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Management profile of rheumatoid arthritis patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A two-year, retrospective chart review

By: Mastewal Belay (MD, Internal Medicine Resident)

Addis Ababa, Ethiopia

December, 2021 GC

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Abstract

Background*:* Rheumatoid arthritis (RA), a chronic systemic inflammatory disease, predominantly affects the joints, leading to functional disability and premature mortality. Standards of care have been established for its treatment. Its management include early aggressive, and persistent use of disease-modifying antirheumatic drugs (DMARDs) to prevent joint damage in people with active inflammation. However, published evidence and guidance for its clinical management are lacking in resource limited countries such as Ethiopia. This research assesses whether care for RA is consistent with current treatment guidelines.

Objective: To assess the management profile of RA patients who attended rheumatology outpatient care center of Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019.

Methodology: A facility-based, cross-sectional study was conducted at rheumatology outpatient care center of TASH, Addis Ababa, Ethiopia. Data was collected using a structured checklist, and then entered and analyzed using SPSS version 26. Descriptive analysis employed to identify the management gaps. Tables and figures were used to present the results.

Results: The study evaluated medical records of 314 RA patients. Their age ranged from 18 to 74 years with a median of 39.5 years and IQR of 30 to 51. Females dominated with a female: male ratio of 5.4:1. RF was positive in 62.1% and anti-CCP was positive in 73.1% of the tested patients. Methotrexate was included in the regimen of most (93.6%) of the patients and chloroquine in 67.2% of them. Overall, 48.7% were on combination therapy. And 85.4% were subjected to steroids for more than six months. Baseline investigations were suboptimal. Objective measures of clinical remission were used in only 17.5% of the total. Successful clinical remission was achieved in 75.8% of patients. Non-pharmacological treatments such as physical therapy and psychological counseling were only delivered to 6.4% and 1% of patients, respectively.

Conclusion: Management gap of RA patients is a common observation in the study setting. The most frequently observed management pitfalls are suboptimal use of DMARDs, use of steroids for extended duration, and underuse of non- pharmacological therapy such as physical therapy and psychological support.

Acronyms/Abbreviations

ACCP	Anticyclic citrullinated peptide
ACR	American College of Rheumatology
CDAI	Clinical Disease Activity Index
CHS	College of Health Science
CRP	C reactive protein
CQ	Chloroquine
DMARDs	Disease Modifying Anti Rheumatic Drugs
ESR	Erythrocyte Sedimentation Rate
EULAR	European Alliance of Associations for Rheumatology
ILD	Interstitial Lung Disease
MTX	Methotrexate
RA	Rheumatoid Arthritis
RAPID3	Routine assessment of patient index data 3
RF	Rheumatoid Factor
TASH	Tikur Anbessa Specialized Hospital
TNFi	Tumor Necrosis Factor inhibitor

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1. Introduction

1.1 Background

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disorder of unknown etiology that primarily involves synovial joints. RA typically affects small joints of the hand and feet symmetrically, and usually leads, if uncontrolled, to destruction of joints due to erosion of cartilage and bone, causing joint deformities and functional impairment. Most patients present with gradual onset of polyarticular disease, but some patients may show acute onset of oligoarticular or monoarticular disease. Diagnosing these patients may be challenging.

RA is a systemic disease which may also lead to a variety of extra-articular manifestations including constitutional symptoms, subcutaneous nodules, ILD, pleural disease, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities.

RA affects ~0.5–1% of the adult population worldwide. The incidence and prevalence of RA varies based on geographic location, both globally and among certain ethnic groups within a country. Liberia and South Africa have reported prevalence rate of 2-3 % and 2.5-3.6% respectively. There is no population-based prevalence study in Ethiopia. The peak age of onset is 50 to 60 years in women and above 70 years in men. Females are two to three times more frequently affected than males.

The treatment of rheumatoid arthritis (RA) is directed towards the control of inflammation and the prevention of articular and extra- articular complications.

Improved outcomes have resulted from the use of potent and well-tolerated conventional synthetic, biologic, and targeted synthetic disease-modifying antirheumatic drugs (DMARDs). They are used alone or in combination to induce and maintain tight control of disease.

The preferred approaches, treat-to-target and tight control of disease, strategies have the potential to control synovitis and slow or stop radiographic progression, than gross assessment of diseases activity.

1.2 Statement of the problem

RA may be considered a potentially curable condition during evolutionary process (from early synovitis to established RA) and the disease course can be changed by early appropriate aggressive treatment.

There are no nationwide or hospital-based studies on RA management profile. So, this study may help to know management gaps and treatment outcome of RA patients in Tikur Anbessa Specialized Hospital.

2. LITERATURE REVIEW

2.1 Gaps in the management of rheumatoid arthritis

According to several studies the management of RA patients often doesn't follow existing guidelines. A population-based study on RA care in the British, Canada and Columbia settings was not consistent with the latest treatment guidelines. They emphasized that efforts to educate family, physicians and patients about the shift in RA treatment paradigms and to improve access to rheumatologists are needed (14).

A longitudinal population-based RA cohort study in British Columbia (BC), Canada has uncovered several gaps in RA care, including loss of follow-up from rheumatology care and suboptimal DMARD use. While some delays in DMARD initiation in new onset RA were observed, timeliness of DMARD use improved over the study period (15).

Another study by EULAR 2019 reveals significant gaps in essential rheumatoid arthritis care across16 patient-centered Standards of Care (SoC) in rheumatoid arthritis, in Europe and between European countries (16). Very little significance is given to rheumatic disease in Africa, with only single rheumatologist providing for the 16 million population of Kenya and thirty for the 40 million South Africans as recently as 2003 (17). The number of published studies in African context that shows the management gaps in Rheumatoid Arthritis is rather scarce.

2.2 DMARD and steroid use in RA patients

Disease-modifying anti-rheumatic drugs (DMARDs) reduce joint destruction and long-term physical disability (1-3). Delays, as brief as 3 months, in instituting DMARDs have been associated with poorer long-term outcomes, including greater physical disability (5–7) and increased radiologic damage (8–10). Therefore, treatment with DMARDs is recommended in all RA patients with active disease (4), and treatment paradigms have shifted towards early, aggressive, and persistent use of DMARDs with the aim of controlling inflammation, thereby preventing joint damage (11–13).

One of the studies on DMARD use at the population level shows, only 43% of the entire RA population had used a DMARD at least once over 5 years, 35% over 2 years, and 31% over 1 year. Use of DMARDs was greatly influenced by specialist care; 76% of people seen at least once by a rheumatologist used a DMARD over a 5-year period, compared with 40% for internists and 10% for family physicians. Results did not differ significantly when looking at 2- and 1-year periods (14).

Another cohort study in BC revealed that rates of DMARD use varied based on whether patients saw rheumatologists and visit timing in relation to measurement year. Rates were low in the entire RA population (35-39% across measurement years). Rates improved but remained suboptimal in patients seeing rheumatologists ever in follow-up or in the past (56%-63%); and were highest (87% in 2014) in patients under active rheumatologist care (i.e., ≥1 visit in measurement year) (15).

Based on the limited data available, during moderate-term treatment periods averaging slightly over 7 months, corticosteroids appeared to be as effective or more effective than alternative therapies in improving several common RA disease activity measures (18). Rheumatoid Arthritis management guidelines advocate using low dose glucocorticoids (≤10 mg daily of a prednisone equivalent) during the initiation of a new disease modifying anti-rheumatic drug and for a relatively short duration (<3 months) when treating flare (19,20).

There is one randomized controlled trial, multinational trial, which investigated the effect of tapering versus continuing oral glucocorticoids in patients with rheumatoid arthritis. The findings show that continuation of low-dose prednisone provided better disease control during the study than tapering prednisone. Of note, treatment success rates were higher with the continued prednisone (77%) compared with the tapered prednisone (65%), and the mean DAS28-ESR change score was better in the continued prednisone group than the taper-prednisone group. (21). ACR recommends Glucocorticoids should be used at the lowest possible dose and for the shortest possible duration to provide the best benefit-risk ratio for the patient. (24)

2.3 Combination therapy in RA patients

Currently available data suggest that treatment should be based on the tight control of disease to reach remission or low disease activity. Sometimes achieving low disease activity and remission is difficult with single drug and combination of DMARDs is required. The TICOR, a single blind randomized controlled trial in Scotland, Patients were randomly assigned to either intensive or routine management. Results showed that mean fall in DAS was greater in the intensive group than in the routine group; patients treated intensively were more likely to have a good response or be in remission (22).

The FINRACo study demonstrated that combination DMARD therapy was more effective than monotherapy at inducing remission in patients with early RA (23). ACR 2015 guideline recommended conditionally Methotrexate monotherapy over double or triple therapy for

DMARD-naive patients with moderate-to-high disease activity. Methotrexate monotherapy is strongly recommended over dual or triple csDMARD therapy for DMARD-naive patients with low disease activity. In patients taking maximally tolerated doses of methotrexate that are not at target, addition of a bDMARD or combination of csDMARD is strongly recommended over continuing DMARD alone. (24)

3. OBJECTIVES

3.1 General objective

- To identify gaps in the management of RA patients attending rheumatology outpatient care center of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019

3.2 Specific objectives

1. To evaluate whether DMARD use meets the guideline recommendations (in terms of dose, frequency & monitoring) among RA patients attending rheumatology outpatient care center of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019
2. To assess whether the use of steroids is consistent with the guideline recommendations among RA patients attending rheumatology outpatient care center of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019
3. To evaluate the use of combination therapy as per the guideline recommendations among RA patients attending rheumatology outpatient care center of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019

4. Methods and Materials

4.1 Study area and period

The study was conducted at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia. TASH is a tertiary hospital located in the capital city of the country. It is the largest & oldest public hospital providing high level of clinical care for millions of people and training to health science students from different parts of the country and the Horn of Africa as well. The hospital has several specialty and sub-specialty clinics delivering specialized care to over half a million patients annually, and it launched digital medical recording system since 2018.

The hospital is the only health organization in the country where there is a well-functioning rheumatology outpatient care center dedicated to patients with various rheumatologic disorders. With rotating four resident physicians and two permanent consultant physicians, it provides service for specialized care twice a week for patients from different parts of the country. The current study was conducted at this facility from March 15 to August 31, 2021.

4.2 Study design

An institution-based, retrospective cross sectional study design was used for this study to address the research objectives considered in this study.

4.3. Population

4.3.1 Source population

The source population were all patients visiting Rheumatology clinic of TASH.

4.3.2 Study population

The study population was patients visiting Rheumatology clinic of TASH during the study period, and who fulfill the inclusion criteria.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

- Patients aging 18 or more years
- Those who visited the rheumatology clinic at least twice
- Those whose charts are retrievable

4.4.2 Exclusion criteria

- Those patients with incomplete or irretrievable medical records

4.5 Sample size and Sampling technique

The study included all RA patients who were in follow-up from January 1, 2018 to December 31, 2019 at rheumatologic clinic of TASH

4.6 Data collection instrument and procedure

Data was collected using a structured questionnaire which was adapted from previously published studies with some modification to ensure applicability to the current study while maintaining validity and reliability. Data was collected by trained data collector under the supervision of the principal investigator. Data collectors were selected from among the rheumatology unit nursing staff. Data collectors had a two-day training on how to extract the required information from record review (iCare system and patient chart) and complete the structured checklist.

4.7 Study Variables

4.7.1 Dependent variable

- Gaps in the management of rheumatoid arthritis

4.7.2 Independent variables

• Sociodemographic variables: age, sex and address

• Lifestyle factors: cigarette smoking

• Clinical and laboratory parameters

4.8 Definition of terms

- **Management gap**: Deviations in the management of RA patient from the 2015 ACR guideline.

- **Rheumatoid arthritis patient:** a patient whose leading diagnosis is rheumatoid arthritis based on ACR or ACR/EULAR classification criteria for RA.

- **Treat-to-target** refers to a systematic approach involving frequent monitoring of disease activity using validated instruments and modification of treatment to minimize disease activity with the goal of reaching a predefined target (low disease activity or remission).

- **Combination therapy:** defined as having received ≥2 DMARDs with overlapping prescription durations.

4.9 Data processing and analysis

Data entering, coding, clearing and statistical analysis was performed using SPSS (Statistical Package for Social science) version 26. Frequency and cross tabulation were used to check for missed values and variables. The demographic and clinical characteristics of patients were computed using descriptive statistics such as mean, standard deviation, frequencies, and percentage. Finally, the study findings were presented using diagrams, tables, and figures.

4.10 Data quality control

To ensure data quality, data collection instrument was prepared after thorough review of relevant literatures and related studies. The tool was pretested before the data collection process in 5% of the total sample size. An English version, pretested checklist was used to collect data. Brief training for the data collectors (two health professionals) about the process of data collection was given before the process of data collection. The data collection procedure was closely supervised, and each day, filled checklists were double-checked manually for consistency and completeness by data collectors and principal investigator before analysis.

4.11 Ethical clearance

Ethical approval was obtained before the beginning of data collection from the Research and Publication Committee (RPC) of the Department of Internal Medicine, College Health Sciences (CHS), TASH. All information in the charts were kept confidential and the information collected were used solely for the intended purpose. Personal Identifier Information (PII), including names of patients were included in the checklist to maintain anonymity, Codes will be used instead and completed checklists were stored safely by the investigator.

4.12 Dissemination of the study findings

The findings of this study will be submitted to the Department of Internal Medicine of College of Health Sciences, Addis Ababa University as a partial fulfillment of specialty certificate in Internal Medicine. The outcome of this study will be presented to other key stakeholders such as annual conferences to reach the wider scientific society. Finally, the manuscript will be submitted to a reputable scientific journal for possible publication.

5. Results

5.1 Sociodemographic characteristics of patients

This study included data derived from 314 adult rheumatoid arthritis patients, who sought care at the rheumatology clinic from January 1, 2018 to December 31, 2019, after excluding 12 patients who didn't fulfill the inclusion criteria. Among the studied patients, majority (265; 84.4%) were females and the remaining 49 (15.6%) were males. And participants' age ranged from 18 to 74 years with a median of 39.5 years and interquartile range of 30 to 51. Of all the studied patients, a little more than half (161; 51.3%) aged 18 to 40 years by the time of data collection while only 27 (8.6%) of the patients belonged to the age range that span from 61 to 74 years (Table 1). 52.4% patients were from Addis Ababa.

Table 1: Distribution by socio-demographic characteristics of RA patients who attended rheumatology outpatient center of TASH, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019

Variable	Frequency	Percent (%)
Sex		
Female	265	84.4
Male	49	15.6
Age group		
≤30	82	26.1
31 to 40	79	25.2
41 to 50	66	21.0
51 to 60	60	19.1
>60	27	8.6
Smoking		
Not documented	226	72.0
No smoking	88	28.0

With respect to history of substance use, while 88 (28%) of the patients were described as nonsmokers as they denied history of any form of cigarette smoking upon questioning by their respective clinicians, the remaining majority 226 (72%) lack a record regarding whether they smoke cigarette or not. Furthermore, clinical data of the studied subjects revealed that

while majority (219;69.8%) of the patients had no recorded preexisting comorbid medical condition, the remaining 95 (30.2%) were documented to have some of form of chronic comorbidity. Among those with comorbidities, hypertension was the most common disease as it was noted in 38 (40%) of the cases and diabetes mellitus appeared in 20 (21.05%) of the patients while 32 (33.7%) patients had other diseases such as chronic kidney disease, HIV/AIDS and bronchial asthma upon review (Figure 1). In addition to this, 4 (1.3%) of patients were observed to have fibromyalgia.

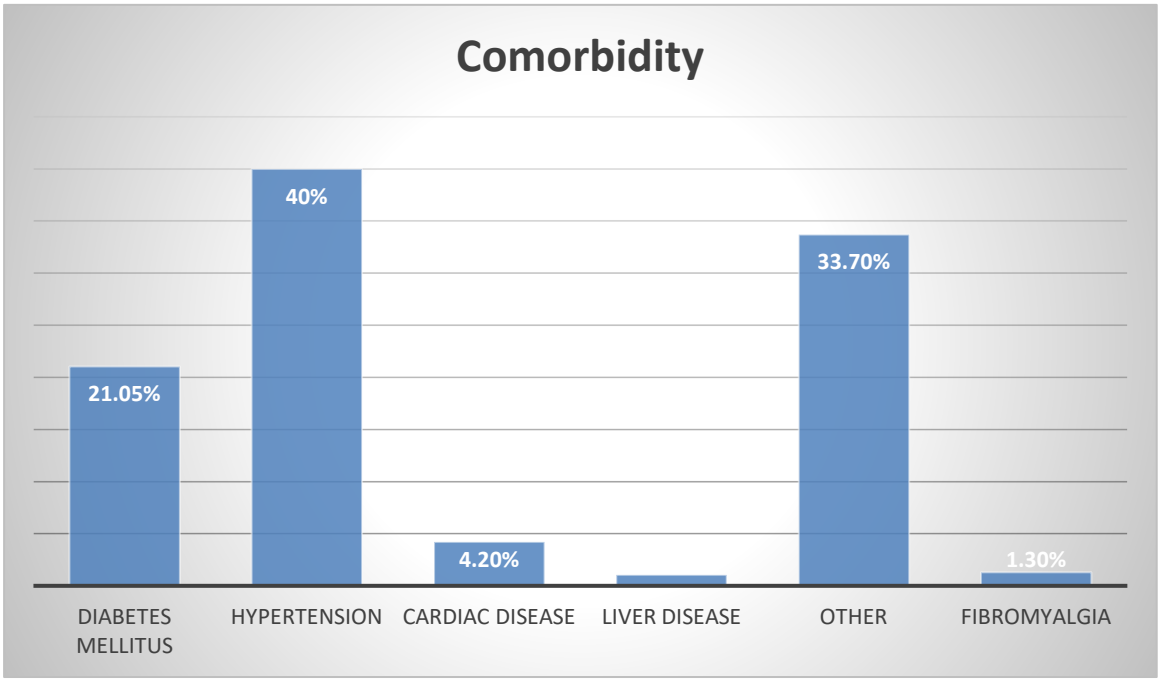

Figure 1. Distribution by comorbidities of RA patients who attended rheumatology outpatient center of TASH, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019 (n=95)

5.2 Laboratory and clinical profiles characteristics

Regarding the serologic markers pertaining to RA, close to one-third (95;30.2%) of the total patients had their rheumatoid factor (RF) determined while 26 (8.3%) had their anti-CCP documented. Of those with documented RF serology, about two-thirds (59;62.1%) were high titers whereas the remaining 36 (37.9%) were described as negative. Likewise, among patients with recorded anti-CCP status, almost three-fourths (19;73.1%) were seropositive while the rest (7;26.9%) were not.

With regard to baseline investigations, almost all (308;98.1%) had full blood count whereas hepatic viral markers were determined for about two-thirds of the patients. Erythrocyte sedimentation rate (ESR) was recorded in one-fourth of the patients (83;26.4%). Radiographs of the hands and feet as baseline imaging were documented in one-fifth (61;19.4%) of the

patients. Likewise, in relation to organ function tests, liver function tests were done in two-thirds (205;65.3%) of the patients while renal function test was collected for half of the patients during the initiation of pharmacotherapy (Table 2).

Table 2: Baseline laboratory and clinical profiles of RA patients who attended rheumatology outpatient center of TASH, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019

Variable	Frequency	Percent (%)
RF (n=95)		
Positive	59	62.1
Negative	36	37.9
Anti-CCP (26)		
Positive	19	73.1
Negative	7	26.9
HBsAg[a]	202	64.3
HCV-Ab[b]	203	64.6
Hand and feet X-ray	61	19.4
Baseline CBC	308	98.1
Baseline ESR	83	26.4
Baseline CXR	74	23.6
Baseline LFT	205	65.3
Baseline RFT	158	50.3
Extra-articular manifestation	5	1.6

Note. a: one patient was seropositive; b: three patients were seropositive; RF: Rheumatoid factor; CBC: complete blood count; ESR: erythrocyte sedimentation rate; CXR: chest x ray; LFT: liver function test; RFT: renal function test

With respect to extra-articular manifestations, only 5 (1.6%) of all patients were described to have extra-articular clinical features such as subcutaneous nodules(2), keratoconjunctivitis(2), and gastrointestinal manifestation (1) (Table 2).

5.3 Pharmacological profile of patients

Short term nonsteroidal anti-inflammatory drugs (NSAIDs) were given to more than half (179;57%) of the patients for immediate pain relief. Most (294;93.6%) were on a regimen that included methotrexate (MTX), and more than two-thirds (211;67.2%) were given chloroquine (CQ) by their physicians to achieve disease remission. Specifically, 18 (5.7%) patients were taking CQ as a monotherapy. In particular, close to half (153;48.7%) of all patients received a combination of MTX and CQ. In addition to this, most (268;85.4%) of the patients received oral prednisolone at some point during their follow up. And, majority (264;84.1%) of the patients were put on a regiment that contains a steroid and certain type of disease modifying anti-rheumatic drug (DMARD). None of the patients received triple therapy that contains any of the aforementioned DMARDs or biological DMARDs(Table 3).

Table 3: Pharmacological profile of RA patients who attended rheumatology outpatient center of TASH, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019

Variable	Frequency	Percent (%)
Medications used		
Methotrexate	294	93.6
Chloroquine	211	67.2
NSAID analgesia	179	57.0
Steroid	268	85.4
Methotrexate + Chloroquine	153	48.7
Steroid + DMARD	264	84.1
MTX starting dose(294)		
< 7.5 mg	73	24.8
7.5 to 15 mg	165	56.1
Unspecified	56	19.05
MTX maintenance dose (292)		
< 15 mg	186	59.2
≥15 mg	128	40.8
Duration of steroid use (268)		
≤ 6 months	39	14.6
> 6 months	229	85.4
Side effects (24)		
Metabolic syndrome	7	29.2
Dyspepsia	6	25
Osteoporosis	6	25
Ophthalmic complication	3	12.5
Others	2	8.3

NSAID: Nonsteroidal anti-inflammatory drugs; DMARD: Disease Modifying Anti Rheumatic Drugs; MTX: Methotrexate

Of all patients taking methotrexate, one-fourth (73) were prescribed on less than the minimum recommended dosage (<7.5mg per week) while 165 (56.1%) were initiated on methotrexate with a dosage that ranged from 7.5 to 15mg once a week. However, the starting MTX dosages for one-fifth (56;19.05%) of the patients was not recorded. Furthermore, more than half of the patients (186;59.2%) of the patients were on maintenance dose of < 15 mg a week, and the remaining 128 (40.8%) were receiving methotrexate ≥ 15 mg per week. Among those taking steroids, majority (229;85.4%) were documented to take it for more than more 6 months (Table 3).

On the other hand, side effects attributed to the DMARDs and steroids were documented in 24 of the patients. Among these, the most frequently observed side effect was metabolic syndrome as it was cited in 7 (29.2%) of the patients. Additionally, dyspepsia affected one-fourth (6) of the patients while osteoporosis accounted for 6 (25%) of the side effect burden (Table 3). Furthermore, 114 (36.3%) of all patients discontinued taking methotrexate during the study period for reasons such as drug unavailability (36;31.6%), pregnancy (27;23.7%) and others (9;7.9%). The remaining 39 (34.2%) were not taking the drug for unspecified reasons, as detailed in Figure 2.

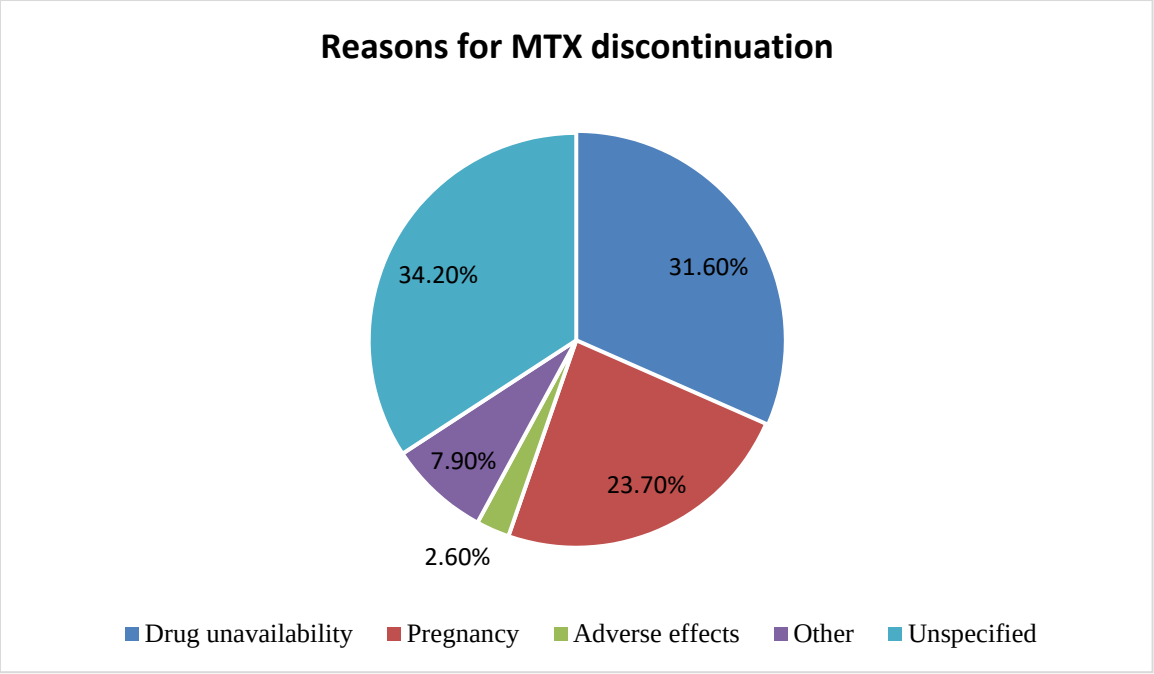

Figure 2. Reasons for methotrexate discontinuation among RA patients who attended rheumatology outpatient center of TASH, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019 (n=114)

5.4 Follow up-related characteristics

In relation to follow up of the patients with acute phase reactants, almost half (154;49.1%) of all patients their ESR determined at least once in the three months preceding the study time. By the same token, only 48 (15.3%) had their C-reactive protein level determined the three-months-time prior to the study period. Moreover, a little more than half (167;53.2%) of the total patients had been investigated with liver function tests while about two-thirds (207;65.9%) had a laboratory workup for kidney function tests (Table 4).

Table 4: Follow up and related characteristics of RA patients who attended rheumatology outpatient center of TASH, Addis Ababa, Ethiopia from January 1st, 2018 to December 31st, 2019

Variable	Frequency	Percent (%)
ESR in 3 months	154	49.1
CRP in 3 months	48	15.3
LFT in 1 year	167	53.2
RFT in 1 year	207	65.9
Disease activity monitoring		
Subjective assessment	258	82.1
Functional assessment	1	0.3
Objective assessment	55	17.5
Type of objective assessment (n=55)		
CDAI	51	92.7
RAPID3	1	1.8
Other	3	5.5
Clinical remission in the last 3 Months (for objectively assessed)		
Yes	33	60
No	22	40
Unspecified	4	1.3
Physical therapy	20	6.4
Psychological counseling	3	1

CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; RAPID3: Routine assessment of patient index data 3

With respect to disease activity monitoring technique, majority (258;82.1%) were assessed subjectively by onsite physicians while (55;17.5%) were followed with objective instruments. Specifically, of those who were monitored objectively, clinical disease activity index (CDAI) was the most frequently used tool (51;92.7%). The remaining 4 (7.5%) patients were followed using other objective tools such as routine assessment of patient index data 3 (RAPID3) (Table 4). Overall, 238 (75.8%) were evaluated by subjective assessment and documented to have controlled disease, but difficult to use the term clinical remission.

Finally, regarding non-pharmacological management, only 20 (6.4%) were ordered to have physical therapy while the remaining majority (294;93.6%) didn't receive any form of physiotherapy at the clinical setting since the start of their follow up. Additionally, 3 (1%) patients were linked to the psychiatry unit for psychological counseling to address disease-related mental problem (Table 4).

6. Discussion

Evaluation of utilization and optimization of DMARDs and steroids in rheumatoid arthritis is important to designing programs for future intervention that would target in furthering patient care, by significantly reducing progressive joint damage, disability and thereby improving overall health-related quality of life. In the current study, therefore, the utilization and optimization of these medications among patients with rheumatoid arthritis was assessed. The results from this study revealed several significant findings.

The present study shows that females outnumbered male with a female: male ratio of 5.4:1, with none having a history of active cigarette smoking. Test for RF were positive in 62.1% of patients and anti-CCP was positive in 73.1% of our patients. Methotrexate was included in the regimen of most (93.6%) of the patients and chloroquine 67.2% of them. Overall, 48.7% were receiving both methotrexate and chloroquine concurrently. Majority (85.4%) took steroid for extended periods. Baseline investigations were suboptimal. Objective measures of clinical remission were used in only 17.5% of the total. Non-pharmacological treatments such as physical therapy and psychological counseling were only delivered to 6.4% and 1% of patients.

The high female to male ratio obtained in this study was in line with the finding reported by Ohagwu et al. in a Nigerian population where female to male ratio was 6.1:1(25). It was also supported by the finding observed by Muia and colleagues in Kenyan population (26). Although smoking has been cited as the strongest modifiable risk factor for a seropositive RA by authors such as Scott (27), none of our patients had history of active cigarette smoking. This finding is supported by Malemba et al. who reported that only 2 out of 114 Congolese patients with RA smoked cigarettes. It is generally assumed that black African's smoke less than their Caucasian counterparts (25).

Although guidelines recommend for exhaustive workups including CBC, creatinine, LFTs, alkaline phosphatase, chest radiograph within previous year, and hepatitis B, and C serology in high-risk patients by the time of initiation of DMARDs, only a sizeable number of patients had those investigations. Few patients had baseline radiography of the affected joints done and very few have chest x-ray. This can be due to the resource constraints in the region which can lead to prioritization of funds for effective healthcare delivery as previously pointed out by Mody et al (28).

This study revealed that 59.2% of patients were receiving suboptimal doses (<15 mg) of MTX although it was prescribed for 93.4% of the patients. Such suboptimal use of DMARDs will result in suboptimal control of disease. Such suboptimal utilization can be a reflection of the severe lack of rheumatologists in the study setting as Lacaille and colleagues highlighted that the strongest determinant for proper DMARD use was specialist care, in their study that included British, Columbian, and Canadian population (14).

In comparison with routine care, previous reports revealed treat to target through more objective and frequent patient assessment was shown to improve clinical outcomes at little cost (22). However, the current study discovered that only 17.5% of the patients received objective clinical assessment. Most (82.1%) of the patients were classified to have achieved clinical remission based on subjective assessment. The csDMARD dosage is suboptimal but the number of patients who are in remission are high making the term "remission" being questionable, in fact the high use of steroid might be helping in terms of good disease control.

An important area of mismanagement noted in this study was long-term steroid use. Although glucocorticoid use is recommended only for short-term, with rapid tapering off over few weeks (30), the steroid schemes lasting over 6 months are applied in 85.4% of patients. This was higher than the Polish report in which steroid schemes lasting over 6 months were applied in 25% of RA patients (31). The discrepancy can be attributed to the varying demographics, disease distribution, clinician's expertise, institutional guidelines and the health care system. For instance, in the current study setting, there were only one adjunct staff rheumatologist and care was offered by nephrologists until recently.

Again, even though periodic funduscopic and visual fields examination is recommended for RA patients taking chloroquine, none of our patients had documented ophthalmic examination. Easterbrook emphasized that patients receiving chloroquine (CQ) need periodic ophthalmologic examinations for early detection of reversible retinal toxicity (32). This management caveat can be partly a result of trained rheumatology nurses in the study setting. At this juncture, it should be pointed out that some part of care such as ocular examinations might have been left undocumented in patients' medical charts inadvertently.

Unfortunately, similar to the Nigerian study, the study confirmed biologic use in the setting of high disease activity and other poor prognostic factors is low due to prohibitive costs especially since most patients pay out of pocket (25). In short, the discrepancies in management confirm the observation suggested by Krüger et al. that time constraints, a shortage of specialists and budget limitations impede the application of 'treat-to-target' principles in real-world practice (33).

Finally, the present study indicated that non-pharmacologic component of care has been given little room in that physical therapy and psychological counseling were only delivered to 6.4% and 1% of patients. This is quite different from the finding of Lacaille and others where physiotherapy was prescribed for about half (47%) of the RA patients and massage therapy and visits to chiropractors, osteopaths, and naturopaths were not uncommon. However, several evidence-based guidelines advocate that optimal management of RA involves more than pharmacologic therapy and that inclusion of such supportive treatment can enhance the overall health-related quality of life of patients. The underutilization and nonconformity with the guidelines can be probably due to lack of access and underestimation of their significance by practitioners. On literature review it was clearly shown that lack of expertise (Rheumatologist) was one of the factors for suboptimal management so I think that effect might be a contributing factor in our clinic during the study period.

7. Strength and Limitation

7.1 Strength

- The assessment of management among RA patients attending rheumatology care center is the first study to be conducted in this setting.
- The study was conducted in the biggest hospital in the country with a big catchment area.
- The fact that the study was a retrospective chart review in its nature and no patient was contacted physically, there was no concern of COVID-19 transmission during the process of data collection.

7.2 Limitation

- The study design was a cross-sectional, and hence it is challenging to make causal inferences and alternative explanations for the findings.
- The study relied on documentation to assess the diseases activity and majority of the physician used subjective methods, the clinical remission results are questionable.
- Physician related characteristics that would contribute to the suboptimal implementation of guideline-directed multidisciplinary care were not addressed in this study.
- The study is a single-centered study; therefore, it might not be generalizable to the general population where differing participants' characteristics, disease distribution, and healthcare infrastructure may exist.

8. Conclusion and Recommendation

8.1 Conclusion

Females are predominantly affected. Methotrexate was included in the regimen of most patients, and more than two-thirds received chloroquine. Overall, 48.7% were receiving both methotrexate and chloroquine concurrently. Use of baseline and follow up investigations were suboptimal. Deviations from the standard management of RA patients is a common observation in the study setting. The most frequently observed management gap is suboptimum use of DMARDs, use of steroids for extended duration, and underuse of non-pharmacological therapy such as physical therapy and psychological support.

8.2 Recommendation

Based on the findings of the study, the following recommendations are forwarded.

To health professionals

- Proper use of the available DMARDs with timely laboratory monitoring should be encouraged.
- Periodic review and ongoing access to the multidisciplinary team including specialist physiotherapy, specialist occupational therapy, and psychological interventions should be available to address the physical and psychosocial impact of rheumatoid arthritis, ensure appropriate medication, and equip the patient with the knowledge, skills, and resources to better cope with this debilitating disease.

To local health policy makers

- Customized guidelines should be designed, and sensitization and training programs should be considered to attain high-quality clinical care of RA patients.
- Efforts to make all types of DMARDs available to RA patients.

To researchers

- Future studies should be comprehensive enough to include potential factors such as “patient voice’’ via direct patient involvement and physician related characteristics that contribute to the suboptimal care.

References

1. Sokka T, Mottonen T, Hannonen P. Disease-modifying antirheumatic drug use according to the "sawtooth" treatment strategy improves the functional outcome in rheumatoid arthritis: results of a long-term follow-up study with review of the literature. Rheumatology (Oxford) 2000; 39:34 – 42.
2. Fries JF, Williams CA, Morfeld D, Singh G, Sibley J. Reduction in long-term disability in patients with rheumatoid arthritis by disease-modifying antirheumatic drug-based treatment strategies. Arthritis Rheum 1996;39:616 –22.
3. Abu-Shakra M, Toker R, Flusser D, Flusser G, Friger M, Sukenik S, et al. Clinical and radiographic outcomes of rheumatoid arthritis patients not treated with disease-modifying drugs. Arthritis Rheum 1998; 41:1190 –5.
4. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 Update. Arthritis Rheum 2002; 46:328 – 46
5. Munro R, Hampson R, McEntegart A, Thomson EA, Madhok R, Capell H. Improved functional outcome in patients with early rheumatoid arthritis treated with intramuscular gold: results of a five-year prospective study. Ann Rheum Dis 1998; 57:88 –93.
6. Tsakonas E, Fitzgerald AA, Fitzcharles MA, Cividino A, Thorne JC, M'Seffar A, et al. Consequences of delayed therapy with second-line agents in rheumatoid arthritis: a 3-year follow-up on the hydroxychloroquine in early rheumatoid arthritis (HERA) study. J Rheumatol 2000;27:623–9.
7. Van der Heide A, Jacobs JW, Bijlsma JW, Heurkens AH, van Booma-Frankfort C, van der Veen MJ, et al. The effectiveness of early treatment with "second-line" antirheumatic drugs: a randomized, controlled trial. Ann Intern Med 1996;124:699 – 707.
8. Lard LR, Visser H, Speyer I, vander Horst-Bruinsma IE, Zwinderman AH, Breedveld FC, et al. Early versus delayed treatment in patients with recent-onset rheumatoid arthritis: comparison of two cohorts who received different treatment strategies. Am J Med 2001; 111:446 –51.
9. Buckland-Wright JC, Clarke GS, Chikanza IC, Grahame R. Quantitative microfocal radiography detects changes in erosion area in patients with early rheumatoid arthritis treated with myocrisine. J Rheumatol 1993;20:243–7.

10. Egsmose C, Lund B, Borg G, Pettersson H, Berg E, Brodin U, et al. Patients with rheumatoid arthritis benefit from early 2ndline therapy: 5-year follow-up of a prospective double blind placebo-controlled study. J Rheumatol 1995; 22:2208 –13.
11. Pincus T, O'Dell JR, Kremer JM. Combination therapy with multiple disease-modifying antirheumatic drugs in rheumatoid arthritis: a preventive strategy. Ann Intern Med 1999;131: 768 –74.
12. Fries JF. Current treatment paradigms in rheumatoid arthritis. Rheumatology (Oxford) 2000;39 Suppl 1:30 –5.
13. Wollheim FA. Approaches to rheumatoid arthritis in 2000. Curr Opin Rheumatol 2001;13:193–201.
14. Lacaille D, Anis AH, Guh DP, Esdaile JM. Gaps in Care for Rheumatoid Arthritis: A population study. Arthritis & Rheumatism (Arthritis Care & Research). 2005;53(2):241–248.
15. Barber CEH, Marshall DA, Szefer E, Barnabe C, Shiff NJ, Bykerk V, et al. Population-based approach to reporting system-level performance measures for rheumatoid arthritis care.
16. Meisters R, Putrik P, Ramiro S, et al. Standards of care for rheumatoid arthritis: gaps in implementation experienced by patients and rheumatologists across 33 European countries. EULAR 2019; Madrid: Abstract OP0307
17. Kalla AA, Tikly M. Rheumatoid arthritis in the developing world. Best Pract Res Clin Rheumatol. 2003 Oct; 17(5):863-75.
18. Criswell KLA, Sems KM, Nettleman MD, Kolluri S. Low-dose corticosteroids in rheumatoid arthritis. A meta-analysis of their moderate-term effectiveness.
19. American college of rheumatology guideline for the treatment of rheumatoid arthritis 2015. Arthritis Rheumatol. 2016; 68: 1-26
20. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017; 76: 960-97.
21. Tapering glucocorticoids in rheumatoid arthritis. The Lancet, 396(10246), 218–219. doi:10.1016/s0140-6736(20)30761-3
22. Grigor C, Capell H, Stirling A, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TI CORA study): a single-blind randomised controlled trial. Lancet 2004; 364: 263-9.

23. Pincus T, Swearingen CJ, Bergman M, Yazici Y. R APID3 (Routine Assessment of Patient Index Data 3), a rheumatoid arthritis index without formal joint counts for routine care: proposed severity categories compared to disease activity score and Clinical Disease Activity Index categories. J. Rheumatol. 2008;35(11), 2136–47.
24. JASVINDER A. SINGH,1 KENNETH G. SAAG,1 S. LOUIS BRIDGES JR.,1 ELIE A. AKL,2 RAVEENDHARA R. BANNURU, (American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis),2015
25. Ohagwu KA, Olaosebikan H, Oba RB, Adelowo OO. Pattern of rheumatoid arthritis in Nigeria; study of patients from a teaching hospital. Afr J Rheumatol 2017;5(1):8-12.
26. Muia GM, Oyoo GO, Kitonyi GW, Wanzala P. Anaemia in patients with rheumatoid arthritis at the Kenyatta National Hospital, Nairobi, Kenya. Afr J Rheumatol. 2015; 3:27-33.
27. Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. Lancet. 2010; 376(9746):1094–1098.
28. Mody GM, Cardiel MH. Challenges in the management of rheumatoid arthritis in developing countries. Best Pract Res Clin Rheumatol. 2008; 22(4): 621–41.
29. Manara M, Bianchi G, Bruschi E, et al. Adherence to current recommendations on the use of methotrexate in rheumatoid arthritis in Italy: results from the MARI study. Clin Exp Rheumatol 2016; 34: 473-9.
30. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017; 76: 960-77.
31. Batko B, Korkosz M, Juś A, Wiland P. Management of rheumatoid arthritis in Poland – where daily practice might not always meet evidence-based guidelines. Arch Med Sci 2021; 17 (5): 1286–93.
32. Easterbrook M. An ophthalmological view on the efficacy and safety of chloroquine versus hydroxychloroquine. J Rheumatol 1999;26:1866–8.
33. Krüger K, Karberg K. “Treat-To-Target” aus der Sicht der niedergelassenen Rheumatologie. Z Rheumatol 2011;70: 664-9.

Annex

Annex I: Information sheet to the director of Tikur Anbessa Specialized Hospital
Department of Internal Medicine, College of Health Sciences, Addis Ababa University

This sheet will be read for the director of Tikur Anbessa Specialized Hospital before collecting any information from the registries.

Greetings. My name is Dr. Mastewal Belay and I am a postgraduate student in Internal Medicine at AAU.

This center was selected to conduct the proposed study "**Management profile of rheumatoid arthritis patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A two-year, retrospective chart review"** as it is leading center in the country dedicated to widespread health care services.

I am humbly requesting your esteemed office to give me permission to conduct the stated study in this hospital. Please read the following information for further understanding:

What the study is about: The purpose of this study to assess management profile of rheumatoid arthritis patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

What I will ask you to do: If you agree to facilitate the undertaking of this study; I will be using a pretested checklist that will include questions about background data and clinical characteristics. I would very much appreciate your cooperation in this study.

Risks and benefits: The result of the study is believed to help responsible body to advance the body of knowledge regarding the management profile of rheumatoid arthritis patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, which can be helpful to improve the overall rheumatology care.

Confidentiality: All information gathered from the participants will be kept confidential. Any of respondents' personal information will not be registered. The records of this study will be kept private. In any sort of public report, any information that will be making it possible to identify the participant will not be included. Research records will be kept in a locked file; only the researcher will have access to the records.

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Annex II: English Version Checklist

Addis Ababa University

Department of Internal Medicine

MRN	Age	Sex	address	Wt. OR BMI	Comorbid illness Type of comorbid illness	Any smoking history	RF and Anti-ccp status	Duration of symptom or classification criteria score (ACR/EULAR 2010 criteria)	hand and feet X-ray Base line chest X-ray Base line RFT and LFT CBC Viral markers ,retinal screen

NO	Questions	Yes	No
1	Is the patient on methotrexate		
2	Duration on methotrexate…		
3	Dose of methotrexate… 1. Starting dose if noted 2. Current dose		
4	Any change in the dose in last three months		
5	If no 4 is yes, is the dose increased?		
6	Is there a time a patient discontinue methotrexate in the past two years?		
7	If no 6 is yes, what is the reason?		
8	Is chloroquine prescribed?		
9	If no 8 is yes, is it prescribed as monotherapy?		
10	Is NSAID prescribed? Does any pain medication prescribed and what pain medication is prescribed?		
11	If no 10 is yes, for how long the patient take it?		
12	Is glucocorticoid prescribed?		

13	If no 12 is yes, what is the dose?		
14	Duration on glucocorticoid therapy?		
15	Any change on the dose? Increased or decreased?		
16	Is glucocorticoid given in other than po route? Like intra articular		
17	Is glucocorticoid given with other DMARD?		
18	If no 17 is yes, which DMARD is given?		
19	Any other csDMARD?		
20	Any biological DMARD use?		
21	Any tsDMARD use?		
22	Is baseline ESR known?		
23	How many ESR Determination in the past three months?		
24	CRP determination in the past three months?		
25	Is LFT determined in the past 3 months?		
26	Does the patient have any medication side effect?		
27	If no 26 is yes, which medication?		

28	If no 26 is yes, what are/is the side effect/s			
29	How was the diseases activity followed?	Subjective assessment	Functional activity of the patient	Objective assessment
30	If the assessment is objective, what method is used for functional assessment	CDAI		RAPID3 Any other, specify
31	Does the patient achieve clinical remission or low disease activity in the past three months?			
32	If number 30 is no, what is diseases activity?	High activity		Moderate disease activity
33	How frequent is the patient followed within 6 months after diagnosis?			
34	How frequent is the patient followed after 6 months of diagnosis?			
35	Does the patient have any extra-articular manifestation?			
36	If no 36 is yes, what is/are the features?			
37	Does the patient prescribe any physical therapy?			
38	Any assistive devise uses?			
39	Any cognitive behavioral therapy prescribed?			

40	Does the patient have fibromyalgia?		
41	If number 41 is yes, what is the disease activity?		
42	Any surgery done?		
43	Any rheumatologist involvement in the management?		

Data collector name

Signature