CLINICAL INVESTIGATION

Disease profile of rheumatoid arthritis and its complications in hispanic population

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease that is associated with functional disability and reduced quality of life. The central pathology of RA is the inflammation of diarthrodial joints, but approximately 40% of patients experience extra-articular manifestations of RA. Extra-articular manifestations are complications of RA that constitute multisystem disorders, associated with genetic and environmental conditions, and increase mortality in RA patients. Observational studies of RA patients have suggested ethnic disparities exist for minority populations; however, less is known about the distribution and prevalence of RA complications and drug-related problems (DRPs). Our objective was to construct a disease profile of RA-related complications in the Hispanic Mexican-American population compared to the non-Hispanic population of El Paso, Texas.

Methods: A retrospective study was conducted in a Texas Tech University Health Science Center El Paso from 2009 to 2019 to assess the prevalence of RA-related complications in the Hispanic vs non-Hispanic population. The primary parameters were RA diagnosis, serological status, RA-treatment modalities, and history of associated complications. Data were extracted by chart review and correlated to disease-related and treatment-related complications. STATA was used to perform statistical analyses. A p-value of < 0.05 determined statistical significance.

Results: One thousand five hundred five (N=1505) patients, diagnosed with RA, were included in this study. Of the cohort, 82.52% of patients were females, 76.81% were Hispanic, and 64.12% had no smoking history. From the total cohort, seven hundred fifty-six (N=756) patients had documentation of serological markers (Rheumatoid factor (RF) and/or Anti-cyclic citrullinated peptide (Anti-CCP)); 78.44% of patients whose serological status was documented, were positive for RF and/or Anti-CCP. Multivariate regression analysis revealed Hispanics have 15% and 17% less risk of overall RA complications and drug-related side-effects, respectively, compared to non-Hispanics (p-value <0.0001). However, within the entire cohort, those with a family history of RA had a 44% more risk of complications compared to those without family history (p-value <0.0001). Additionally, modifiable risk factors, i.e., active smoking and alcohol use had a higher complication risk, 19% and 21%, respectively (p-value <0.0001). Significantly, all patients seropositive for RF, and/or anti-CCP had a lower prevalence of RA-related and drug-related complications. However, non-Hispanic patients seropositive for RF or anti-CCP had a higher prevalence of specific complications of RA and DRPs compared to Hispanic patients.

Conclusion: In our retrospective review, analysis of sociodemographic characteristics reveals that Hispanic patients paradoxically have less risk of disease-related and treatment-related complications compared to non-Hispanic populations in El Paso, Texas. Genetic predisposition, modifiable environment/lifestyle factors had a higher prevalence of RA complications, congruent with established studies. Further analysis reveals that seropositive RA-patients have decreased complication prevalence compared to seronegative cohorts.

Key Indexing Terms: Rheumatoid arthritis and related complications; Epidemiological profile; Hispanic population. **[Am J Med Sci 2023;■(■):1–8.]**

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic, systemic autoimmune disease associated with long-term adverse outcomes.[1] The central pathology of RA involves the symmetrical inflammation of the synovium of diarthrodial joints; however, extra-articular RA manifestations, also known as multisystem disorder complications of RA, i.e. cardiovascular (pericarditis), respiratory (Caplan syndrome), and small vasculitis are frequent (18 to 41%) and are associated with increased

morbidity and mortality.[2–4] Multiple genetic and environmental factors are associated with increased risk for RA and disease sequela.[5,6] Of these, the strongest associations have been seen with female sex, individuals with comorbid conditions, smoking history, low socioeconomic status (SES), and family history.[5]

Autoantibodies play a critical role in the pathogenesis of RA. Rheumatoid factor (RF), IgM autoantibody to the Fc component of IgG, and IgG anti-cyclic citrullinated peptide (anti-CCP) are prognostic serological autoantibodies in RA patients.[7] Approximately 70-80% of RA patients are 'seropositive' for autoantibodies.[7] Seropositive patients have more pronounced joint destruction and a higher prevalence of RA complications than seronegative patients.[8] Current literature suggests that higher titers of RF increase the incidence of rheumatoid nodules, vasculitis, and pleuropulmonary complications.[9,10] Anti-CCP seropositive patients show evidence of atherosclerotic damage and more active disease sequelae than seronegative patients.[9]

RA affects approximately 0.6% to 1% of the US adult population.[11] While RA has been noted in all ethnic groups, conflicting evidence has emerged regarding whether RA-associated ethnic disparities in clinical outcomes exist.[12–14] Some evidence shows that minority populations, i.e. Hispanic and African American, have worse functional outcomes than non-minority groups.[15] However, other studies have shown that Hispanics have equal or lower mortality rates (among specific pathologies) compared to non-Hispanic populations, despite lower SES and higher rates of other co-morbidities.[16] Thus, the extent to which RA ethnic disparities persist in minority populations has yet to be fully examined. Furthermore, little data exists regarding ethnic disparities in the development of RA complications and pattern of disease according to serological status.[11,15,17,18] Most studies of RA complications have typically examined homogenous patient populations.[19–21] Thus, accurately understanding the epidemiology of RA by RA complications and serological phenotype may provide insights into the pathophysiology of RA and implications for the course of disease management.

This study aims to examine a multiethnic cohort of patients with RA to determine the prevalence and manifestations of RA complications between different ethnic groups and to identify specific RA complications and DRPs differing between the Hispanic Mexican-American population and non-Hispanic populations in El Paso, Texas.

METHODS

Population

A retrospective chart review was performed using single center data of patients diagnosed with RA based upon ICD9 and ICD10 code identification from 2009 to 2019. One thousand five-hundred and five patients (N=1505) diagnosed with RA were enrolled in the study. Misdiagnosed patients (as documented in their charts) and individuals < 18 years of age were excluded from the study.

Collection of data

Baseline characteristics, RA complications, and DRPs of each participant were obtained based upon ICD9 and ICD10 code diagnosis of RA and analyzed from the clinic admission date to September 2021. Baseline data consisted of demographic information (gender, age, race, ethnicity, employment status, insurance type), social factors (tobacco and alcohol use), number of years diagnosed with RA, and RF/Anti-CCP seropositive status. RF seropositivity was demonstrated at >14 IU/mL per laboratory results, or as documented in patient history. Anti-CCP seropositivity was demonstrated at >20 units/mL, or as documented in patient history. The complications of RA that were evaluated include: amyloidosis, anemia, ankylosing spondylitis, anxiety, arrhythmia, bronchiectasis, bronchiolitis, Caplan syndrome, cardiovascular disease, cervical myelopathy, conduction defects, depression, diabetes mellitus, eye inflammation, Felty syndrome, gastritis, gastroesophageal reflux disease, gastrointestinal intolerance, infection, insomnia, interstitial lung disease, joint deformity, keratoconjunctivitis sicca, liver disease, lung cancer, lymphoma/lymphoproliferative disease, mononeuritis multiplex, nerve entrapment, neutrophilic dermatosis, cutaneous nodules, osteoarthritis, osteoporosis, pericardial effusion, pericarditis, peripheral neuropathy, peripheral vascular disease, pleural effusion, pleuritis, pulmonary fibrosis, pulmonary hypertension, pulmonary nodules, renal disease, Sjogren syndrome, ulcers, valvular defects, vasculitis, and xerostomia. All complications of RA were included if diagnosed at the same time as or following diagnosis of RA. These complications were excluded if proven to be caused by conditions other than RA, as documented in the medical records. Furthermore, medication-related adverse events (DRPs) were included only if they occurred following medication administration. If a complication of RA coincided with a possible medication adverse event, it was included in both data sets. The DRPs that were evaluated include: alopecia, anaphylaxis, anemia, bone-marrow suppression, demyelinating disease, depression, dizziness, elevation of liver function tests/hepatotoxicity, eye toxicity, gastritis, gastroesophageal reflux disease, gastrointestinal intolerance, headache, heart failure, hypertension, hyperglycemia, infection, infusion/injection site reactions, insomnia, interstitial lung disease, liver disease, lymphoproliferative disease, mucositis, osteoporosis, peptic ulcers, photosensitivity, pneumonitis, post-dosing fatigue/fatigue, pulmonary fibrosis, rashes, renal disease, and stomatitis. RA medications included in this study were; steroids, nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs (DMARDs) (methotrexate, leflunomide, hydroxychloroquine, sulfasalazine, azathioprine),

mycophenolate mofetil, cyclosporine, minocycline, penicillamine, cyclophosphamide, gold thiomalate, biological DMARDs (tumor necrosis factor alpha inhibitors, t-cell co-stimulation blockers, interleukin-1 blockers, rituximab, tocilizumab, sarilumab), and JAK inhibitors (tofacitinib, baricitinib).

Statistical analysis

The prevalence of the RA complications and DRPs was performed and reported in total patients and according to RF and anti-CCP seropositivity. Complications and side effects were reported in absolute number and percentage and categorized according to ethnicity. Fisher's exact test was utilized to determine the association between two independent categorical variables. Poisson regression analysis was conducted to determine the association of sociodemographic characteristics with RA complications, drugs-related side effects, and reported incidence rate ratios (IRR) with 95% confidence interval (CI). STATA 17.0 program was used to conduct statistical analyses. A p-value of < 0.05 was considered statistically significant.

Ethics statement

This study protocol was reviewed by the Institutional Review Board for the Protection of Human Subjects (El Paso IRB #00009946) and classified as exempt from formal IRB review in accordance with 45 CFR 46.104(d)(4)(iii).

RESULTS

Patient demographics

The study sample consisted of N=1505 patients diagnosed with RA: N=1156 identified as Hispanic and N=237 as non-Hispanic. A description of patient characteristics is provided in [Table 1]. Median age was 63 (interquartile range 53-72) years, and women constituted 82.52% of the total study population. There were no significant differences in the number of RA complications between gender or current patient age [Table 2]. Those with a family history of RA within the entire study population have a 44% more risk of complications of RA compared to those without a family history of RA (95% CI, 1.36-1.53: p-value <0.0001). Those with a family history of RA have a 62% more risk of DRPs compared to those without a family history of RA (95% CI, 1.51-1.75: p-value <0.0001). Those who have had RA longer have 12% more risk of complications of RA (95% CI, 0.99-1.002: p-value <0.0001). Those who have had RA longer have 1% more risk of DRPs (95% CI, 1.013-1.02: p-value <0.0001).

TABLE 1. Baseline characteristics of rheumatoid arthritis (RA) patients.

Characteristics	Number	Percentage
Participants	1505	100%
Gender		
Female	1242	82.52%
Race		
White	1208	80.27%
Ethnicity		
Hispanic	1156	76.81%
Family History of RA		
Yes	178	11.83%
Smoking status		
Non-smoker	965	64.12%
Former smoker	378	25.12%
Current smoker	152	10.10%
Alcohol Use		
None	1145	76.08%
Former	9	0.60%
Current	238	15.81%
Employment status		
Employed	405	26.91%
Insurance type		
Uninsured	159	10.56%
Private	463	30.76%
Medicaid/Medicare	800	53.16%
RF seropositivity		
Negative	270	17.94%
Positive	502	33.36%
Anti-CCP seropositivity		
Negative	306	20.33%
Positive	359	23.85%
RF and/or Anti-CCP		
Negative	163	21.56%
Positive	593	78.44%

RA, rheumatoid arthritis; RF, rheumatoid factor; Anti-CCP, anti-cyclic citrullinated peptide antibodies. Patients whose descriptive characteristic status was unknown were not included in this table.

Substance use

Former smokers have 13% more risk of complications of RA compared to non-smokers (95% CI, 1.07-1.19: p-value <0.0001). Former smokers have 11% more risk of DRPs compared to non-smokers (95% CI, 1.04-1.18: p-value 0.001). Current smokers have 19% more risk of complications of RA compared to non-smokers (95% CI, 1.11-1.28: p-value <0.0001). There were no significant differences in the number of DRPs between current smokers and non-smokers [Table 2].

Current alcohol users have 21% more risk of complications of RA compared to non-alcohol users (95% CI, 1.14-1.28: p-value <0.0001). Current alcohol users have 24% more risk of DRPs compared to non-alcohol users (95% CI, 1.15-1.34: p-value <0.0001). There were no significant differences in the number of RA complications or DRPs between former alcohol use and no alcohol use [Table 2].

Employment status and insurance coverage

Those who are currently employed have 8% more risk of complications of RA compared to unemployed

TABLE 2. Multivariable Poisson regression of sociodemographic characteristics with number of rheumatoid arthritis (RA) complications and drug-related problems (DRPs).

	RA complications				DRPs			
Variable	**IRR**	**95% CI**		**p-value**	**IRR**	**95% CI**		**p-value**
Female	1.14	1.07	1.21	<.0001	1.14	1.06	1.23	0.001
Ethnicity								
Hispanic (ref: Non-Hispanic)	0.86	0.81	0.91	<.0001	0.81	0.76	0.87	<.0001
RA family history								
Yes (ref: No)	1.38	1.30	1.47	<.0001	1.54	1.43	1.66	<.0001
Smoking status								
Former smoker (ref: non-smoker)	1.13	1.07	1.19	<.0001	1.11	1.04	1.18	0.002
Current smoker (ref: non-smoker)	1.12	1.04	1.20	0.003	0.98	0.88	1.08	0.679
Alcohol status								
Former (ref: no alcohol use)	0.91	0.66	1.24	0.541	0.92	0.6	1.39	0.682
Current (ref: no alcohol use)	1.14	1.07	1.21	<.0001	1.16	1.07	1.25	<.0001
Employment								
Employed (ref: unemployed)	1.15	1.08	1.21	<.0001	1.16	1.08	1.25	<.0001
Insurance Type								
Private (ref: uninsured)	1.21	1.11	1.33	<.0001	1.42	1.25	1.59	<.0001
Medicaid/Medicare (ref: uninsured)	1.37	1.26	1.49	<.0001	1.65	1.47	1.85	<.0001
Years with RA	1.01	1.01	1.01	<.0001	1.014	1.011	1.017	<.0001
Age	1.00	0.99	1.00	0.057	1.00	0.99	1.002	0.998

(95% CI, 1.03-1.13: p-value 0.003). Those who are currently employed have 10% more risk of DRPs compared to unemployed (95% CI, 1.03-1.17: p-value 0.002).

Those with private insurance has 27% more risk of complications of RA compared to uninsured (95% CI, 1.16-1.38: p-value <0.0001). Those with private insurance has 48% more risk of DRPs compared to uninsured (95% CI, 1.32-1.67: p-value <0.0001). Those with Medicaid/Medicare have 38% more risk of complications of RA compared to uninsured (95% CI, 1.27-1.51: p-value <0.0001). Those with Medicaid/Medicare have 63% more risk of DRPs compared to uninsured (95% CI, 1.46-1.83: p-value <0.0001).

Ethnicity and RA complications

Hispanics have 15% less risk of overall RA complications compared to non-Hispanics (95% confidence interval [CI], 0.81-0.9; p-value <0.0001). Hispanic patients had a lower prevalence of arrhythmia (10.47% vs 15.61%, p-value 0.032), bronchiolitis (7.44% vs 11.39%, p-value 0.05), conduction defects (7.87% vs 13.92%, p-value 0.005), Felty syndrome (8.13% vs 13.08%, p-value 0.024), interstitial lung disease (8.30% vs 12.66, p-value 0.046), mononeuritis multiplex (8.30% vs 12.66%, p-value 0.046), pleuritis (7.44% vs 13/08%, p-value 0.007), renal disease (11.42% vs 18.99%, p-value 0.003), and more than 4 complications total (49.13% vs 59.49%, p-

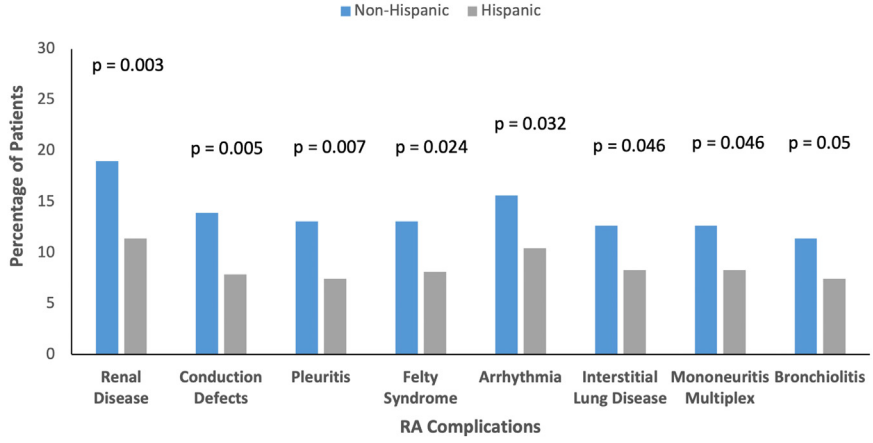

FIGURE 1. Significant RA complications by ethnicity.

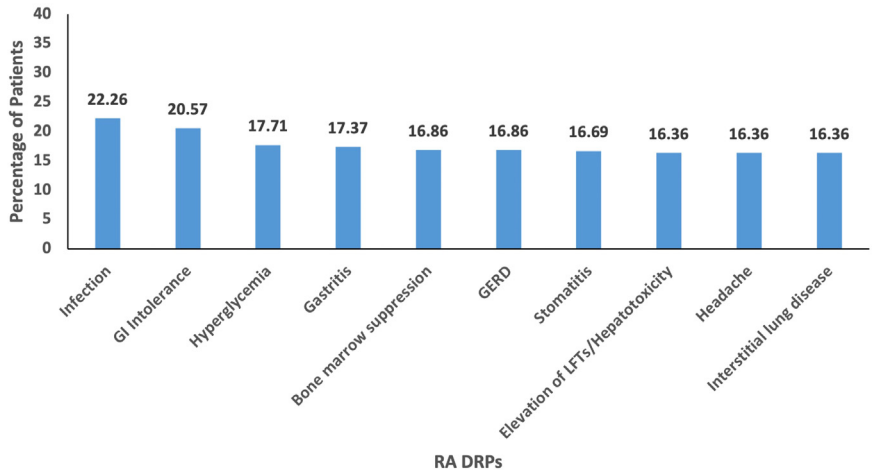

FIGURE 2. Overall highest prevalence of DRPs.

value 0.004) compared to non-Hispanic patients [Figure 1]. There were no significant differences in the prevalence of amyloidosis, anemia, ankylosing spondylitis, anxiety, bronchiectasis, Caplan syndrome, cardiovascular disease, cervical myelopathy, depression, diabetes mellitus, eye inflammation, gastritis, gastroesophageal reflux disease (GERD), gastrointestinal (GI) intolerance, infection, insomnia, joint deformity, keratoconjunctivitis sicca, liver disease, lung cancer, lymphoma/lymphoproliferative disease, nerve entrapment, neutrophilic dermatoses, subcutaneous nodules, osteoarthritis, osteoporosis, pericardial effusion, pericarditis, peripheral neuropathy, peripheral vascular disease, pleural effusion, pulmonary fibrosis, pulmonary hypertension, pulmonary nodules, Sjogren's syndrome, ulcers, valvular defects, vasculitis, or xerostomia.

Ethnicity and DRPs

The highest prevalence of DRPs overall includes: infection (22.26%), GI intolerance (20.57%), hyperglycemia (17.71%), gastritis (17.37%), bone marrow suppression (16.86%), GERD (16.86), stomatitis (16.69%), elevated LFTs/hepatotoxicity (16.36%), headache (16.36%), and interstitial lung disease (16.36%) [Figure 2]. Hispanics have 17% less risk of overall DRPs compared to non-Hispanics (95% CI, 0.77-0.89: p-value <0.0001). Hispanic patients also had a lower prevalence of the following DRPs: headache (10.81% vs 16.88%, p-value 0.011), peptic ulcers (7.44% vs 12.24%, p-value 0.019), and more than 2 DRPs (46.97% vs 57.81%, p-value 0.003) compared to non-Hispanic patients [Table 3]. There were no significant differences in the prevalence of alopecia, anaphylaxis, anemia, bone marrow suppression, demyelinating disease, depression, dizziness, elevation of liver function tests/hepatotoxicity, eye toxicity, gastritis, GERD, GI intolerance, hypertension, hyperglycemia, infection, infusion/injection site reactions, insomnia, interstitial lung disease, liver disease, lymphoproliferative disease, mucositis, osteoporosis, photosensitivity, pneumonitis, post-dosing fatigue, pulmonary fibrosis, rashes, renal disease, or stomatitis.

RF and anti-CCP seropositivity

Additionally, patients' RF and anti-CCP seropositivity were analyzed in relation to RA complications and DRPs. Patients seropositive for RF and/or anti-CCP had a lower prevalence of anxiety (14.50% vs 22.09%, p-value 0.023), peripheral neuropathy (12.48% vs 26.38%, p-value <0.001), peripheral vascular disease (14.33% vs 21.47%, p-value 0.03), vasculitis (13.49% vs 23.93%, p-value 0.002), and more than 4 complications total (79.43% vs 90.18%, p-value 0.001) compared to those who were seronegative for these markers [Table 4 Supplemental]. Patients seropositive for RF and/or anti-CCP had a lower prevalence of the following DRPs: depression (p-value 0.018), dizziness (p-value 0.028), insomnia (p-value 0.001), pneumonitis (p-value 0.005), and more than 2 DRPs compared to those who were seronegative for these markers [Table 5 Supplemental].

RF seropositivity

Patients seropositive for RF had a lower prevalence of the following RA complications: anxiety (14.14% vs 20.74%, p-value 0.025), arrhythmia (15.54% vs 21.48%, p-value 0.047), Felty syndrome (12.95% vs 18.52%, p-value 0.044), peripheral neuropathy (11.35% vs 21.85%, p-value <0.001), valvular defects (12.35% vs 18.89%, p-value 0.019), vasculitis (12.15% vs 22.22%, p-value <0.001), and more than 4 complications total (77.49% vs 89.26%, p-value <0.001) compared to those who were seronegative for RF. Patients seropositive for RF had a higher prevalence of xerostomia (17.53% vs 11.85%, p-value 0.038) compared to those who were seronegative for RF [Table 4 Supplemental]. Patients seropositive for

TABLE 3. Prevalence of drug-related problems (DRPs) by ethnicity.

Factor	Not Hispanic	Hispanic	p-value
N	237	1156	
Alopecia	25 (10.55%)	97 (8.39%)	0.31
Anaphylaxis	28 (11.81%)	97 (8.39%)	0.1
Anemia	25 (10.55%)	128 (11.07%)	0.91
Bone marrow suppression	33 (13.92%)	132 (11.42%)	0.27
Demyelinating disease	28 (11.81%)	97 (8.39%)	0.1
Depression	27 (11.39%)	125 (10.81%)	0.82
Dizziness	33 (13.92%)	143 (12.37%)	0.52
Elevation of LFTs/Hepatotoxicity	26 (10.97%)	115 (9.95%)	0.64
Eye Toxicity	23 (9.70%)	99 (8.56%)	0.61
Gastritis	34 (14.35%)	123 (10.64%)	0.11
GERD	40 (16.88%)	139 (12.02%)	0.054
GI Intolerance	48 (20.25%)	196 (16.96%)	0.22
Headache	40 (16.88%)	125 (10.81%)	0.011
Heart failure	26 (10.97%)	103 (8.91%)	0.33
Hypertension	46 (19.41%)	175 (15.14%)	0.12
Hyperglycemia	29 (12.24%)	126 (10.90%)	0.57
Infection	35 (14.77%)	162 (14.01%)	0.76
Infusion/Injection site reactions	19 (8.02%)	84 (7.27%)	0.68
Insomnia	25 (10.55%)	92 (7.96%)	0.2
Interstitial lung disease	27 (11.39%)	112 (9.69%)	0.41
Liver disease	26 (10.97%)	108 (9.34%)	0.47
Lymphoproliferative disease	26 (10.97%)	107 (9.26%)	0.4
Mucositis	28 (11.81%)	91 (7.87%)	0.055
Osteoporosis	24 (10.13%)	112 (9.69%)	0.81
Peptic ulcers	29 (12.24%)	86 (7.44%)	0.019
Photosensitivity	21 (8.86%)	95 (8.22%)	0.7
Pneumonitis	28 (11.81%)	118 (10.21%)	0.48
Post-dosing fatigue/Fatigue	26 (10.97%)	101 (8.74%)	0.27
Pulmonary fibrosis	26 (10.97%)	102 (8.82%)	0.32
Rashes	28 (11.81%)	158 (13.67%)	0.53
Renal Disease	28 (11.81%)	114 (9.86%)	0.35
Stomatitis	25 (10.55%)	108 (9.34%)	0.55
Medication side effect score			0.003
≤2	100 (42.19%)	613 (53.03%)	
>2	137 (57.81%)	543 (46.97%)	

RA, rheumatoid arthritis; LFTs, liver function tests; GI, gastrointestinal. Patients whose descriptive characteristic status was unknown were not included in this table.

RF had a lower prevalence of the following DRPs: depression (14.54% vs 21.11%, p-value 0.026), dizziness (15.54% vs 22.96%, p-value 0.014), insomnia (10.16% vs 18.52%, p-value 0.002), peptic ulcers (12.15% vs 17.41%, p-value 0.050), photosensitivity (11.35% vs 19.26%, p-value 0.003), pneumonitis (15.54% vs 22.22%, p-value 0.024), pulmonary fibrosis (12.35% vs 21.11%, p-value 0.002), rashes (13.94% vs 22.22%, p-value 0.005), and more than 2 DRPs (74.10% vs 88.15%, p-value <0.001) compared to those who were seronegative for RF [Table 5 Supplemental].

Non-Hispanic patients seropositive for RF had a higher prevalence of the following RA complications: cardiovascular disease (25.30% vs 15.00%, p-value 0.022), mononeuritis multiplex (22.89% vs 13.75%, p-value 0.035), pleuritis (20.48% vs 12.00%, p-value 0.039), and pulmonary fibrosis (25.30% vs 14.00%, p-value 0.010) compared to Hispanic patients seropositive for RF [Table 6 Supplemental]. Non-Hispanic patients seropositive for RF also had a higher prevalence of headaches (28.92% vs 12.75%, p-value <0.001) as a DRP compared to Hispanic patients seropositive for RF [Table 7 Supplemental].

Anti-CCP seropositivity

Patients seropositive for anti-CCP had a lower prevalence of the following RA complications: vasculitis (14.48% vs 20.59%, p-value 0.040) and more than 4 complications (82.45% vs 91.83%, p-value <0.001) compared to those who were seronegative for anti-CCP.

Patients seropositive for anti-CCP had a lower prevalence of the following DRPs: bone marrow suppression (15.88% vs 23.53%, p-value 0.014), depression (14.48% vs 22.88%, p-value 0.007), eye toxicity (13.93% vs 19.93%, p-value 0.047), infusion/injection site reactions (10.86% vs 16.34%, p-value 0.040), lymphoproliferative disease (13.65% vs 21.90%, p-value 0.006) and more than 2 DRPs (79.39% vs 92.48%, p-value < 0.001) compared to those who were seronegative for anti-CCP [Table 5 Supplemental].

Non-Hispanic patients seropositive for anti-CCP had a higher prevalence of pulmonary fibrosis (28.77% vs 15.38%, p-value 0.008) as a complication of RA compared to Hispanic patients seropositive for anti-CCP [Table 6 Supplemental]. Non-Hispanic patients seropositive for RF also had a higher prevalence of headaches (34.25% vs 13.92%, p-value <0.001) as a DRP compared to Hispanic patients seropositive for RF [Table 7 Supplemental].

DISCUSSION

Our report augments existing literature on RA-related complications and provides a detailed epidemiological profile of a minority population. In this study, we investigated a heterogenous border population of Hispanic and non-Hispanic patients with RA to determine the prevalence of specific RA complications and DRPs based upon ethnicity. Previous studies have described RA disease activity in minority populations according to the Clinical Disease Activity Index, Disease Activity Score in 28 Joints, Health Assessment Questionnaire (HAQ), Multidimensional HAQ, and self-report measures.[12-15] In each of these studies, minorities had worse outcomes than their non-Hispanic matched counter.[12-15] However, in most of these studies, the majority of each population were non-Hispanic and none of these studies examined the role of RA complications and DRPs in evaluation of RA severity. Other studies have demonstrated that Hispanics have equal or lower mortality rates compared to non-Hispanic populations, despite having higher disease burden.[16] Our evidence concludes that Hispanic patients have less risk and lower prevalence of RA complications and DRPs. Significantly, our analysis shows decreased prevalence of RA complications including arrhythmia, bronchiolitis, conduction defects, Felty syndrome, ILD, mononeuritis multiplex, pleuritis, and renal disease. These findings could contribute to the phenomenon of "Hispanic paradox" as many studies have linked RA complications with increased morbidity and mortality.[2-4,9]

There is limited research regarding the development of RA complications according to serological status,[11,15,17,18] and even less reported on heterogenous border populations.[19,20] Unlike prior research, which found that seropositivity for RF and/or anti-CCP was correlated with increased severity of RA,[8-10] our research found that seropositivity for either marker was associated with decreased prevalence of RA complications and DRPs in Hispanic patients compared to non-Hispanic patients. This is possibly secondary to the already decreased prevalence of RA complications and DRPs in Hispanics, or it could be specific to RA disease severity rather than a marker of RA complications or DRPs. A combination of the contribution of genetic factors and autoantibodies interaction with environmental factors likely contributes to disease susceptibility.[15]

Important limitations of our study include that we did not measure the titers of RF or anti-CCP and the extent of seropositivity could also affect patient outcomes.[8-10] Furthermore, many of the patient charts indicating seropositivity or seronegativity of RF and anti-CCP were based upon historical documentation from prior providers as these outcomes were not directly measured in the clinic for the majority of our participants. Additional factors that could contribute to the unique finding of decreased complications or DRPs in overall seropositive participants in our study could be due to the smaller population of non-Hispanic compared to Hispanic participants, lack quantified disease activity, lack of titers of RF/anti-CCP.[12-15] Other studies have demonstrated that the underlying genetic features for the development of RA and seropositivity for RF varies across racial and ethnic groups.[15] Further research is needed to elucidate the exact origin of these new findings.

In concordance with prior research, our results demonstrate that those with a family history of RA, former/current smoker status, current alcohol use, and have had RA for a longer period have an increased risk of both RA complications and DRPs.[5] Incidentally, our study also found that those who are employed or have medical insurance are at a higher risk of RA complications and DRPs. The comparison group for those employed were all those unemployed, which includes patients who were retired or on disability. These groups could not be examined separately, as not all charts indicated employment status, making this sample inadequate to be representative of the population. Additionally, it is possible that those with medical insurance are at higher risk of RA complications and DRPs because they are more likely to seek medical care and exhibit more data in their charts from additional visits later in the disease course. Both circumstances warrant additional investigation in future studies.

CONCLUSION

Rheumatoid arthritis is a chronic, debilitating disease associated with increased mortality and financial burden. While RA has been extensively studied, much less is reported regarding extra-articular manifestation and treatment-associated adverse sequela. Even less is known regarding RA complications and DRPs concerning minority and serological status. Our epidemiological profile of Hispanic patients in a heterogenous, border population seeks to fill in the gap. Our study provides evidence of reduced morbidity and mortality associated

with specific RA complications and DRPs in the Hispanic population. Significantly, we provide evidence of the reduced prevalence of RA complications and DRPs in serological positive, Hispanic patients, contrary to current established literature. While the scope of this study is limited by retrospective analysis and moderate sample size, it provides another avenue of research towards a less well understood niche for RA complications, management, and population health outlook.

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DECLARATION OF COMPETING INTEREST

The authors have no personal or institutional interest with regards to the authorship and/or publication of this manuscript.

SUPPLEMENTARY MATERIALS

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