

Changes in the Spectrum of Systemic Autoimmune and Autoinflammatory Diseases in Sub-Saharan Africa: A Cohort Study of 1,006 Patients in Senegal

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Abstract

Introduction: Data on systemic diseases in sub-Saharan Africa remain limited despite a widening clinical spectrum and recognition of their contribution to chronic disease burden. In tropical environments, these conditions are often characterized by significant diagnostic delays and severe visceral involvement. This study reports on the comprehensive disease spectrum within a major Senegalese internal medicine department. **Methods:** We performed a descriptive, retrospective cohort study of all patients managed for systemic diseases in the Internal Medicine Department of Dalal Jamm National Hospital from August 29, 2016, to August 18, 2021. Diagnoses were cross-referenced against international criteria based on full clinical and paraclinical evidence. **Results:** During the study period, a total of 1,136 medical records were screened, and 130 were excluded due to insufficient data, resulting in 1,006 unique medical records analyzed. The mean age was 48.11 years, ranging from 3 to 91 years, with a clear female predominance of 82.03% and a sex ratio of 0.219. The median time to diagnosis was 3 years (range: 0 - 46 years; mode: 1 year). Chief complaints were dominated by joint involvements in 83.73% of cases, primarily presenting as polyarthritis in 60.6% of patients. A family history of inflammatory rheumatism was identified in 23.76% of the cohort. Autoimmune diseases represented 67.1% of the total cases, followed by autoinflammatory diseases at 19.4%, undifferentiated connective tissue diseases at 10.9%, systemic

vasculitides at 2.1%, and granulomatoses at 0.5%. In the autoimmune group, rheumatoid arthritis predominated with 499 cases; Systemic Lupus Erythematosus (SLE) accounted for exactly 34 cases (3.4%). Among autoinflammatory conditions, polygenic forms like ankylosing spondylitis led with 89 cases, while a single monogenic case of Familial Mediterranean Fever was recorded with a diagnostic delay of 20 years. Behçet's disease led the vasculitis group with 14 cases. Methotrexate was the most common disease-modifying antirheumatic drug utilized, prescribed to 54.20% of patients on maintenance therapy. **Conclusion:** This cohort demonstrates a broad, diverse spectrum of systemic conditions in tropical settings, dominated by polygenic autoimmune and autoinflammatory disorders. Marked diagnostic delays persist for rare or monogenic diseases, arguing for the establishment of regional registries to support large-scale clinical trials.

Keywords

Autoimmune Diseases, Autoinflammatory Diseases, Connective Tissue Diseases, Rheumatoid Arthritis, Familial Mediterranean Fever, Senegal

1. Introduction

Systemic diseases comprise a heterogeneous group of immunologically based conditions affecting multiple organ systems simultaneously or sequentially [1]. When mediated by autoimmune mechanisms, they fall under the category of connective tissue diseases [1]. Despite major advances in understanding their pathophysiology, their underlying mechanisms of onset remain complex and multifactorial [1] [2]. Historically, these conditions were considered rare in sub-Saharan Africa, a perception supported by the hygiene hypothesis and clinical masking by major infectious endemic diseases.

However, hospital-based observations in sub-Saharan Africa indicate a shift in the clinical landscape [3]. Urbanization, changes in lifestyle, and increased life expectancy are accompanied by the emergence of noncommunicable diseases (NCDs), including chronic inflammatory and autoimmune conditions [3]. Despite this increase, regional epidemiological data remain limited, often restricted to fragmented hospital series [3]. In tropical settings, these patients face significant diagnostic delays, exposing them to severe and irreversible visceral damage [3].

In recent years, increased access to expertise in clinical immunology and the development of laboratory facilities have begun to reveal the true diversity of this spectrum. Characterizing this epidemiological landscape is essential for optimizing the allocation of healthcare resources and improving patient outcomes. This study reports on the clinical spectrum, recent epidemiological profile, and diagnostic challenges of a cohort of 1,006 patients treated at a referral internal medicine department in Dakar, Senegal.

2. Patients and Methods

2.1. Study Setting and Design

We conducted a retrospective, descriptive cohort study over a 5-year period from August 29, 2016, to August 18, 2021, within the Internal Medicine Department of the Dalal Jamm National Hospital Center (CHN Dalal Jamm) in Dakar, Senegal. The end of this period coincided with the outbreak of SARS-CoV 2 pandemic, during which the department was partially integrated into the epidemic treatment center, disrupting the usual rhythm of outpatient visits and hospitalizations.

2.2. Inclusion and Classification Criteria

A total of 1,136 medical records of patients seen in the outpatient clinic or hospitalized for a systemic condition were initially screened. Among these, 130 records were excluded because they were incomplete or did not allow for the extraction of basic demographic or diagnostic data. This selection process resulted in a final cohort of 1,006 unique patients, ensuring the transparency of our sampling frame and final cohort selection. Inclusion was based on diagnostic confirmation according to validated international classification criteria [4]:

- 1) Rheumatoid arthritis (RA): 2010 ACR/EULAR criteria [5] [6].
- 2) Systemic lupus erythematosus (SLE): 2019 ACR/EULAR criteria or SLICC criteria [7]-[9].
- 3) Primary Sjögren's syndrome (PSS): 2016 ACR/EULAR criteria [10].
- 4) Systemic sclerosis (SSc): 2013 ACR/EULAR criteria [11].
- 5) Idiopathic inflammatory myopathies (IIM): Hoogendijk or Troyanov criteria [12] [13].
- 6) Familial mediterranean fever (FMF): Tel Hashomer diagnostic criteria [14].
- 7) Ankylosing spondylitis (AS): Modified New York criteria [15].
- 8) Juvenile idiopathic arthritis (JIA): Edmonton criteria [16].
- 9) Systemic vasculitides: Definitions from the 2012 Chapel Hill Consensus Conference [17].
- 10) Sarcoidosis: Consensus clinical, radiological, and histopathological criteria [18].

2.3. Data Collection and Analysis

Data were collected using a standardized questionnaire assessing demographic information, reasons for consultation, time to diagnosis, comorbidities (particularly cardiovascular risk factors), gynecological and obstetric history, and treatment regimens received.

The time to diagnosis was defined as the interval between the onset of the first clinical symptom and formal diagnostic classification based on international criteria. Symptom onset was retrospectively identified and extracted from the history of the disease section of the medical records, as documented during the patient's initial internal medicine consultation. To address uncertain or partially missing dates, a standardized imputation rule was applied: when only the year of onset

was known, the onset was set to the midpoint of that year (July 1st); if only the season or month was recalled, the midpoint of that specific period was utilized.

Statistical analysis was performed using Excel and SPSS software. Quantitative variables are expressed as means and standard deviations, qualitative variables as counts and percentages. Bibliographic management was conducted using Zotero software according to the Vancouver system. The study received the required administrative approvals, and patient anonymity was strictly maintained.

3. Results

3.1. Demographic Profile and Time to Diagnosis

A total of 1,006 patients were included. The mean age of the cohort was 48.11 years, with a high concentration of patients (74.64%) in the 25 - 64 age group. There was a clear predominance of females (82.03%), resulting in a sex ratio (M/F) of 0.219. The time to diagnosis was documented for 675 patients. The distribution was heavily skewed with a mean of 4.34 ± 5.88 years, a mode of 1 year, and a median of 3 years (range: 0 to 46 years). Subgroup variations are presented in **Figure 1** and **Table 1** (p. 3). The mean time to diagnosis (from the first symptom to formal classification) was 4.34 years, varying across pathological subgroups (**Figure 1**) (**Table 1**):

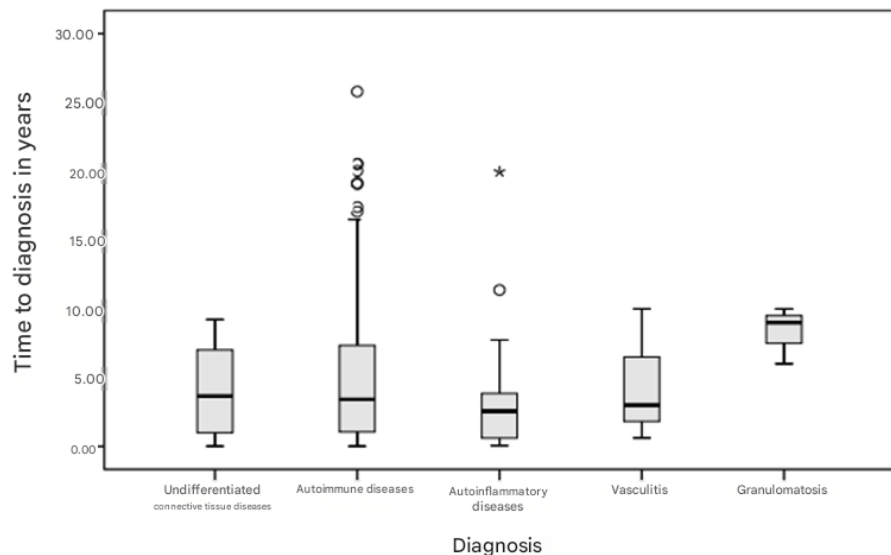


Figure 1. Variation in diagnostic delays according to the spectrum of systemic diseases.

Table 1. Epidemiological aspects according to the spectrum of systemic diseases.

Disease Entity/Spectrum	Age Mean (SD)	Female (N)	Male (N)	Male-to-Female Ratio	Time to Diagnosis Mean (SD)
Autoimmune Diseases	48 (15)	587	88	0.15	5 (7)
Systemic Lupus Erythematosus	39 (14)	32	2	0.06	4 (3)
Inflammatory Myopathy	39 (15)	23	4	0.17	4 (8)

Continued

Rheumatoid Arthritis	49 (14)	431	68	0.16	5 (7)
Atrophic Polychondritis	50 (-)	1	0	0.00	-
Primary APS (SAPL)	46 (18)	4	0	0.00	12 (14)
Systemic Sclerosis	42 (21)	7	1	0.14	4 (-)
Multiple Autoimmune Syndrome	65 (5)	3	0	0.00	5 (3)
Overlap Syndrome	47 (15)	62	3	0.05	4 (5)
Sharp Syndrome	62 (12)	1	1	1.00	-
Primary Sjögren's Syndrome	52 (17)	29	3	0.10	3 (4)
Undifferentiated Conn. Tissue Disease	46 (17)	88	22	0.25	5 (6)
Autoinflammatory Diseases	51 (19)	130	65	0.50	4 (3)
Juvenile Idiopathic Arthritis	15 (6)	11	4	0.40	1 (1)
Familial Mediterranean Fever	27 (-)	1	0	0.00	20 (-)
Gout	64 (13)	31	29	0.94	3 (2)
Still's Disease	27 (-)	0	1	1.00	4 (0)
Systemic IBD	38 (28)	1	2	2.00	2 (2)
Polymyalgia Rheumatica (PPR)	63 (8)	22	3	0.14	3 (3)
Psoriatic Arthritis	40 (-)	1	0	0.00	4 (-)
Ankylosing Spondylitis	43 (15)	63	26	0.41	4 (3)
Systemic Vasculitides	37 (10)	8	11	1.38	3 (2)
Granulomatosis with Polyangiitis	50 (-)	1	1	1.00	-
Behçet's Disease	32 (6)	4	10	2.50	3 (2)
Giant Cell Arteritis	72 (-)	0	1	1.00	4 (0)
Polyarteritis Nodosa (PAN)	57 (-)	1	0	0.00	3 (-)
Microscopic Polyangiitis	48 (11)	2	0	0.00	4 (-)
ANCA-Associated Vasculitis	40 (-)	1	0	0.00	18 (-)
Granulomatoses	48 (26)	2	3	1.50	7 (3)
Rosai-Dorfman Disease	3 (-)	0	1	1.00	-
Kimura's Disease	59 (11)	1	1	1.00	10 (1)
Sarcoidosis	60 (2)	1	1	1.00	5 (1)

Note: ***Legend:** APS/SAPL: Antiphospholipid Syndrome; SD: Standard Deviation; IBD: Inflammatory Bowel Disease.

3.2. Clinical Manifestations and Comorbidities

The reasons for consultation were dominated by joint manifestations (83.73%), primarily of the polyarthritis type (60.6%). Cardiovascular risk profiles were comprehensively documented for a subset of 594 patients; data were missing for the remaining 412 patients primarily due to the acute/emergency context of certain admissions or incomplete long-term retrospective charting. Within this analyzed subset of 594 patients with a complete cardiovascular profile, 37.21% had at least one

cardiovascular risk factor: hypertension (25.79%), diabetes (7.57%), dyslipidemia (2.35%), stroke (0.33%), and peripheral arterial disease (0.33%). In terms of gynecological and obstetric history, 6.38% of the women in the series (n = 51) reported at least one history of spontaneous abortion [19] [20].

3.3. Distribution of the Systemic Spectrum

The cohort was divided into defined immunopathological subgroups (**Figure 2**) (**Table 2**):

1) Systemic autoimmune diseases (67.1%, n = 675): Largely dominated by rheumatoid arthritis (49.7%, n = 499), followed by overlap syndromes (6.5%, n = 65), systemic lupus erythematosus (3.4%, n = 34), primary Sjögren's syndrome (3.2%, n = 32), inflammatory myopathies (2.7%, n = 27), systemic sclerosis (0.6%, n = 8), primary SAPL (0.4%, n = 4), multiple autoimmune syndromes (0.3%, n = 3), Sharp syndrome (0.2%, n = 2), and atrophic polychondritis (0.1%, n = 1).

2) Undifferentiated connective tissue diseases: These accounted for 10.9% (n = 110) of the entire cohort.

3) Autoinflammatory diseases (19.4%, n = 195): Primarily composed of polygenic forms: ankylosing spondylitis (8.8%, n = 89), gout (6.0%, n = 60), rhizomelic pseudo-polyarthritides (2.5%, n = 25), juvenile idiopathic arthritis (1.5%, n = 15), systemic IBD (0.3%, n = 3), adult-onset Still's disease (0.1%, n = 1), and psoriatic arthritis (0.1%, n = 1). A single case of a monogenic form was identified: Familial Mediterranean Fever (FMF) (0.1%).

4) Systemic vasculitides (2.1%, n = 21): Including Behçet's disease (1.4%, n = 14), granulomatosis with polyangiitis (n = 2), microscopic polyangiitis (n = 2), giant cell arteritis (n = 1), ANCA-associated vasculitides (n = 1), and nodular periarteritis (n = 1).

5) Granulomatoses (0.5%, n = 5): Represented by Kimura disease (n = 2), sarcoidosis (n = 2), and Rosai-Dorfman disease (n = 1).

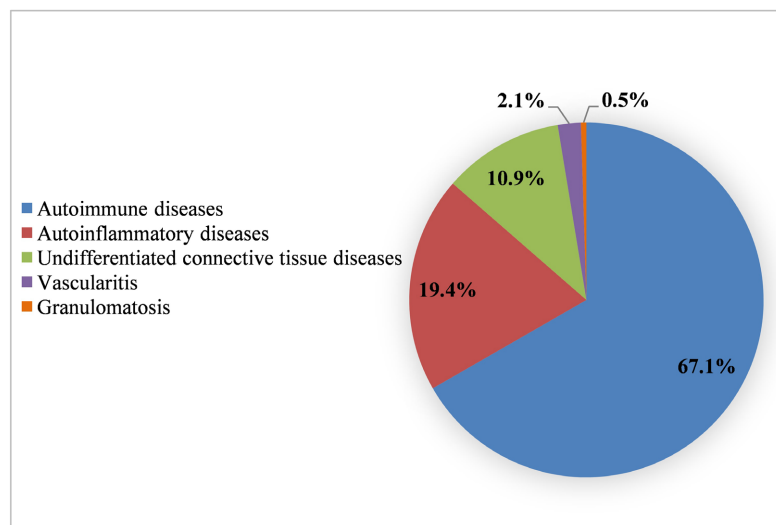


Figure 2. Distribution of patients according to the spectrum of systemic diseases.

Table 2. Distribution of patients by diagnosis.

Main Spectrum and Diagnostic Groups	Number (N)	Percentage (%)
Systemic Autoimmune Diseases	675	67.1
Rheumatoid Arthritis	499	49.7
Overlap Syndrome	65	6.5
Systemic Lupus Erythematosus	34	3.4
Primary Sjögren's Syndrome	32	3.2
Inflammatory Myopathies	27	2.7
Systemic Sclerosis	8	0.6
Primary SAPL (APS)	4	0.4
Multiple Autoimmune Syndrome	3	0.3
Sharp Syndrome	2	0.2
Atrophic Polychondritis	1	0.1
Undifferentiated Connective Tissue Diseases	110	10.9
Autoinflammatory Diseases	195	19.4
Ankylosing Spondylitis	89	8.8
Gout	60	6.0
Polymyalgia Rheumatica Syndrome	25	2.5
Juvenile Idiopathic Arthritis	15	1.5
Systemic IBD	3	0.3
Familial Mediterranean Fever	1	0.1
Still's Disease	1	0.1
Psoriatic Arthritis	1	0.1
Vascular Diseases/Vasculitides	21	2.1
Behçet's Disease	14	1.4
Granulomatosis with Polyangiitis	2	0.2
Microscopic Polyangiitis	2	0.2
Giant Cell Arteritis	1	0.1
Nodular Periarteritis (PAN)	1	0.1
ANCA-Associated Vasculitis	1	0.1
Granulomatoses	5	0.5
Kimura Disease	2	0.2
Sarcoidosis	2	0.2
Rosai-Dorfman Disease	1	0.1
Total Cohort	1006	100.0

3.4. Therapeutic Approaches

Long-term maintenance treatment was initiated in 583 patients. The remaining

423 patients did not receive long-term csDMARDs or maintenance therapy because they either defaulted immediately after diagnostic confirmation, elected to pursue traditional alternative medicine, or presented with self-limiting acute conditions requiring only short-term symptomatic interventions.

Among the 583 treated patients, Methotrexate was the most commonly prescribed drug (54.20%, $n = 316$), followed by hydroxychloroquine (43.34%, $n = 253$), sulfasalazine (12.03%, $n = 70$), allopurinol (7.03%, $n = 41$), azathioprine (4.46%, $n = 26$), mycophenolate mofetil (0.51%, $n = 3$), and leflunomide (0.34%, $n = 2$). Dual therapy was utilized in 22.47% of these cases, whereas triple therapy was observed in only two patients. Access to biologic therapy (Rituximab) remained rare (0.17%, $n = 1$) [21] (Table 3).

Table 3. Distribution of patients by monotherapy maintenance treatment.

Maintenance Therapy	Frequency (n)	Percentage (%)*
Methotrexate	316	54.20
Hydroxychloroquine	253	43.34
Salazopyrin (Sulfasalazine)	70	12.03
Allopurinol	41	7.03
Azathioprine	26	4.46
Mycophenolate Mofetil	3	0.51
Leflunomide	2	0.34
Rituximab	1	0.17

*Note: Percentages sum to greater than 100% due to patients undergoing overlapping dual/triple regimens.

4. Discussion

4.1. Evolution of the Phenotypic Spectrum and Epidemiological Transition

Our study describes one of the largest single-center cohorts of systemic diseases in West Africa. Our results demonstrate that the immunological landscape in tropical settings is far broader and more complex than previously recognized. While 20th-century paradigms suggested a relative rarity of autoimmune diseases among African populations with dark skin, the analysis of these 1,006 cases documented over 5 years reflects an increasing detection rate in specialized clinical structures [22].

Consistent with global data, RA is the most common condition, accounting for nearly half of our cohort (49.7%). Its prevalence aligns with Kane's multicenter studies in Dakar [22]. It is interesting to note geographical and recruitment variations on a continental scale: while our series places lupus (3.4%) and undifferentiated connective tissue diseases (10.9%) behind RA, series in Ouagadougou report a predominance of systemic sclerosis [23], and teams in Abidjan describe lupus as the leading condition [24]. These discrepancies likely reflect the density

of specialists in rheumatology or internal medicine across different capitals rather than actual genetic gradients [25].

The mean age (48.11 years) and the strong female predominance (sex ratio of 0.219) align with data from the international literature, confirming the role of sex hormones in modulating the immune response. Furthermore, the high prevalence of cardiovascular risk factors (37.21%), particularly hypertension (25.79%), underscores that the development of accelerated atherosclerosis induced by chronic systemic inflammation represents a major prognostic challenge in Africa [6] [20].

4.2. The Major Challenge of Diagnostic Delay: The Critical Case of FMF

The overall median diagnostic delay of 3 years (mean: 4.34 years) constitutes a major obstacle to optimal management, as uncontrolled chronic inflammation leads to irreversible structural or visceral damage [22]. However, detailed analysis by disease reveals that this diagnostic delay is particularly extreme for rare or underrecognized conditions in our region. In our series, the longest diagnostic delay was observed for a monogenic autoinflammatory condition, Familial Mediterranean Fever (FMF), where the gap between the age of symptom onset in the patient and the age at diagnosis reached 20 years [26].

This delay is considerably longer than those reported in countries where the disease is classically described. In Morocco, a country with a high prevalence of this condition, the average diagnostic delay within a national cohort is only 10.75 years [27]. These results clearly demonstrate that diagnostic delay for FMF remains the norm in our context [26]. This critical delay is largely due to a lack of awareness of the disease among our frontline healthcare professionals, who rarely consider monogenic autoinflammatory syndromes when faced with recurrent febrile episodes or serositis in tropical settings, mistakenly preferring to perform multiple tests for infectious or parasitic causes.

4.3. Prominent Role of Polygenic Autoinflammatory Diseases

While FMF illustrates the complexity of monogenic forms linked to innate immunity [4], the autoinflammatory diseases (AIDs) in our cohort are largely dominated by polygenic entities (19.4% of the overall cohort) [22]. Ankylosing spondylitis (8.8%) and gout (6.0%) constitute the main core of these conditions [22]. Long underestimated among Black Africans, ankylosing spondylitis emerges here as a major reason for seeking care in tropical rheumatology, despite the historically low prevalence of the HLA-B27 allele in this subregion, suggesting other polygenic pathways or environmental factors specific to the tropical setting [28].

Gout, for its part, represents a polygenic metabolic IAM whose rising incidence reflects the Westernization of diets and the increase in metabolic syndromes in urban Africa [29]. Finally, polymyalgia rheumatica (PPR) (2.5%) demonstrates that inflammatory conditions in the elderly are actively emerging in Senegal, in parallel with increasing life expectancy. These polygenic forms share a critical

challenge in tropical regions: their tendency to mimic septic arthritis or post-infectious reactive arthropathies, frequently leading to inappropriate antibiotic prescriptions and delaying the initiation of csDMARDs or colchicine [9].

4.4. Systemic Granulomatoses: Differential Diagnostic Challenges in Tuberculosis-Endemic Areas

Although granulomatous diseases account for only 0.5% (n = 5) of our cohort, their relevance in tropical internal medicine is critical due to the diagnostic pitfalls they share with granulomatous infectious diseases, foremost among which is tuberculosis. Sarcoidosis (2 cases) and Rosai-Dorfman disease (1 case) are characterized by lymphadenopathy and systemic involvement, the clinical and radiological presentation of which closely mimics lymph node or multifocal tuberculosis. In West Africa, identifying the precise origin of such respiratory signs remains a cornerstone of clinical practice, as pleuropulmonary manifestations are common features of underlying connective tissue diseases [30]. In tropical settings, the practice of routinely treating all granulomatous diseases as tuberculosis (due to endemicity) exposes these patients to unnecessary drug toxicity and delays the initiation of life-saving corticosteroid therapy [18].

The presence of two cases of Kimura's disease, a cutaneous-lymph node eosinophilic granulomatosis that is extremely rare in dark-skinned individuals, illustrates the extreme diversity of our center's patient population [19]. When faced with a presentation of skin nodules and lymphadenopathy associated with massive hypereosinophilia in a tropical setting, the clinician legitimately and primarily considers filariasis or another invasive helminthiasis. The absence of microfilariae and histopathological confirmation of a granulomatous infiltrate rich in immunoblasts and eosinophils without caseous necrosis allow the diagnosis to be revised in favor of Kimura's disease, thereby avoiding repeated courses of ineffective anthelmintics [19].

4.5. Profile of Vasculitides: Predominance of Behçet's Disease and Prevalence of Secondary Forms

Within our vasculitis subgroup (2.1%, n = 21), Behçet's disease was the predominant form with 14 cases (66.6% of vasculitides), a finding fully consistent with Kane's observations [22]. To contextualize these data, it is worth referring to the seminal work by Ndongo *et al.* on systemic vasculitides in Senegal [31]. In their study of 27 cases collected in hospitals in Dakar, the authors had already highlighted the overall rarity of primary systemic vasculitides in sub-Saharan Africa, while confirming the predominant role of Behçet's disease within this spectrum [31].

A crucial element shared by the observations of Ndongo *et al.* concerns the importance of secondary vasculitides in our setting [32]. In tropical African settings, presentations of vasculitis occur very frequently during the course of major, long-standing underlying connective tissue diseases [32]. This is the case with rheumatoid vasculitis complicating severe and neglected rheumatoid ar-

thrititis or lupus vasculitis, which is particularly favored by delayed diagnosis [32]. Furthermore, clinicians must distinguish these forms of vasculitis from those associated with chronic endemic infections (e.g., hepatitis B and C viruses, HIV), which often present as cryoglobulinemia or secondary leukocytoclastic vasculitis mimicking primary forms [32]. This phenotypic duality requires absolute diagnostic rigor to avoid serious therapeutic errors based on indiscriminate immunosuppression.

4.6. Strengths and Limitations of the Study

The main strength of this study lies in its large sample size (1,006 patients) recruited from a single university center, ensuring relative homogeneity of clinical criteria. Conversely, its retrospective nature results in missing data. Furthermore, technical limitations (unavailability or high cost of certain specific immunological tests, such as detailed ANCA testing or genetic testing for autoinflammatory diseases) may have limited diagnostic accuracy, explaining the rate of connective tissue diseases classified as “undifferentiated” (10.9%).

Additionally, because our department serves as a major national tertiary referral center, the study cohort is subject to a significant selection bias. The observed cases represent hospital-based frequencies within a specialized setting rather than the true prevalence or incidence of these conditions in the general population.

5. Conclusion

Our study highlights a rich, balanced, and diverse spectrum of systemic autoimmune, autoinflammatory, and granulomatous diseases in Senegal, definitively refuting the hypothesis that these conditions are rare in tropical settings. While rheumatoid arthritis remains the predominant condition, the emergence of polygenic autoinflammatory diseases and the diagnostic challenge posed by granulomatoses (particularly in relation to tuberculosis) necessitate a reassessment of our clinical management algorithms. Significant diagnostic delays (illustrated by the 20-year diagnostic odyssey for FMF) and limited access to targeted therapies are the main obstacles to improving prognosis. There is an urgent need to integrate clinical immunology into national public health programs and to strengthen training for healthcare professionals to end diagnostic delays.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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