

# OUTPATIENT CARE ASPECTS OF RHEUMATIC PATIENTS IN LATVIA: REAL LIFE DATA IN THE CONTEXT OF THE FIRST MONTH OF THE COVID-19 PANDEMIC

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*The aim of this study was to analyse the rheumatic disease profile and treatment aspects of the patients consulted in the outpatient department of Pauls Stradiņš Clinical University Hospital during the first month of the COVID-19 pandemic from 2020 March 13 till April 14. A total of 457 (76.04%) remote and 144 (23.96%) face-to-face consultations were analysed, totalling 601 patients: 434 (72.21%) females and 167 (27.79%) males with mean age 51.40 ± 14.73 years. Rheumatoid arthritis (223 (37.10%)), psoriatic arthritis (93 (15.47%)) and ankylosing spondylitis (80 (13.31%)) were the most frequently consulted conditions. Disease modifying antirheumatic drugs (DMARDs) or immunosuppressants (IS) were taken by 515 (85.69%) patients. These included synthetic DMARD (242 (46.99%)), mainly methotrexate; and biologic DMARD (156 (30.29%)), mainly tumour necrosis factor inhibitor. More than one-half of the cohort (427 (71.05%)) was not taking a glucocorticoid (GC). NSAIDs were used in 391 (65.08%) patients, mainly on demand (354 (90.54%)). Most patients (401 (66.72%)) had no comorbidities (hypertension, diabetes, malignancy and/or chronic respiratory disease). The profile of patients consulted in the outpatient department consisted mainly of middle-age females with autoimmune inflammatory arthritis treated by DMARD. Most of the patients did not use GCs, they did not regularly use NSAIDs and did not have comorbidities. Telemedicine is an acceptable way of care delivery for chronic rheumatic patients with previously known disease and treatment, especially during a pandemic.*

**Keywords:** ambulatory, rheumatic profile, telemedicine, COVID-19 pandemic, comorbidities.

## INTRODUCTION

Since the beginning of the COVID-19 pandemic, throughout the world there has been a change of the consulting approach in the clinical medicine, including in the field of rheumatology. Following the epidemiological recommendations of the World Health Organization for interpersonal distancing, thus limiting the spread of the SARS-CoV-2 infection in the society, the state of emergency in Latvia was declared for a time period of 13 March till 14 April with

two subsequent month long extensions in 2020 and reintroduction of it from 9 November till the beginning of April 2021. During the last week of March 2020, the standard care approach was modified by significantly reducing the number of face-to-face consultations and implementing telemedicine in the work of outpatient departments.

In the outpatient department of the Centre of Rheumatology of Pauls Stradiņš Clinical University Hospital, face-to-face consultations were available till 20 March 2020 and then

exceptionally during the following period till the end of April 2020 (for example, exceptions were made in cases of exacerbation of the disease with the necessity to assess disease activity and adjust treatment based on physical examination). From the last week of March, planned face-to-face consultations were substituted with remote consultations using phone calls with subsequent emailing of recommendations to the patient and/or to his family doctor. The remote consultations were mainly held for patients with previously known diagnosis (so-called returning patients) of the Centre and in a significantly smaller extent — for general practitioners if they had patients with suspected rheumatic disease in an acute state. This decision was matched with the Adult Rheumatology Society of Latvia and supported by the Ministry of Health of Latvia, taking into consideration aspects of rheumatology. These included a broad variety of symptoms and involved organ systems and significance of full physical examination, including palpation of joints and peripheral pulses, auscultation of lungs etc. in the context of the interpretation of the patient's story, thus making correct conclusions for the diagnosis and immunomodulatory treatment prescription if indicated. The absence of physical examination for new (previously unknown) patients during remote consultations can be the leading reason of misdiagnosis and unsafe treatment, outweighing the risk of delayed rheumatic disease diagnosis. Therefore, such a selective approach for remote consulting highlighted the main group of patients (returning patients) who were under the supervision of the rheumatologist in the largest adult rheumatology centre in Latvia.

Rheumatology is characterised by a large variety of diseases, not only inflammatory rheumatic and systemic diseases, but also degenerative joint and spine diseases, soft tissue rheumatism, and metabolic bone diseases (Vanhoof *et al.*, 2002). Rheumatological practice can include all of these. The key question is about the proportion of diseases showing the main professional directions of certain rheumatological practice, educational and training resources and needs as well as aspects of healthcare planning and financial and social impacts.

This study aimed to analyse the rheumatic disease profile and treatment aspects of the patients consulted in the outpatient department of Pauls Stradiņš Clinical University Hospital during the first month of COVID-19 pandemic.

## MATERIALS AND METHODS

Data was collecting from face-to-face and remote consultations in the outpatient department of the Centre of Rheumatology of Pauls Stradiņš Clinical University Hospital in the time period from 13 March to 14 April 2020, which was the first period of the state of emergency in Latvia due to the COVID-19 pandemic. There were ten rheumatologists in 2020 in the Centre of Rheumatology of Pauls Stradiņš Clinical University Hospital. The overall number of adult rheumatologists in Latvia was 26.

The data were extracted from the local database and included the following variables: 1) sex, 2) age, 3) diagnosis, 4) groups of medications used for the treatment of rheumatic disease (conventional or targeted synthetic or biologic disease modifying antirheumatic drug (csDMARD, tsDMARD, bDMARD, respectively), immunosuppressants (IS) (cyclophosphamide, mycophenolate mofetil, azathioprine) (Isaacs and Burmester, 2020; Mikuls *et al.*, 2020), glucocorticoids (GCs), non-steroidal anti-inflammatory drug (NSAID)), 5) modification of therapy made during the consultation (defined as dosage increase or initiation of treatment, switch to another medicine of the same DMARD group, switch to biosimilar bDMARD, switch to another group of DMARD, cessation of treatment due to side effects, prolongation of treatment interval, treatment cessation due to remission, treatment cessation for a definite time period, dosage reduction); and 6) comorbidities (cardiovascular disease (including hypertension), diabetes mellitus, malignancy (present or past), and chronic respiratory disease).

During distant consultations, the assessment of disease activity and subsequent treatment modification if needed was performed based on subjective data (patient's complaints) and recent blood tests (inflammatory markers, full blood count, and immunological data) if available in the electronic system.

All analyses were performed using IBM SPSS Statistics, version 23.0.

## RESULTS

The data of 457 (76.04%) distant consultations and 144 (23.99%) face-to-face consultations were analysed. The study included 601 patients, of whom 434 (72.21%) were females and 167 (27.79%) were males, with the age  $51.40 \pm 14.73$  (range 18–89) years. The largest number of patients (156 (25.96%)) had age from 50 to 59 years followed by the age group from 60 to 69 years — 120 (19.97%) patients and age group 40 to 49 years — 119 (19.8%) patients. The smallest number of patients was in the group older than 80 years — 7 (1.16%). Fifty-nine (25.96%) consulted patients had age younger than 30 years and 64 (10.65%) patients were in the age group from 70 to 79 years.

Figure 1 shows the spectrum of diagnosis managed during one month in the outpatient department. The most frequent seven diagnoses among 24 were rheumatoid arthritis (RA) — 223 (37.10%) patients, psoriatic arthritis (PsA) — 93 (15.47%), ankylosing spondylitis (AS) — 80 (13.31%), peripheral spondyloarthritis (SpA) (also defined as undifferentiated SpA or reactive arthritis) — 42 (6.99%), juvenile idiopathic arthritis — 37 (6.16%), systemic lupus erythematosus — 30 (4.99%) and osteoarthritis/spondylosis — 27 (4.49%) patients. Significantly less common diseases were systemic sclerosis (eight (1.33%) cases), primary Sjogren's syndrome (8 (1.33%)), granulomatosis with polyangiitis (five (0.83%)), and polymyalgia rheumatica (four (0.67%)). There were three (0.50%) cases of crystal induced arthropathy.

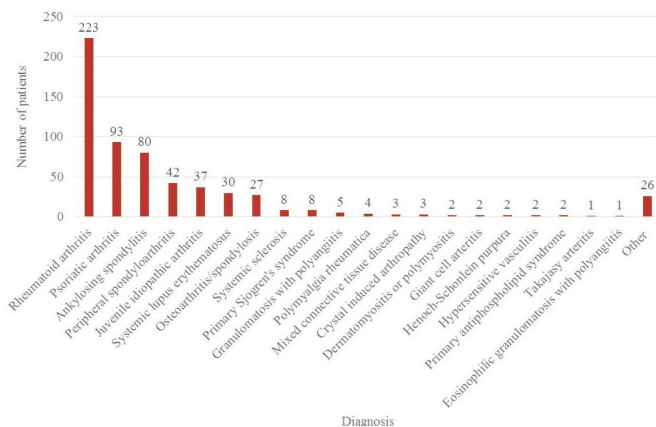


Fig. 1. Diagnosis distribution of the patients.

thy and three (0.50%) cases of mixed connective tissue disease. One or two cases of different small and large vessel vasculitides were consulted and there were a few patients with dermatomyositis and primary antiphospholipid syndrome. The category of other cases (26 (4.33%)) included one or two cases of the following diseases: sarcoidosis, bullous pemphigoid, arthralgia, joint hypermobility syndrome, undifferentiated connective tissue disease, Lyme disease, diffuse idiopathic skeletal hyperostosis, SAPHO syndrome, osteogenesis imperfecta, granulomatous mastitis, relapsing polychondritis, retroperitoneal fibrosis, IgG4 disease, undifferentiated vasculitis, thoracic outlet syndrome, soft tissue rheumatism, and adult onset Still's disease.

Among the groups of medicines used to treat patients, 515 (85.69 %) patients were taking DMARDs, and 86 (14.31%) patients were not taking DMARDs. Features of intake of DMARDs are represented in Table 1. Most of the patients were treated with csDMARD or IS monotherapy — 242 (40.27%) patients or bDMARD monotherapy — 157 (26.12%) patients. A small number of patients was treated with tsDMARD (tofacitinib) monotherapy — 8 (1.33%) patients or combined therapy — four (0.67%) patients.

Table 2 shows the intake of certain medicines of the different DMARDs groups, independent on the use as monotherapy or combined treatment. Among synthetic DMARDs (sDMARDs), the most frequently used medicine was methotrexate, which was taken by 156 (25.96%) patients, followed by sulfasalazine taken by 92 (15.31%) patients and hydroxychloroquine — 65 (7.49%) patients. Leflunomide was used by 45 (7.49%) patients. Immunosuppressive medications such as azathioprine were taken by 18 (3.00%) patients, mycophenolate mofetil — 12 (2.00%) patients, oral cyclophosphamide — one (0.17%). The tsDMARD tofacitinib was taken by 12 (1.82%) patients. The most frequently prescribed bDMARD was tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) inhibitor, used by 198 (32.95%) patients, followed by interleukin-17A (IL-17A) inhibitor — 23 (3.83%) and IL-6 inhibitor — 20 (3.33%) patients. Other bDMARDs such as IL-12/IL-23 inhibitor, abatacept and rituximab were prescribed for less than ten patients (seven (1.16%), eight (1.33%), and five (0.83%) patients, respectively).

Table 1. Treatment profile of patients

Group of medications	Number of patients (n = 601)	Frequency, %
None	86	14.31
csDMARDs or IS	242	40.27
tsDMARDs	8	1.33
bDMARDs	157	26.12
csDMARDs and bDMARDs	104	17.30
csDMARDs and tsDMARDs	4	0.67

DMARD – disease modifying antirheumatic drugs, csDMARDs – conventional synthetic DMARDs, IS – immunosuppressant, tsDMARDs – targeted synthetic DMARDs, bDMARDs – biologic DMARDs

Table 2. Profile of the treatment with disease modifying antirheumatic drugs

DMARDs group	Medicine	Patients (n)	Frequency, %	
			Medicines (n = 661)	Patients (n = 601)
csDMARDs and immuno suppressants	Methotrexate	156	23.60	25.96
	Sulfasalazine	92	13.92	15.31
	Leflunomide	45	6.81	7.49
	Hydroxychloroquine	65	9.83	10.82
	Azathioprine	18	2.72	3.00
	Cyclophosphamide	1	0.15	0.17
tsDMARDs	Mycophenolate mofetil	12	1.82	2.00
	Tofacitinib	12	1.82	2.00
bDMARDs	TNF $\alpha$ inhibitors (adalimumab, etanercept, golimumab, infliximab)	198	29.95	32.95
	IL-6 inhibitor (tocilizumab)	20	3.03	3.33
	IL17A inhibitor (secikunimab)	23	3.48	3.83
	IL12/IL23 inhibitor (ustekinumab)	7	1.06	1.16
	Abatacept	8	1.21	1.33
	Rituximab	5	0.76	0.83

DMARDs – disease modifying antirheumatic drugs, csDMARDs – conventional synthetic DMARDs, tsDMARDs – targeted synthetic DMARDs, bDMARDs – biologic DMARDs, TNF – tumour necrosis factor, IL – interleukin

More than a half of the studied cohort (427 (71.05%) patients) was not taking a glucocorticoid (GC). The rest of the cohort (174 (28.95%) patients) was taking a GC and for the most of them (114 (65.52%) patients) the dosage was not changed during the consultation. For 41 (23.56%) patients, the dosage was tapered or its intake was discontinued. The change of GCs dosage (increase, tapering or cessation) was not dependent on sex ( $p = 0.12$ ,  $V = 0.16$ ), age group ( $p = 0.35$ ,  $V = 0.19$ ), diagnosis ( $p = 0.21$ ,  $V = 0.34$ ) or the group of DMARD used in the treatment of the disease ( $p = 0.78$ ,

V = 0.14). The average dosage of GCs was 6.74 +/- 4.86 mg (interval from 1.25 mg to 40.00 mg) (95% CI, 6.00–7.48). The median for GCs users was 5.00 mg, IQR 2.5.

Most of the patients used a NSAID on demand (354 (58.90%) and less than 10% regularly (37 (6.16%). A total of 210 (34.94%) patients did not take a NSAID.

Table 3 represents the characteristics of the most common diseases managed in the outpatient rheumatological department during one month. The most frequent diagnosis was RA — 223 (37.10%) patients, mainly females (190 (85.20%)) with mean age 58 (SD 11.62) years. Methotrexate alone and methotrexate in combination with TNF $\alpha$  inhibitor was the most frequently used treatment in this case. A total of 103 (46.19%) RA patients used GCs. Among the cohort, 144 (64.57%) patients used NSAIDs on demand, 10 (4.48%) patients regularly and 69 (30.94%) patients did not use it. The most frequent next time visit for RA patients was at three to six months.

During 601 consultations, treatment was modified in 98 (16.31%) cases. Table 4 shows that the modification of

treatment for the DMARD group was mainly done during remote consultations (68 cases). There was no statistically significant difference in treatment modification according to the type of consultation ( $p = 0.18$ ). The most frequent modification of treatment was dosage increase or initiation of DMARD treatment: 26 (38.24%) among distant consultations and 20 (62.50%) cases among face-to-face consultations. Most of the modifications were for the group of csDMARDs — 57 (58.16%) cases.

Cessation of DMARD treatment due to undesirable side effects was made in 9 (9.00%) cases. The reasons were hepatotoxicity (one), eczema (one), alopecia (one), stomatitis (one), subfebrile temperature (one), lung damage (one) and three cases without description of the treatment cessation reason. Detailed information is presented in Table 5.

NSAIDs were used in the treatment of 391 (65.08%) patients, of whom 37 (6.16%) took this medication regularly and 354 (58.90%) used it on demand. Analysis of the intake of NSAIDs according to the most common disease by age group is presented in Table 6.

Table 3. The profile of the most frequent treated diseases

Characteristics	Diagnosis (number (%))							
	RA	PsA	AS	Peripheral SpA	OA/Sp	JIA	SLE	
Patients	223 (37.10)	93 (15.47)	80 (13.31)	42 (6.99)	27 (4.49)	37 (6.16)	30 (4.99)	
Sex (M/F)	33 (14.80) / 190 (85.20)	39 (41.94) / 54 (58.06)	55 (68.75) / 25 (31.25)	11 (26.19) / 31 (73.81)	1 (3.70) / 26 (96.30)	9 (24.32) / 28 (75.68)	3 (10.00) / 27 (90.00)	
Mean age (SD)	58.06 (11.62)	50.78 (11.95)	44.85 (10.96)	44.21 (13.96)	61.19 (13.24)	28.16 (11.26)	49 (13.08)	
Not used DMARD/IS	9 (4.04)	4 (4.30)	2 (2.50)	9 (21.43)	24 (88.89)	2 (5.41)	4 (13.33)	
DMARDs group*:								
csDMARD or IS	100 (46.73)	32 (35.96)	10 (12.82)	29 (87.88)	3 (100.00)	9 (25.71)	26 (100.00)	
tsDMARD	8 (3.74)	–	–	–	–	–	–	
bDMARD	44 (20.56)	41 (46.07)	55 (70.51)	4 (12.12)	–	11 (31.43)	–	
csDMARD + bDMARD	58 (27.10)	16 (17.98)	13 (16.67)	–	–	15 (42.86)	–	
csDMARD + tDMARD	4 (1.87)	–	–	–	–	–	–	
The most frequent* DMARD or IS used in:								
monotherapy	MTX	TNF	TNF	SSZ	NA	TNF	HOQ	
	39 (18.22)	22 (24.72)	48 (62.82)	23 (69.7)		8 (22.86)	15 (57.69)	
combined therapy	MTX + TNF	MTX + TNF	SSZ + TNF	NA	NA	MTX + TNF	HOQ + AZA	
	25 (11.68)	11 (12.36)	8 (10.26)			10 (28.57)	5 (19.23)	
GCs usage	103 (46.19)	9 (9.68)	9 (11.25)	2 (4.76)	2 (7.41)	3 (8.11)	19 (63.33)	
NSAID	No	69 (30.94)	29 (31.18)	19 (23.75)	3 (7.14)	9 (33.33)	14 (37.84)	20 (66.67)
	On demand	144 (64.57)	60 (64.52)	54 (67.50)	28 (66.67)	17 (62.96)	21 (56.76)	10 (33.33)
	Regular intake	10 (4.48)	4 (4.30)	7 (8.75)	11 (26.19)	1 (3.70)	2 (5.41)	–
The most frequent next visit time	3–6 months	3–6 months	3–6 months	3–6 months	As needed	3–6 months	3–6 months	
	163	71	70	18	16	34	22	
	(73.42)	(76.34)	(87.50)	(42.86)	(59.26)	(91.89)	(73.33)	

M – male, F – female, RA – rheumatoid arthritis, PsA – psoriatic arthritis, AS – ankylosing spondylitis, JIA – juvenile idiopathic arthritis, SLE – systemic lupus erythematosus, OA/Sp – osteoarthritis/spondylosis, GCs – glucocorticoids, NSAID – nonsteroidal antiinflammatory drug, NA – not applicable, IM – immunomodulatory, IS – immunosuppressant, csDMARD – conventional synthetic disease modifying antirheumatic drug, tsDMARD – targeted synthetic disease modifying antirheumatic drug, bDMARD – biologic disease modifying antirheumatic drug; \*Frequency (%) calculated from patients with comorbidity/use of DMARDs.



Table 4. Profile of DMARDs treatment modification during consultations

Treatment modification	Type of consultation			
	distant		face-to-face	
	number of patients	frequency, %	number of patients	frequency, %
Dosage increase / initiation of treatment	26	38.24	20	62.50
Switch to another medication of the same DMARD group or IS	4	5.88	0	0.00
Switch to biosimilar bDMARD	5	7.35	0	0.00
Switch to another group of DMARD or IS	6	8.82	3	9.38
Cessation of treatment due to side effects	8	11.76	1	3.13
Prolongation of treatment interval	4	5.88	1	3.13
Treatment cessation due to remission	5	7.35	1	3.13
Treatment cessation for definite time period	7	10.29	2	6.25
Dosage reduction	3	4.41	4	12.50
Total	68	100.00	32	100.00
<i>p</i>	0.18			
<i>V</i>	0.35			

DMARD – disease modifying antirheumatic drug, IS – immunosuppressant, bDMARD – biologic disease modifying antirheumatic drug

Table 5. Profile of undesirable treatment side effects

Side effect	Treatment	Diagnosis, age (years), sex
Hepatotoxicity (blood tests)	Methotrexate	Rheumatoid arthritis, 70, female
Skin rash (eczema)	TNF $\alpha$ inhibitor	Ankylosing spondylitis, 37, male
Alopecia	Leflunomide	Rheumatoid arthritis, 44, female
Stomatitis	Sulfasalazine	Peripheral spondyloarthritis, 52, female
Subfebrile temperature	Methotrexate	Juvenile idiopathic arthritis, 25, female
Lung damage	Methotrexate	Rheumatoid arthritis, 64, female
Not defined	TNF $\alpha$ inhibitor	Rheumatoid arthritis, 44, female
Not defined	Sulfasalazine	Peripheral spondyloarthritis, 40, female
Not defined	Leflunomide	Rheumatoid arthritis, 60, male

TNF $\alpha$  – tumour necrosis factor  $\alpha$

Comorbidities (cardiovascular disease, diabetes, chronic respiratory disease, past or present malignancy) were absent in most patients (401, 66.72%) (Table 7). Two hundred (33.28%) patients had a single comorbidity (164 cases), compared with 36 cases as a combination of different

Table 6. The frequency of NSAID intake according to the most common disease of the certain age group

Age group (years)	The most common disease in the certain age group	NSAIDs intake (patients (frequency within the disease group))		
		No	On demand	Regular
Younger than 30	JIA	9 (36.00)	15 (60.00)	1 (4.00)
31–39	AS	6 (31.58)	12 (63.16)	1 (5.26)
40–49	RA	8 (22.86)	25 (71.43)	2 (5.71)
50–59	RA	17 (28.81)	41 (69.49)	1 (1.69)
60–69	RA	25 (32.47)	47 (61.04)	5 (6.49)
70–79	RA	11 (33.33)	21 (63.64)	1 (3.03)
Older than 80	RA	2 (6.67)	1 (3.33)	–

JIA – juvenile idiopathic arthritis, AS – ankylosing spondylitis, RA – rheumatoid arthritis.

Table 7. The frequency of comorbidities

Comorbidity	Patients, n	Frequency, %
None	401	66.72
Cardiovascular disease	113	18.80
Diabetes mellitus	7	1.16
Chronic respiratory disease	30	4.99
Malignancy	14	2.33
Diabetes mellitus and chronic respiratory disease	3	0.50
Cardiovascular disease and diabetes mellitus	21	3.49
Cardiovascular disease, diabetes mellitus and chronic respiratory disease	4	0.67
Cardiovascular disease and chronic respiratory disease	6	1.00
Cardiovascular disease and malignancy	1	0.17
Cardiovascular disease, diabetes mellitus and malignancy	1	0.17

comorbidities. The most common comorbidity as a moncategory or a combination of different comorbidities was cardiovascular disease mentioned — 146 (24.29%) cases in total, 113 (18.80%) cases as a single and 33 (5.51%) cases as a combination of comorbidities. The second frequently mentioned comorbidity was chronic respiratory disease — 43 (7.16%) cases in total — 30 (4.99%) cases as a single comorbidity and 13 (2.17%) cases as a combination. Diabetes mellitus was noted in seven (1.16%) cases as a single comorbidity and in 29 (4.83%) as a combination of several comorbidities. Malignancy was mentioned in 16 (2.67%) cases (14 (2.33%) as a single comorbidity and two (0.34%) as a combination.

There was no significant association between the rheumatic diseases and studied comorbidities ( $p = 0.06$ ,  $V = 0.14$ ).

## DISCUSSION

The COVID-19 pandemic encouraged creation of an alternative care approach for patients with rheumatic and mus-

culoskeletal diseases (RMDs). Due to the lack of vaccines or effective treatment at that time, social distancing and quarantine regulations were the only widely available interventions (Wiersinga *et al.*, 2020). Thus, telemedicine (distant consultations) was applied as a solution to provide ongoing care for patients with chronic diseases. Despite many social advantages of telemedicine, it was not a widely applied medical care approach before the COVID-19 pandemic — for example, less than 1% of all physician visits in the United States were conducted via telehealth (Amwell Physician and Consumer Survey, 2020). During the COVID-19 lockdown, telemedicine use increased significantly in just a few weeks. For example, in a specialised centre in Bogota, Colombia, telecounselling of a RA cohort was done for 92% patients, in comparison with 8% of conventional face-to-face follow-up visits during a period of eight weeks (Santos-Moreno *et al.*, 2020). The same trend was seen in our centre — during the first four weeks of the COVID-19 pandemic, the majority of consultations (76.04%) occurred using telemedicine.

In this study, we examined the real time one-month data of the remote and face-to-face outpatient consultations for patients with a specific profile, who were under the supervision of the largest centres of adult rheumatology in Latvia. The COVID-19 pandemic forced us to use a selective approach for the telemedicine care — consultations were made mainly for existing (known or returning) patients and exceptionally for general practitioners with acute rheumatic questions. Thus, these data helped us recognise the spectrum of rheumatic diseases mainly seen by rheumatologists in routine practice.

The most frequently (approximately one-third of the patients) consulted condition was rheumatoid arthritis (223/601, 37.10%), followed by psoriatic arthritis (93/601, 15% of cases) and ankylosing spondylitis (80/601, 13% of cases). These data are in agreement with the information reported in several scientific publications about rheumatological outpatient practices. For example, analysis of the prevalence of inflammatory rheumatic diseases in a rheumatologic outpatient clinic in Iran showed that the most common diseases were rheumatoid arthritis (47%), followed by spondyloarthropathies (17%) and systemic *lupus erythematosus* (17%) (Jokar and Jokar, 2018). The data obtained are also in line with the prevalence of the rheumatic diseases in the general population. For example, in the USA, the prevalence of RA 0.5 is 1.00%, overall spondyloarthritides 0.3–1.3% and SLE — 0.07–0.14% (Berghea *et al.*, 2021); although it varies considerably among different populations.

Noticeably, patients with osteoarthritis (27/601, 4.49%) were consulted significantly less frequently than patients with autoimmune inflammatory arthritis. This difference shows that osteoarthritis treatment follow-up is mainly made by general practitioners and/or physiotherapists and/or orthopaedic surgeons. Primary osteoarthritis remains the main general differential diagnosis in case of pain in joints for elderly people. The data collected indirectly

showed the significance of cooperation between rheumatologists and general practitioners, as well as other specialists who performed screening before the first referral to the rheumatologist, and thus excluding patients not satisfying inflammatory arthritis criteria.

According to sex and age of patients, most were females (434/601, 72.21%) and the largest number of patients was of age 50 to 69 years. These results are in an agreement with data from clinical trials where RA patients were examined (Myasoedova *et al.*, 2020).

The most frequently used medications were methotrexate as csDMARD and TNF $\alpha$  inhibitors as bDMARDs. These results are in accordance with the profile of patients (mainly rheumatoid arthritis or spondyloarthropathy) consulted in the Centre. Methotrexate is the gold standard for the treatment of rheumatoid arthritis (Smolen *et al.*, 2020) and psoriatic arthritis (Gossec *et al.*, 2020) as the first choice and thereafter as part of a combination therapy with bDMARD. In some cases of axial spondyloarthritis, it is also used for the reduction of the risk of immunogenicity in addition to bDMARD (Ducourau *et al.*, 2020). The leading number of TNF $\alpha$  inhibitor users can be explained by several factors: 1) discovery time — the first original biologic drugs registered for rheumatoid arthritis were TNF $\alpha$  inhibitors (McInnes and Gravallesse, 2021), which entered the market one by one, and followed by biosimilars in the last few years; 2) the rules of reimbursement (country dependent); 3) clinical experience of rheumatologists from clinical trials; and 4) routine work encouraging to give preference for already known medicines. At that time, in Latvia, the first reimbursed bDMARD (after inefficacy and contraindications of sDMARDs, including methotrexate for RA and PsA or sulfasalazine for AS) was TNF $\alpha$  inhibitor biosimilar adalimumab ([www.vmnvd.gov.lv](http://www.vmnvd.gov.lv)).

The majority of patients using GCs had RA (103 out of 223 RA patients, 46.19%, and 103 out of 601 patients of the cohort, 17.14%). GCs are still widely used in RA (Hua *et al.*, 2020). These medications appear to be used in approximately 50% of patients with RA, with varied duration and dosage among the studies (Sokka *et al.*, 2007). However, a recent study of an Australian cohort of patients with RA showed that the probability of GC use throughout follow-up decreased over time, from 55% in 2001 to 39% in 2012 ( $p < 0.001$ ) (Black *et al.*, 2017). In contrast, another observational cohort study showed that the proportion of patients initiating GCs was higher in the group from 1995 to 2007 compared with the earlier group from 1980 to 1994 (68% vs. 36%), but the cumulative dose did not differ over the first year (Makol *et al.*, 2014; Hua *et al.*, 2020). In our cohort, GCs were used in half of RA patients, raising the question about full efficacy of the basic treatment with DMARD. One of the limitations of our study is the lack of data analysis about duration, dosage, type of DMARDs and a disease activity in the case of GCs usage. Thus, we have no data about the strategy for using GCs using in the examined cases — whether it was bridging therapy during the

initiation of DMARD or flare treatment or maintenance treatment.

One-third of patients (34.94%) in the cohort did not use NSAID, while more than a half (58.90%) used it on demand and a small part (6.16%) on a regular basis. Based on the data of a retrospective two-year observational study conducted in the United States, the use of prescribed NSAIDs was found to be common among patients with AS (68.1%), PsA (51.1%) and RA (61.1%) (Hunter *et al.*, 2021). However, the reported use of these co-medications after biologic initiation significantly decreased in the first year of treatment (Hunter *et al.*, 2021). Thus, for the correct interpretation of the use of NSAIDs, several additional questions, such as the exact reason of intake, pain pattern, disease activity etc., are important for informed decision making in case of basic treatment modification and/or safety aspects of the prolonged pain reduction treatment.

During remote consultations for returning patients, the treatment was modified in 98 (16.31%) cases, mainly by dosage increase or initiation of treatment with DMARD (38.24%), thus showing the significance of cooperation between a doctor and a patient with chronic disease. This is a significant point that underlines the equal value of telemedicine in comparison to face-to-face consultations. Every treatment modification means subjective and objective treatment tolerance evaluation (including laboratory tests), which requires good knowledge of the patient's about the main aspects of his/her disease.

Telemedicine is an efficient way of care delivery for patients with chronic diseases, especially during a pandemic. However, based on a survey conducted in the Netherlands (Bos *et al.*, 2021) and our clinical experience, the time (not included in the statistical analysis during this study) spent on a teleconsultation equals that of the face-to-face consultations. It may also not be as easy as is often assumed. It entails new skills from both patients and care providers, and technical issues also play an important role in conducting a smooth conversation with the patient (Bos *et al.*, 2021). Thus, these aspects should be taken into account in providing similar quality regarding efficacy and a safety of telemedicine in comparison to standard care.

During the one-month period covered by this study, nine cases with undesirable side effects responsible for treatment cessation were found. None of them were serious. The spectrum of the adverse events is consistent with clinical data obtained from registries and clinical trials (Ruderman, 2012; D'Angelo *et al.*, 2018; Sepriano *et al.*, 2020). In one RA case, methotrexate usage was stopped due to unspecified lung damage. Over the years, multiple publications have appeared in the scientific literature linking methotrexate usage with various types of "lung damage", including fibrotic interstitial lung disease (ILD). The latest systematic review of methotrexate safety aspects concerning progressive fibrotic ILD in case of RA argues against this link, thus suggesting beneficial rather than a harmful effect of methotrexate on lungs (Dawson *et al.*, 2021). In very rare

cases (reported in 1% of RA patients), it can cause hypersensitivity pneumonitis (Sathi *et al.*, 2012). A dose-dependent favourable effect of methotrexate on the risk of ILD in RA patients was demonstrated additionally by another study published in 2021. Thus, the link between "lung damage" and methotrexate in this certain clinical case from the cohort should be carefully analysed to clarify the pattern of lung injury. In three other cases, there were no data for the reason for interruption of the drug intake. These missed safety aspects underline the significance of a uniform approach for the information included in the database.

RA, PsA and axial SpA (mainly AS) are all associated with a high prevalence of comorbidities, including cardiovascular diseases, kidney diseases, lung diseases, infections, malignancies, osteoporosis, gastrointestinal diseases and depression (Stouten *et al.*, 2021). The coexistence of these diseases often complicates or limits the recommended management of rheumatic diseases, due to the interaction of drugs, polypharmacy, or drug intolerance (Filipowicz-Sosnowska, 2019). Rheumatologists should consider management of comorbidities as one of the primary tasks involved in the care of a patient. Collaboration with other healthcare providers, including primary care physicians and other specialists is a key to optimising holistic management for every patient (Stouten *et al.*, 2021).

Comorbidities were noted in 200 (33.28%) of patients, with the most frequently detected cases being for cardiovascular disease (as a single or combination of diseases) (146 (24.29%) cases). Malignancies (present or past) were identified in around 3% of patients. In general, these findings on cardiovascular disease (the leader position among comorbidities) and malignancy (a number of cases) are consistent with the COMORD study from Lebanon published in 2020 (Ziade *et al.*, 2020). In this study, data of 769 patients (RA, SLE, axial and peripheral SpA, OA) were analysed. We did not identify any association between the rheumatic diseases and studied comorbidities ( $p = 0.06$ ). In the COMORD study, the total number of comorbidities per patient was highest for OA (1.8) and lowest for axSpA (0.8),  $p < 0.001$ . It should be noted that in the COMORD study, four rheumatic diseases were analysed and the number of OA patients included was significantly higher than in our cohort (213 vs 27 cases, respectively). The second frequently detected comorbidity was chronic respiratory disease (43 (7.16%) cases), followed by diabetes (36 (6.00%) cases). Further analysis of the frequency of both conditions should be done in the context of additional information, such as respiratory damage pattern, specific rheumatic disease (lung injury as a systemic manifestation of chronic autoimmune disease or "parallel" not associated condition), smoking, usage of glucocorticoids, occupancy, age, work etc. In the COMORD study, diabetes was found in 10.4% of patients (highest in OA 14.6% and lowest in axial SpA 5.8%,  $p = 0.144$ ). Considering the heterogeneity of our cohort — more than 20 diseases were included with predominance of autoimmune inflammatory arthritis or connective tissue diseases — it is impossible to accurately compare our results



to other clinical trials, but the trends of frequency of comorbidities are comparable with data from different clinical trials of specific rheumatic diseases (Radner, 2016).

This is the first study in Latvia evaluating the profile of rheumatic patients in the outpatient care unit, which includes data obtained through remote consultations. Study limitations include lack of several clinically significant data (including smoking, duration of the disease, duration of treatment, work etc.), no follow-up data for remote consultations relevant for the analysis of its quality (cross-sectional study), no comparative analysis of time spent on face-to-face or remote consultations. Due to the small numbers of patients in several subgroups (diseases), it is impossible to conclude about trends, for example, comorbidities, in comparison with other cohorts. This study unequivocally showed the significance of and the need for validity, accuracy and consistency of clinical data included in medical records based on a standardised approach.

The scientific aim of this study was to examine the remote approach, which was used for the first time in ambulatory care of rheumatic patients in Latvia. As discussed in our study, telemedicine is developing approach used in rheumatology. There are still debates about its accuracy and safety in rheumatology (Jackson *et al.*, 2022; Piga *et al.*, 2022).

In summary, the profile of patients consulted in the outpatient department consisted mainly of middle age females with autoimmune inflammatory arthritis treated by DMARD. Most of the cohort patients did not use GCs and regularly NSAIDs and did not have comorbidities. The results of this study provide insight into the outpatient care aspects of rheumatic diseases in Latvia and should improve understanding of a real-life healthcare needs. Telemedicine seems an acceptable way of care delivery organisation for chronic rheumatic patients with previously known disease and treatment, especially during the pandemic restrictions. Further prospective investigation is needed to evaluate advantages and disadvantages of its implementation in the routine practice of outpatient care for rheumatic patients beyond the pandemic.

## ETHICS

The study was approved by the Ethics Committee of Pauls Stradiņš Clinical University Hospital (280520–19L) and conducted in accordance with the ethical principles of the Helsinki Declaration.

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## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## REFERENCES

- Berghea, F., Berghea, C. E., Zaharia, D., Trandafir, A. I., Nita, E. C., Vlad, V. M. (2021). Residual pain in the context of selecting and switching biologic therapy in inflammatory rheumatic diseases. *Front. Med. (Lausanne)*, **8**, 712645. DOI: 10.3389/fmed.2021.712645.
- Black, R. J., Lester, S., Buchbinder, R., Barrett, C., Lassere, M., March, L., Whittle, S., Hill, C. L. (2017). Factors associated with oral glucocorticoid use in patients with rheumatoid arthritis: A drug use study from a prospective national biologics registry. *Arthritis Res. Ther.*, **19** (1), 253.
- Bos, W. H., van Tubergen, A., Vonkeman, H. E. (2021). Telemedicine for patients with rheumatic and musculoskeletal diseases during the COVID-19 pandemic; a positive experience in the Netherlands. *Rheumatol. Int.*, **41** (3), 565–573.
- D'Angelo, S., Carriero, A., Gilio, M., Ursini, F., Leccese, P., Palazzi, C. (2018). Safety of treatment options for spondyloarthritis: A narrative review. *Expert Opin. Drug Saf.*, **17** (5), 475–486.
- Dawson, J. K., Quah, E., Earnshaw, B., Amoasii, C., Mudawi, T., Spencer, L. G. (2021). Does methotrexate cause progressive fibrotic interstitial lung disease? A systematic review. *Rheumatol. Int.*, **41**, 1055–1064.
- Ducourau, E., Rispens, T., Samain, M., Dernis, E., Le Guilchard, F., Andras, L., Perdriger, A., Lespessailles, E., Martin, A., Cormier, G., *et al.* (2020). Methotrexate effect on immunogenicity and long-term maintenance of adalimumab in axial spondyloarthritis: A multicentric randomised trial. *RMD Open*, **6** (1), e001047. DOI: 10.1136/rmdopen-2019-001047.
- Filipowicz-Sosnowska, A. (2019). Comorbidities and multimorbidity in rheumatic diseases. *Reumatologia*, **57** (1), 1–2.
- Gossec, L., Baraliakos, X., Kerschbaumer, A., de Wit, M., McInnes, I., Dougados, M., Primdahl, J., McGonagle, D. G., Aletaha, D., Balanescu, A., *et al.* (2020). EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann. Rheum. Dis.*, **79**, 700–712.
- Hainer, R., O'Riordan, B. (2020). From virtual care to hybrid care: COVID-19 and the future of telehealth insights from the 2020 Amwell Physician and Consumer Survey. <https://static.americanwell.com/app/uploads/2020/09/Amwell-2020-Physician-and-Consumer-Survey.pdf> (accessed 13.06.2021).
- Hua, C., Buttgereit, F., Combe, B. (2020). Glucocorticoids in rheumatoid arthritis: Current status and future studies. *RMD Open*, **6** (1), e000536. DOI: 10.1136/rmdopen-2017-000536.
- Hunter, T., Nguyen, C., Birt, J., Smith, J., Shan, M., Tan, H., Lisse, J., Isenberg, K. (2021). Pain medication and corticosteroid use in ankylosing spondylitis, psoriatic arthritis, and rheumatoid arthritis in the United States: A retrospective observational study. *Rheumatol. Ther.*, **8**, 1371–1382.
- Isaacs, J. D., Burmester, G. R. (2020). Smart battles: Immunosuppression versus immunomodulation in the inflammatory RMDs. *Ann. Rheum. Dis.*, **79** (8), 991–993.
- Jackson, L. E., Edgil, T. A., Hill, B., Owensby, J. K., Smith, C. H., Singh, J. A., Danila, M. I. (2022). Telemedicine in rheumatology care: A systematic review. *Semin. Arthritis Rheum.*, **56**, 152045. DOI: 10.1016/j.semarthrit.2022.152045.
- Jokar, M., Jokar, M. (2018). Prevalence of inflammatory rheumatic diseases in a rheumatologic outpatient clinic: Analysis of 12626 cases. *Rheumatol. Res.*, **3** (1), 21–27.
- Makol, A., Davis, J. M. 3rd, Crowson, C. S., Thorneau, T. M., Gabriel S. E., Matteson, E. L. (2014). Time trends in glucocorticoid use in rheumatoid arthritis: Results from a population-based inception cohort, 1980–1994 versus 1995–2007. *Arthritis Care Res.*, **66** (10), 1482–1488.
- McInnes, I. B., Gravallesse, E. M. (2021). Immune-mediated inflammatory disease therapeutics: past, present and future. *Nat. Rev. Immunol.*, **13**, 1–7.
- Mikul, T. R., Johnson, S. R., Fraenkel, L., Arasaratnam, R. J., Baden, L. R., Bermas, B. L., Chatham, W., Cohen, S., Costenbader, K., Gravallesse, E. M., *et al.* (2020). American College of Rheumatology Guidance for the



- Management of Rheumatic Disease in Adult Patients During the COVID-19 Pandemic: Version 1. *Arthritis Rheumatol.*, **72** (8), 1241–1251.
- Myasoedova, E., Davis, J., Matteson, E. L., Crowson, C. S. (2020). Is the epidemiology of rheumatoid arthritis changing? Results from a population-based incidence study, 1985–2014. *Ann. Rheum. Dis.*, **79** (4), 440–444.
- Piga, M., Floris, A., Congia, M., Chessa, E., Cangemi, I., Cauli, A. (2022). Telemedicine in rheumatology: high specificity and sensitivity of follow-up virtual video consultations during COVID-19 pandemic. *Rheumatology* (Oxford), **61** (5), 1795–1801.
- Radner, H. (2016). Multimorbidity in rheumatic conditions. *Wien. Klin. Wochenschr.*, **128** (21–22), 786–790.
- Ruderman, E. M. (2012). Overview of safety of non-biologic and biologic DMARDs. *Rheumatol.*, **51** (6), 37–43.
- Santos-Moreno, P., Chavez-Chavez, J., Hernández-Zambrano, S. M., Rivera-Triana, D. P., Castiblanco-Montañez, R. A., Aza, A., Buitrago-García, D., Villarreal, L., Rojas-Villarraga, A. (2021). Experience of telemedicine use in a big cohort of patients with rheumatoid arthritis during COVID-19 pandemic. *Ann. Rheum. Dis.*, **80**, e65. DOI: 10.1136/annrheumdis-2020-218165.
- Sathi, N., Chikura, B., Kaushik, V. V., Wiswell, R., Dawson, J. K. (2012). How common is methotrexate pneumonitis? A large prospective study investigates. *Clin. Rheumatol.*, **31**, 79–83.
- Sepriano, A., Kerschbaumer, A., Smolen, J. S., van der Heijde, D., Dougados, M., van Vollenhoven, R., McInnes, I. B., Bijlsma, J. W., Burmester, G. R., de Wit, M., Falzon, L., Landewé, R. (2020). Safety of synthetic and biological DMARDs: A systematic literature review informing the 2019 update of the EULAR recommendations for the management of rheumatoid arthritis. *Ann. Rheum. Dis.*, **79** (6), 760–770.
- Smolen, J. S., Landewé, R. B. M., Bijlsma, J. W. J., Burmester, G. R., Dougados, M., Kerschbaumer, A., McInnes, I. B., Sepriano, A., van Vollenhoven, R. F., de Wit, M., *et al.* (2020). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann. Rheum. Dis.*, **79** (6), 685–699.
- Sokka, T., Kautiainen, H., Toloza, S., Mäkinen, H., Verstappen, S. M., Lund Hetland, M., Naranjo, A., Baecklund, E., Herborn, G., Rau, R., *et al.* (2007). QUEST-RA: Quantitative clinical assessment of patients with rheumatoid arthritis seen in standard rheumatology care in 15 countries. *Ann. Rheum. Dis.*, **66** (11), 1491–1496.
- Stouten, V., Pazmino, S., Verschuere, P., Mamouris, P., Westhovens, R., de Vlam, K., Bertrand, D., Van der Elst, K., Vaes, B., De Cock, D. (2021). Comorbidity burden in the first three years after diagnosis in patients with rheumatoid arthritis, psoriatic arthritis or spondyloarthritis: a general practice registry study. *RMD Open*, **7**, e001671. DOI: 10.1136/rmdopen-2021-001671.
- Tornero-Molina, J., Sánchez-Alonso, F., Fernández-Prada, M., Bris-Ochaita, M. L., Sifuentes-Giraldo, A., Vidal-Fuentes, J. (2021). Tele-rheumatology during the COVID-19 pandemic. *Reumatol. Clin.*, **18** (3), 157–163. DOI: 10.1016/j.reumae.2020.10.002.
- Vanhoof, J., Declerck, K., Geusens, P. (2002). Prevalence of rheumatic diseases in a rheumatological outpatient practice. *Ann. Rheum. Dis.*, **61**, 453–455.
- Wiersinga, W. J., Rhodes, A., Cheng, A. C., Peacock, S. J., Prescott, H. C. (2020). Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A review. *JAMA*, **324** (8), 782–793.
- Ziade, N., El Khoury, B., Zoghbi, M., Zoghbi, M., Merheb, G., Abi Karam, G., Mroue, K., Messaykeh, J. (2020). Prevalence and pattern of comorbidities in chronic rheumatic and musculoskeletal diseases: The COMORD study. *Sci. Rep.*, **10** (1), 7683. DOI:10.1038/s41598-020-64732-8.

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## REIMATISKO PACIENTU AMBULATORĀS APRŪPES ASPEKTI LATVIJĀ: KLĪNISKĀS PRAKSES DATI COVID-19 PANDĒMIJAS PIRMĀ MĒNEŠĀ KONTEKSTĀ

Pētījuma mērķis bija analizēt reimatisko slimību profilu un terapijas aspektus pacientiem, kuri konsultēti Paula Stradiņa Klīniskās universitātes slimnīcas ambulatorajā daļā no 2020. gada 13. marta līdz 14. aprīlim, kas atbilst COVID-19 pandēmijas pirmajam mēnesim. Šajā periodā tika veiktas 457 (76,04%) attālinātās un 144 (23,96%) klātienē konsultācijas, kopumā konsultējot 601 pacientu ( $51,40 \pm 14,73$  gadi): 434 (72,21%) sievietes un 167 (27,79%) vīrieši. Visbiežāk tika konsultēti pacienti ar reimatoīdo artrītu (223 (37,10%)), psoriātisku artrītu (93 (15,47%)) un ankilozējošo spondilītu (80 (13,31%)). 515 (85,69%) pacienti lietoja slimību modificējošos antireimatiskos medikamentus (SMARM) vai imūnsupresantus (IS), no tiem 242 (46,99%) gadījumos lietoti sintētiskie SMARM, galvenokārt metotreksāts, vai 156 (30,29%) gadījumos — bioloģiskie SMARM, galvenokārt tumora nekrozes faktora alfa inhibitori. Lielākā daļa pacientu (427 (71,05%)) nelietoja glikokortikoidus (GK). NSPIL lietoja 391 (65,08%) pacients, galvenokārt pēc vajadzības. Lielākajai pacientu daļai nebija blakusslimību (hipertensija, cukura diabēts, malignitāte un/vai hroniskā plaušu slimība). Konsultēto pacientu profilu veidoja galvenokārt vidējā vecuma sievietes ar autoimūno iekaisuma artrītu, kas ārstēts ar SMARM. Reimatisko pacientu ambulatorā aprūpē, nodrošinot attālinātās konsultācijas, iespējams sekmīgi izvērtēt pacientu reimatisko slimību klīniskos aspektus un vadīt terapiju, ja pacients iepriekš atradies dinamiskā novērošanā pie reimatologa.