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## Comorbidities and extra-articular manifestations of Rheumatoid arthritis in sub-Saharan Africa

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### Abstract

Rheumatoid arthritis is a systemic auto-immune disorder that preferentially affects the joints. Extra-articular manifestations and comorbidities observed during rheumatoid arthritis are multiple and frequent. They are the cause of high morbidity and mortality in this population and make rheumatoid arthritis serious. Systematic screening for the extra-articular manifestations and comorbidities is therefore necessary in order to optimize its management in affected subjects. The various studies carried out on rheumatoid arthritis in developing countries have explored less the extra-articular manifestations as well as the comorbidities. This work reviews the literature on the extra-articular manifestations as well as the comorbidities encountered in subjects with rheumatoid arthritis in Sub saharia Africa in order to draw the attention of the nursing medical staff to their extent in order with a view to systematic screening and treatment.

**Keywords:** Rheumatoid arthritis; Comorbidities; Extra-articular manifestations; Sub-Saharan Africa

### 1. Introduction

Rheumatoid arthritis is one of the most common systemic autoimmune diseases; it affects 0.24% in the world population and 0.42% in Africa [1]. It is responsible for primary damage to the joints leading to their inflammation and progressive destruction in the absence of let alone without rapid and adequate treatment [2]. Extra-articular manifestations are also frequent with a frequency that can reach 50% with the progression of the disease [3]. Rheumatoid arthritis impairs the quality of life due to its joint damage but is also associated with high mortality. Epidemiological data highlight the high mortality in rheumatoid arthritis compared to the general population [4, 5]. This high mortality is attributable to extra-articular manifestations, in particular visceral [6], with a risk of death from cardiovascular diseases which can reach 50% in the case of rheumatoid arthritis [7]. Several situations promote the occurrence or aggravation of these extra-articular manifestations, including the environment, age, male sex, but also certain modifiable factors such as smoking, diet, obesity, dyslipidemia, high blood pressure or diabetes [8, 9]. To these, we also (add) cite depression favored by the pain felt by the patient, impaired quality of life, extra-articular manifestations and comorbidities [10, 11]. The latter are already present in a third of patients screened for polyarthritis and can reach 80% in the long term in developed countries and a higher prevalence in developing countries [12]. In sub-saharia Africa, there are few data on extra-articular manifestations and comorbidities of rheumatoid arthritis. Many patients are still treated without screening for these manifestations or comorbidities. Systematic screening for the latter is therefore necessary in order to optimize care in affected subjects, especially in developing countries which have fewer resources and which are increasingly confronted with non-communicable diseases and transferable ones. The only studies available address only a few extra-articular manifestations and/or comorbidities therefore requiring clarification. The present study identifies through a literature review the different extra-articular manifestations and comorbidities observed in patients followed for rheumatoid arthritis. Emphasis will also be placed on lifestyle that can

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promote comorbidities and worsening of rheumatoid arthritis. The results of this study will give an overview of the extent of these manifestations and comorbidities in order to draw the attention of caregivers and patients to their prevention, screening and management.

## 2. Material and methods

### 2.1. Study setting

The study concerned the countries of Sub saharia Africa, particularly in West Africa (Benin, Burkina Faso, Togo, Côte d'Ivoire, Niger, Nigeria, Mali, Senegal, Guinea), Central Africa (Democratic Republic of Congo, Cameroon), East Africa (Uganda, Ethiopia, Sudan), Southern Africa (South Africa).

### 2.2. Type of study

This was a retrospective and descriptive study

### 2.3. Study population

It consists of all people living with rheumatoid arthritis.

### 2.4. Sampling

An exhaustive inventory of publications dealing with rheumatoid arthritis and concerning which concerned subjects living in Africa south of the Sahara was made. Publications addressing the manifestations and comorbidities of rheumatoid arthritis were included. Articles dealing with clinical cases or with a sample size of less than 10 were not included in the study.

### 2.5. Variables

The variables studied related to general characteristics (sex, age, lifestyle, nutritional status), comorbidities and extra-articular manifestations of rheumatoid arthritis. Comorbidities represented all diseases observed that were not directly related to rheumatoid arthritis. Extra-articular manifestations are the locations outside the known joints of rheumatoid arthritis.

### 2.6. Data collection technique

Data collection was done by listing all publications on Pub Med, Cochrane Library, Cochrane central Register of Controlled Trials, Santé Psy, LiSSA, Bibnet.org, Pub Med central, Science direct, LILACS, Springer Link, Wiley Online Library, Cairn. A data collection sheet and other appropriate tools were used.

### 2.7. Data processing and analysis

Data were entered using Word and Excel software.

## 3. Results

### 3.1. General characteristics of the study population

**Table 1** General characteristics of subjects living with rheumatoid arthritis in sub-Saharan Africa

Authors	Country	Size	Age (year)	Women (%)	Alcohol (%)	Tabacco (%)
Mabusela et al. [11]	South Africa	110	56.6±11.9	90.9	-	13.6
Singwe-Ngandeu et al. [1]	Cameroon	50	51±14.8	78	8	2
Bogale et al. [2]	Ethiopia	73	50.7±10.3	87.6	11	4
Mulumbe et al. [4]	DRC	75	51.8±14.6	80	28	2.66
Zomaletho et al. [26]	Benin	68	49.9±12.1	95.6	-	-
Kamissoko et al. [13]	Guinea	17	48.2±11.9	82.4	-	5.9

DRC : Democratic Republic of Congo

The study population of different publications ranged from 17 to 500 subjects. A female predominance was observed with a proportion varying between 78 and 95.6%. The average age varied between  $48.2 \pm 11.9$  and  $56.6 \pm 11.9$  years (old). The frequency of alcohol consumption varied between 8 and 28% [1-2, 4]. Tobacco consumption was observed in 2-13.6% of subjects [1-2, 4, 11, 13]. **(Table 1)**

### 3.2. Comorbidities

The prevalence of arterial hypertension varied between 11.7 and 70% [1, 12, 14-18], that of diabetes between 4.3 and 15.3% [4, 6, 12, 15-18] and that of obesity between 40 and 58.8% [1, 11, 13, 17] of subjects. Between 2 and 70.5% had depression [1, 11, 15], 2% cancer [1, 12] and between 23.5 and 74.2% dyslipidemia [1, 6, 12]. The prevalence of asthma varied between 2.3 and 4.3% [14, 18] and gout was reported in 5.8% [17] of subjects. HIV infection was present in 2.1 to 9.3% of the subjects surveyed [11-12, 15]. (Table II)

**Table 2** Comorbidities encountered in subjects living with rheumatoid arthritis in sub Saharian Africa

Authors	Size	Comorbidities (%)						
		HTA	DM	Depression	HIV	Obesity	Gastritis	Others
Lala et al. [12]	500	70	15.3	-	9.3		64	Cancer 2 Dyslipidemia 74.2
Ouedraogo et al. [14]	23	30.3	-	-	-	-	-	Asthma 4.3
Bongomin et al. [15]	49	54.2	6.3	70.8	2.1	-	-	-
Mulumba et al. [4]	75		13.33	-	-			
Kakpovi et al. [16]	92	10.9	4.3	-	-	-	-	-
Garba et al. [17]	17	29.4	5.88	-	-	29.41	-	Gout 5.88
Mabusela et al. [11]	110	-	-	67	7.3	40	-	-
Singwe-Ngandeu et al. [1]	50	36	-	2	-	46	32	Cancer 2 Dyslipidemia 50
Kamissoko et al. [6]	17	-	17.2	-	-	58.8	-	Dyslipidemia 23.5
Gondanga[18]	128	11.7	5.5	-	-	-	-	Asthma 2.3

HTA : Hypertension; DM : Diabetes mellitus; HIV : Human Immunodeficiency Virus

### 3.3. Extra-articular manifestations

**Table 3** Extra-articular manifestations encountered in subjects living with rheumatoid arthritis in sub Saharian Africa

Authors	Size	Extra-articular manifestations (%)					
		Nodule	Heart	Sicca syndrome	Lung	Anemia	Others
Ouedraogo et al. [19]	120	5		15		36.6	
Singwe-Ngandeu et al[1]	50		2				Stroke 6 Infection 58
Lala et al. [12]	500	31	7.2		3.2	78.2	Vascularite 1.4 Infection 11.2
Garba et al. [17]	17	41.17		52.94		23.52	
Mulumba et al. [4]	75	16	32	4	2.7		
Ndongo et al. [20]	35	3		34	6	17	Adenopathy 6
Niasse et al. [21]	400	5		38.2	8.9	58.8	Adenopathy 1.5 Fever 1.5
Balde et al.[22]	22	-	-	86.36			Eye damage 18.88
Abdullahi et al. [23]	74	-	-	39.2	-	-	Eye damage 41.9
Gondanga [18]	128	8.2	-		4.9	67.2	Eye damage 4.92

Nodules were observed in 3 to 41.17% [4, 12, 17-20], pulmonary involvement in 2.7 to 8.9% [4, 12, 18, 20-21] and cardiac involvement in 4 to 32% of subjects [1, 4, 12]. The prevalence of sicca syndrome varied between 2 and 86.36% [17-21] and anemia between 17 and 78.2% [12, 17-21]. The other manifestations observed were infection 11.2-58% [1, 12], ocular involvement 4.92-41.9% [18, 22-23], lymphadenopathy 1.5-6% [20 -21], fever in 1.5% [21], cerebrovascular accidents in 6% [1] and vasculitis in 1.4% [12] of subjects. (Table III)

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#### 4. Discussion

Rheumatoid arthritis is a systemic disease not often rarely diagnosed in developing countries due to limited technical means. It is a debilitating disease because it is responsible for joint damage but above all serious because of comorbidities and complications in the event of late screening and management; common frequent situations in developing countries. The present study is one of the few to focus on the comorbidities and complications encountered in rheumatoid arthritis. At the end of this study, the following essential points should be noted.

It is a disease that mainly affects women and a population of young adults in accordance with the results reported in the literature [24-26]. The lifestyle of patients was characterized by smoking in 2-13.6%. The frequency of tobacco consumption was also reported by Lin et al. [27] in China (15%), Uribe-Reina et al. [28] in Colombia (6.14%), and Gheita et al. [29] in Egypt (8.2%). This practice should be avoided by patients insofar as smoking is a cardiovascular risk factor but promotes the citrullination of proteins entering the etiopathogenic phenomena of rheumatoid arthritis [25].

The comorbidities encountered were arterial hypertension (11.7-70%), diabetes (4.3-15.3%), obesity (40-58.8%), depression (2-70.5 %), cancer (2%), dyslipidemia (23.5-74.2%), asthma (2.3-4.3%), gout (5.8%) and (HIV infection) infection with HIV (2.1-9.3%). Results similar to those of the present study have been reported. In studies by Bentaleb et al. [30] in Morocco and McFarlane et al. [31] in the United States, the prevalence of arterial hypertension was 15.6-16% and 66.6% respectively. Okais et al. [32] in Lebanon and Harrold et al. [33] in the United States reported a prevalence of diabetes of 3.3-18% and 8.5% respectively. The prevalence of obesity varied between 9-53.2% in Morocco [30] and was 37.2% in the United States [31]. Bentaleb et al. [30] reported a prevalence of depression that varied between 2 to 62.11% and that of cancer at 2%. The frequency of dyslipidemia in patients was observed in the study by Varela et al [34] and Santos-Moreno et al. [35] with respectively a prevalence of 26.7% and 45%. Harold et al. [33] reported an asthma prevalence of 2.1%.

The main extra-articular manifestations encountered were nodules (3-41.17%), pulmonary involvement (2.7-8.9%), cardiac involvement (4-32%), sicca syndrome (2 -86.36%), anemia (17 and 78.2%), infection (11.2-58%) and ocular involvement (4.92-41.9%). The diversity of extra-articular damage reflects the multisystem nature of rheumatoid arthritis highlighted by several studies. Trabelsi et al. [36] in France reported that extra-articulars were present in 20% of subjects and reached 40% according to Wu et al. [37] in South Korea in case of late diagnosis. The frequency of rheumatoid nodules in the studies by Kaeley et al. [38] in India and Zafar et al. [39] in Pakistan were 14.6% and 9.9% respectively. Lung involvement was reported with a proportion of 10-30% according to Laria et al. [40] and 21% according to Bentaleb et al. [30]. Cardiovascular manifestations are above all the severity of the disease and are very frequent [41]. Kumar et al. [42] in Pakistan and Yao-Wei et al. [43] in South Korea reported a frequency of 58.2% and 10.9% respectively. Sicca syndrome was also common; Bentaleb et al. [30] reported a prevalence of 81.9% and Uribe-Reina et al. [28] 19.7%. Sicca syndrome mainly affects the lacrimal and salivary glands. Apart from the ocular involvement of sicca syndrome, other ocular manifestations such as uveitis or conjunctivitis have been reported by Uribe-Reina et al. [28] and Chen et al. [41]. The mean hemoglobin level was low (11.6 g/dl) according to Gheita et al. [29] and the prevalence of anemia varying between 28.8 and 23% according to Bentaleb et al. [30]. The infection was reported by Harrold et al. [33] and Varela et al. [34] respectively 5.1% and 14.6%. The occurrence of infections in this population may also be favored by immunosuppressants frequently used in the treatment of polyarthritis; they are often pulmonary and urinary [34, 40, 44].

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#### 5. Conclusion

Comorbidities and extra-articular manifestations are very common in rheumatoid arthritis. Their screening and management must be systematic within this population for therapeutic optimization. Emphasis should be placed on preventing modifiable comorbidities through behavior change communication.

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## Compliance with ethical standards

### *Acknowledgments*

All authors cited in this article.

### *Disclosure of conflict of interest*

No conflict of interest.

### *Statement of ethical approval*

This is a study that referred to studies already carried out and published with free access. However, respect for patient confidentiality and fidelity to the information provided by the authors have been guaranteed.

### *Statement of informed consent*

The informed consent and the anonymity of the patients included in the various studies have been obtained by the authors.

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## References

- [1] Singwe-Ngandeu M, Essouma M, Moor VJA, Musa AJ, Menanga AP, Ngoufack C et al. Cardiovascular Risk Burden in Sub-Saharan Africans with Rheumatoid Arthritis: A Hospital-Based Study in Yaounde, Cameroon. *Open Journal of Rheumatology and Autoimmune Diseases* 2016; 6 : 1-9.
- [2] Bogale Z, Feleke Y. Prevalence, Clinical Manifestations, and Treatment Pattern of Patients with Rheumatoid Arthritis Attending the Rheumatology Clinic at Tikur Anbessa Specialized Hospital, Ethiopia: A Cross-Sectional Study, *Open Access Rheumatology: Research and Reviews* 2022 ; 14 : 221-9
- [3] Gbadamassi AG, Adjoh KS, Fiany A, Adambounou T, Aziagbe A, Efalou P. Rheumatoid arthritis-associated lung disease in black Africans: Descriptive study of 28 cases in Lomé. *Afr J Thoracic Crit Care Med* 2020;26(4):129-32
- [4] Mulumba C, Lebugbe P, Mbuji-Muamba JM, Makulo JR, Lepira F, Mukaya J et al. Prevalence and associated factors of subclinical atherosclerosis in rheumatoid arthritis at the university hospital of Kinshasa. *BMC Rheumatology* 2019 ; 3 : 37-44
- [5] Dessie G, Tadesse Y, Demelash B, Genet S. Assessment of Serum Lipid Profiles and High-sensitivity C-reactive Protein Among Patients Suffering from Rheumatoid Arthritis at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Cross-Sectional Study. *Open Access rheumatology* 2020 ; 12 : 223-32
- [6] Kamissoko AB, Barry IS, Sanda M, Houngebegnon CD, Diallo ML, Barry A et al. Asymptomatic Cardiac Manifestations in Rheumatoid Arthritis in Conakry (Guinea). *Open Journal of Rheumatology and Autoimmune Diseases* 2022 ; 12 : 57-64.
- [7] Solomon A, Stanwix AE, Castaneda S, Llorca J, Gonzalez-Juanatey C, Hodgkinson B et al. Points to consider in cardiovascular disease risk management among patients with rheumatoid arthritis living in South Africa, an unequal middle income country. *BMC Rheumatology* 2020 ; 4 : 42-57
- [8] Meyer P, Anderson R, Ker J, Ally M. Rheumatoid arthritis and risk of cardiovascular disease. *Cardiovascular journal of africa* 2018 ; 29(5) : 317-21
- [9] Ghammo H, Mitha M, Connolly C, Nyamande K. Rheumatoid Arthritis Associated Interstitial Lung Disease in KwaZulu-Natal, South Africa: A Retrospective 5-Year Review. *Int J Respir Pulm Med* 2020, 7(2):132-4
- [10] Zabsonré Tiendrébéogo W, Kaboré F, Nanema D, Binta S, Alassane D, Sougué C et al. Frequency and Factors Associated with Depression in Rheumatoid Arthritis in African Black Patients: Case-Control Study. *Open Journal of Rheumatology and Autoimmune Diseases*, 2019, 9, 35-41
- [11] Mabusela M, Tomita A, Paruk S, Paruk F. Prevalence of depressive symptoms in patients with rheumatoid arthritis at a regional hospital in KwaZulu-Natal, South Africa. *S Afr J Psychiat.* 2022;28 : 1-7
- [12] Lala V, Tikly M, Musengue E, Govind N. Comorbidities in Black South Africans with established rheumatoid arthritis. *Int J Rheum Dis.* 2022;25:699–704

- [13] Kamissoko A, Edikou T, Barry A, Sanda M, Fofana K, Lou N et al. Sexuality of Women with Rheumatoid Arthritis in a West African Hospital. *Open Journal of Rheumatology and Autoimmune Diseases*, 2021, 11, 152-159
- [14] Ouedraogo AR, Ouedraogo G, Boncounkou K, Zabsonre-Tiendrebeogo J, Kambou-Tiemtoré B, Maiga S et al. Respiratory manifestations during rheumatoid arthritis in Ouagadougou, Burkina Faso. *Rev Pneumol Trop* 2018 ; 29 : 67-71
- [15] Bogomin F, Natukunda B, Sekimpi M, Olum R, Baluchu JB, Makhoba A et al. High Prevalence of Depressive Symptoms Among Ugandan Patients with Rheumatoid Arthritis. *Open Access Rheumatology: Research and Reviews* 2021 ; 93-102
- [16] Kakpovi K, Koffi-Tessio V, Houzou P, Fianyo E, Kolou M, Kueviakoe M et al. Profile of rheumatoid arthritis in consultation rheumatology in Lome (Togo). *European Scientific Journal* 2017 ; 13(15) : 125-52
- [17] Garba AA, Andia A, Taofik M, Laouali MC, Kader AA, Adéhossi E. Epidemiological, clinical, paraclinical, therapeutic and evolutionary profile of the first cases of rheumatoid arthritis (RA) at the National Hospital of Zinder (HNZ). *Rafmi* 2020 ; 7(2) : 7-12
- [18] Godanga J. Frequency of seronegative rheumatoid arthritis in the rheumatology department at the CHU du point G. University of Sciences, Techniques and Technologies of Bamako, Faculty of Medicine and Odontostomatology, Medical Thesis, N°1254, 2022, 92 pages
- [19] Ouedraogo NCJ, Zabsonre /Tiendrebeogo JWS, Traore S, Kabore F, Guira O, Ouedraogo DD et al. Particularities of male rheumatoid arthritis (RA) at the University Hospital of Bogodogo. *Rhum Afr Franc* 2020 ; 3 (2) : 19 -25
- [20] Ndongo S, Pouye A, Ouedraogo L, Azankpan E, Diack N, Diop TM. Rheumatoid Arthritis of Man: A Study of 35 Cases in a Senegalese Hospital. *Open Journal of Internal Medicine*, 2014, 4, 137-42
- [21] Niasse M, Kane BS, Ndiaye AA, Ndao AC, Djiba B, Fall S et al. Severity of the Rheumatoid Arthritis in Sub-Saharan Africa: Study of 403 Senegalese Observations. *Open Journal of Internal Medicine*, 2017, 7, 151-9
- [22] Balde AI, Kamissoko AB, Camara F, Diane S, Yombouno E, Lelano A et al. Ocular Manifestations during Rheumatoid Arthritis in Conakry. *Open Journal of Ophthalmology*, 2022, 12, 373-81
- [23] Abdullahi MH, Pam V, Oladigbolu KK, Umar AA, Muhammad RC. Prevalence and Spectrum of Eye Disorders Among Patients With Rheumatoid Arthritis and Systemic Lupus Erythematosus in a Tertiary Hospital in Northern Nigeria. *J West Afr Coll Surg* 2022; 12:48-54.
- [24] Almutairi K, Inderjeeth C, Preen DB, Keen H, Nossent J. The prevalence of rheumatoid arthritis in Western Australia. *BMC Rheumatology* 2022 ; 3 : 93-100
- [25] Rauwel B, Degboé Y, Nigon D, Boyer JF, Abravanel F, Izopet J et al. Reduced progression of bone erosion in cytomegalovirus seropositive rheumatoid arthritis patients. *Arthritis research and therapy* 2020 ; 22 : 13-8
- [26] Zomaletho Z, Assogba C, Dossou-Yovo H. Impact of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection and disease-2019 (COVID-19) on the quality of life of rhumaoid arthritis patients in Benin. *The egyptian rheumatologist* 2021 ; 43 : 23-7
- [27] Lin J, Chen C, Ma J, Mo Y, Li Q, Chen L et al. Neglected extra-articular manifestations in rheumatoid arthritis patients with normal body mass index: reduced skeletal muscle overlapping overfat. *Ther Adv Chronic dis* 2020 ; 11 : 1-18
- [28] Uribe-Reina P, Munoz-Ortiz J, Cifuentes-Gonzalez C, Reyes-Guanes J, Terreros-Dorado W, Lopez-Rojas C et al. Ocular Manifestations in Colombian Patients with Systemic Rheumatologic Diseases. *Clinical Ophthalmology* 2021;15 2787-802
- [29] Gheita TA, Raafat HA, El-Bakry SA, Elsaman A, El-Saadany HM, Hammam N et al. Rheumatoid arthritis study of the Egyptian College of Rheumatology (ECR): nationwide presentation and worldwide stance. *Rheumatology International* 2023 ; 43 : 667-76
- [30] Bentaleb I, Rostom S, Bouayad S, Oulkadi L, Bahiri R. Inventory of comorbidities and extra-articular manifestations during rheumatoid arthritis in Morocco. *Moroccan Journal of Rheumatology* 2020; 54:20-33
- [31] McFarlane IM, Leon S, Bhamra MS, Burza A, Waile SA, Alvarez MR et al. Assessment of Cardiovascular Disease Risk and Therapeutic Patterns among Urban Black Rheumatoid Arthritis Patients. *Med. Sci.* 2019, 7, 31-40
- [32] Okais J, Fayad F, Baddoura R, Tabesh OA, Aouad K, Ghoubar M et al. Association between Diabetes and Rheumatoid Arthritis: A Systematic Literature Review. *The open journal Rheumatology Journal* 2022 ; 16 : 1-20

- [33] Harrold LR, Shan Y, Rebello S, Kramer N, Connolly SE, Akemo E et al. Prevalence of Sjögren's syndrome associated with rheumatoid arthritis in the USA: an observational study from the Corrona registry. *Clinical Rheumatology* 2020 39:1899-905
- [34] Varela DC, Monroy JC, Ribero MJ, Villota C, Rodriguez-Jiménez M, Hernández RD et al. Multimorbidity burden in rheumatoid arthritis. *Ann Rheum Dis* 2022 ; 1282-82
- [35] Santos-Moreno P, Rodriguez-Vargas G, Martinez S, Ibata L, Rojas-Villarraga A. Metabolic Abnormalities, Cardiovascular Disease, and Metabolic Syndrome in Adult Rheumatoid Arthritis Patients: Current Perspectives and Clinical Implications *Open Access Rheumatology: Research and Reviews* 2022:14 255-67
- [36] Trabelsi M, Romand X, Gilson M, Vaillant M, Guerne P, Hayem G et al. Rheumatoid Meningitis a Rare Extra-Articular Manifestation of Rheumatoid Arthritis: Report of 6 Cases and Literature Review. *J. Clin. Med.* 2020, 9, 1625-33
- [37] Wu D, Luo Y, Li T, Zhao X, Lv T, Fang G et al. Systemic complications of rheumatoid arthritis: Focus on pathogenesis and treatment. *Front. Immunol.* 2022 ; 13 : 1-13
- [38] Kaeley N, Ahmad S, Pathania M, Kakkar R. Prevalence and patterns of peripheral neuropathy in patients of rheumatoid arthritis. *J Family Med Prim Care* 2019; 8:22-6.
- [39] Zafar ZA, Alam MA, Sarfraz M, Ahmad T, Saeed HA, Rehman A. Frequency of extra-articular manifestations in cohort of Pakistani patients presented with RA at Independent University Hospital Faisalabad. *Professional Med J* 2021; 28(6):819-27.
- [40] Laria A, Lurati AM, Zizzo G, Zaccara E, Mazzocchi D, KA et al. Interstitial Lung Disease in Rheumatoid Arthritis: A Practical Review. *Front. Med.* 2022 ; 9 : 1-14
- [41] Chen X, Zhang M, Wang T, Li Y, Wei M. Influence factors of extra-articular manifestations in rheumatoid arthritis. *Open Medicine* 2020; 15: 787-95
- [42] Kumar P, Kalpana F, Khamuani M, Lohana S, Dembra S, Jahangir M et al. Frequency of Cardiovascular Manifestation in Patients With Rheumatoid Arthritis. *Cureus* 2021 ; 13(4):1-5
- [43] Yao-Wei Z, Qian-Hua L, Jing-Wel G, Jie P, Jian-Da M, Le-Feng C et al. Association Between Metabolic Dysfunction-Associated Fatty Liver Disease and Cardiovascular Risk in Patients With Rheumatoid Arthritis: A Cross-Sectional Study of Chinese Cohort. *Frontiers in cardiovascular medicine* 2022 ; 9 : 1-10
- [44] Tanase DM, Gosav EM, Petrov D, Teodorescu D, Buliga-Funis O, Ouatu A et al. MicroRNAs (miRNAs) in Cardiovascular Complications of Rheumatoid Arthritis (RA): What Is New? *Int. J. Mol. Sci.* 2022 ; 23 : 1-15