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Trends in Internal Medicine

Immune-Mediated Inflammatory Diseases Diagnosed In Internal Medicine Department at the University Hospital Center of the Point G: An Epidemiological and Clinical Overview

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ABSTRACT

Background: *Immune-mediated inflammatory diseases (IMIDs) characterized by three nosological entities, autoimmune diseases, auto inflammatory diseases and inflammatory diseases of undetermined mechanism, share in common the inflammatory process but their clinical and biological expressions are extremely diverse. A panoramic study of IMIDs could contribute to identify the epidemiological, immuno-genetical, environmental, pathophysiological and clinical disparities. We aimed in this work to describe epidemiological and clinical aspects of all IMIDs diagnosed in internal medicine department.*

Methods: *We retrospectively analyzed data from patients hospitalized for IMIDs between 2018 and 2019.*

Results: *921 patients hospitalized from 2018 to 2019, 205 patients (56.10% female) presented with immune-mediated inflammatory disease, of which two cases of associations, which is 207 cases of IMIDs (22.48%). IMIDs were dominated by inflammatory diseases of undetermined mechanism (113 cases) followed by autoimmune diseases (84 cases) and auto inflammatory diseases (10 cases). Organ-specific autoimmune diseases (72 cases) dominated the autoimmune diseases: type 1 diabetes (40 cases), Graves' disease (13 cases) versus systemic autoimmune diseases (12 cases): rheumatoid arthritis (04 cases), systemic lupus erythematosus (03 cases). There were no cases of monogenic forms. "organ-specific" polygenic forms (07 cases) dominated the polygenic auto-inflammatory diseases: gout (02 cases), ulcerative colitis (02 cases) versus "systemic" polygenic forms (03 cases): Horton's disease (01 case). Inflammatory diseases of undetermined mechanism were dominated by neoplasia (109 cases): Solid tumor (77 cases) [hepatocellular carcinoma (14 cases), breast cancer (09 cases)] and hematological malignancies (31 cases) [non-Hodgkin's malignant lymphoma (14 cases), chronic myeloid leukemia (8 cases)] followed by paraneoplastic syndromes (02 cases) and inflammatory diseases of iatrogenic origin (02 cases).*

Conclusion: *IMIDs is frequently diagnosed in internal medicine and dominated by inflammatory diseases of undetermined mechanism followed by autoimmune diseases and auto inflammatory diseases.*

Keywords
Immune-mediated inflammatory diseases, Internal medicine, Mali.

Introduction
Immune-mediated inflammatory diseases (IMIDs) amongst which type 1 diabetes, spondylosing arthritis, juvenile idiopathic arthritis, coeliac disease, inflammatory bowel disease, graft versus host disease and colon cancer are diseases in which our immune system is defective and causes chronic tissue damage [1]. IMIDs are characterized by three nosological entities and their nosological sub-entities: (i) autoimmune diseases (systemic autoimmune diseases, organ-specific autoimmune diseases), (ii) autoinflammatory diseases (monogenic autoinflammatory diseases, polygenic autoinflammatory diseases: "systemic" polygenic autoinflammatory diseases and "organ-specific" polygenic autoinflammatory diseases) and (iii) inflammatory diseases of undetermined mechanism (neoplasms, paraneoplastic syndromes and inflammatory diseases of iatrogenic origin) [2-5]. These nosogical groups have in common the inflammatory process, but their clinical and biological expressions are extremely diverse. A panoramic study of IMIDs could contribute to identify the epidemiological, immuno-genetical, environmental, pathophysiological and clinical disparities; and notably the main commonalities of some IMIDs. Thus, the resulting findings could direct research of the same therapeutic targets and new approaches for preventive medicine for a large number of IMIDs. Although the prevalence of IMIDs has already been estimated in the Western society at 5-7% [3], IMIDs patients represented about 4% of the population according to two US healthcare datasets [6], the overall prevalence of some selected IMIDs was estimated by 2258 per 100 000 inhabitants [7], the African literature seems to be on the fringes of this new concept in rheumatology. However, epidemiological aspects of some nosological entities and sub-entities of IMIDs have been reported there as connective tissue diseases [8-10,5], autoinflammatory diseases [5,11], neoplasms [12]. We aimed in this work to describe epidemiological and clinical aspects of all IMIDs diagnosed in internal medicine department at the University Hospital Center of the Point G.

Methods
This was a descriptive study with a retrospective data collection on the medical records of patients hospitalized for IMIDs in the department of internal medicine at the University Hospital Center of Point G for a study period of 02 years from January 1, 2018 to December 31, 2019. Patients seen in the outpatient consultation for IMIDs in the internal medicine department at the University Hospital Center of the Point G and patients hospitalized for IMIDs in the internal medicine department at the University Hospital Center of the Point G outside the study period were not included in this study. This was an exhaustive sampling of all cases of IMIDs during the study period. Diagnosis for IMIDs was established based on clinical and paraclinical data and/or validated diagnostic criteria according to the type of IMIDs. The data were collected on the pre-established survey form, including epidemiological (age, sex, profession, residence) and clinical (discharge diagnosis) characteristics. Data entry and analysis were done using SPSS version 22 software. Quantitative data were presented as mean and standard deviation if the distribution was normal, otherwise as median and interquartile range. Qualitative data were presented as numbers and percentages.

Results
Of 921 patients hospitalized from 2018 to 2019, 205 patients presented with immune-mediated inflammatory disease, of

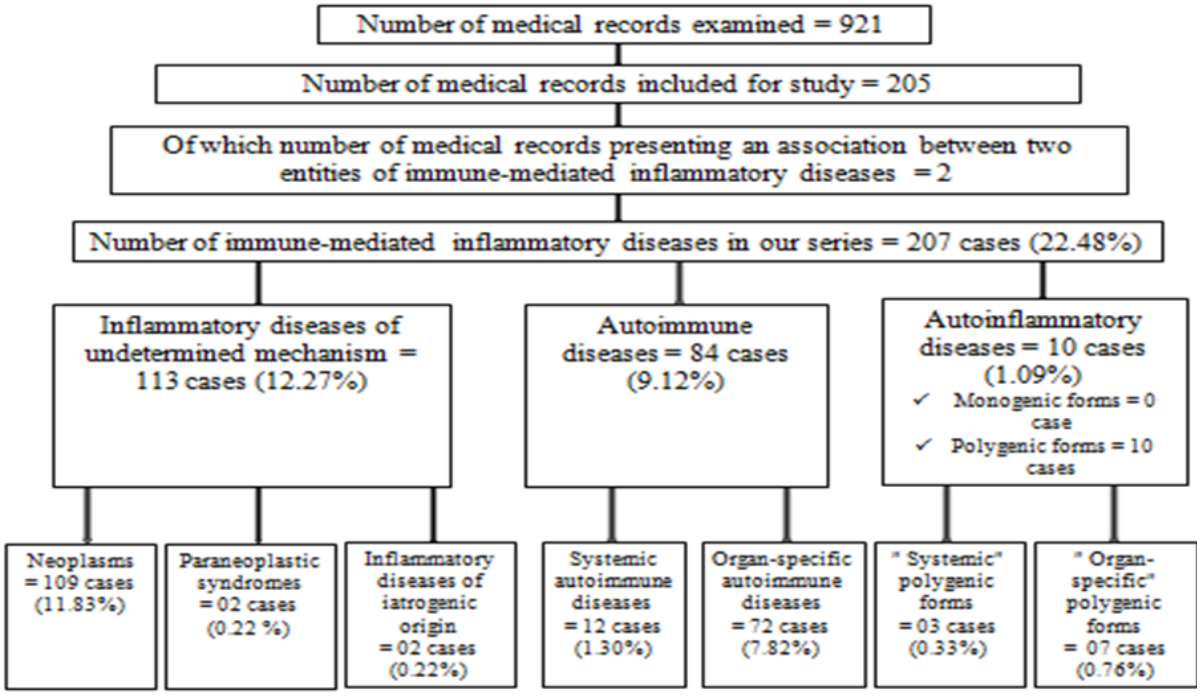

Figure 1: Overall distribution of patients according to immune-mediated inflammatory diseases.

Table 1: Distribution of patients by sociodemographic data.

Socio-demographic data	Number of cases (N= 205)	Percentage
Gender		
Male	90	43.90
Female	**115**	**56.10**
Age group		
0 - 19 years	31	15.12
20 - 39 years	**79**	**38.54**
40 - 59 years	61	29.76
60 - 79 years	32	15.61
≥ 80 years	2	0.98
Profession		
Houseworker	**64**	**31.22**
Pupils/Etudent	28	13.66
Trader	16	7.80
Farmers*	22	10.73
Worker	9	4.39
Civil servant	21	10.24
Not employed	1	0.49
Others	3	1.46
No information	23	11.22
Artisans	12	5.85
Liberale profession	6	2.93
Residence		
Urbain	**146**	**71.22**
Rural	26	12.68
Outside of Mali	7	3.41
No information	26	12.68

Farmers*: Cultivator/Breeder/Fisherman.

Table 2: Distribution of patients by autoimmune diseases.

Autoimmune diseases			Number	Percentage
Systemic autoimmune diseases (12 cases/84; 14.9% of cases)	**Rheumatoid arthritis**		**4**	**33.33**
	Systemic lupus erythematosus		3	25.00
	Systemic scleroderma		1	8.33
	Dermato-polymyositis		1	8.33
	Sharp Syndrome/Mixed Connective tissue diseases (2 cases; 16.67% of cases)	Systemic lupus erythematosus + rheumatoid arthritis	1	8.33
		Systemic lupus erythematosus + rheumatoid arthritis + dermato-polymyositis + systemic scleroderma	1	8.33
	Gougerot-Sjogren syndrome		1	8.33
	Total		12	100.00
Organ-specific autoimmune diseases (72 cases/84; 85.71% of cases)	**Type 1 diabetes**		**40**	**55.56**
	Grave's disease		13	18.06
	Autoimmune hemolytic anemia		5	6.94
	Biermer's disease		3	4.17
	Autoimmune polyendocrinopathy		2	2.78
	Guillain Barre syndrome		2	2.78
	Myasthenia gravis		2	2.78
	De Quervain's thyroiditis		1	1.39
	Hashimoto's thyroiditis		1	1.39
	Autoimmune adrenal insufficiency		1	1.39
	Autoimmune hepatitis		1	1.39
	Immunological thrombocytopenic purpura		1	1.39
	Total		72	100.00

Table 3: Distribution of patients by autoinflammatory diseases.

Autoinflammatory diseases			**Number**	**Percentage**
Monogenic autoinflammatory diseases			0	0.00
Polygenic autoinflammatory diseases			**10**	**100.00**
"Systemic" polygenic autoinflammatory diseases (3/10 cases; 30.00% of case)	**Horton's disease**		1	33.33
	Systemic Sarcoidosis		1	33.33
	Still's disease		1	33.33
	Total		3	100.00
"Organ-specific" polygenic autoinflammatory diseases (7 cases/10; 70.00% of cases)	**Chronic inflammatory rheumatism (n= 4 cases; 57.14% of cases)**	**Microcrystalline arthropathies (gout)**	**2**	**28.57**
		Spondylarthropathies (Ankylosing spondylitis)	1	14.29
		Pseudo rheumatoid arthritis	1	14.29
	Chronic inflammatory bowel diseases (n= 3 cases; 42.86% of cases)	Ulcerative colitis	**2**	28.57
		Crohn's disease	1	14.29
	Total		7	100.00

Table 4: Distribution of patients by inflammatory diseases of undetermined mechanism

Inflammatory diseases of undetermined mechanism				**Number**	**Percentage**
Neoplasms (109 cases/113; 96.46% of cases)	**Solid tumors (77 cases/109; 70.64% of cases)**	**Hepatocellular carcinoma**		**14**	**18.18**
		Breast cancer		9	11.69
		Stomach cancer		8	10.39
		Prostate cancer		5	6.49
		Imaging and/or cytological and/or histological documented metastasis without highlighted primary cancer		5	6.49
		Kaposi sarcoma		5	6.49
		Uterine cervix cancer		4	5.19
		Colorectal cancer		4	5.19
		Bladder cancer		3	3.90
		Prostate benign tumor		3	3.90
		Esophageal cancer		2	2.60
		Benign and malignant kidney tumor		1	1.30
		Bronchopulmonary cancer		1	1.30
		Oto-rhino-laryngological cancer		1	1.30
		Benign and malignant brain tumor		1	1.30
		Others neoplasms		11	14.29
		Total		77	100.00
	Hematological malignancies (31 cases/109; 28.44% of cases)	**Non-Hodgkin lymphoma**		**14**	**45.16**
		Chronic myeloid leukemia		8	25.81
		Hodgkin lymphoma		5	16.13
		Dysmyelopoiesis		1	3.23
		Acute lymphoid leukemia		1	3.23
		Chronic lymphoid leukemia		1	3.23
		Multiple myeloma		1	3.23
		Total		31	100.00
	Association entre solid tumors and hematological malignancies (1 case/109; 0.92% of cases	Non-Hodgkin lymphoma + hepatic and peritoneal documented metastasis without specified primary cancer		1	100.00
		Total		1	100.00
Paraneoplastic syndromes (02 cases/113; 1.77% of cases)	Paraneoplastic arthritis			1	50.00
	Paraneoplastic lower limb thrombophlebitis			1	50.00
	Total			2	100.00
Inflammatory diseases of iatrogenic origin (02 cases/113; 1.77% of cases)	Drug-induced inflammatory rheumatisms		Pyrazinamide-induced gout	1	50.00
			Others	0	0.00
	Drug-induced inflammatory osteopathies		Dexamethasone induced fragility osteopathy	1	50.00
			Others	0	0.00
	Drug-induced inflammatory myopathies			0	0.00
	Total			2	100.00

which two patients presented an association between two entities of IMIDs, which is 207 cases of IMIDs (22.48%). IMIDs were dominated by inflammatory diseases of undetermined mechanism (113 cases) followed by autoimmune diseases (84 cases) and autoinflammatory diseases (10 cases) (Figure 1). Of the 205 patients included, 56.10% were female, for a sex ratio of 0.78. The age group of 20 to 39 years represented 38, 54% of the study population. The mean age of the patients was 38.48 ± 18.29 years with extremes ranging from 04 to 88 years. Homemakers represented 31.22% of the study population. In our study, 71.22% of our patients were urban residents (Table 1). Organ-specific autoimmune diseases (72 cases) dominated the autoimmune diseases: type 1 diabetes (40 cases), Graves' disease (13 cases) versus systemic autoimmune diseases (12 cases): rheumatoid arthritis (04 cases), systemic lupus erythematosus (03 cases) (table 2). There were no cases of monogenic forms. “organ-specific” polygenic forms (07 cases) dominated the polygenic auto-inflammatory diseases: gout (02 cases), ulcerative colitis (02 cases) versus "systemic" polygenic forms (03 cases): Horton's disease, systemic sarcoidosis and Still’s disease (01 case each) (Table 3). Inflammatory diseases of undetermined mechanism were dominated by neoplasms (109 cases): Solid tumor (77 cases) [hepatocellular carcinoma (14 cases), breast cancer (09 cases)] and hematological malignancies (31 cases) [non-Hodgkin's malignant lymphoma (14 cases), chronic myeloid leukemia (8 cases)] followed by paraneoplastic syndromes (02 cases): paraneoplastic polyarthritis (1 case), paraneoplastic lower limb thrombophlebitis (1 case), and inflammatory diseases of iatrogenic origin (02 cases): pyrazinamide-induced gout (1 case), dexamethasone induced fragility osteopathy (1 case) (Table 4).

Discussion

Methodology

The retrospective survey of our single-center study with mainly adult recruitment did not allow us to optimize the collection of certain epidemiological information. The interpretation of the results obtained must therefore take into account the pitfalls (information bias as non-completeness of hospitalization records , confusion bias as difficulties to perform certain specialized para-clinical examinations for the confirmatory diagnosis of certain IMIDs, selection bias such patients followed as outpatients or patients hospitalized outside the internal medicine department, and generalization bias due to the mode of hospital single-center recruitment) associated with this methodological approach to the study. This observational, cross-sectional and descriptive study with retrospective survey from January 1, 2018 to December 31, 2019 focusing on the epidemiological and clinical aspects of IMIDs has allowed us to apprehend the extent of the problematic of IMIDs in internal medicine at the University Hospital Center of the Point G.

Immune-mediated inflammatory diseases: overall results and sociodemographic aspects

We collected 207 cases of IMIDs i.e., a frequency of 22.48% from 205 medical records with two cases of associations according to our inclusion criteria out of 921 hospitalized patients. The prevalence of IMIDs in the Western society was estimated at 5 - 7% [3] and at 4% of the population according to two US healthcare datasets [6]. The high frequency of IMIDs in our study could be explained by an exhaustive recruitment of all IMIDs cases whose internal medicine department is known to be a site of predilection for difficult, rare and multiple conditions diagnosis and management. IMIDs were dominated by inflammatory diseases of undetermined mechanism (113 cases) followed by autoimmune diseases (84 cases) and autoinflammatory diseases (10 cases). Our result is consistent with the literature, as demonstrated by Soukho et al. [5] in 2021 that autoimmune diseases (291 cases) were more prevalent than autoinflammatory diseases (40 cases), but their study did not take into account the third entities of IMIDs. Of the 205 patients included, 56.10% were female, for a sex ratio of 0.78 and the mean age of the patients was 38.48 ± 18.29 years with extremes ranging from 04 to 88 years. Soukho et al. found a similar finding in their work on autoimmune and autoinflammatory diseases with sex ratio of 0. 54 and the mean age at 35.27 ±16.27 years [5].

Autoimmune diseases

In our series, autoimmune diseases were found in 84 patients (9. 12 % of study population) and accounted for 40, 58% of the IMIDs. Our result is inferior to those observed by Soukho et al. [5] in internal medicine who reported 291 cases (4.56%) of autoimmune diseases. This difference could be explained by the study period shorter in our series but recent with constant improvement of diagnostic tools in our countries. Further, Garba et al. [13] reported a prevalence of autoimmune diseases of 7% in internal medicine.

Connective tissue diseases or systemic autoimmune diseases in our study were noted in 12 patients (1. 30% of study population) and constituted 5. 80% of IMIDs and 14. 29% of the autoimmune diseases. Our result was comparable to those found by Soukho and Zouna in Mali [5. 14] who reported respectively a frequency of 1.10% and 2.05% but was higher than those were found by Teclessou et al. [8] and Mijiyawa et al. [10] in Togo who found respectively a frequency of 0.19% and 0.20%. Systemic autoimmune diseases were dominated in our study by rheumatoid arthritis (04 cases), systemic lupus erythematosus (03 cases). A similar finding is noted by Soukho et al. [5] in Mali (systemic lupus erythematosus with 63.35% of cases followed by rheumatoid arthritis with 21.27% of cases), Teclessou et al. in Togo [8] (Systemic lupus erythematosus with 50.22% followed by rheumatoid arthritis with 21.64%), Dioussé et al. in Senegal [9] (Systemic lupus erythematosus with 65.2% followed by scleroderma with 21%).

Organ-specific autoimmune diseases in the study population were recorded in 72 patients (7. 82% of study population) and represented 34. 78% of the IMIDs and 85. 71% of the autoimmune diseases. The frequency of organ-specific autoimmune diseases was 3.46% in the series of Soukho et al. [2]. In Niger, Garba et al. [13] in 2019 reported a prevalence of organ-specific autoimmune diseases at 1.15%. Type 1 diabetes (40 cases) followed by Graves' disease (13 cases) were the most frequent organ-specific autoimmune diseases in our study. Our result is consistent with those of Soukho et al. [5] (type 1 diabetes with 63.35% of the cases followed by

Graves' disease with 21.27% of the cases) but not consistent with those of Garba et al. (Graves' disease followed by immunologic thrombocytopenic purpura) [13]. The recruitment period between these studies may explain these variable distributions of organ-specific autoimmune diseases.

Autoinflammatory diseases

In our study population, auto-inflammatory diseases were found in 10 patients with a frequency of 1. 09% of cases and constituted 4. 83% of the IMIDs. There were no cases of monogenic forms. Our result was higher than those observed by Soukho et al. [5] in Mali who reported a frequency of auto-inflammatory diseases at 0.63% of cases. Further, NZenze et al. [15] reported a prevalence of auto-inflammatory diseases at 2.34% in Gabon, Fall et al. [11] a prevalence of auto-inflammatory diseases at 8.1% in Senegal. This disparity between our results could be explained by the study period and the recruitment sites, which differed in our respective studies.

"Systemic" polygenic autoinflammatory diseases were recorded in 03 patients (0, 33% of study population) and represented 1, 45% of the IMIDs and 30, 00% of the polygenic autoinflammatory forms. Our result is similar to those obtained by Soukho et al. [5]. They noted a frequency of "systemic" polygenic autoinflammatory diseases at 0.13%. Horton's disease, systemic sarcoidosis and Still's disease (01 case each) were the 03 cases of "systemic" polygenic autoinflammatory diseases in our series. Soukho et al. in Mali reported 02 cases of Horton 's disease [5], Konaté et al. [16] and Sougué et al. [17] in Burkina Faso reported 01 case of systemic sarcoidosis in their study, Kane et al. [18] in Senegal, reported 03 cases of Still's disease.

"Organ-specific" polygenic inflammatory diseases were noted in 7 patients (0. 76% of study population) and accounted for 3. 38% of the IMIDs and 70. 00% of the polygenic autoinflammatory forms. This result is comparable to those obtained by Soukho et al. [5] who reported the frequency of "organ-specific" polygenic inflammatory diseases at 0. 50%. Gout (02 cases), ulcerative colitis (02 cases) were the most frequent "organ-specific" polygenic inflammatory diseases in our study. A similar finding is made in Gabon by Nzenze et al. [15] who found that gout was the most frequent inflammatory arthropathy with 31.6% of cases, in Mali by Soukho et al. [5] who noted that gout was the most common "organ-specific" polygenic autoinflammatory disease with 50.00% of cases. In contrast, the spondyloarthropathy was more frequent than gout according to the series of Fall et al. [11] in Senegal and Divengi et al. [19]. Sites of recruitment could be explain these observed differences, some with internal medicine monocentric and multicentric recruitment and others rheumatologic monocentric recruitment.

Inflammatory diseases of undetermined mechanism

Inflammatory diseases of undetermined mechanism were found in 113 patients with a frequency of 12. 27% of study population and constituted 54. 59 % of the IMIDs. With a well-conducted search through Medline, Google Scholar and so on, we did not find any epidemiological panorama study of this entity of IMIDs in literature. To our knowledge, it would be a first epidemiological panorama of inflammatory diseases of undetermined mechanism. However, we found data from their nosological sub-entities as neoplasms, paraneoplastic syndromes and inflammatory diseases of iatrogenic origin. Although the immunological mechanism that underlies this entity is not fully specified compared to the first two entities, but it is extremely important to address and analyze them together both within it and within IMIDs.

Neoplasms were noted in 109 patients (11. 83% of study population) and accounted for 52. 66% of the IMIDs and 96. 46% of the inflammatory diseases of undetermined mechanism.

Solid tumor in 77 cases (70, 64% of neoplasms) dominated hepatocellular carcinoma (14 cases) followed by breast cancer (09 cases) and stomach cancer (08 cases). Our finding is inconsistent with the literature. According to data from the Mali cancer registry from January 1986 to December 2005, i.e. 20 years, the five most frequent cancers of all sexes combined were liver 1553 cases (19.9%), stomach 1058 cases (13.5), cervix Uterine 1033 cases (13.2%), breast 610 cases (7.8%), bladder 423 cases (5.4%) [12]. According to WHO, the most common new cases of cancer in 2020 were: breast (2.26 million cases), lung (2.21 million cases), colon and rectum (1.93 million cases), prostate (1.41 million cases), skin (non-melanoma) (1.20 million cases) and stomach (1.09 million cases) [120]. The internal medicine department single-center recruitment could explain these disparities in their distribution.

Hematological malignancies were recorded in 31 cases (28.44% of neoplasms) dominated by non-Hodgkin's malignant lymphoma (14 cases), chronic myeloid leukemia (8 cases). Similar findings are made by Keïta et al. [21] in internal medicine, who reported 18 cases of hematological malignancy, which was a hospital frequency of 4. 69%. It was essentially about the chronic myeloid leukemia (04 cases) followed by acute myeloid leukemia and non-Hodgkin's malignant lymphoma (03 cases each).

In our study the paraneoplastic syndrome was noted in 02 patients (0.22% of study population) and represented 0.97% of the IMIDs and 1.77 % of inflammatory diseases with undetermined mechanism. These were paraneoplastic polyarthritis (1 case) and paraneoplastic lower limb thrombophlebitis (1 case). Gassara et al. reported seven paraneoplastic rheumatologic syndromes in a rheumatology department over 20 years [22]. Arbia Boudjelthia et al. in internal medicine collected 41 cases (52.56%) of thrombophlebitis of paraneoplastic origin in 78 patients with cancer and thrombophlebitis [23].

The inflammatory diseases of iatrogenic origin were recorded in 02 patients (0. 22% of study population) and constituted 0.97% of the IMIDs and 1.77% of the inflammatory diseases of undetermined mechanism, including pyrazinamide-induced gout (1 case), dexamethasone induced fragility osteopathy (1 case).

Conclusion

It appears from our study that IMIDs are frequently diagnosed in internal medicine and characterized by their frequent occurrence

in women and preferably between 20 and 39 years of age. Inflammatory diseases of undetermined mechanism followed by autoimmune diseases and autoinflammatory diseases dominate iMIDs.

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