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Prevalence, comorbidities, and diseaserelated complications of rheumatoid arthritis in Colombia: a national cross-sectional study based on administrative claims data



Kevin Maldonado-Cañón^{1*}, Giancarlo Buitrago^{2,3} and Gerardo Quintana-López^{1,4,5,6}

Abstract

Background To date, there has been limited exploration, particularly on a national scale, of the prevalence patterns of comorbidities and complications associated with rheumatoid arthritis (RA) in Colombia. We aimed to analyze the prevalence patterns of comorbidities and disease-related complications of RA patients enrolled in Colombia's contributory healthcare regime.

Methods We performed a nationwide observational descriptive cross-sectional study using administrative claims data. We used a set of sensitive and specific electronic algorithms (i.e., a set of rules) applied to linked data based on ICD-10 codes and unique medication use codes. We compared all those algorithms with several sources, including governmental agencies and scientific literature, to identify all the known adults treated for RA.

Results A total of 123,080 RA cases for 2018 were identified, corresponding to a point prevalence of 0.86 (95% CI 0.86–0.87) per 100. Compared to a non-RA reference population, hypertension (68.2 vs. 20.0%), osteoarthritis (43.6 vs. 6.1%), and osteoporosis (18.6 vs. 1.1%) provided larger standardized mean differences. Lupus (30.04; 95%CI 29.3–30.8), multiple sclerosis (7.18; 95%CI 6.6–7.8), and osteoporosis (5.57; 95%CI 5.5–5.6) provided higher age- and sex-adjusted prevalence ratios. Disease-related complications were found in 62.2% of cases.

Conclusions We describe the first comprehensive assessment of the prevalence patterns of disease-related complications and comorbidities that define the RA burden of disease within a multimorbidity profile. Also, our study provides a narrower and more reliable point prevalence estimate for RA in Colombia.

Keywords Latin America, Comorbidity, Complications, Prevalence, Rheumatoid arthritis

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Background

Rheumatoid Arthritis (RA) is a systemic, chronic, and autoimmune inflammatory disease [1]. Worldwide, a point prevalence of 0.45% (95% CI 0.38–0.53%) has been reported, with a pooled period prevalence of 0.46% (95% CI 0.36% and 0.57%) [2]. Factors influencing the variations within these ranges include the heterogeneity of sample sizes in primary studies, geographical location, and the level of risk of bias assessment [2, 3]. Furthermore, the estimation methods are paramount. Linked data has been recommended to reduce the risks of selection bias and bias by indication and addresses the drawbacks of the lack of randomization when using straightforward registry data, which may induce underestimations [2, 4].

In Colombia, rheumatoid arthritis has been described as the most common inflammatory rheumatic disease, with a prevalence ranging from 0.52 to 1.98 per 100 inhabitants [5–7]. However, these are estimates obtained from heterogeneous methodologies with significant constraints. The straightforward use of registry data has severe limitations: the sampling bias is unmistakable in the RIPS database (Individual Registry of Health Services in Spanish *Registros Individuales de Prestación de Servicios de Salud*), which is the most widely used for such studies [6], considering the lack of regulation and validation for the information report process [8, 9].

On the other hand, although the cross-sectional study that utilized the COPCORD questionnaire made an effort towards a more reliable approach, the concomitance of the chikungunya fever epidemic at the time of its application and the fact that in some specific cities, the desired sample size was not achieved due to healthcare perception barriers [5], brought significant selection bias. Finally, few studies, and none on a national scale, have considered prevalence patterns of comorbidities and complications alone and compared with a non-RA reference population.

Methods

The aim of this study was to assess the prevalence patterns of comorbidities and disease-related complications of RA patients enrolled in Colombia's contributory healthcare regime in 2018 using a set of sensitive and specific electronic algorithms (i.e., a set of rules) applied to linked data based on ICD-10 codes and unique medication use codes. Secondarily, we compared the patterns of comorbidities with a non-RA reference population to indirectly identify the RA disease burden in a multimorbidity profile.

Study design and data source

We performed a nationwide observational descriptive cross-sectional study using data from the Capitation

Sufficiency Database from the Colombian Ministry of Health as the primary source of information. Since the database is used to estimate the insurance premium that the health system pays to health insurers (unit per capitation (UPC)), each health provider is responsible for reporting deidentified patient-level data on the consumption of healthcare services and associated ICD-10 codes yearly.

The UPC database includes claims of services provided by insurers, comprising approximately 80% of the contributory regime -individuals with formal employment- covering 48% (22.19 million individuals) of the total population in 2016. The remaining population is part of the subsidized regime (individuals without formal employment in low-resource settings) and other forms of health insurance (e.g., those for the military forces, police officers, and certain groups like public universities and oil industry workers) [10]. This data is then verified through a validation process by the Colombian Ministry of Health, where inconsistencies are corrected, thus providing a highly standardized source of information with little underreporting previously used in several national studies [11–14].

As complementary sources of information, we used the Unique Enrollees Database (*Base de Datos Única de Afiliados* [BDUA] in Spanish) to identify the total number of enrollees affiliated with any of the insurers who provided information for the UPC database for the corresponding period. A unique coded number allowed for referencing the anonymized records, so authors had no access to information that could identify individual participants during or after data collection. Data were accessed on the 7th of March, 2022, for research purposes.

RA cases identification

Given that the UPC database does not include clinical information such as symptoms, physical assessments, or the results of diagnostic tests, an electronic algorithm (i.e., a set of rules) was designed to identify the RA cases based on ICD-10 codes and unique medications codes (*Clasificación Única de Medicamentos* [CUM] in Spanish) -derived from the international anatomical therapeutic chemical (ATC) classification-. A similar approach was previously utilized on the same database for several other conditions [11–14].

To identify adult (\geq 18 years old) patients with RA diagnosis, we developed two types of electronic algorithms: sensitive and specific. First, via the sensitive algorithm we identified patients with any ICD-10 code for RA (M05.0, M05.1, M05.2, M05.3, M05.8, M05.9, M06.0, M06.1, M06.2, M06.3, M06.4, M06.8, or M06.9); second, via the specific algorithms we identified patients with any ICD-10 code for RA and at least one CUM code associated with the pharmacological treatment of RA -Analgesics

(including NSAIDs and paracetamol), corticosteroids (prednisolone), DMARDs (Methotrexate, Leflunomide, Chloroquine, Sulfasalazine, Azathioprine, and Cyclosporin), and bDMARDs (Etanercept, Abatacept, Infliximab, Adalimumab, Certolizumab, Golimumab, Rituximab, Tocilizumab, Tofacitinib, and Baricitinib)-.

Afterward, we carried out a sensitivity analysis where each type of algorithm (sensitive and specific) was applied over a period of 4 years from 1 January 2015 to 31 December 2018 and had its ICD-10 diagnostic persistence time adjusted in 1 to 6 nonconsecutive months. This allowed us to identify the patients listed in the 2018 database who met any algorithm variants (when applied to the 2015 to 2018 period) and consumed any health resource in 2018. Finally, we estimated the point prevalence for each algorithm variant. Given the recommendations on identifying RA patients from administrative databases [4] and a priori considerations on how physicians use certain medications and code visits and having previous local prevalence estimates and their risks of over- or underestimation as comparators, we selected the most reliable approach.

History or current evidence of comorbidities

A set of 37 comorbidities (neoplasms, endocrine, psychiatric, cardiovascular, pulmonary, gastrointestinal, skin, musculoskeletal, and urogenital) was selected by clinical relevance and previous reports [15]. Following the Oliveros et al. approach validated for our database for calculating the Charlson Comorbidity Index [16], if at least one ICD-10 code from 2015 to 2018 was identified, the disease was assumed to be prevalent; however, given the focus of the study, we raised the detection threshold to have at least two ICD-10 codes to improve specificity.

Complications

We identified musculoskeletal complications through unique health procedure codes (UHPCs) associated with orthopedic joint-replacement procedures (total hip, knee, ankle, wrist, elbow, shoulder, and spinal joint replacement). Similarly, cardiovascular complications (i.e., acute myocardial infarction) were identified through the combination of a related ICD-10 code (I21-I24) and at least one UHPC associated with a heart catheterization procedure. Infectious complications were also identified through ICD-10 codes (J12-J18, N30, N390, G00-G09, L00-L08, A00-A09, A15-A19, A30-A49, A54-A79, A50-A64, A80 - B10, and B15-B19).

Statistical analysis

Disease, comorbidity, and complications point prevalence for 2018 are reported per 100 persons. The denominator used for calculating the prevalence of RA was the total number of enrollees at the end of 2018 affiliated with any of the insurers who provided information for the UPC database for this period. Prevalence is reported by region (Atlántica, Bogotá, Central, Oriental, Orinoquía – Amazonía, and Pacífica), age groups (18–34, 35–44, 45–54, 55–64, 65–74, and \geq 75), and sex (male, female). The corresponding 95% CI was calculated through bootstrapping with 1,000 subsamples. Further, a choropleth map was constructed to show the variability of prevalence across all 33 departments.

To assess whether the observed comorbidities and complications differed between subgroups, stratified analyses were made by age and sex. Further, 2-sample z-tests for equality of proportions with continuity correction, standardized mean differences and crude and sexand age-adjusted prevalence ratios (PRs) using a modified Poisson model [17, 18] were calculated to compare the prevalence of comorbidities in RA cases with a non-RA reference adult population, consisting of all individuals older than 18 without RA diagnosis enrolled with the same insurers -who reported information for the UPC database- as of 2018, in whom comorbidities were also identified within a timeframe between 2015 and 2018 using the approach of at least two ICD-10 codes. Standardized mean differences, unlike other statistical tests of hypothesis, are not influenced by sample size. Values of 0.2, 0.5, and 0.8 represent small, medium, and large effect sizes, meaning systematic differences are observed when comparing two samples [19, 20]. All figures and analyses were done using the statistical language R (version 4.0.3; R Core Team, 2020) (RRID: SCR_001905) [21], except for the 95% CI calculation through bootstrapping done using STATA MP 17.0 (RRID: SCR_012763) [22].

Results

Algorithm selection

The results of 12 different electronic algorithms, six sensitive and six specific, and the comparisons with the local values reported in the literature are shown in Fig. 1. What stands out in this figure are the differences between the number of cases identified through the sensitive vs. the specific algorithms and the rapid decrease in the number of cases after adjusting the ICD-10 diagnostic persistence in increasing amounts of nonconsecutive months.

From a total of 294,472 potential RA cases identified through the sensitive algorithm and 246,939 identified through the specific algorithm. The algorithm variant resulting from combining the specific algorithm with the ICD-10 diagnostic persistence in two nonconsecutive months was deemed the most reliable approach since it meets a priori considerations of the current realworld standard of care and contrasts with previous local over- and underestimates. A comparison of estimates excluding NSAIDs and Paracetamol is provided as supplementary material (Fig. S1).



Fig. 1 Electronic algorithms variants performance and comparison with the literature. CAC: High-Cost Disease Fund (Cuenta de Alto Costo in Spanish)

 Table 1
 Adult point prevalence of rheumatoid arthritis (2018)
 stratified by sociodemographic characteristics

	Number of RA cases	Total population	Prevalence per 100 (95%
			CI)
Sex			
Female	101,105 (82.1%)	7,496,953	1.35 (1.34–1.36)
Male	21,975 (17.9%)	6,746,654	0.33 (0.32–0.33)
Age Group			
18–34	11,137 (9.0%)	5,375,484	0.21 (0.20-0.21)
35–44	14,399 (11.7%)	2,822,459	0.51 (0.50–0.52)
45–54	26,099 (21.2%)	2,336,645	1.12 (1.10–1.13)
55-64	33,550 (27.3%)	1,889,023	1.78 (1.76–1.80)
65–74	23,751 (19.3%)	1,102,856	2.15 (2.13–2.18)
≥ 75	14,144 (11.5%)	717,140	1.97 (1.94–2.01)
Region			
Atlántica	13,702 (11.1%)	1,753,202	0.78 (0.77–0.80)
Bogotá	39,846 (32.4%)	4,376,279	0.91 (0.90–0.92)
Central	33,698 (27.4%)	5,084,180	0.66 (0.66–0.67)
Oriental	16,461 (13.4%)	1,006,125	1.64 (1.61–1.66)
Orinoquía	677 (0.6%)	130,809	0.52 (0.48–0.56)
- Amazonía			
Pacífica	18,696 (15.2%)	1,893,012	0.99 (0.97–1.00)
Overall	123,080 (100%)	14,243,607	0.86 (0.86–0.87)

Patient characteristics and disease prevalence

The algorithm variant mentioned above allowed us to identify 123,080 RA cases enrolled in Colombia's contributory healthcare regime for 2018 and provides an estimated point prevalence of 0.86 (95% CI 0.86–0.87) per 100. The mean age was 57.09 years (SD 14.96), and most

cases were females (82.1%). Table 1 provides a detailed description of the RA cases and the prevalence estimates stratified by sociodemographic characteristics. Furthermore, as shown in Fig. 2, RA prevalence is higher in the Oriental region.

Prevalence of comorbidities

In our RA cases, the most frequent comorbidities were hypertension (68.2%), osteoarthritis (43.6%), gastritis (33.5%), hypothyroidism (29.1%), and hyperlipidemia (29.1%). Further, depression was prevalent in only 9.2% of the RA cases. The most frequent comorbidities were similar in our non-RA reference population of 14,120,527 subjects, yet they were less frequent. Significant differences were found for all listed comorbidities (i.e., 2-sample z-tests p-values of < 0.005); however, standardized mean differences less than 0.1 (i.e., absence of systematic differences) were found for sebaceous gland disorders, emphysema, lung neoplasms, Parkinson's disease, gastric ulcer, multiple sclerosis, colorectal neoplasms, and stroke. Higher standardized mean differences corresponded to hypertension (68.2 vs. 20.0%), osteoarthritis (43.6 vs. 6.1%), osteoporosis (18.6 vs. 1.1%), hypothyroidism (29.1 vs. 6.7%), gastritis (33.5 vs. 11.2%), diabetes (20.6 vs. 5.8%), and lupus (8.7 vs. 0.2%). Likely, we identified significant raw and age- and sex-adjusted PRs for all listed comorbidities: lupus, multiple sclerosis, osteoporosis, and psoriasis, the higher ones. A detailed description of SMDs and PRs can be found in Tables 2 and 3; Fig. 3.



Fig. 2 Adult point prevalence of rheumatoid arthritis (2018) per region (A) and department (B). Since too few enrollees belonged to Guainía for the 2018 period (n = 3), the prevalence was not calculated

Differences in the prevalence of comorbidities by considering having at least one vs. two ICD-10 codes can be found in Supplementary Table S1.

When assessing the differences in complications and comorbidities among subgroups, notable are the higher rates for older age groups for severe musculoskeletal complications and certain chronic diseases, as well as the variations between males and females in urinary tract infections, acute myocardial infarction, osteoporosis, hypothyroidism, osteoarthritis, and gastritis. Detailed descriptions of the stratified analyses are provided in Table 4.

Discussion

Our study uses an unprecedently large, linked dataset based on ICD-10 and unique medication use codes to assess the prevalence patterns of comorbidities and disease-related complications of RA patients enrolled in Colombia's contributory healthcare regime. After applying sensitive and specific electronic algorithms (i.e., a set of rules) to all persons enrolled in the UPC database between 2015 and 2018, we deemed the algorithm with the ICD-10 diagnostic persistence in two nonconsecutive months and at least one medication associated with the pharmacological treatment of RA as the most reliable approach. We uncovered a total of 123,080 RA cases enrolled in Colombia's contributory healthcare regime for 2018, corresponding to an estimated point prevalence of 0.86 (95% CI 0.86-0.87) per 100. We also observed a higher frequency and standardized mean differences compared with a non-RA reference population of certain comorbidities such as hypertension, osteoarthritis, hypothyroidism, gastritis, osteoporosis, diabetes, and lupus and higher age- and sex-adjusted PRs for lupus, multiple sclerosis, osteoporosis, and psoriasis. Further, we identified disease-related complications in 62.2% of the RA cases, with cardiovascular or infectious complications broadly more frequent than musculoskeletal complications.

When considering prevalence distribution by age and sex, our estimates are consistent with worldwide data, which found higher prevalence in females than in males as well as in 55- to 64- and 65- to 74-year-olds [23]. On the other hand, our findings accord with earlier local reports for Colombia [5–7]. Using administrative claims data, Díaz-Rojas et al. identified a prevalence of 0.9% for 2005 [7], and Fernández-Avila a prevalence of 0.52%. for 2012–2016 [24]. It is important to bear in mind the possible bias due to the use of an ICD-10 code alone as a case definition and to the lack of regulation and validation of the RIPS database [6].

Other studies using a different methodological approach, however, have presented varied estimates: the cross-sectional study that utilized the COPCORD questionnaire found a prevalence of 1.49% (95% CI: 1.12– 1.98); yet the desired sample size was not achieved, and the concurrent chikungunya fever epidemic at the time affects its external validity [5]. More recently, based on data from the High-Cost Disease Fund, Castillo-Cañón et al. discovered surprisingly lower estimates for 2019 (0.24% (95% CI: 0.23–0.24)); however, this estimate might be misleading and should be cautiously interpreted for

Variables	RA cases	(n = 123,080)	Non-RA popu	SMD	
	n	Prevalence per 100 (95% CI)		Prevalence per 100 (95% CI)	
Neoplasms					
Colorectal Neoplasms	1158	0.94 (0.89–1.00)	32,942	0.23 (0.23–0.24)	0.09
Lung Neoplasms	406	0.33 (0.30–0.36)	8719	0.06 (0.06–0.06)	0.06
Skin Neoplasms	3,67	2.98 (2.89–3.07)	116,641	0.83 (0.82–0.83)	0.16
Endocrine					
Hypothyroidism	35,864	29.14 (28.89–29.39)	945,82	6.70 (6.68–6.71)	0.61
Diabetes	25,311	20.56 (20.34–20.79)	815,064	5.77 (5.76–5.78)	0.45
Psychiatric					
Depression	11,344	9.22 (9.06–9.38)	280,101	1.98 (1.98–1.99)	0.32
Anxiety	13,853	,853 11.26 (11.08–11.43) 461,292		3.27 (3.26–3.28)	0.31
Neurologic					
Parkinson's Disease	889	0.72 (0.68–0.77)	27,142	0.19 (0.19–0.19)	0.08
Multiple Sclerosis	633	0.51 (0.48–0.56)	5,539	0.04 (0.04–0.04)	0.09
Migraine	13,169	10.70 (10.53–10.87)	961,921	6.81 (6.80–6.83)	0.14
Cardiovascular					
Hyperlipidemia	27,278	22.16 (21.93–22.39)	1,332,862	9.44 (9.42–9.46)	0.35
Hypertension	83,946	68.20 (67.95–68.46)	2,829,972	20.04 (20.02-20.07)	1.11
Angina	3838	3.12 (3.03-3.21)	120,758	0.86 (0.85–0.86)	0.16
Acute Myocardial Infarction	4502	3.66 (3.56–3.76)	96,086	0.68 (0.68–0.68)	0.21
Coronary Artery Disease	6609	5.37 (5.25–5.49)	210,288	1.49 (1.48–1.50)	0.21
Arrhythmias	5402	4.39 (4.28–4.50)	184,046	1.30 (1.30–1.31)	0.19
Heart Failure	4155	3.38 (3.28–3.48)	105,069	0.74 (0.74–0.75)	0.19
Stroke	1181	0.96 (0.91–1.01)	34,124	0.24 (0.24–0.24)	0.09
Pulmonary					
Chronic Sinusitis	4269	3.47 (3.37–3.57)	146,947	1.04 (1.04–1.05)	0.16
Chronic Bronchitis	2636	2.14 (2.06-2.22)	76,774	0.54 (0.54–0.55)	0.14
Emphysema	237	0.19 (0.17–0.22)	4711	0.03 (0.03–0.03)	0.05
COPD	13,294	10.80 (10.63–10.98)	288,22	2.04 (2.03–2.05)	0.36
Asthma	6621	5.38 (5.26–5.50)	239,95	9,95 1.70 (1.69–1.71)	
Gastrointestinal					
GERD	11,989	9.74 (9.58–9.91)	388,125	2.75 (2.74–2.76)	0.29
Gastric Ulcer	756	0.61 (0.57–0.66)	18,022	0.13 (0.13-0.13)	0.08
Gastritis	41,222	33.49 (33.24–33.75)	1,582,287	11.21 (11.19–11.22)	0.56
Inflammatory Bowel Disease	5734	4.66 (4.55–4.77)	341,262	2.42 (2.41–2.42)	0.12
Diverticulitis	2112	1.72 (1.65–1.79)	45,614	0.32 (0.32–0.33)	0.14
Skin					
Eczema	20,959	17.03 (16.82–17.24)	997,176	7.06 (7.05–7.08)	0.31
Psoriasis	3139	2.55 (2.47–2.64)	46,162	0.33 (0.32–0.33)	0.19
Sebaceous Gland Disorders	1,887	1.53 (1.47–1.60)	201,667	1.43 (1.42–1.43)	0.01
Musculoskeletal					
Osteoarthritis	53,714	43.64 (43.37–43.91)	859,675	6.09 (6.08–6.10)	0.96
Lupus	10,686	8.68 (8.53–8.84)	24,767	0.18 (0.17–0.18)	0.42
Discopathy	16,282	13.23 (13.04–13.42)	489,892	3.47 (3.46–3.48)	0.36
Osteoporosis	22,868	18.58 (18.37–18.79)	151,697	1.07 (1.07–1.08)	0.62
Urogenital					
Urolithiasis	8686	7.06 (6.92–7.19)	569,134	4.03 (4.02–4.04)	0.13
Cystitis	6596	5.36 (5.24–5.48)	313,821	2.22 (2.21–2.23)	0.16

Table 2 Prevalence of comorbidities in RA patients

CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; GERD: Gastroesophageal Reflux Disease; RA: rheumatoid arthritis; SMD: Standardized mean differences. The bolded SMD values denote systematic differences between the two cohorts (SMD > 0.2)

Table 3 Raw and age- and sex-adjusted prevalence ratios of comorbidities in RA patients compared to non-RA individuals who consumed any resources during 2018

Comorbidities	PR (95% CI)	Age- and sex-adjusted PR (95% Cl)		
Neoplasms				
Colorectal Neoplasms	3.09 (2.91-3.27)	1.90 (1.79–2.01)		
Lung Neoplasms	4.09 (3.7-4.52)	2.38 (2.15–2.63)		
Skin Neoplasms	2.76 (2.67–2.85)	1.68 (1.63–1.74)		
Endocrine				
Hypothyroidism	3.33 (3.3–3.36)	1.94 (1.92–1.96)		
Diabetes	2.73 (2.7–2.76)	1.64 (1.62–1.65)		
Psychiatric	, , , , , , , , , , , , , , , , , , ,	, , , , , , , , , , , , , , , , , , ,		
Depression	3.56 (3.49–3.62)	2.39 (2.35–2.43)		
Anxiety	2.64 (2.6–2.68)	1.82 (1.79–1.85)		
Neurologic		(,		
Parkinson's Disease	2.88 (2.69–3.07)	1.70 (1.59–1.82)		
Multiple Sclerosis	10.04 (9.24–10.89)	7.18 (6.6–7.82)		
Migraine	1.20 (1.18–1.22)	1.27 (1.25–1.29)		
Cardiovascular				
Hyperlipidemia	1.80 (1.78–1.82)	1.21 (1.2–1.22)		
Hypertension	2.60 (2.59–2.62)	1.61 (1.6–1.62)		
Angina	2 79 (2 7–2 88)	1 76 (1 7–1 82)		
Acute Myocardial Infarction	4 11 (4-4 24)	2 79 (2 7–2 87)		
Coronary Artery Disease	2 76 (2 69–2 83)	1 78 (1 74–1 82)		
Arrhythmias	2.58 (2.51-2.65)	1 55 (1 51–1 59)		
Heart Failure	3 47 (3 37-3 58)	2.02 (1.96-2.08)		
Stroke	3.04 (2.87-3.22)	1.80 (1.7–1.91)		
Pulmonary	5.01 (2.07 5.22)	1.00 (1.) 1.5 1)		
Chronic Sinusitis	2 55 (2 48-2 63)	2 00 (1 94–2 06)		
Chronic Bronchitis	3 02 (2 9-3 13)	1 77 (1 71–1 84)		
Emphysema	4.42 (3.88-5.03)	2 78 (2 44-3 17)		
COPD	4.05 (3.98-4.12)	2.76 (2.77 3.77)		
Acthma	2 A2 (2 27 2 A8)	1.88 (1.84 1.03)		
Gastrointestinal	2.72 (2.37 2.70)	1.00 (1.0+ 1.75)		
GERD	2 71 (2 67_2 76)	1 80 (1 85_1 02)		
Gastric I IIcor	2.71 (2.07 2.70)	2.47 (2.3_2.66)		
Castritic	2.00 (2.72 2.20) 2.20 (2.27 2.21)	2.47 (2.3 2.00)		
Inflammatory Bowel Disease	2.29(2.27-2.31)	1.70 (1.75-1.78)		
Divorticulitic	1.40 (1.44-1.51)	1.54 (1.5-1.50) 2 10 (2 00 2 22)		
Skin	4.07 (3.89-4.23)	2.10 (2.00-2.27)		
Eczomo	1 05 /1 02 1 07)	162 (16 164)		
Eczeriid	1.00 (1.02-1.07) E 07 (E 76 - 6.10)	1.02(1.0-1.04)		
PSUIIdSIS Sebacaaus Cland Disorders	0.92 (0.70 0.96)	3.04 (4.60-3.23)		
Sebaceous Gianu Disorders	0.82 (0.79–0.80)	1.79(1.71-1.07)		
		202 (201 204)		
Usteoartnintis	5.49 (5.45-5.52)	2.83 (2.81-2.80)		
Lupus	57.09 (57.00-56.75)	50.04 (29.29_30.82)		
Disconathy	2 92 (2 88-2 96)	207 (201-21)		
Osteoporosis	13.24 (13.07_13.41)	5 57 (5 5_5 6A)		
Urogenital	13.27 (13.07-13.41)	5.57 (5.5-5.04)		
Urolithiasis	1 34 (1 31_1 37)	1 43 (1 4–1 46)		
Cyctitic	1.85 (1.8-1.90)	1 36 (1 22_1 20)		
CYDUUD	1.0.2 (1.0 = 1.0.2)	1.00 (1.00) = 1.091		

CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; GERD: Gastroesophageal Reflux Disease; RA: rheumatoid arthritis; PR: Prevalence Ratio. All PR provided a p-value < 0.001

two reasons: first, the comprehensiveness of High-Cost Disease Fund data depends on the rate of reporting by insurers - with no report on the percentage of adherence and compliance by insurers to the obligation of reporting data - and second, an important selection bias cannot be ruled out considering that the healthcare providers reporting are primarily institutions specialized in RA care.

Previous analyses on the prevalence of RA based on administrative claims data vary. Based on the 2015-2016 Alberta Health Care Insurance Plan, RA crude prevalence was 1.08% (95% CI 1.07-1.09) [25]. When analyzing data from 2001 to 2015 of the health insurance registry (FIPA), hospital discharges (MedEcho), physician-billing claims (RAMQ), and the provincial death registry databases, a prevalence of 0.8% was estimated for Quebec, Canada [26]. Through the National Database of Health Insurance Claims and Specific Health Checkups of Japan, Nakajima et al. found a lower estimate of 0.65% in 2017 [27]. This is similar to the broadly referenced range of 0.41 to 0.54% from 2004 to 2014 based on US administrative health insurance claims databases (Truven Health MarketScan® Research database and IMS PharMetrics Plus database) [28] and of 0.28 to 0.32% from 2009 to 2012 based on Korean National Health Insurance claims data [29]. Differences from our estimate can be explained by increases in age-standardized incidence rates for our region described in the 2019 and 2021 Global Burden of Disease Studies [23, 30]; our estimated prevalence is rather lower than those reported for Southern and Andean Latin America (0.26 (0.23 to 0.30) and 0.43 (0.36 to 0.48)); however, it seems possible that these differences can be attributed to the data sparsity, particularly from low-income and middle-income regions like ours [30]. Also, the lack of a standardized RA case definition should be considered when making direct comparisons.

One could argue that including NSAID prescriptions in the specific algorithms reduces their specificity; however, only a minor difference (3.7%; 4,536 fewer cases) was observed when comparing estimates excluding NSAIDs. When excluding paracetamol, the difference was over 25% (32,118 fewer cases). This interesting finding is likely related to our real-world local practices: according to the High-Cost Disease Fund 2018 data -without ruling out the previously discussed selection bias- about 62.1% of patients were treated by a rheumatologist, and 72.3% were prescribed DMARDs [31]. This raises questions regarding the effect of access-to-specialized-care barriers and gaps between current treatment guidelines and actual daily practices. To develop a complete picture, additional studies will be needed to assess the extent and effects of this phenomenon nationwide.

The prevalence patterns of comorbidities and diseaserelated complications have not been previously described



Fig. 3 Standardized mean differences and age- and sex-adjusted prevalence ratios when comparing RA cases with a non-RA reference population. SMD: Standardized mean differences; PR: Prevalence ratio. The vertical lines denote thresholds for identifying differences between the two cohorts (SMDs of 0.1 and 0.2 and PR of 1)

for the Colombian population. A recent report from the PANLAR's (Panamerican League of Associations for Rheumatology) register of rheumatic diseases (PANRED) provides lower prevalence estimates for hypertension (40.6 vs. 68.2%), type II Diabetes (13.8 vs. 20.1%), and COPD (3.4 vs. 10.8%) yet higher for dyslipidemia (36.5 vs. 22.2%) [32]. This discrepancy could be attributed to PANRED's lower sample size and convenience sampling technique. When comparing our results to those of the COMORA study, similar patterns arise, such as the frequency of depression (15 vs. 12.5%) and asthma (6.6 vs. 5.4%) [33].

Conversely, other administrative claims database studies have also further supported the RA disease burden within a multimorbidity profile: Luque Ramos et al. found similar values for the most common comorbidities i.e., osteoarthritis (44 vs. 43.6%) and osteoporosis (26 vs. 18.6%), yet we had slightly lower estimates for depression (32 vs. 9.2%) [34]. Tidblad reported for Sweden a higher risk of respiratory and endocrine diseases, with similar frequencies to ours in coronary artery disease (5.3) vs. 5.4%), heart failure (2.2 vs. 3.4%), and stroke (1.3 vs. 1.0%), but lower in COPD (2.5 vs. 10.8%), asthma (2.6 vs. 5.4%), and depression (2.0 vs. 9.2%) [35]. Differences in respiratory diseases could be attributed to a high prevalence of expositional risk factors, such as the widespread practice of cooking with coal stoves in poorly ventilated spaces, which was common in Colombia until a couple of decades ago [36].

While higher sex- and age-adjusted PRs for osteoporosis might be explained by the chronic use of prednisolone, those for lupus and psoriasis can be attributed to the similarities in the pathological mechanisms and clinical presentation of these conditions, as well as the fact that during the diagnostic work-up, they may be considered differential diagnoses. A causal or risk association could not be assessed by our study, considering its cross-sectional nature. On the other hand, PRs for multiple sclerosis reveal something about the complex nature of autoimmunity and are supported by prior studies [37, 38]. Overall, the significant PRs for all listed comorbidities are expected and match those observed in earlier studies [15, 33, 35].

Contrasts in comorbidities prevalence patterns stratified by age and sex can be mainly explained by those characteristics alone rather than by a plausible interaction with the RA diagnosis; nevertheless, additional causal-inference-orientated research is needed to better understand the insights provided by this description previously unknown for our population.

Since the study was limited to patients identified by the healthcare system, there is a risk of underestimation. Given Colombia's broad health coverage, potential differences are assumed to be insignificant [39]. Conversely, there is a risk of overestimating cases where an ICD-10 diagnosis of RA is recorded to validate the use of medications not covered by the health system for another disease. However, employing a logical generalization algorithm that considers a minimum number of

Table 4 Prevalence of complications and comorbidities in RA cases stratified by age and sex

Variables	Age group Sex						Total
	18–49 (n=33,624)	50–64 (n=48,580)	65–74 (n=24,964)	≥75 (<i>n</i> =15,912)	Female (n = 101,105)	Male (n=21,975)	
Infectious							
complications							
Viral and bacterial pneumonia	5.91 (5.66–6.18)	8.71 (8.46–8.96)	12.85 (12.44–13.28)	19.40 (18.79–20.02)	9.97 (9.80–10.15)	11.07 (10.65–11.50)	10.17 (10.00–10.34)
Urinary tract infection	7.77 (7.48–8.06)	8.05 (7.80–8.30)	8.22 (7.87–8.58)	7.77 (7.35–8.21)	9.10 (8.93–9.27)	2.78 (2.57–3.01)	7.97 (7.83–8.12)
Central nervous system infection	0.53 (0.46–0.61)	0.53 (0.47–0.60)	0.66 (0.57–0.77)	0.58 (0.47–0.72)	0.54 (0.50–0.59)	0.67 (0.57–0.79)	0.56 (0.52–0.61)
Skin and subcutane- ous tissue infections	19.70 (19.29–20.12)	21.35 (20.98–21.72)	21.61 (21.10–22.13)	23.15 (22.49–23.82)	20.95 (20.72–21.19)	22.25 (21.68–22.82)	21.18 (20.96–21.41)
Intestinal infectious diseases	41.44 (40.91–41.97)	33.36 (32.94–33.79)	31.15 (30.58–31.73)	31.81 (31.10–32.54)	35.34 (35.06–35.61)	33.01 (32.39–33.64)	34.92 (34.66–35.18)
Tuberculosis	2.61 (2.44–2.79)	2.98 (2.83–3.13)	2.49 (2.31–2.69)	2.06 (1.85–2.30)	2.45 (2.36–2.55)	3.62 (3.39–3.87)	2.66 (2.57–2.75)
Other bacterial diseases	0.79 (0.69–0.89)	0.74 (0.66–0.82)	0.77 (0.67–0.89)	0.88 (0.74–1.04)	0.75 (0.70–0.80)	0.91 (0.79–1.04)	0.78 (0.73–0.82)
Sexually transmitted infections	4.04 (3.83–4.26)	2.05 (1.92–2.18)	1.58 (1.43–1.74)	1.41 (1.24–1.61)	2.20 (2.12–2.29)	3.38 (3.15–3.62)	2.41 (2.33–2.50)
Viral infections	15.41 (15.01–15.81)	16.55 (16.21–16.89)	16.76 (16.30–17.23)	15.02 (14.46–15.60)	16.29 (16.08–16.51)	15.11 (14.63–15.60)	16.08 (15.88–16.29)
Viral hepatitis	1.73 (1.59–1.88)	1.58 (1.48–1.69)	1.38 (1.24–1.53)	0.90 (0.77-1.07)	1.40 (1.33–1.47)	1.93 (1.75–2.13)	1.49 (1.43–1.56)
Acute myocardial infarction	0.10 (0.07–0.14)	0.35 (0.30–0.40)	0.80 (0.69–0.92)	1.14 (0.98–1.32)	0.35 (0.31–0.39)	1.04 (0.91–1.19)	0.47 (0.44–0.51)
Musculoskeletal complications							
Total Hip Replacement	0.23 (0.18–0.28)	0.54 (0.47–0.60)	0.79 (0.69–0.92)	0.99 (0.85–1.16)	0.55 (0.51–0.60)	0.62 (0.53–0.74)	0.56 (0.52–0.60)
Total Knee Replacement	0.15 (0.11–0.20)	0.83 (0.75–0.91)	1.65 (1.50–1.82)	1.65 (1.47–1.86)	0.92 (0.86–0.98)	0.91 (0.80–1.05)	0.92 (0.87–0.97)
Ankle Joint Replacement	0.00 (0.00-0.02)	0.01 (0.00–0.02)	0.02 (0.01–0.05)	-	0.01 (0.00–0.02)	0.01 (0.00–0.04)	0.01 (0.01–0.02)
Elbow Joint Replacement	0.02 (0.01–0.04)	0.08 (0.06–0.10)	0.09 (0.06–0.14)	0.04 (0.02–0.09)	0.06 (0.04–0.07)	0.07 (0.04–0.12)	0.06 (0.05–0.07)
Shoulder Joint Replacement	0.01 (0.01–0.03)	0.08 (0.06–0.11)	0.26 (0.21–0.34)	0.42 (0.33–0.54)	0.16 (0.13–0.18)	0.09 (0.06–0.14)	0.14 (0.12–0.17)
Comorbidities							
Hypertension	49.92 (49.39–50.45)	65.92 (65.49–66.35)	82.44 (81.96–82.91)	91.48 (91.03–91.91)	67.91 (67.63–68.19)	69.55 (68.94–70.16)	68.20 (67.95–68.46)
Osteoarthritis	19.50 (19.09–19.92)	46.66 (46.21–47.11)	58.88 (58.27–59.49)	61.53 (60.79–62.26)	45.70 (45.41–46.00)	34.17 (33.54–34.80)	43.64 (43.37–43.91)
Gastritis	25.36 (24.91–25.81)	34.73 (34.31–35.16)	38.95 (38.35–39.56)	38.32 (37.58–39.07)	34.87 (34.59–35.14)	27.17 (26.58–27.76)	33.49 (33.24–33.75)
Hypothyroidism	22.88 (22.45–23.32)	27.91 (27.51–28.31)	35.01 (34.43–35.60)	36.91 (36.17–37.65)	31.21 (30.93–31.48)	19.62 (19.08–20.17)	29.14 (28.89–29.39)
Hyperlipidemia	8.71 (8.41–9.03)	26.36 (25.98–26.75)	30.45 (29.88–31.02)	24.77 (24.10–25.45)	22.32 (22.08–22.57)	21.43 (20.88–22.00)	22.16 (21.93–22.39)
Diabetes	7.46 (7.18–7.75)	19.46 (19.11–19.83)	30.17 (29.60–30.74)	36.56 (35.82–37.30)	20.22 (19.99–20.45)	22.14 (21.58–22.72)	20.56 (20.34–20.79)
Osteoporosis	2.94 (2.76–3.14)	15.38 (15.06–15.72)	32.59 (32.01–33.17)	39.40 (38.67–40.14)	21.09 (20.85–21.32)	7.05 (6.72–7.39)	18.58 (18.37–18.79)
Eczema	15.44 (15.05–15.85)	17.36 (17.02–17.71)	18.16 (17.69–18.64)	17.58 (17.00–18.19)	17.44 (17.22–17.66)	15.15 (14.67–15.65)	17.03 (16.82–17.24)
Discopathy	8.99 (8.68–9.31)	14.82 (14.50–15.15)	15.38 (14.94–15.83)	13.96 (13.41–14.53)	13.18 (12.99–13.38)	13.43 (12.98–13.90)	13.23 (13.04–13.42)
Anxiety	9.03 (8.72–9.35)	12.64 (12.34–12.94)	11.78 (11.39–12.20)	10.91 (10.42–11.42)	12.13 (11.94–12.32)	7.23 (6.89–7.57)	11.26 (11.08–11.43)

Variables	Age group	Age group				Sex	
	18–49 (<i>n</i> = 33,624)	50–64 (<i>n</i> = 48,580)	65–74 (n=24,964)	≥75 (<i>n</i> =15,912)	Female (<i>n</i> = 101,105)	Male (n=21,975)	
COPD	2.46 (2.30–2.64)	6.87 (6.65–7.10)	16.47 (16.02–16.94)	31.52 (30.81–32.24)	10.02 (9.85–10.20)	14.39 (13.92–14.87)	10.80 (10.63–10.98)
Migraine	17.30 (16.90–17.71)	11.14 (10.86–11.43)	5.67 (5.38–5.97)	3.30 (3.03–3.59)	12.03 (11.84–12.23)	4.56 (4.31–4.83)	10.70 (10.53–10.87)
GERD	5.57 (5.33–5.82)	10.95 (10.68–11.24)	12.29 (11.88–12.71)	10.86 (10.37–11.37)	10.29 (10.11–10.47)	7.21 (6.88–7.55)	9.74 (9.58–9.91)
Depression	7.86 (7.57–8.16)	10.04 (9.78–10.31)	9.09 (8.72–9.46)	9.77 (9.30–10.26)	9.79 (9.62–9.97)	6.56 (6.25–6.89)	9.22 (9.06–9.38)
Lupus	14.15 (13.78–14.54)	8.44 (8.20–8.69)	5.30 (5.03–5.60)	3.15 (2.89–3.44)	9.50 (9.33–9.68)	4.91 (4.65–5.19)	8.68 (8.53–8.84)

COPD: Chronic Obstructive Pulmonary Disease; GERD: Gastroesophageal Reflux Disease. Prevalence is provided per 100 with the corresponding 95% confidence interval (CI)

There were no identified hand, wrist, or spinal joint replacement cases

diagnoses over time and the specific medications utilized for this condition can reduce the likelihood of this happening. Furthermore, the generalizability of these results depends on the information source. While this limitation is inherent in administrative claim databases, the use of a novel approach involving a set of sensitive and specific electronic algorithms applied to real-world linked data based on ICD-10 codes and unique medication use codes has been deemed reliable for estimating the prevalence of complex health conditions in Colombia [11–14], where the absence of a comprehensive country-level clinical registry hinders the adoption of more precise methods.

Taken together, we present the first comprehensive assessment of the prevalence patterns of disease-related complications and comorbidities of RA in Colombia as part of the RA disease burden within a multimorbidity profile, compared with a non-RA reference population. We also provide a narrower and more reliable RA point prevalence estimate for Colombia's contributory healthcare regime. These findings should be interpreted with caution; however, this innovative approach offers insights into three key aspects: the use of specific and sensitive electronic algorithms for more reliable disease identification in administrative databases, moving beyond simple reliance on the ICD-10 code; the flexibility to adjust distinct parameters within these algorithms to evaluate their performance in terms of case identification capacity; and the reliability provided by linked databases in studies on the prevalence of RA.

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s42358-025-00437-8.

Supplementary Material 1

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Author contributions

Conceptualization and Methodology: KMC, GB, and GQL. Formal analysis: KMC. Writing - original draft preparation: KMC; Writing - review and editing: KMC, GB, and GQL. Supervision: GB and GQL. All authors read and approved the final manuscript.

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Data availability

Data cannot be shared publicly because of a confidentiality agreement between Universidad Nacional de Colombia and the Ministry of Health of Colombia. However, data are available from the Ministry of Health of Colombia's integrated information system (https://www.sispro.gov.co/Pages /Home.aspx) for researchers who meet the criteria for access to confidential data. R and STATA codes are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the IRB of the School of Medicine of the National University of Colombia on October 27, 2021 [N. 020–191]. Individual informed consent was not obtained due to the nature of the data.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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