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Original Article

Clinical Characteristics of IgG4-Related Disease in the United Arab Emirates: A Retrospective Single-Center Study

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ABSTRACT

Background: Demographic and clinical data of IgG4-related disease affecting solely the native population of the UAE, known as Emiratis**,** does not exist in the literature. **Aim:** To explore the demographic and clinical characteristics of IgG4-related disease in a well-defined population of Emirati patients attending Cleveland Clinic Abu Dhabi, a large tertiary center in the Middle East. **Patients and Methods:** The data presented is part of a retrospective cohort study, in which 15 Emirati patients with IgG4-related disease (IgG4-RD) were evaluated over 5 years from April 2015 to September 2020 at the rheumatology outpatient clinic at Cleveland Clinic Abu Dhabi. The demographic and clinical data were recorded. Descriptive statistics of the variables were applied. **Results:** Fifteen Emirati patients with an established diagnosis of IgG4-RD were assessed. There was a male predominance (53%) with a median age at the time of diagnosis of 47 ± 11.2 years. A 6-year lag period was noted from the initial presentation until a diagnosis of IgG4-RD was established. The most frequent comorbidities observed were hematological conditions (63%), hypertension (47%), diabetes mellitus (40%), and gastroesophageal reflux disease (40%). An elevated serum IgG4 was observed in the majority of patients at the initial presentation. Rheumatoid factor was detected in 13% and low titer of immunofluorescence antinuclear antibody in 7%. 86% of patients had a tissue biopsy with marked lymphocytic and plasmacytic infiltration being the most reported finding in 86%. Methotrexate, azathioprine, and rituximab were the most frequently prescribed disease-modifying agents. **Conclusion:** We report the first comprehensive analysis on a small cohort

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of Emirati patients with IgG4-RD. We describe disease features unique to UAE patients and demonstrate that IgG4-RD has a significant disease burden. Our results underscore the need for the IgG4-RD UAE-wide national registry to improve the quality of care of these patients.

Keywords: IgG4, IgG4-RD, native-populations, rheumatology, UAE

Introduction

IgG4-related disease (IgG4-RD) includes a group of immune-mediated fibroinflammatory disorders that share a dense lymphoplasmacytic infiltration with a predominance of IgG4 positive plasma cells in the affected tissue accompanied by some degree of fibrosis, obliterative phlebitis, and an increased number of eosinophils.[1] IgG4-RD can involve one or multiple organs, including the salivary glands, orbits, lymph nodes, pancreas, hepatobiliary tree, kidneys, and the retroperitoneal space. Several IgG4-RD cohorts report variability in disease characteristics according to the affected population. Most of the IgG4-RD cohorts show a slight predominance of the disease in middle-aged and older men with variability in gender distribution and organ involvement.[2-4] Nevertheless, most of the currently available data come from studies carried out in Europe and the United States with very few reports, if any, from the Middle East and North Africa region. We retrospectively sought to describe the clinical and demographic characteristics of IgG4-RD affecting solely the native Emirati population in the UAE.

Patients and Methods

Subjects

We performed a detailed retrospective chart review of clinical characteristics of all patients diagnosed with IgG4-RD attending Cleveland Clinic Abu Dhabi between April 01, 2015 and September 31, 2020. Patients were identified using the EPIC database, and search terms including IgG4-RD, retroperitoneal fibrosis, and raised serum IgG were used as keywords. The inclusion criteria included subjects more than 18 years of age who had more than two follow-up visits with the rheumatology clinic over 6 months. We excluded subjects <18 years, those who missed follow-up visits, those with multiple missing laboratory data, and subjects with other types of inflammatory arthritis. We applied both the ACR/EULAR 2019 criteria for IgG4-RD[5] and the comprehensive diagnostic criteria for IgG4-RD[6] to validate the diagnosis IgG4-RD. Patients fulfilling either classification criterion were enrolled in this cohort. A total number of 15 patients met the inclusion/exclusion criteria included in this current analysis.

Study variables

The medical records of all the subjects were reviewed, and demographics, clinical, laboratory, and treatment data were collected. We recorded lifestyle habits and comorbidities, including body mass index, cigarette smoking, marital status, dyslipidemia, hypertension, diabetes mellitus (DM), thyroid disease, chronic kidney disease (CKD), coronary artery disease, gastrointestinal disease, nonmalignant hematological disorders (iron deficiency anemia, sickle cell anemia, thalassemia), asthma, chronic obstructive airway disease, osteoporosis, depression, and malignancies. Furthermore, laboratory variables including rheumatoid factor (RF), anti-CCP, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), immunofluorescence antinuclear antibody (IF-ANA), anti-Ro/SSA, anti-La/SSB, double-stranded DNA, C3, and C4 were recorded. Medications used, including oral corticosteroids, conventional synthetic disease-modifying antirheumatic drugs (DMARDs) (hydroxychloroquine, methotrexate, azathioprine, and mycophenolate mofetil), and biologic DMARDs (rituximab) were documented.

Statistical analysis

Descriptive statistics (means, medians, and percentages) were used to summarize the characteristics of the cohort. Continuous variables are summarized as the mean ± standard deviation (SD), while skewed continuous variables are summarized with the median ± standard deviation. Statistical

analyses were performed using R 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

In a total of 15 Emirati patients who fulfilled the ACR/EULAR 2019 IgG4-RD criteria, 8 (53%) were from Abu Dhabi, 4 (27%) from Dubai, 2 (13%) from Sharjah, and 1 (7%) from Ajman. The median age of patients at the time of the initial symptoms was 44 ± 14.7 years (median ± SD) and at the time of diagnosis was 47 ± 11.2 years (median ± SD) with 6 years lag period between initial presentation and establishing a diagnosis. The majority of patients were males (53%) with a male-to-female ratio of 1.14:1. 87% of the patients (13 out of 15 patients) had a biopsy-proven diagnosis of definitive Ig4-RD [Table 1].

Comorbidities and modifiable risk factors

Forty percent of the patients were smokers and obese [Table 1]. The most frequent comorbidities observed in this cohort were atopy, hematological disease, followed by hypertension, DM, and gastrointestinal disease [Table 1]. Other comorbidities observed included cardiac disease, CKD, osteoporosis, respiratory disease, thyroid disease, malignancy, cardiac disease and depression [Table 1]. A total of 5 patients were tested positive for either latent tuberculosis, hepatitis B, or C at baseline screening, and one patient had a history of varicella-zoster infection.

Clinical manifestations and organ involvement

The most commonly reported clinical manifestations were constitutional symptoms (67%), including fatigue, unintentional weight loss, and fever [Table 1]. This was followed by those with mass effects such as lower back pain, flank pain, oliguria or anuria, and lymphadenopathy [Table 1]. Other manifestations included vision changes (20%), shortness of breath, and mid-thoracic back pain. Sixty-seven percent of the patients had a single organ involvement, and the most frequently involved organ was the kidney, mainly involving the renal pelvis and/or the ureter, followed by the aorta, lacrimal gland, and submandibular gland [Table 1]. Two-organ involvement (lymphadenopathy and kidneys) was manifested only in 33% of the patients.

Inflammatory markers, autoantibody profile, imaging, and biopsy findings

The median value of ESR and CRP levels at baseline were 70 ± 28 (normal reference range 0-20 mm/hr) and 38 ± 27 (normal reference range <5 mg/L), respectively [Table 2]. The baseline serum total IgG levels were 15.99 ± 3.5 g/L, and the serum IgG4 levels were 1.93 ± 0.59. Autoantibody screening was performed on all 15 patients; 13%

Table 1: Demographic characteristics, comorbidities, and clinical manifestations

Characteristics	Value*
Demographics	
Number of cases	15
Sex (male:female ratio)	1.14:1
Median age at the disease onset	44±15
Median age at diagnosis	47±11
Biopsy	13
BMI (kg/m2)	30±3
Smoking (%)	40
Comorbidities (%)**	
DM	40
Hypertension	47
Thyroid disease	13
Dyslipidemia	36
Cardiac disease	7
Chronic kidney disease	29
Gastrointestinal disease	40
Hematological disease	63
Osteoporosis	14
Respiratory disease	14
Depression	7
Malignancy	13
Atopy	73
Clinical manifestations (%)**	
Lower back pain	60
Flank pain	60
Mid thoracic back pain	13
Lymphadenopathy	40
Shortness of breath	13
Vision changes	20
Constitutional symptoms	67
Oliguria or anuria	47
Mass location	
Renal pelvis or/and ureter	53
Aorta	20
Lacrimal gland	20
Submandibular	8

*Results are shown as frequencies, percentages of the whole group or median±SD, **Frequency of medications are not mutually exclusive. SD: Standard deviation, BMI: Body mass index, DM: Diabetes mellitus

had a positive RF, and 7% had a positive IF-ANA. Otherwise, the remainder of the autoimmune profile was unremarkable, including SS-A, SS-B, anti-CCP, ds-DNA antibodies, and complements. Computed tomography scan of the chest, abdomen, and pelvis with and without contrast was performed in all patients at baseline. Thirteen patients had a tissue biopsy confirming the diagnosis of IgG4-RD. The most frequent findings were marked lymphocytic and plasmacytic infiltration (83%), followed by IgG4 positive plasma cells of more than in the% on high power field (75%). Other reportable findings were storiform fibrosis (67%) and a ratio of serum IgG4/total IgG of more than 40% (58%).

Medications

All patients received oral prednisone at the time of diagnosis at a dose of 0.5-1 mg/kg depending on the severity of symptoms, which was tapered gradually during the follow-up period. The most commonly received DMARD was methotrexate, followed by azathioprine [Table 3]. Other DMARDs prescribed were mycophenolate mofetil and hydroxychloroquine. Rituximab was the most frequently used intravenous biologic synthetic DMARD.

Discussion

IgG4-RD is a heterogeneous disease with variable clinical presentation and characteristics. The prevalence of the disease varies between countries depending on multiple factors, including sample size, age, gender, genetic background, and ethnic distribution of the population.[7] Data on clinical characteristics of IgG4-RD in the Middle East and Gulf region are very scarce. We retrospectively analyzed the clinical and histological features of 15 patients diagnosed with IgG4-RD attending Cleveland Clinic Abu Dhabi over 5 years (April 2015 to September 2020).

Of the total 15 patients included in the study, the majority were males, with a male-female ratio (M:F) of 1.14:1 and a median age of 47 years at the time of diagnosis. Our results are comparable to the North-American cohort with a male-to-female ratio of 1.6:1 and the median age at the time of diagnosis of 50 years.[8] On the other hand, in both the Turkish[9] and the Japanese cohorts,[10] the median age of the affected individuals was in the fifth and sixth decade of life, respectively, with a high male prevalence (M:F: 4:1) in the Japanese cohort,[10] and no sex difference in the Turkish cohort.[9] This variability in age between countries could be explained by either a real difference due to genetic variation or other factors such as health care accessibility. However, the full explanation for why the disease is so common in men remains elusive.

We observed a median delay of 6 ± 6 years between the initial symptoms and the diagnosis of IgG4-RD. The magnitude of diagnostic delay is longer in the current cohort when compared to the North-American cohort (median: 5.2 ± 8.5 years)[8]

Table 2: Salient laboratory investigations and frequency of various biopsy findings

Details of findings	Results
Laboratory*	
ESR (mm/h)	70±28
CRP (mg/L)	38±27
Eosinophilia	0.24±0.10
IF-ANA	7
Rheumatoid factor	13
Anti-CPP	0
SSA/SSB	0
Low C4	0
Low C3	0
Elevated ds DNA	0
Serum IgG 4 (mg/dl)	1.93±0.59
Biopsy findings**	
Marked lymphocytic and plasmocytic infiltration	83
Storiform fibrosis	67
Ratio of IgG4/IgG>40%	58
IgG4 positive plasma cells/HPF>10	75

*Results are shown as percentages of the whole group or median±SD, **Frequency of medications are not mutually exclusive. SD: Standard deviation, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, IF-ANA: Immunofluorescence antinuclear antibody, CCP: Cyclic citrullinated peptide, HPF: High-power field, SSA: Anti-Sjogren syndrome A autoantibodies, SSB: Anti-Sjogren syndrome B autoantibodies

Table 3: Management of the study populations

Treatment	Value*
Prednisone	100
Methotrexate	67
Hydroxychloroquine	8
Azathioprine	42
Mycophenolate mofetil	17
Rituximab	17

*Results are shown as percentages of the whole group. Frequency of medications are not mutually exclusive

and the French cohort (mean: 3.8 years).[11] This lengthier delay in our cohort is likely explained by the fact that this is a relatively new disease entity. Access to specialized medical care may be difficult for some patients.

The most frequently affected organs reported in most of the cohorts published were lymph nodes, submandibular and lacrimal glands, pancreas, and retroperitoneum [Table 4].[8,10-14] The most frequently affected organs in our cohort were retroperitoneal involvement of the kidneys (53%), lymph nodes (40%), aorta (20%), lacrimal gland (20%), and submandibular gland (8%), which is similar to the findings reported from the Turkish cohort, where 44.2% of patients had retroperitoneal fibrosis. The majority of the cohorts have shown that the[9,12,13] pancreas was one of the most frequently affected organs (60%, 38.5%, and 23.1%, respectively), and in contrast, none of the patients in our cohort had a pancreatic involvement. In addition, the majority of patients were found to have two or more organs affected, with a variable proportion between 41% and 88%. However, most of the patients in our cohort (67%) had a single organ involvement, and only 33% had a two-organ affected.

Two-thirds of patients had elevated serum IgG4 levels at baseline, defined as more than 1.35 g/L with median serum levels of 1.93 g/L. Serum IgG4 positivity was higher in our cohort when compared to the USA[8] and Spanish cohorts,[15] which was reported to be approximately 50%. It was lower than that reported from the French[11] and Chinese cohorts.[14] All patients had an elevated baseline serum IgG4 level**,** given that this was part of the inclusion criteria to be enrolled into both cohorts. A minor percentage of patients had a positive RF and IF-ANA, and none of the patients had elevated complements levels, which echo what was previously reported in the literature.[12]

In our cohort, 13 patients had a biopsy-proven diagnosis. However, the other two patients were diagnosed through reliable clinical and imaging features, in addition to an adequate and notable response to empirical treatment. Regarding treatment, all patients in this study received glucocorticoids, either as monotherapy or in combination therapy with methotrexate and azathioprine, the most frequently used steroid-sparing DMARDs. Rituximab was the most frequently prescribed injectable DMARD in refractory disease not responding to conventional synthetic DMARDs. These findings are compbatile with previously reported literature where azathioprine and methotrexate were the most frequently prescribed DMARDs, limiting the use of rituximab to patients lacking response to steroids.[14,15]

In summary, we report a comprehensive description of the clinical features of 15 Emirati patients with IgG4-RD, attending a large tertiary center in Abu Dhabi, UAE, between 2015 and 2020. Since there are no population databases or registries in the country, our findings provide important information regarding the understanding of IgG4-RD in the region. The present study is the first to examine a wide range of IgG4-RD variables in a local homogenous Emirati population. In addition, we revealed that our findings were similar to larger published cohorts [Table 4]. However, we identified unique characteristics in this current cohort, including median age. This is likely since the current study population is younger than what was observed in the Japanese population. The other interesting findings were the lack of pancreatic involvement, the higher percentage of single organ involvement, and the marked elevation in the serum IgG4 levels. Our study has some limitations, including the small number of patients enrolled cohort, the retrospective nature of the study, and the fact that biopsy was not performed on two patients diagnosed based on clinical and imaging findings.

Conclusion

Our study demonstrates that IgG4-RD is not uncommon in the Emirati population and has a significant disease burden. Our findings highlight the need for a national registry for IgG4-RD patients to identify the actual disease prevalence and to increase awareness about this disease among the general population and physicians in the UAE.

Authors contribution

All authors contributed to the conception, conduct, data analysis, and drafting and revising of the manuscript.

Table 4: Comparison of the clinical characteristics of the IgG4-related disease cohorts in the literature

Variables (number of patients)	UAE (15)	Turkey (52)	USA (125)	USA (57)	Spain (55)
Male:female ratio	1.14:1	1:1	1.6:1	1.7:1	3:1
Age at diagnosis (years)	Median 47±11	Mean: 51.1±12.7	Mean: 50.3±14.9	Mean: 58±14.8	Median: 53
Mean disease duration prior diagnosis (years)	6	NA	5.0±7.5	NA	NA
BMI	30±3	NA	NA	28.9±7.3	NA
Main comorbidities	Hematological, gastrointestinal, DM, and hypertension. atopy (73%)	Hashimoto's thyroiditis	NA	NA	Hashimoto's thyroiditis
Main organs involved	RPF, lacrimal	RPF, pancreas	Submandibular glands, lymph nodes, orbits, pancreas	Pancreas (26.4%), pericardium, gallbladder, liver	Retroperitoneum (27%), orbital Pseudotumor (22%), salivary gland (16%), pancreas (16%)
IgG4≥135 mg/dL (%)	67	67.3	51.4	12	NA
Serologies	ANA (7%), RF (13%)	ANA titer≥1/160 (7%)	Low C3 (20%) Low C4 (19%)	NA	NA
Biopsy (%)	86	25	50	100	100
Glucocorticoids (%)	100	71	51.2	45.6	85.5
DMARDS (%)	80	57.5	36.8	MTX 14.3 AZA 14.3	34.5
DMARDS used	MTX, HCQ, AZA, MMF	MTX, AZA, CYC	MTX, MMF, tamoxifen, AZA, CYC, IVIG	MTX, AZA RTX	MTX, AZA, MMMF, CYC, RTX
Rituximab (*n*)	3	24	7	5	3

Variables (number of patients)	Spain (15)	France (25)	Italy (41)	Japan (235)	China (118)
Male:female ratio	4:1	2.6:1	1.9:1	4:1	2.3:1
Age at diagnosis (years)	Median 60.7±14.8	Mean: 58	Median: 62	Median: 67	Mean: 53.1
Mean disease duration prior diagnosis (years)	NA	3.8	NA	NA	NA
BMI	NA	NA	NA	NA	NA
Main comorbidities	NA	NA	Urticaria, conjunctivitis, rhinitis, bronchial asthma, or gastrointestinal symptoms, (30%)	Allergic diseases and type 2 DM (39%)	61.8% allergy
Main organs involved	Lymph nodes (60% patients), kidneys (40%), salivary glands (33.3%), pancreas (20%),	lymph nodes (76%), pancreas (52%), salivary glands (44%), kidney (44%), biliary duct (32%), and retroperitoneum (32%	Pancreas, retroperitoneum	Pancreatitis (61%), sialadenitis (34%), tubulointerstitial nephritis (23%), dacryoadenitis (23%), periaortitis (20%)	Lymphadenopathy 65.3%, sialadenitis 64.4%, dacryoadenitis 50.8%, autoimmune pancreatitis 38.1%
IgG4≥135 mg/dL (%)	682.33	52	73	Median: 470 mg/dL	97.5
Serologies	Low C3 and C4 33.3%	ANA titer≥1:100 (16%) Low C3 and/or C4 56.25% (was analyzed on 16 patients only)	ANA (1:80-1:320) 17% Low C3 and/or C4 (14%)	positive ANA with≥40 titers in 50% and≥80 in 23%	Positive ANA 11%
Biopsy (%)	67	100	75	64	57.6

Contd...

Table 4: Contd...

Variables (number of patients)	Spain (15)	France (25)	Italy (41)	Japan (235)	China (118)
Glucocorticoids (%)	100	92	100	69	96.6
DMARDS (%)	33.3	48	41	Non used	60.1
DMARDS used	Tarcolimus, MTX, RTX	MTX, AZA, RTX, CYC, TOC, tamoxifin, imatinib	MTX, AZA, RTX, CYC	Non used	Used not reported
Rituximab (*n*)	1	3	1	0	0

RPF: Retroperitoneal fibrosis, BMI: Body mass index, DMARDs: Disease-modifying antirheumatic drugs, ANA: Antinuclear antibody, C3 and C4: Serum complement 3 and 4, MTX: Methotrexate, AZA: Azathioprine, CYC: Cyclophosphamide, RTX: Rituximab, IVIG: Intravenous immunoglobulin, DM: Diabetes mellitus, RF: Rheumatoid factor, HCQ: Hydroxychloroquine, MMF: Mycophenolate mofetil, TOC: Table of contents

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Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

The Institutional Review Board approved the study at Cleveland Clinic Abu Dhabi (A-2020-070).

References

1. Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, *et al.* Consensus statement on the pathology of IgG4-related disease. Mod Pathol 2012;25:1181-92.
2. Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012;366:539-51.
3. Quero M, Draibe J, Solanich X, Rama I, Gomà M, Martínez-Valenzuela L, *et al*. Clinical features and outcomes in a cohort of patients with immunoglobulin G4-related disease at a university hospital in Spain. Clin Kidney J 2019;12:829-35.
4. Wang L, Zhang P, Zhang X, Lin W, Tang H, Li J, *et al*. Sex disparities in clinical characteristics and prognosis of immunoglobulin G4–related disease: A prospective study of 403 patients. Rheumatology 2019;58:820-30.
5. Wallace ZS, Naden RP, Chari S, Choi HK, Della-Torre E, Dicaire JF, *et al.* The 2019 American College of Rheumatology/European League against Rheumatism classification criteria for IgG4-related disease. Ann Rheum Dis 2020;79:77-87.
6. Umehara H, Okazaki K, Nakamura T, Satoh-Nakamura T, Nakajima A, Kawano M, *et al.* Current approach to the diagnosis of IgG4-related disease – Combination of comprehensive diagnostic and organ-specific criteria. Mod Rheumatol 2017;27:381-91.
7. Martínez-Valle F, Fernández-Codina A, Pinal-Fernández I, Orozco-Gálvez O, Vilardell-Tarrés O. IgG4-related disease: Evidence from six recent cohorts. Autoimmun Rev 2017;16:168-72.
8. Wallace ZS, Deshpande V, Mattoo H, Mahajan VS, Kulikova M, Pillai S, *et al.* IgG4-related disease: Clinical and laboratory features in 125 patients. Arthritis Rheum 2015;67:2466-75.
9. Karadağ Ö, Erden A, Ayhan EA, Bölek EÇ, Kalyoncu U, Armağan B, *et al.* The clinical features and outcomes of Turkish patients with IgG4-related disease: A single-center experience Turk J Med Sci 2017;47:1307-14.
10. Inoue D, Yoshida K, Yoneda N, Ozaki K, Matsubara T, Nagai K, *et al.* IgG4-related disease: Dataset of 235 consecutive patients. Medicine (Baltimore) 2015;94:e680.
11. Ebbo M, Daniel L, Pavic M, Sève P, Hamidou M, Andres E, *et al.* IgG4-related systemic disease: Features and treatment response in a French cohort: Results of a multicenter registry. Medicine (Baltimore) 2012;91:49-56.
12. Carruthers MN, Topazian MD, Khosroshahi A, Witzig TE, Wallace ZS, Hart PA, *et al.* Rituximab for IgG4-related disease: A prospective, open-label trial. Ann Rheum Dis 2015;74:1171-7.
13. Campochiaro C, Ramirez GA, Bozzolo EP, Lanzillotta M, Berti A, Baldissera E, *et al.* IgG4-related disease in Italy: Clinical features and outcomes of a large cohort of patients. Scand J Rheumatol 2016;45:135-45.
14. Lin W, Lu S, Chen H, Wu Q, Fei Y, Li M, *et al.* Clinical characteristics of immunoglobulin G4-related disease: A prospective study of 118 Chinese patients. Rheumatology (Oxford) 2015;54:1982-90.
15. Fernández-Codina A, Martínez-Valle F, Pinilla B, López C, DeTorres I, Solans-Laqué R, *et al.* IgG4-related disease: Results from a multicenter Spanish registry. Medicine (Baltimore) 2015;94:e1275.

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