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COMPARISON OF ELDERLY AND YOUNG ONSET RHEUMATOID ARTHRITIS

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ABSTRACT – *Objective:* To describe demographic, clinical, paraclinical and therapeutic characteristics of elderly onset (EORA) compared to young-onset (YORA) rheumatoid arthritis.

Patients and Methods: We studied 50 EORA and 100 YORA. Socio-demographic characteristics, clinical and paraclinical data of the disease were collected as well as the treatments assigned to patients. EORA patients were defined as disease onset ≥ 60 years.

Results: At the study visit, EORA patients had a mean age of 68.3 ± 6.4 years old and YORA patients were aged 42.5 ± 9.1 years old. A male predominance was noted in EORA group than the YORA group (38% *vs.* 12%, p <0.001). The onset of disease in EORA was more acute (p <0.001) with more systemic symptoms (p <0.001). EORA patients had higher Disease Activity Score of 28 joints (DAS28) (p=0.03) and higher erythrocyte sedimentation rate (ESR) (40 [10-110] *vs.* 28 [2-88], p=0.015). There was no significant difference in seropositive character, prevalence of radiographic erosions or joint deformity. The EORA patients had a higher Health Assessment Questionnaire (HAQ) (1 [0.4-2.2] *vs.* 0.6 [0.2-2], p<0.001) and more comorbidities (84% *vs.* 37%, p<0.001). Methotrexate was the most conventional synthetic disease-modifying antirheumatic drugs used in the two groups (95% in the YORA and 96% in the EORA; p=0.740). The EORA group received fewer biologic drugs than the YORA group (30% *vs.* 47 %; p=0.041).

Conclusions: There were more male in EORA group. Activity and HAQ was higher in the EORA group. The EORA had more comorbidities which may explain the lesser use of biological treatments.

KEYWORDS: Rheumatoid arthritis, Elderly onset, Young-onset, Disease activity, Life quality, Comorbidities, Disease modifying antirheumatic drugs.

LIST OF ABBREVIATIONS: RA-Rheumatoid arthritis, EORA-Elderly-onset rheumatoid arthritis, YORA-Young-onset rheumatoid arthritis, ESR-Erythrocyte sedimentation rate, CRP-C-reactive protein, DAS28-Disease Activity Score of 28 joints, HAQ-Health Assessment Questionnaire, ACPA-Anti–citrullinated protein antibody, RF-Rheumatoid factor, cDMARDS-Synthetic disease-modifying antirheumatic drugs, bDMARDS-Biologic disease-modifying antirheumatic drugs, SD-Standard deviation, IQR-Interquartile range, PMR-Polymyalgia rheumatica, RTX-Rituximab, Anti-TNFα -Anti-tumor necrosis factor-alpha, Anti-IL6-Interleukin 6 inhibitors, WHO-World Health Organization.

INTRODUCTION

Rheumatoid arthritis (RA) is the most common rheumatic disease typically beginning in young women between 30-50 years old. By 2030, the number of people ≥ 60 years old will increase by 56%, from 962 million (2017) to 1.4 billion (2030) and will exceed the number of children under 10 (1.41 billion against 1.35 billion)[1]. Since life expectancy has been increasing, the age of onset of multiple diseases increased too. Rheumatoid arthritis affects 2% of people over 60[2]. Rheumatoid arthritis (RA) that develops in people over the age of 60 or 65 is known as elderly-onset rheumatoid arthritis (EORA), also known as late-onset RA[3].

The characteristics of EORA appear to have more acute onset, systemic involvement, and worse functional outcomes than those of young onset RA[4].

However, the age may have an effect on how the disease is assessed. Erythrocyte sedimentation rate (ESR) does in fact rise with aging, increasing the value of the Disease Activity Score of 28 joints (DAS28-ESR). On the other hand, older persons may have higher results on the Health Assessment Questionnaire (HAQ), which can be related to higher prevalence of comorbidities in this population. The prevalence of comorbidity may also affect therapy choice depending on the population's age.

The aim of this study was to characterize and to compare the demographic, clinical, paraclinical and therapeutic features of elderly-onset RA with those of young-onset RA (YORA).

PATIENTS AND METHODS

Patients

Adult RA patients who met ACR/EULAR 2010 rheumatoid arthritis classification criteria of the Department of Rheumatology at El Ayachi Hospital from August 2019 to September 2020 were included in this retrospective, observational and case control group study.

We included YORA patients and EORA patients defined by an age of onset ≥ 60 years. We restricted patients to ≤10 years of disease duration.

We took into account EORA and YORA patients with onset ages under 60. We limited the patients' disease duration to 10 years or less.

Data collection

Data about demographics, clinical and biological features including joint counts, DAS28 score activity, ESR, C-reactive protein test (CRP), anti–citrullinated protein antibody (ACPA) and rheumatoid factor (RF) status were collected. Extra-articular features and comorbidities have been noted. Functional capacity was assessed by the HAQ.

Statistical analysis

Statistical analysis was performed using SPSS software, version 13.0 (SPSS Inc., Chicago, IL, USA). The T-Student and Mann-Whitney tests for quantitative variables and the Chi2 test for qualitative variables were used to compare the two groups. Results with $p \leq 0.05$ were considered statistically significant.

RESULTS

At the study visit, EORA patients' mean age was 68.3 ± 6.4. The mean age at illness onset was 64.54 ± 5.77. Patients with YORA were 42.5 ± 9.1 years old, with a mean age at disease onset of 37 ± 8.4. The EORA group had more males than the YORA group (38% *vs.* 12%, p <0.001). The EORA group had a low educational level (p <0.001). The EORA group had a larger percentage of smokers (18% *vs.* 3%, p=0.006) (Table 1).

In EORA, the disease onset was more acute (p <0.001) with more systemic symptoms (p <0.001). EORA patients had higher DAS28 ESR (p=0.03). No significant difference was seen in seropositive character, frequency of radiographic erosions or joint deformity (Table 2).

Table 1. Comparison of demographic characteristics of EORA and YORA patients.

	CYORA (n=100)	EORA (n=50)	Total (n=150)	*p*-value
***Gender*[1]**				
Female	88 (88)	31 (62)	119	<0.001
Male	12 (12)	19 (38)	31	
***Age*[2]**	42.5 ± 9.1	68.3 ± 6.4	51.1±14.7	-
***Marital status*[1]**				
Single	19 (19)	3 (6)	22 (14.7)	0.014
Married	78 (78)	41 (82)	119 (79.3)	
Widower	1 (1)	5 (10)	6 (4)	
Divorced	2 (2)	1 (2)	3 (2)	
***Educational level*[1]**				
Illiterate	34 (34)	37 (74)	71 (47.3)	<0.001
No university/college degree	63 (63)	12 (24)	75 (50)	
University/college degree	3 (3)	1 (2)	4 (2.7)	
***Work status*[1]**				
Working	34 (34)	11 (22)	45 (30)	0.131
Not working or retiree	66 (66)	39 (78)	105 (70)	
***Smoking*[1]**				
Smoker	3 (3)	9 (18)	12 (8)	0.006
Non-smoker	97 (97)	41 (82)	138 (92)	
***Age at onset (years)*[2]**	37±8.4	64.54 ± 5.77	46.19±15.11	<0.001
***Age at diagnosis (years)*[2]**	38.09 ±8.67	65.48 ±5.76	47.22±15.12	<0.001
***Disease duration (years)*[3]**	5 [0-10]	2.7 [0-10]	4.77 [0-10]	0.001

[1]number and percentage, [2]mean ± SD, [3]Median and IQR.

Abbreviations: EORA, elderly-onset rheumatoid arthritis; YORA, young-onset rheumatoid arthritis

The HAQ score of the EORA patients was higher (1 [0.4-2.2] *vs.* 0.6 [0.2-2], *p* <0.001) and they also had more comorbidities. Hypertension (40% *vs.* 6%, *p*<0.001), diabetes (20% *vs.* 4%, *p*=0.001), hyperlipidemia (8% *vs.* 1%, *p*=0.024), osteoporosis (60% *vs.* 21%, *p*<0.001) and ocular disease (18% *vs.* 3%, p=0.001) were higher in the EORA group (Table 3).

Methotrexate was the most conventional synthetic disease-modifying antirheumatic drugs (cDMARDs) used in the 2 groups (95% in the YORA and 96% in the EORA; *p*=0.740). Additionally, there were no statistical differences in the two groups' oral corticosteroid usage. Less biologic medication was administered to the EORA group than the YORA group (30% *vs.* 47 %; *p*=0.041) (Table 4).

DISCUSSION

Elderly onset RA has become more common[5]. We must distinguish between RA that appears beyond the age of 60 and RA that appears in elderly people early in life[6]. 50 EORA were included in this study. Patients with EORA differ from YORA patients in a few ways. These variations have implications for prognosis and treatment.

Table 2. Clinical features and laboratory test results of EORA and YORA patients.

	CYORA (n=100)	EORA (n=50)	Total	*p*-value
***Start mode*[1]**				
Acute	4 (4)	27 (54)	31 (20.7)	<0.001
Progressive	96 (96)	23 (46)	119 (79.3)	
***Systemic symptoms*[1]**				
Yes	13 (13)	31 (62)	44 (29.3)	<0.001
Asthenia	10 (76)	28 (90.32)	38 (25.3)	
Weight loss	6 (46.15)	16 (51.6)	22 (14.7)	
Anorexia	3 (23)	8 (25.8)	11 (7.3)	
Fever	0 (0)	3 (9.67)	3 (2)	
No	87 (87)	19 (38)	106 (70.7)	
***Painful joint counts (28 joints)*[2]**	3.5 [0-18]	5 [0-16]	4 [0-18]	0.101
***Swolen joint counts (28 joints)*[2]**	2 [0-15]	3 [0-11]	2 [0-15]	0.374
***ESR*[2]**	28 [2-88]	40 [10-110]	30 [2-110]	0.015
***CRP*[2]**	9 [0-94]	12 [1-83]	10 [0-94]	0.111
***DAS28*[3]**	3.68 ± 1.34	4.6 ± 1.05	3.8 ± 1.2	0.03
Remission < 2.6[1]	27 (27)	3 (6)	30 (20)	0.002
Low activity 2.6 –3.2[1]	15 (15)	10 (20)	25 (16.7)	0.439
Moderate activity 3.3–5.1[1]	43 (43)	31 (62)	74 (49.3)	0.028
High activity > 5.1[1]	15 (15)	6 (12)	21 (14)	0.618
***Seropositivity (ACPA and/or RF)*[1]**	87 (87)	46 (92)	133 (88.7)	0.362
***Erosions*[1]**	70 (70)	40 (80)	110 (73.3)	0.192
***Deformed joints*[1]**	33 (33)	21 (42)	54 (36)	0.279

[1]number and percentage, 2 Median and IQR, 3 mean ± SD.

Abbreviations: EORA, elderly-onset rheumatoid arthritis; YORA, young-onset rheumatoid arthritis; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein test; DAS28, Disease Activity Score of 28 joints; ACPA, anti–citrullinated protein antibody; RF, rheumatoid factor.

RA is known to be a disease of young women. In the EORA group, they were more males than the YORA. Our findings are comparable to other studies[3,7-9]. Seropositive RA was predominant in both groups. In a Colombian population, the RF and ACPA frequency was lower in EORA patients[10]. Thus, it has been shown that EORA patients had less positive RF[3,11]. In 5 individuals (10%), a very late onset after age 70 was noted.

Our study's findings demonstrate that RA with an elderly start has different clinical features. Most EORA patients have more acute onset and systemic symptoms, such as asthenia, weight loss and fever. The involvement of large joint, especially the shoulders may evoke a similar presentation to polymyalgia rheumatica (PMR)[12]. Additionally, several studies reevaluated the ultimate diagnosis among PMR patients and found that over 20% of patients later received a diagnosis of PR[13]. This confusion arises primarily when the PR is seronegative[14]. Despite being thought of as two different diseases, PR seronegative and PMR really have many similarities. A destructive arthritis or symmetrical damage to the metacarpal and/or proximal interphalangeal joints may help distinguish between the two diseases. In our study, 18% of the YORA group had shoulder involvement (p=0.001). We shouldn't ignore the degenerative illness in this population, though.

Table 3. Quality of life and comorbidities of EORA and YORA patients.

	CYORA (n=100)	EORA (n=50)	Total	*p*-value
***HAQ*[1]**	0.6 [0.2-2]	1 [0.4-2.2]	0.8 [0.2-2.2]	<0.001
< 0.52	38 (38)	3 (6)	40 (26.7)	<0.001
0.5–1.52	59 (59)	41 (82)	98 (65.3)	0.005
>1.52	3 (3)	6 (12)	9 (6)	0.029
***Comorbidity*[2]**	37 (37)	42 (84)	79 (52.7)	<0.001
***Hypertension*[2]**	6 (6)	20 (40)	26 (17.3)	<0.001
Cardiovascular*[2] *disease	3 (3)	2 (4)	5 (3.3)	0.748
***Diabetes*[2]**	4 (4)	10 (20)	14 (9.3)	0.001
***Hyperlipidemia*[2]**	1 (1)	4 (8)	5 (3.3)	0.024
***Pulmonary disease*[2]**	3 (3)	5 (10)	8 (5.3)	0.072
***Infection*[2]**	5 (5)	2 (4)	7 (4.7)	0.784
***Liver disease*[2]**	2 (2)	0 (0)	2 (1.3)	0.314
***Cancer*[2]**	0 (0)	0 (0)	0 (0)	—
***Osteoporosis*[2]**	21 (21)	30 (60)	51 (34)	<0.001
***Renal disease*[2]**	1 (1)	1 (2)	2 (1.3)	0.615
***Ocular disease*[2]**	3 (3)	9 (18)	12 (8)	0.001
***Depression*[2]**	3 (3)	0 (0)	3 (2)	0.216
***Other*[2]**	2 (2)	0 (0)	2 (1.3)	0.314

[1]Median and IQR, [2]number and percentage.

Abbreviations: EORA, elderly-onset rheumatoid arthritis; YORA, young-onset rheumatoid arthritis; HAQ, Health Assessment Questionnaire

The number of swollen joints did not differ significantly between the two groups, while DAS28 ESR was higher in EORA patients (p=0.03). Also, there were more patients in the YORA group who were in remission (27% *vs.* 6 %, p=0.002). The ESR increases with age and can explain higher DAS 28 (ESR) in

Table 4. Treatments used in EORA and YORA patients.

	CYORA (n=100)	EORA (n=50)	Total	*p*-value
***Corticosteroïd*[1]**	94 (94)	43 (86)	137 (91.3)	0.101
***Dose of corticosteroid mg/day*[2]**	5.8±3.1	6.3±2.8	6.02 ± 3.03	0.472
***Methotrexate*[1]**	95 (95)	48 (96)	143 (95.3)	0.740
***Biologics*[1]**	47 (47)	15 (30)	62 (41.3)	0.041
Rituximab[1]	42 (89.36)	12 (40)	54 (87)	
Anti-TNFα[1]	4 (8.5)	2 (6.66)	6 (9.67)	
Anti-IL6[1]	1 (2.12)	1 (3.33)	2 (3.22)	

[1]number and percentage, [2]mean ± SD.

Abbreviations: EORA, elderly-onset rheumatoid arthritis; YORA, young-onset rheumatoid arthritis.

elderly individuals independent of joint counts[15]. Additionally, the EORA group's patients reported more pain and weariness with a significant statistical difference (p=0.006 and p<0.001 respectively). Similar to earlier research, there was no discernible difference between the two groups in terms of the occurrence of radiography erosions and joint deformities[7,16]. Patients with YORA do not perform any better than those with EORA. In fact, the lack of timely access to care in some circumstances may prevent effective early intervention and explain the severe forms in young subjects. Our findings, however, continue to be in line with the research. Despite the fact that bone erosion causes functional disability, it is a surrogate sign of the disease's future development and does not always correspond to the current level of functional disability. In contrast to YORA, HAQ increased in EORA. It was less than 0.5 at 38% in YORA group (p<0.001). Furthermore, it was observed that functional disability is associated with age of disease onset and disease duration[17,18]. Despite RA, multiple factors can explain this difference. EORA group has poorer physical status and higher prevalence of comorbidities than YORA groups which reduces their self-care activities. In our study, 60% of EORA patients had osteoporosis, 40% had hypertension, 20% had diabetes, 18% had ocular disease and 8% had hyperlipemia.

Regarding therapy, the use of prednisolone was the same in the two groups without any significant statistical difference in the daily dose. In spite of the fact that using glucocorticoids can raise cardiovascular risk in this population[19], some investigations indicated that older patients used them just as frequently or more frequently[13,20]. The most used cDMARD in our context is methotrexate, which may be discontinued due to socioeconomic issues. Indeed, treatment was stopped in 88 of the 199 patients who got methotrexate (39.3%), and the methotrexate maintenance rate was 91.1 at 1 year, 87.1% at 2 years, and 68.3 at 5 years[21]. In our setting, the most frequently prescribed biological therapy is Rituximab (74%; n = 166). Tocilizumab was the second (13.6%; n = 31) and finally, anti-TNF is in third place (12.4%; n = 28). Following multivariate analysis, insurance type was linked to the decision to use Rituximab as the first biologic[22]. The first cDMARD in both groups was methotrexate; however, the combination therapy was less common in the EORA group than the YORA. Methotrexate has been demonstrated to be equally effective across all age groups while typically requiring lower dosages[23]. Also, the use of biologic therapy was less in EORA than YORA patients. This can probably be related to the presence of more comorbidities in this group. Rituximab (RTX) was the most prescribed biologic disease-modifying anti-rheumatic drug (bDMARD). A French study analyzed the efficacy of rituximab in elderly patients showed that RTX is slightly less effective in this group[24]. Furthermore, low educational level, financial status, and polymedication can make therapy management difficult in elderly patients.

Most statistics indicate that women are more prevalent than men to have RA in the African population, and that it appears to have an early age of onset[25]. However, the prevalence of elderly onset RA was 10.5% in Senegal and 29.3% in Egypt[26,12]. However, there are some contradictory findings. Egyptian EORA, in contrast to Senegalese EORA, were more active and had less deformity. In terms of therapy, Egyptian YORA patients used methotrexate somewhat more frequently than our EORA patients, and their use of DMARD (57.9%) or biological drugs (0.8%) was much lower.

Our study has some limits. The information provided came from the last visit, thus we are unable to assess the disease prognosis or the effectiveness and safety of treatments.

CONCLUSIONS

EORA and YORA patients had different demographic characteristics. Most EORA patients have an acute onset and more systemic symptoms. Despite higher activity and HAQ in the EORA group, their treatment was less aggressive.

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REFERENCES

1. Decade of Healthy Ageing 2020-2030 WHO Global strategy on ageing and health.
2. Rasch EK, Hirsch R, Paulose-Ram R, Hochberg MC. Prevalence of rheumatoid arthritis in persons 60 years of age and older in the United States: effect of different methods of case classification. Arthritis Rheum 2003; 48: 917-926.
3. Soubrier M, Mathieu S, Payet S, Dubost II, Ristori JM. Elderly-onset rheumatoid arthritis. Joint Bone Spine 2010; 77: 290-6.
4. Turkcapar N, Demir O, Atli T, Kopuk M, Turgay M, Kinikli G, Duman M. Late onset rheumatoid arthritis: clinical and laboratory comparisons with younger onset patients. Arch Gerontol Geriatr 2006; 42: 225-231.
5. Myasoedova E, Crowson CS, Kremers HM, Therneau TM, Gabriel SE. Is the incidence of rheumatoid arthritis rising ? : results from Olmsted County, Minnesota, 1955–2007. Arthritis Rheum 2010; 62: 1576-1582.
6. Rasch E, Hirsch R, Paulose-Ram R, Hochberg M. Prevalence of rheumatoid arthritis in persons 60 years of age and older in the United States: effect of different methods of case classification Arthritis Rheum 2003; 48: 917-926.
7. Tan TC, Gao X, Thong B Y-H, Leong KP, Lian TY, Law WG, Kong KO, Howz HS, Chng HH, Koh ET and the TTSH Rheumatoid Arthritis Study Group Comparison of elderly- and young-onset rheumatoid arthritis in an Asian cohort. Int J Rheum Dis 2016; 20: 737-745.
8. Bajocchi G, La Corte R, Locaputo A, Govoni M, Trotta F. Elderly onset rheumatoid arthritis: clinical aspects. Clin Exp Rheumatol 2000; 18: S49-50.
9. Ruban TN, Jacob B, Pope JE, Keystone EC, Bombardier C, Kuriya B. The influence of age at disease onset on disease activity and disability: results from the Ontario Best Practices Research Initiative. Clin Rheumatol 2016; 35: 759-763.
10. Spinel-Bejarano N, Quintana G, Heredia R, Yunis JJ, Caminos JE, Garcés MF, Rondon F, Iglesias-Gamarra A. Comparative study of elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis in a Colombian population: clinical, laboratory and HLA-DRB1 findings. Clin Exp Rheumatol 2013; 31: 40-46.
11. Chen DY, Hsieh TY, Chen YM, Hsieh CW, Lan JL, Lin FJ. Proinflammatory cytokine profiles of patients with elderly-onset rheumatoid arthritis: a comparison with younger-onset disease. Gerontology 2009; 55: 250-8.
12. El-Labban AS, Omar HA, El-Shereif RR. Pattern of young and old onset rheumatoid arthritis (YORA and EORA) among a group of egyptian patients with rheumatoid arthritis. Clin Med Insights Arthritis Musculoskelet Disord 2010; 3: 25-31.
13. Kobak S, Bes C. An autumn tale: Geriatric rheumatoid arthritis. Ther Adv Musculoskelet Dis 2018; 10: 3-11.
14. Manzo C, Emamifar A. Polymyalgia rheumatica and seronegative elderly-onset rheumatoid arthritis: two different diseases with many similarities. EMJ 2019; 4: 111-119.
15. Ito H, Ogura T, Hirata A, Ali F, El-Mansoury TM. Global assessments of disease activity are age-dependent determinant factors of clinical remission in rheumatoid arthritis. Semin Arthritis Rheum 2017; 47: 310-4.
16. Mueller RB, Kaegi T, Finckh A, Haile SR, Schulze-Koops H, von Kempis J, SCQM physicians. Is radiographic progression of late-onset rheumatoid arthritis different from young onset rheumatoid arthritis? Results from the Swiss prospective observational cohort. Rheumatology (Oxford) 2014; 53: 671-7.
17. Calvo-Ale´n J, Corrales A, Sanchez-Andrada S, Fernández-Echevarría MA, Peña JL, Rodriguez-Valverde V. Functional outcome and subset identification in RA patients from meridional Europe: analysis of a Spanish cohort. Clin Rheumatol 2003; 22: 77-83.
18. Cho SK, Sung YK, Choi CB, Cha HS, Choe JY, Chung WT, Hong SJ, Jun JB, Kim J, Kim TH, Kim TJ, Koh EM, Lee HS, Lee J, Lee SS, Lee SW, Yoo DH, Young Yoon B, Bae SC, Korean Observational Study Network for Arthritis (KORONA) Investigators. Do patients with elderly-onset rheumatoid arthritis have severe functional disability? Semin Arthritis Rheum 2012; 2: 23-31.
19. Listing J, Kekow J, Manger B, Burmester GR, Pattloch D, Zink A, Strangfeld A. Mortality in rheumatoid arthritis: the impact of disease activity, treatment with glucocorticoids, TNFα inhibitors and rituximab. Ann Rheum Dis 2015; 74: 415-421.
20. Teoh L, Suppiah R, Gow P. Late-onset rheumatoid arthritis in the Counties Manukau District Health Board region of New Zealand: an observational study of treatment. N Z Med J 2014; 127: 40-48.
21. Oulkadi L, Rostom S, Hmamouchi I, El Binoune I, Amine B, Abouqal R, Achemlal L, Allali F, El Bouchti I, El Maghraoui A, Ghozlani I, Hassikou H, Harzy T, Ichchou L, Mkinsi O, Niamane R, Bahiri R. Therapeutic Maintenance Level of Methotrexate in Rheumatoid Arthritis: A RBSMR Study. Mediterr J Rheumatol 2022; 33: 224-231.
22. Eddaoudi M, Rostom S, Hmamouchi I, El Binoune I, Amine B, Abouqal R, Achemlal L, Allali F, El Bouchti I, El Maghraoui A, Ghozlani I, Hassikou H, Harzy T, Ichchou L, Mkinsi O, Niamane R, Bahiri R. The first biological choice in patients with rheumatoid arthritis: data from the Moroccan register of biotherapies. Pan Afr Med J 2021; 17; 38: 183.
23. Díaz-Borjón A. Guidelines for the use of conventional and newer disease-modifying antirheumatic drugs in elderly patients with rheumatoid arthritis. Drugs Aging 2009; 26: 273-293.
24. Payet S, Soubrier M and Perrodeau E. Efficacy and safety of rituximab in elderly patients with rheumatoid arthritis enrolled in a French Society of Rheumatology registry. Arthritis Care Res (Hoboken) 2014; 66: 1289-1295.
25. Adelowo O, Mody GM, Tikly M, Oyoo O, Slimani S. Rheumatic diseases in Africa. Nature Reviews Rheumatology 2021; 17: 363-374.
26. Ndongo S, Tiendrebeogo J, Pouye A, Lekpa FK, Ka MM, Diop TM. Effect of Age on Rheumatoid Arthritis in a Black Senegalese Population. Rheumatology 2011; 48: 1111-3.