase levels	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)

*Sum of diagnostic tests does not equal total number of patients in categories because one patient may have multiple diagnostic tests. [+]Sum of total number of biopsies does not equal the total number of biopsies because one patient may have multiple biopsies. [#]Blood cultures helped establish the diagnosis in one case of disseminated fungal infection, one case of disseminated TB infection, and one case of endocarditis. TB: tuberculosis; NAAT: nucleic acid amplification test; IgM: M class immunoglobulin; CSF: cerebrospinal fluid.

Complete blood count (CBC) was the most frequently orienting test for inflammatory causes (Table 4). Apart from basic hematology and chemistry laboratories, the most frequently performed tests were chest X rays (100%), followed by chest CT (92%), biopsies (85.7%), abdominal CT (79.5%), and lactate dehydrogenase (75%). Echocardiography was obtained for 56.3% of patients, but results proved useful in only 6.3% (n = 4) of tests. Bone marrow cultures were performed in 32.1% of cases, but only 1 was informative. Similarly, cytomegalovirus (CMV) viral load was obtained for 30.4% of patients, but none proved helpful, even in HIV cases. One positron-emission CT and 5 radio-labeled leukocyte scintigraphies were performed, with no helpful findings. Final diagnosis was reached most frequently with the help of biopsy of any organ in 35 cases (31.2%) in infectious, inflammatory, and neoplastic cases (Table 5).

Overall, 22 patients (19.6%) died during hospitalization. Patients diagnosed with neoplastic diseases had a higher in-hospital mortality rate (50%) than patients with infectious (14.3%), unknown (14.3%), and inflammatory causes (13%). It was not possible to establish survival after hospital discharge, as long-term follow-up was not available for most patients.

Discussion

Our study reports one of the largest series of FUO in Latin America. Similar to findings in previous reports worldwide, this work confirms that infectious diseases dominate as causes of FUO, with tuberculosis as the main cause. It thoroughly describes the use of diagnostic tests in the workup of these conditions, reaffirming the importance of contrast-enhanced CT and biopsies. The results also highlight a low diagnostic yield of frequently used tests such as echocardiograms and bone marrow cultures.

In a systematic review that included 3,164 patients from 18 case series, Fusco *et al.* [9] found that the most common causes of FUO were infectious diseases, followed by non-infectious inflammatory diseases and neoplasms, with undiagnosed cases accounting for as many as 20% of cases. This proportion varied depending on geographic location, though South American studies were not included. The present study's findings resemble those of the systematic review, except for the proportion of undiagnosed cases, which was higher in the present series. Case series from Colombia and Latin America also describe infectious diseases as the main cause of FUO [7,10,11], except for a report from Havana, Cuba, where neoplasms composed most cases [12]. Interestingly, the present study found a gradual decrease in the proportion of undiagnosed cases over time, contrary to reports in prior analyses of multiple case series [13] perhaps due to more availability of specialized tests in later years.

In many FUO series, TB has been particularly relevant. Clinical manifestations of TB are usually nonspecific, including disseminated disease without the characteristic miliary pattern on chest X rays or CT, or with single organ involvement of liver, spleen, kidneys, or lymph nodes [14,15]. In this study the most common individual FUO cause was TB, with extrapulmonary, pulmonary, and disseminated disease cases distributed almost evenly.

It is recommended that healthcare professionals look for potentially diagnostic clues (PDC) during the investigation of FUO. A retrospective study showed lower chances of reaching a diagnosis when PDC were absent [16], though other authors did not find such an association [17]. In the present series, arthralgia, arthritis, myalgia and skin lesions were more common in inflammatory etiologies and lymph node enlargement was more common in malignancies. However, all other signs or symptoms were not associated with finding a definite diagnosis, since even undiagnosed cases debuted with a wide variety of symptoms. This remarks the importance of performing a systematic diagnostic approach that includes first line diagnostic tests besides thorough anamnesis and physical examination.

Basic laboratory and imaging tests (blood cultures, serological tests for microbial pathogens, rheumatological diseases tests, blood chemistry, chest X-rays, and abdominal ultrasound) may help find a diagnosis in about one-fourth of FUO cases [18]. When diagnosis remains unclear, chest and abdominal CTs are usually performed, with helpful findings in 20% to 30% of cases, according to previous reports [19,20]. Findings in this study were similar, with helpful results in 37% of abdominal CTs and 31% of chest CTs. This study also found that more than half of patients had echocardiography, but it was useful in only four cases (6.3%) which is consistent with reports in other publications [17,19]. Head CT, bone marrow culture, and CMV viral load were also frequently performed (30.4% to 35.7% of patients), with poor diagnostic effectiveness (0% to 2.5%).

Although clinical symptoms and standard diagnostic testing suggest an etiology for a major subset of patients, the remaining cases require invasive procedures, including biopsies. The diagnostic contribution of biopsies has changed in the last 20

years. In a study performed in 2003, Vanderschueren *et al.* described a contribution rate of 9% to 34% [21]. Mete *et al.* in 2012 found that the diagnostic yield of invasive studies was 59% for infectious diseases, 19% for inflammatory/autoimmune diseases, and 100% for neoplasms [22]. These findings align with those of the present study (57.1%, 34.8%, and 87.5%, respectively). Bone marrow biopsy (BMB) is frequently part of systematic workup protocols for FUO. The present study found a diagnostic yield of 37.5% for BMB in neoplasms, similar to that reported by Benito *et al.* in patients with HIV infection [23]. Other studies, however, have reported a lower diagnostic yield (20%) in people without HIV [24].

Labeled leukocyte scintigraphy (LLS) and positron emission tomography (PET-CT) have been proposed as part of the systematic workup for FUO when a diagnosis remains elusive after extensive investigations [25,26]. Some studies, however, have found limited diagnostic yield for such exams [25]. In a meta-analysis by Bharucha *et al.* including 18 studies and 905 patients, PET-CT contributed to the diagnosis of FUO in 56% of cases [27]. Keidar *et al*. conducted a single-center prospective study in Israel; that documented the cause of FUO with PET-CT in 22 of 48 patients (46%) [28]. Only one PET-CT and five LLS were performed in our series, and none helped find a final diagnosis. A possible reason is that PET-CT is a costly test that is not readily available in the majority of institutions in Colombia. Considering the cited studies, it is likely that a higher use of PECT-CT may help decrease the rate of cases that remain undiagnosed.

The main limitation of this study is that our patients are drawn from a single center, were resources may be significantly different from those available at other institutions in the region. This may limit the external validity of our findings. However, we accept patients from all over the country and from different socioeconomic background. Another limitation is the retrospective nature of the study. The authors have taken steps to mitigate these biases by utilizing software to screen for cases and double-confirming inclusion and exclusion criteria. This approach helps to reduce the likelihood of human error. Another significant limitation is the lack of follow-up for many patients, which hinders the ability to estimate mortality rates for categories of causes beyond hospitalization.

Conclusions

This study suggests that causes of FUO in Colombia are not significantly different from those of developed countries, with infectious causes as the main category of FUO, and with a high proportion of cases remaining undiagnosed. Notably, in contrast to reports from developed countries, and despite the limited availability of resources in Colombia, the proportion of undiagnosed cases has decreased over recent years in our series. The study also highlights the significance of a comprehensive diagnostic process, with CT scans and biopsies playing a pivotal role.

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