Health disparities in rheumatoid arthritis

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Abstract: Rheumatoid arthritis (RA) is an autoimmune disease characterized by joint inflammation that involves symmetric polyarthritis of small and large joints. Autoimmune rheumatic diseases represent a significant socioeconomic burden as they are among the leading causes of death and morbidity due to an increased risk of cardiovascular disease. Health disparities in patients with rheumatoid arthritis affect outcomes, prognosis, and management of the disease.

Keywords: rheumatoid arthritis, health disparities

Epidemiology of rheumatoid arthritis

Rheumatic disorders collectively pose a significant socioeconomic burden for healthcare systems and are among the leading causes of mortality and morbidity due to an increased risk of cardiovascular disease. Rheumatoid Arthritis (RA) is an autoimmune condition characterized by symmetric inflammation of small and large joints.

The Centers for Disease Control (CDC) defines health disparities as ‘preventable differences in the burden of disease, injury, violence, or in opportunities to achieve optimal health experienced by socially disadvantage racial, ethnic, and other population groups, and communities’. As the population of the United States continues to diversify, there has been an emergence of significant health disparities that disproportionately affect marginalized minorities such as African Americans and Hispanic Americans. This has led to poorer health outcomes with higher mortality and morbidity in non-Caucasians versus Caucasians.

Numerous studies have investigated the impact of ethnicity, race, age, and gender on the clinical manifestations and disease outcomes of RA in the United States (US), which we aim to describe in this article.

Based on a study done in 2010, the overall age- and sex-adjusted annual RA incidence is 40.9/100,000 population and the age-adjusted incidence in women is 53.1/100,000 population (versus 27.7/100,000 population in men). The incidence of RA has increased from 1985 to 2007 with a reported RA incidence of 32.7/100,000 from 1985 to 1994.

A systematic review on the global burden of RA showed a global prevalence of 0.24%. Studies did not show a clear linear trend in age-adjusted prevalence of RA between men and women between 2005 and 2018, instead exposing the impact of race and education on the development of RA, with higher risk of RA in African Americans, those with educational level less than high school and low family income.

From a geographical point of view, there were variations with higher estimates in polar countries, lower estimates in tropical countries, and lower estimates (or perhaps underreporting) in some African and Asian countries. In 2009, the prevalence rates of RA in developed countries remained approximately 0.5–1% for the adult population group. In 2010, the prevalence in the United States was noted to be around 0.6% versus Canada, which had a prevalence of RA of 0.9%.

Interestingly, newer studies from 2017 done in United States show the prevalence of RA during the period of 2004 to 2014 has increased from 0.41 to 0.54%, respectively, affecting approximately 1.3 million adults. This rise could be attributed to the increasing emphasis on early diagnosis of RA, regular monitoring of disease activity, increased life expectancy, as well as a growing elderly population.
The prevalence of RA in Europe is very well described. In Spain it was described between 0.9% and 0.5% in France it was found to be 0.31%, in Italy 0.41% and in Lithuania 0.55%. Batko et al. described 0.9% prevalence in the Polish population, and 0.35% in Serbia.

Oceania has a high prevalence among both the indigenous Australian population (2.7%) and the non-indigenous Australian population (1.9%). High rates of RA in indigenous populations have been described in Pima (5.3%), Chippewa (6.8%), and Qom (2.4%) peoples. Another study done by Silman and Pearson demonstrated again that the prevalence of RA is relatively constant in many populations, at 0.5–1.0%, with a high prevalence reported similar rates in indigenous populations such as Pima Indians and the Chippewa Indians. In Asia, the highest prevalence was reported in India (0.75%) and the lowest prevalence in Pakistan (0.142%) and South Korea (0.2%). While some studies report a prevalence of 0.2% in China and 0.3% in Japan, other studies showed a much higher prevalence in Japan 0.6% to 1%. Low prevalence has also been shown in China and Taiwan.

In Africa, the prevalence was reported as 0.13% in Algeria, 0.2% in Egypt, and 0.5% in Nigeria. The highest prevalence was reported in Congo and South Africa at 0.9%.

The prevalence described in Latin America include 0.2–0.94% in Argentina and 1.6% in Mexico. As described, rheumatic diseases are global phenomena, and the distribution is ubiquitous.

**Differences in disease manifestations in RA**

RA is a chronic, symmetric, inflammatory arthritis that affects multiple small and large joints. Patients typically present with joint pain, swelling, warmth, erythema, and prolonged morning stiffness lasting more than 30 minutes with an insidious onset. These symptoms can be accompanied by systemic manifestations such as fatigue, weight loss or low-grade fever. Long-term radiographic changes to affected joints include periarticular structural damage and erosions.

As per American College of Rheumatology (ACR), the criteria for diagnosing rheumatoid arthritis include at least one joint with clinic synovitis that is not explained by other inflammatory arthritis associated with either positive rheumatoid factor (RF) and/or anti-citrullinated peptide antibody (anti-CCP), elevated inflammatory markers [C-reactive protein and/or erythrocyte sedimentation rate (ESR)] with a duration of symptoms of more than 6 weeks. Most of the patients are found to have positive rheumatoid factor (in 60–80% cases with a specificity of 80%) and/or a positive anti-CCP, which has a sensitivity of 50–70% and specificity of 95–99%. The susceptibility to rheumatoid arthritis (RA) is associated with defined HLA-DRB1 alleles, however, most African Americans are HLA-DR4 negative, despite being seropositive or seronegative and this finding was not associated with a higher risk of disease severity. Positivity for rheumatoid factor was weakly associated with more severe disease in these patients.

Extraarticular manifestations (EAMs) of RA range from skin involvement to lungs, heart, central nervous system, kidneys, eyes, and the hematopoietic system.

Hata and Kavanaugh described the main dermatologic manifestations of RA. These included rheumatoid nodules, which are the most common EAM. They are seen in approximately 30% of the patients with RA and in 75% of those with Felty syndrome. They are more prevalent in Caucasian males.

Esposito et al. described lung involvement in RA, including interstitial lung disease (ILD), airway disease, pleural disease, and drug-induced toxicity. Pulmonary complications occur in 60% to 80% of patients with RA. ILD is the most common RA-related lung condition. The risk of developing RA-associated ILD (RA-ILD) is nine times higher than ILD in the general population. The main risk factors associated with an increased risk of developing RA-ILD include antibody positivity (RF and/or anti-CCP, mainly the latter), older age, and male sex with four times higher risk in males than females. Usual interstitial pneumonia (UIP) is a pattern of ILD that is mostly seen in older male patients with a history of smoking and carries a poor prognosis. A study published by Samhouri et al. showed that the presence of severe EAMs, smoking history, and age at incidence were the major factors associated with ILD. Interestingly, this study did not find an association between male sex and RA-ILD. Pleural involvement (pleural thickening or pleural effusions) was seen in 70% of the patients;
however, only few of them (5%) will develop symptoms. It was reported mainly in males (24%) versus females (16%). Risk factors for developing pleural effusions are age older than 35, male sex, and presence of rheumatoid nodules.

Another study done at Mayo Clinic in Rochester MN,23 showed that the risk of developing ILD was 7.7% in patients with RA versus 0.9% in control population. The main risk factors included older age at the time of diagnosis, males, and severe RA. This study was done on the population in Rochester, which mainly consists of Caucasian patients with socioeconomic characteristics similar to Caucasian US population.

In 2019, McFarlene et al.24 published a study done on 32 patients with RA-ILD from New York City Hospitals in Brooklyn, NY. Of these patients, 89% were African Americans. Women were predominant in this cohort, 88.5% accounting for African Americans and 9.2% for Hispanics. In this study population, with smoking history prevalence of 31% (less than half in Mayo Clinic cohort) and prevalence of ILD was 6.36% with higher risk on women (93.7%).

Nearly all the cardiac structures can be affected in patients with RA and it is well known that coronary artery disease (CAD) is the most common cause of death in this population.25 RA-related autoantibodies (rheumatoid factor and anti-CCP) are an independent risk factor for subclinical atherosclerosis and subsequent cardiovascular events. A study done on the Multi-Ethnic Study of Atherosclerosis (MESA) cohort noticed that RA-related autoantibodies, without clinical diagnosis of RA, were associated with clinical cardiovascular disease (CVD) events in African American women.26 More specifically, IgA RF and anti-CCP were associated with coronary artery calcium (CAC) by computer tomography $\geq 300$ (with a score of 0 meaning no calcium seen in the coronary arteries, 100–300 meaning moderate plaque deposition and $> 300$ showing very high to severe disease with high risk of cardiovascular events) in African American women. There was no similar trend in White women or men.26

Furthermore, another study involving African Americans with diagnosis of RA demonstrated the increased risk for atherosclerotic cardiovascular disease (ASCVD) in this cohort.27 The rate of ASCVD is 37.4% in African Americans compared with 20.5% in Caucasians with a prevalence ratio of 4.0 versus 2.5, respectively. Interestingly, in African Americans, RA along with concomitant diagnosis of another connective tissue disease (CTD) has a lower ASCVD rate (34.2%) compared with RA alone, which has a prevalence of 39%. The same trend is seen for Caucasian patients with ASCVD rate 19.8% in RA with another CTD compared with 20.9% in RA diagnosis only.27

An important factor in reducing CVD in RA patients is disease activity control, which plays an important role for decreasing the risk of atherosclerotic disease, especially in African American population. However, only 0.9% of RA patients treated in the public sector receive biologic disease-modifying antirheumatic drugs (DMARD) if they fail conventional synthetic DMARD,28 based on a study done in Sub-Saharan population. This study was focused on the comorbidities in the population diagnosed with RA, and found that most of the Sub-Saharan African black population have lower income and therefore seek medical care within public healthcare centers where resources are limited compared with the private medical sector. This cohort of Sub-Saharan African black RA patients have higher risk for ASCVD.

Patients with RA are also more susceptible to mental health disorders such as anxiety, depression, or cognitive impairment. Depression is two times more common in RA population versus general population. This may be contributing to higher disease activity and lower treatment responsiveness.29

Patients with RA have an increased mortality risk compared with the general population, therefore early diagnosis may improve the outcomes of the disease.

Differences in rheumatic disease outcomes: mortality, morbidity/disability, access to treatment, remission

Mortality rates in patients with RA are higher when compared with expected rates in the general population. There is an increased trend toward RA-associated mortality rates in the older population groups.6 The most common causes of increased mortality in RA are due to cardiovascular, infectious, hematologic, gastrointestinal, and respiratory diseases.
Disease severity and disease activity markers in RA (for example, extra-articular manifestations, ESR, seropositivity, higher joint count, and functional status) have also been shown to be associated with increased mortality in the Indigenous population, where RA prevalence is higher compared with Caucasians, the morbidity and mortality from CVD was higher in Pima Indians when compared with other races. In this population, the diagnosis of RA, high serum RF, proteinuria, older age, and male sex were the major risk factors for mortality. Studies demonstrated the critical role of inflammation in RA-associated premature mortality. Methotrexate has been shown to have a positive effect on survival and newer studies show that tumor necrosis factor (TNF) inhibitors may reduce mortality in women but not men with RA.

The health disparities in life expectancy between African Americans and Caucasians have been well-identified. A recent study focusing on reviewing the socioeconomic status and health in African American population from Washington, D.C. showed that African Americans were expected to live 12 years less when compared with Caucasians.

RA is also associated with progressive disability, with limitation in work and physical activity. Race and socioeconomic status are important factors for disability in patients with RA.

The findings from the study by Ma et al. revealed a 44% 10-year work disability prevalence and 39% inability to work 10 years after early-stage rheumatoid arthritis, with a total of US$8.4 (US$10.6) billion for annual direct cost and US$30.8 billion for annual indirect cost with a total annual cost of US$39.2 billion costs for excess healthcare costs in the form of copays and medications. About 30% of the RA patients were more likely to need help with personal care and RA patients were twice as likely to have a health-related activity limitation.

A recent multicenter study on 184,722 RA patients in the United States, performed by Dowell et al., showed that the type of the insurance (Medicare/Medicaid) was associated with higher disease activity and burden. Interestingly, upon comparing demographics, there was no significant difference in disease activity between Caucasians versus African Americans or distance to specialty care.

RA can lead to irreversible joint deformities and loss of function with 25% of patients requiring total joint arthroplasty (TJA). A study done by Young et al. documents that there has been a decrease in total elbow arthroplasty (TEA) performed on Caucasian patients with RA, but the percentage among African American patients is increasing. For total shoulder arthroplasty (TSA), the proportion of Caucasians decreased over time while the African American proportion remained unchanged. Studies demonstrated that, despite African Americans undergoing total knee arthroplasty (TKA) less often than Caucasians, they experience more perioperative complications with worse pain, function, and overall they achieve less clinical improvement. Postoperative complications after undergoing total hip arthroplasty (THA) are influenced by race disparities, with African Americans having a higher rate of prolonged operative time, total length of hospital stay more than 5 days, and discharge to non-home facility when compared with Caucasian patients. Also, as demonstrated in the work of Shahid and Singh, surgical approach (total arthroplasty) and their outcomes were influenced by race differences, and this was not explained by a single cause. Further research and interventions are needed to dissipate the racial disparities.

The role race disparities play in rehabilitation was demonstrated by a recent study performed in an African American population. The study showed that severe disability was associated with increased rehabilitation, but not with disease activity.

Race disparities have significant impact on disability as discussed above. Based on self-reported Health Assessment Questionnaire Disability Index (HAQ-DI; 0–3; 3 = unable to do), Caucasians with RA have the least amount of disability (HAQ-DI 1.24) compared with African Americans (HAQ-DI 1.28), with African Americans having lower education and multiple comorbidities. Pain was also reported as higher in African Americans (39.3/100) versus Caucasians (33.3/100). Higher scores were also translated in Global Health where African Americans reported 42.4/100 compared with 39.3 in Caucasians.

A multicenter study done in the United States on 9363 patients compared disease activity measures (CDAI and HAQ-DI) between visit 1 (2013–2015) and visit 2 (2018–2020). The CDAI scores were higher for Hispanics when compared with Caucasians in both visits 1 and 2, with a lower
disease activity and remission rates in the Hispanic population. Although CDAI scores improved at visit 2 in the Hispanic patients, they overall improved less when compared with Caucasians. HAQ-DI was also higher in Hispanics and Blacks at visit 1 and visit 2 when compared with Caucasians.43

Another study43 showed that Patient Global Assessment was also higher in African American RA patients (56%) when compared with Hispanic Americans (43%), Asian/Pacific Islanders (47%), and Caucasians (36%). Interestingly, African Americans had lower mean total joint count (TJC)5 when compared with Hispanic Americans and Caucasians5 and Asians. Swollen joint count (SJC) was same for all ethnic groups. ESR has also been more elevated in minority groups with African Americans having higher ESR (41 mm/h) than Hispanic Americans (30 mm/h) and Caucasians (23 mm/h). Overall, a higher mean score of DAS28 was observed in non-White population with African Americans score of 4.4 compared with Asian/Pacific Islanders (4.2), Hispanics (4.0), and Caucasian (3.3). There are also notable differences in HAQ scores between African Americans (1.5) compared with Hispanics and Asian/Pacific Islanders (1.3) and Caucasians (1.0).43

Over the past decade, there has been an improvement in achieving a lower disease activity, however, the racial disparities persist. Between 2005 and 2007, 54.7% of Caucasian, 62.8% of Asian, and 43.3% of African American patients would achieve low disease activity compared with 64.5% of Caucasians, 65.5% of Asians, and 58.4% of African Americans who would achieve low disease activity between 2010 and 2012.44

There have been steady improvements in achieving remission from 2005 to 2007 and 2010 to 2012, with an increase from 21.4 to 29.0% in Caucasians, from 23.8 to 28.4% in Asians, and from 14.7 to 22.8% in African American patients.44 Despite overall improvement, racial disparities persisted for both time periods, African American patients had worse outcomes in terms of disease activity and achieving remission when compared with Caucasian patients.

Nowadays, there are multiple therapeutic options for patients with RA. However, there is less access to medications for African Americans versus Caucasians. According to the treat-to-target recommendations per ACR/European League Against Rheumatism (EULAR),45 the primary target for RA treatment is clinical remission, which is defined as the absence of signs and symptoms of significant inflammatory disease in patients with RA, or low disease activity. A systematic review done by Yu et al.46 noted that the rate of remission was increased with longer follow-up duration, with predictive factors for remission including male sex, higher education level, younger age, and low disease activity at baseline. Use of steroids at the time of diagnosis was associated with lower rate of remission. Racial disparities have a significant effect on remission and achieving low disease activity.

Access to treatment has been lower for African American patients and race is a strong predictive factor of acceptance of treatment. A study done by Navarro et al. highlighted the differences in people who filed with Medicare and Medicaid before 65 years old. African Americans were least likely to receive biologic disease-modifying anti-rheumatic drugs (bDMARDs; 49.3%) compared with Caucasians (53.3%) but Hispanics had higher chance to receive bDMARDs (60.9%). Kerr et al.47 compared the use of conventional standard DMARDs and biologics between Caucasians and non-Caucasians. DMARD use in Ethnic Minority Rheumatoid Arthritis Consortium (EMRAC) was greater in non-White population but similar in all Veterans Affairs Rheumatoid Arthritis Registry (VARA) patients. However, there was significantly more biologic use in EMRAC versus VARA (37% versus 22%), greater in Caucasian population compared with African Americans (45% versus 33%). A higher rate of biologic use is associated with younger age, advanced education, long-standing disease, and severe disease.47 Applying for disability in African American population with RA led to high opioid prescription with more than 66% of Medicare/Medicaid beneficiaries to receive chronic opioid, which suggests that this population presents with more pain and joint deformities and lower access to treatment could be an explanation of this.48

Interventions to reduce disparities in rheumatic disease outcomes

Delay in diagnosis of RA can lead to more severe disease manifestations and irreversible bony destruction, disability, and loss of function.
We consider that access to healthcare specialists, especially in areas where there is a lack of specialists, developing Early Arthritis Clinics (EAC) versus Routine Care Clinics, education of primary care physician (PCP) on recognizing inflammatory arthritis and early referral to specialists along with improvement in acceptance and adherence to treatment from patient are a few key modalities to improve healthcare disparities.

In the primary care setting, new-onset RA is less common than low back pain, osteoarthritis, gout, fibromyalgia, or psoriasis, but is more common than polymyalgia rheumatica (PMR), systemic lupus, or septic arthritis.19 EACs were initially set up as research clinics but showed promising results. 'Early RA' is defined by 2–4 weeks of joint pain, irrespective of synovial inflammation, positive RF or anti-CCP antibody, and positive family history in one first-degree relative.40 EAC healthcare services focus to facilitate early diagnosis and improve treatment. Patients with early inflammatory arthritis symptoms are referred to EACs as early treatment can prevent long-term functional disability.50 A study done by Farina et al.51 showed that patients seen in EACs had early diagnosis and treatment with subsequently less need of second-line biologic medications. Another study done by Niemantsverdriet et al.52 showed that being seen by a rheumatologist within 6 weeks of symptom onset had benefits for achieving sustained DMARD-free remission, but not for radiographic progression.

One of the causes of delay in presenting to a specialist would be lack of access to a rheumatologist due to geographic distance. A study done by FitzGerald et al.53 showed there are some areas with population of greater than 200,000 people without a rheumatologist within travel distance of 94 miles or for smaller metropolitan areas within a distance of 200 miles. A greater number of rheumatologists per core-based statistical area was associated with larger populations and fellowship program. The presence of a rheumatology training program is associated with a greater density of rheumatologists. ACR is leading an initiative of increasing rheumatology fellowship programs in rural areas, with subsequently improving access to rheumatology specialists.

Socioeconomic status is another reason for delaying health service access for RA. A study done by Cifaldi et al.54 found that uninsured and Medicaid patients in the United States were 17% and 13% less likely to visit a rheumatologist, respectively. This may be addressed by developing more outreach clinics potentially attached to major academic centers where rheumatology fellows or faculty can volunteer to provide care for uninsured patients.

Differences in the ways patients self-evaluate the risk and benefits of treatment seem to have an impact on medication adherence. Distrust of medical recommendations among different races continue to persist. When presented with the same information of risks and benefits of the medications, a study showed that African American patients were more concerned about medication toxicities, particularly serious adverse effects, and gave less importance to the benefit from the treatment.55 Caucasian patients were more open to aggressive treatment compared with African Americans (51% Caucasians versus 16% African Americans), in part due to differences in spirituality, health beliefs, perceptions of benefit, and trust.56 A study done on the general population,57 showed that African American older adults hold different beliefs related to their physician’s capacity of prescribing medications and are more likely to express negative and suspicious beliefs related to their doctors decisions and care. This can be translated in higher rate of non-adherence in African Americans. More training and education for physicians to improve communication with minority patients is needed to increase acceptance for more aggressive medications and treatments for rheumatoid arthritis.

The patients’ socio-economic status, cultural background, as well as their personal beliefs and values are influencing acceptance of biologic treatment as demonstrated by a Canadian study including African Americans and Indigenous populations. One of the proposed solutions to rebuild trust in the medical system is increasing the African American and Indigenous population exposure to health care professionals from an early age (summer camps, career days, scholarships).58

The health disparities in patients with rheumatoid arthritis affect the outcomes, the prognosis, and the management of the disease. Unfortunately, despite novel and better treatments discovered over time, not all ethnic groups have access to them. Untreated disease has poor prognosis in the long term and new strategies are needed to reduce the gap between different ethnic populations.
Declarations

**Ethics approval and consent to participate**
Not applicable.

**Consent for publication**
Not applicable.

**Author contributions**

**Elena I. Ciofoaia:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Validation; Visualization; Writing – original draft; Writing – review & editing.

**Anjani Pillarisetty:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – review & editing.

**Florina Constantinescu:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources.

**Acknowledgements**
None.

**Funding**
The authors received no financial support for the research, authorship, and/or publication of this article.

**Competing interests**
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Availability of data and materials**
Not applicable.

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