

SUPPLEMENTARY MATERIAL

Delayed referral, socioeconomic status, and disease characteristics as factors associated with disabilities in rheumatoid arthritis patients: a multicenter observational study

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Supplementary Table 1. Definitions used in the study.

| Category | Variable | Definition/Classification |
|---------------------------------------|-------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Demographic data | Age | Age at recruitment (in years). |
| | Gender | Male or female. |
| | Duration of RA at presentation | Time from onset of initial symptoms or signs attributable to RA. |
| | Total disease duration | Time from onset of RA at presentation + follow-up duration at recruitment. |
| Initial presentation | Earliest symptom/sign | First symptom, sign, or joint affected within the first 6 weeks as recalled by the patient. |
| | Initial joint involvement | First joint(s) affected within the first 6 months of RA. |
| Pattern of joint involvement | Upper limb | Joints of hand knuckles, shoulders, etc. |
| | Lower limb | Joints of knees, feet, etc. |
| | All joints (polyarticular) | Involvement of both upper and lower limb joints. |
| | Other than joints | Neck, back, or non-joint areas. |
| | Polyarticular presentation | Pain in multiple areas including both upper and lower limb joints. |
| Oligoarthritic presentation | Defined separately (≤ 4 joints involved). | |
| Socioeconomic classification | Modified scale (reference 15) | Upper-lower + lower \rightarrow <i>lower class</i> ; lower-middle \rightarrow <i>middle class</i> ; upper + upper-middle \rightarrow <i>upper class</i> |
| Extra-articular manifestations | Rheumatoid nodules | Subcutaneous firm nodules, clinically diagnosed. |
| | Ocular involvement | Keratoconjunctivitis sicca, scleritis, or episcleritis, documented clinically. |
| | Neurologic involvement | Peripheral neuropathy confirmed clinically/electrophysiologically. |
| | Cutaneous involvement | Vasculitic lesions, ulcers, or purpura, clinically evident. |
| | Hematologic involvement | Anemia, leukopenia, or thrombocytopenia attributable to RA. |
| | Cardiovascular involvement | Pericarditis or other RA-related cardiac disease diagnosed clinically or by imaging. |
| | Pulmonary involvement | Interstitial lung disease, pleuritis, or pulmonary nodules diagnosed clinically or radiologically. |

RA, rheumatoid arthritis.

Supplementary Table 2. The Rheumatoid Arthritis Articular Damage score: definition for scoring damage in individual joints.

| Joint type | Definitions for scoring irreversible articular damage | Max score |
|---------------------|-----------------------------------------------------------------------------------------|-----------|
| Cervical spine | 1: severe limitation of motion, ankylosis, or known cervical subluxation | 2 |
| | 2: history of medullary compression or surgical fusion | |
| Shoulder | 1: external rotation <45° {anatomical limitation, not due to pain}, or severe crepitus | 4 |
| | 2: ankylosis or prosthesis | |
| Elbow | 1: flexion contracture <30° | 4 |
| | 2: flexion contracture >30°, ankylosis, history of radial head resection, or prosthesis | |
| Wrist | 1: extension or flexion <30°, or volar/ulnar/radial shift | 4 |
| | 2: ankylosis, prosthesis or history of ulnar head resect on | |
| MCP | 1: ulnar deviation | 20 |
| | 2: subluxation, ankylosis, or prosthesis | |
| PIP | 1: flexion contracture | 20 |
| | 2: Swan neck or boutonniere deformity, ankylosis, or prosthesis | |
| Hip | 1: internal rotation <10° | 4 |
| | 2: prosthesis or Girdlestone pseudarthrosis | |
| Knee | 1: medial or lateral deviation >10° due to arthritis, or Hexion contracture <20° | 4 |
| | 2: flexion contracture >20°or prosthesis | |
| Ankle | 1: fixed valgus deformity <20° | 4 |
| | 2: prosthesis, ankylosis, arthrodesis, or valgus deformity >20° | |
| MTP | 1: visible deformity due to arthritis | 4 |
| | 2: history of Kates. Kessel or other arthr-0plasty of the forefoot | |
| Maximum total score | | 70 |

MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint; MTP, metatarsophalangeal joint.

Supplementary Table 3. Clinical characteristics, extra-articular features, and disease activity measures of rheumatoid arthritis patients categorized by severity of joint damage.

| (n=4213) | | | | |
|------------------------------------------------------------|--------------------------|-------------------------|-----------------------|---------------------|
| Parameters | Severe damage (n=378) | Moderate damage (n=387) | No damage (n=3448) | p-value |
| First RA-related symptom | | | | |
| Upper limb joints | 95 (25.13%) | 123 (31.78%) | 599 (17.37%) | <0.001* |
| Lower limb joints | 67 (17.72%) | 98 (25.32%) | 457 (13.25%) | |
| Polyarticular presentation | 62 (16.4%) | 76 (19.64%) | 283 (8.21%) | |
| Other than joints | 7 (1.85%) | 2 (0.52%) | 19 (0.55%) | |
| Unknown | 147 (38.89%) | 88 (22.74%) | 2090 (60.61%) | |
| Extra-articular features | | | | |
| Rheumatoid nodules | 39 (31.2%) | 29 (23.2%) | 57 (45.6%) | <0.001* |
| Pulmonary fibrosis | 19 (5.03%) | 14 (3.62%) | 21 (0.61%) | <0.001* |
| Pulmonary nodules | 0 (0%) | 0 (0%) | 1 (100%) | 1.000 [^] |
| Pleural thickening | 0 (0%) | 0 (0%) | 1 (100%) | 1.000 [^] |
| Pleural effusion | 0 (0%) | 0 (0%) | 1 (100%) | 1.000 [^] |
| Rheumatoid lung | 0 (0%) | 0 (0%) | 2 (100%) | 1.000 [^] |
| Vasculitis | 1 (0.26%) | 2 (0.52%) | 2 (0.06%) | 0.045 [^] |
| Cutaneous | 1 (0.26%) | 0 (0%) | 0 (0%) | 0.090 [^] |
| Ulcerative | 0 (0%) | 0 (0%) | 1 (100%) | 1.000 [^] |
| Sjogren's features | 18 (4.76%) | 15 (3.88%) | 29 (0.84%) | <0.001* |
| Raynaud's phenomenon | 3 (0.79%) | 1 (0.26%) | 2 (0.06%) | 0.005 [^] |
| Dermatitis | 2 (0.53%) | 0 (0%) | 0 (0%) | 0.008 [^] |
| Systemic features | 30 (7.94%) | 11 (2.84%) | 16 (0.46%) | <0.001* |
| Disease activity and functional assessment measures | | | | |
| Visual analog scales (VAS) | 0 (0%) | 1 (0.26%) | 0 (0%) | 0.182 [^] |
| VAS pain scale | 4.28±2.31 (0-10) | 4.02±2.14 (0-10) | 3.22±2.44 (0-10) | <0.001 [#] |
| VAS physicians global scale | 2.79±2.43 (0-9) | 3.12±2.12 (0-9) | 1.25±1.91 (0-10) | <0.001 [#] |
| VAS patient global assessment scale | 3.02±2.7 (0-9) | 3.14±2.24 (0-10) | 1.23±1.96 (0-10) | <0.001 [#] |

*Chi-square; [#]analysis of variance; [^]Fisher exact test, NA - the variables were not treated as continuous due to their significant skewness and were instead considered categorical. Similarly, the Rheumatoid Arthritis Articular Damage score, which was significantly right-skewed, was also treated as a categorical variable.

Supplementary Table 4. Clinical and demographic characteristics of rheumatoid arthritis patients stratified by total probable duration of illness.

| Descriptive (n=4213) | | | | | |
|-----------------------------------------------------|-------------------|------------------------|--------------------------|----------------------|---------------------|
| Parameters | <2 years (n= 382) | 2 to 5 years (n = 796) | 5 to 10 years (n = 1192) | >10 years (n = 1843) | P value |
| Rheumatoid nodules | 2 (0.52%) | 6 (0.75%) | 12 (1.01%) | 34 (1.84%) | 0.043 [^] |
| Pulmonary fibrosis | 0 (0%) | 0 (0%) | 1 (0.08%) | 0 (0%) | 0.563 [^] |
| Pulmonary Nodules | 0 (0%) | 0 (0%) | 1 (0.08%) | 0 (0%) | 0.563 [^] |
| Pleural Thickening | 0 (0%) | 0 (0%) | 1 (0.08%) | 0 (0%) | 0.563 [^] |
| Pleural effusion | 0 (0%) | 0 (0%) | 1 (0.08%) | 0 (0%) | 0.563 [^] |
| Rheumatoid lung | 0 (0%) | 0 (0%) | 1 (0.08%) | 1 (0.05%) | 1.000 [^] |
| Vasculitis | 0 (0%) | 0 (0%) | 3 (0.25%) | 2 (0.11%) | 0.591 [^] |
| Cutaneous | 0 (0%) | 0 (0%) | 1 (0.08%) | 0 (0%) | 0.563 [^] |
| Ulcerative | 0 (0%) | 0 (0%) | 1 (0.08%) | 0 (0%) | 0.563 [^] |
| Raynaud's Phenomenon | 0 (0%) | 0 (0%) | 3 (0.25%) | 3 (0.16%) | 0.576 [^] |
| Dermatitis | 1 (0.26%) | 0 (0%) | 0 (0%) | 1 (0.05%) | 0.209 [^] |
| Systemic features | 7 (1.83%) | 16 (2.01%) | 14 (1.17%) | 20 (1.09%) | 0.212 [*] |
| Sjogren's features | 2 (0.52%) | 12 (1.51%) | 17 (1.43%) | 31 (1.68%) | 0.398 [^] |
| Disease activity and functional assessment measures | | | | | |
| Visual analogue scales (VAS) | 0 (0%) | 0 (0%) | 1 (0.08%) | 0 (0%) | 0.563 [^] |
| VAS pain scale | 3.33±2.46 (0-10) | 3.07±2.32 (0-10) | 3.18±2.35 (0-10) | 3.67±2.5 (0-10) | <0.001 [#] |
| VAS physicians global Scale | 1.44±2.02 (0-8) | 1.67±2.02 (0-10) | 1.67±2.10 (0-10) | 1.47±2.11 (0-9) | 0.022 [#] |
| VAS patient global assessment Scale | 1.46±2.21 (0-9) | 1.71±2.16 (0-9) | 1.66±2.17 (0-10) | 1.47±2.19 (0-10) | 0.013 [#] |
| Joint involvement RAAD scores | | | | | |
| Neck RAAD score | 9 (2.36%) | 9 (1.13%) | 23 (1.93%) | 34 (1.84%) | 0.417 [*] |
| Upper limb joints RAAD score | 38 (9.95%) | 71 (8.92%) | 161 (13.51%) | 414 (22.46%) | <0.001 [*] |
| Lower limb joints RAAD score | 20 (5.24%) | 40 (5.03%) | 104 (8.72%) | 264 (14.32%) | <0.001 [*] |

RAAD, Rheumatoid Arthritis Articular Damage; *Chi-square; #analysis of variance; ^Fisher exact test, NA - the variables were not treated as continuous due to their significant skewness and were instead considered categorical. Similarly, the RAAD score, which was significantly right-skewed, was also treated as a categorical variable.

Supplementary Table 5. Distribution of drug usage among rheumatoid arthritis patients according to severity of joint damage (n=4213).

| Parameters | Severe damage (n=378) | Moderate damage (n=387) | No damage (n=3448) | p-value |
|----------------------|-----------------------|-------------------------|--------------------|---------|
| AZA | 4 (1.06%) | 1 (0.26%) | 25 (0.73%) | 0.411* |
| HCQ | 199 (52.65%) | 184 (47.55%) | 2047 (59.36%) | <0.001* |
| Steroids | 154 (40.74%) | 150 (38.76%) | 1232 (35.73%) | 0.097* |
| DMARD | 4 (1.06%) | 9 (2.32%) | 32 (0.93%) | 0.040* |
| Methotrexate | 285 (75.40%) | 297 (76.74%) | 2756 (79.93%) | 0.053* |
| Sulfasalazine | 51 (13.49%) | 62 (16.02%) | 402 (11.66%) | 0.033* |
| Leflunomide | 129 (34.13%) | 117 (30.23%) | 932 (27.03%) | 0.008* |
| Supplement | 128 (33.86%) | 102 (26.36%) | 714 (20.71%) | – |
| NSAID | 186 (49.21%) | 151 (39.02%) | 1355 (39.30%) | – |
| MMF | 4 (1.06%) | 2 (0.52%) | 33 (0.96%) | 0.665* |
| Tofacitinib | 12 (3.17%) | 9 (2.33%) | 34 (0.98%) | <0.001* |
| CYC | 0 (0%) | 0 (0%) | 1 (0.03%) | 0.895* |
| Rituximab | 4 (1.05%) | 3 (0.77%) | 15 (0.43%) | 0.215* |
| Iguratimod | 2 (0.53%) | 3 (0.78%) | 33 (0.95%) | 0.678* |
| Tacrolimus | 10 (2.65%) | 6 (1.55%) | 93 (2.70%) | 0.402* |
| Penicillamine | 0 (0%) | 0 (0%) | 1 (0.03%) | – |
| Others | 111 (29.37%) | 71 (18.35%) | 851 (24.68%) | – |

Patients could receive multiple medications simultaneously; therefore, percentages are not mutually exclusive and may exceed 100% when summed across drug categories.

Methotrexate and other DMARDs were frequently used in combination; accordingly, patients receiving combination therapy were included in each relevant medication category.

AZA, azathioprine; HCQ, hydroxychloroquine; DMARD, disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug; MMF, mycophenolate mofetil;

CYC, cyclophosphamide; *Chi-square; #analysis of variance; ^Fisher exact test.

Supplementary Table 6. Distribution of drug usage across multiple centers.

| Descriptive (n=4213) | | | | | | | | | |
|----------------------|------------------|--------------------|-------------------|-----------------|-----------------|-----------------|----------------|------------------|---------|
| Drugs used | Centre 1 (n=383) | Centre 2 (n = 565) | Centre 3 (n=2490) | Centre 4 (n=91) | Centre 5 (n=41) | Centre 6 (n=72) | Centre 7 (n=5) | Centre 8 (n=566) | p-value |
| AZA | 1 (0.26%) | 2 (0.35%) | 24 (0.96%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 3 (0.53%) | 0.525* |
| HCQ | 148 (38.64%) | 390 (69.03%) | 1599 (64.22%) | 16 (17.58%) | 11 (26.83%) | 41 (56.94%) | 0 (0%) | 225 (39.75%) | <0.001* |
| Steroids | 69 (18.02%) | 244 (43.19%) | 818 (32.85%) | 72 (79.12%) | 18 (43.9%) | 61 (84.72%) | 0 (0%) | 254 (44.88%) | <0.001* |
| DMARD | 0 (0%) | 4 (0.71%) | 29 (1.16%) | 3 (3.3%) | 0 (0%) | 0 (0%) | 0 (0%) | 2 (0.35%) | 0.043* |
| Methotrexate | 264 (68.93%) | 466 (82.48%) | 2146 (86.18%) | 49 (53.85%) | 31 (75.61%) | 40 (55.56%) | 0 (0%) | 342 (60.42%) | <0.001* |
| Sulfasalazine | 106 (27.68%) | 153 (27.08%) | 202 (8.11%) | 6 (6.59%) | 7 (17.07%) | 0 (0%) | 0 (0%) | 41 (7.24%) | <0.001* |
| Leflunomide | 131 (34.2%) | 70 (12.39%) | 867 (34.82%) | 6 (6.59%) | 3 (7.32%) | 0 (0%) | 0 (0%) | 101 (17.84%) | <0.001* |
| Supplement | 289 (75.46%) | 39 (6.9%) | 551 (22.13%) | 0 (0%) | 16 (39.02%) | 1 (1.39%) | 0 (0%) | 48 (8.48%) | |
| NSAID | 255 (66.58%) | 21 (3.72%) | 1050 (42.17%) | 47 (51.65%) | 12 (29.27%) | 23 (31.94%) | 0 (0%) | 284 (50.18%) | |
| MMF | 6 (1.57%) | 7 (1.24%) | 23 (0.92%) | 1 (1.1%) | 0 (0%) | 0 (0%) | 0 (0%) | 2 (0.35%) | 0.602* |
| Tofacitinib | 8 (2.09%) | 7 (1.24%) | 10 (0.4%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 30 (5.3%) | <0.001* |
| CYC | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (0.18%) | 0.488* |
| Rituximab | 6 (1.57%) | 10 (1.77%) | 2 (0.08%) | 2 (2.2%) | 1 (2.44%) | 0 (0%) | 0 (0%) | 1 (0.18%) | <0.001* |
| Iguratimod | 0 (0%) | 35 (6.19%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 3 (0.53%) | <0.001* |
| Tacrolimus | 0 (0%) | 0 (0%) | 108 (4.34%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (0.18%) | <0.001* |
| Penicillamine | 0 (0%) | 0 (0%) | 1 (0.04%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | |
| Others | 160 (41.78%) | 55 (9.73%) | 740 (29.72%) | 16 (17.58%) | 5 (12.2%) | 18 (25%) | 0 (0%) | 39 (6.89%) | |

AZA, azathioprine; HCQ, hydroxychloroquine; DMARD, disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug; MMF, mycophenolate mofetil; CYC, cyclophosphamide; *Chi-square; #analysis of variance; ^Fisher's exact test.