

## Opportunities for Prescribers to Be Effectively Engaged In the Model of ‘Shared-Care’ Treatment of Rheumatoid Arthritis. A Cross-Sectional Study from Pakistan.

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### Abstract

**Aim:** This descriptive, cross-sectional study aimed to explore the perceptions and knowledge of prescribers in Islamabad and Rawalpindi cities towards adherence to standard treatment guidelines for rheumatoid arthritis.

**Method:** A semi-structured questionnaire was distributed to a random sample of sample of 382 prescribers specifically treating rheumatoid arthritis. The data were collected, computed and analyzed using SPSS, version 16 program and descriptive analysis was conducted. The Kruskal–Wallis and Mann–Whitney tests ( $P \leq 0.05$ ) were used to compare the knowledge scores of prescribers about standard rheumatoid arthritis regimens by profession, length of experience, type of health-care facility, gender, sector and city.

**Results:** A majority of prescribers were of the view that patient-related factors (63.62%), availability of STGs for reference (19.12%), lack of awareness of prescribers regarding STGs (68.07%), prescribers' experience (62.06%) and lack of enforcement of STGs (65.4.5%) were the main factors contributing towards lack of adherence to STGs in the management of rheumatoid arthritis in Pakistan. Most of the prescribers were of the view that indomethacin (76.43%) and ibuprofen (68.84%) were the most effective NSAID and methotrexate (82.72%) and prednisolone (77.48%) as disease modified anti rheumatoid drugs and steroids in management of rheumatoid arthritis.

**Conclusion:** The overall knowledge of prescribers regarding standard treatment regimens for rheumatoid arthritis in the 2 cities of Pakistan was moderate. More than half of the prescribers were aware of correct standard treatment regimens of NSAIDs and DMARDs used in the management of arthritis. Prescribers working as general practitioners possessed comparatively better knowledge than their counterparts.

**Keywords:** Knowledge, perceptions, prescribers, general practitioners, rheumatoid arthritis, Pakistan.

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### I. Introduction

Rheumatoid arthritis has been ranked among the 40<sup>th</sup> leading cause of disability across the world(1). It is a chronic inflammatory condition of multiple joints that primarily attacks synovial joints, leading to articular destruction and functional disability resulting in decreased quality of life and premature disability (2-4). Cultural and economic differences between societies affect work disability as an outcome measure for RA (5). Work disability rates remain high among people living in developing countries but they remain working with high levels of disability and disease activity. Treatment of RA is costly. The direct and indirect estimated cost of RA reported per year is approximately \$26–\$32 billion in USA and £4 billion in UK (6)(7). Early diagnosis plays a crucial role by reducing further progression of the disease. Guidelines for management of RA demands early diagnosis within three month. Most patients ignore the early sign and symptoms of RA. Optimal management require early detection of disease and continuous monitoring of remission of disease that reduces long term joint damage and improve functional outcomes (8, 9). Guidelines are designed by converting research and expert opinion into recommendations for everyday practice, but health care providers are often slow to incorporate these guidelines into their daily treatment practices. Unfortunately, guidelines are not routinely followed. Several studies have reported low compliance of prescribers with standard treatment guidelines (4, 10, 11). The reasons for suboptimal adherence to published guidelines might be due to the shortage of rheumatologists and lack of awareness of other prescribers to these guidelines as compared to rheumatologists (12). Although, rheumatologists in some countries tend to follow most of the guidelines but they are deficit in managing non pharmacological care like occupational therapy and patient counseling which can reduce the rate of hospital admissions (13). Rheumatoid arthritis is neglected in term of specific treatment and most of these patients are treated by GP's and primary care physicians due to inadequate number of rheumatologists in Pakistan. This

study will be the first ever study conducted in Pakistan to the best of our knowledge which will assess the current prescribing trends and adherence to standard treatment guidelines for the management of rheumatoid arthritis. Thus, the main objective of the study was to assess the knowledge and perceptions of prescribers towards adherence to standard treatment guidelines for rheumatoid arthritis in twin cities of Pakistan.

## II. Methodology

### Study design

A descriptive, cross-sectional study design was used to evaluate the knowledge and perceptions of prescribers regarding adherence to standard treatment regimen for rheumatoid arthritis in the 2 major cities of Pakistan: Islamabad (the national capital) and Rawalpindi (its twin city). Approval was obtained for the study from the Ethical Committee of Hamdard University. Moreover in Pakistan, questionnaire-based studies do not need any Ministry of Health endorsement. Despite that, prior information was sent to the Ministry of Health, Government of Pakistan for the execution of this research among prescribers practicing in the twin cities. Beside this, approval for the data collection was also taken from MS of the respective hospitals.

### Sampling of facilities and respondents

This study was conducted from May to July 2015. The study population included prescribers from Islamabad and Rawalpindi. Calculations of sample size were performed using *Raosoft* R sample size calculator to determine the size of sample that represents the population of registered prescribers [15]. Considering the current population of registered prescribers ( $N = 5615$ ), a sample size of 382 was required to achieve 95% confidence level with 5% margin of error. A sample of 382 prescribers specifically treating rheumatoid arthritis was selected randomly from the 2 cities. The prescribers were contacted and given an explanation of the purpose of the study, and their verbal consent to participate in the study was obtained. None of the prescribers refused to participate in the study.

### Study tool

A questionnaire was developed through focus group discussions by using the WHO standard treatment guideline for treatment of rheumatoid arthritis as a reference. Two focus group discussions were carried out at different time intervals with 4 different groups of experts including clinicians, specialists, physicians and doctors from academia. Each group comprised 3–4 participants for the development, finalization, face and content validity of the data collection tool. Pilot testing was carried out on 38 prescribers (10%) of the total sample size before beginning the final study. A Cronbach alpha value of 0.692 confirmed the reliability and internal consistency of the questionnaire.

The questionnaire comprised 5 sections. The first section included information regarding prescriber's demographic characteristics: gender, city, sector (public/private), type of health facility, profession and years of experience. In the second section, perceptions of prescribers regarding current treatment practices for rheumatoid arthritis in the country were explored. In the third section the perceptions of prescribers regarding contributing factors towards lack of adherence to STGs were explored, including patient-related factors, availability and accessibility of the guidelines for reference, prescriber's experience/personal preference and lack of guideline enforcement. Sections 2 and 3 of the questionnaire included a set of statements in which respondents were asked to indicate their level of agreement using a 5-point Likert scale where 1 = strongly disagree, 2 = disagree; 3 = neutral, 4 = agree and 5 = strongly agree was used. In the fourth section, the perceptions of prescribers regarding the effectiveness of different currently available NSAIDs and disease modified anti rheumatoid drugs and steroids were explored. In the last section, the knowledge of prescribers regarding standard treatment regimens for NSAIDs and disease modified anti rheumatoid drugs and steroids was assessed in 2 subscales. Responses were assigned as 1 = yes/correct and 2 = no/incorrect. Subscale 1 included 5 questions regarding standard treatment regimens for NSAIDs (score 5–10) while subscale 2 included 5 questions regarding standard treatment regimens for disease modified anti rheumatoid drugs and steroids (score 5–10). The composite score range was 10–20 and a lower score indicated better knowledge.

### Data collection

Two teams, one in each city, with 10 data collectors in each team, were trained by the group of experts including the principal investigator. The questionnaire was hand-delivered to prescribers by the data collectors. Informed and verbal consent for participation was taken from the respondents. Respondents were assured about the confidentiality of information verbally and were shown an undertaking signed by the principal investigator. The questionnaire was self-completed by the prescribers and was collected from them on the same day.

### Data analysis

The data were computed and analyzed using *SPSS*, version 16 program and descriptive analysis was conducted. The results of each item in the questionnaire were reported as percentages and frequencies. The

Kruskal–Wallis test ( $P \leq 0.05$ ) was used to compare the knowledge scores of prescribers about standard rheumatoid arthritis regimens by profession, length of experience and type of health-care facility, and the Mann–Whitney test ( $P \leq 0.05$ ) was used to compare the knowledge of prescribers by gender, sector and city.

### III. Results

#### Background characteristics

Out of 382 prescribers, 58.38 % were male while 41.62 % were female. Just over two-thirds (61.26%) of the total prescribers were working in the public sector, while 38.74 % were from the private sector. A total of 67.80 % were working in tertiary health-care facilities (providing specialized health care in large research and teaching hospitals), 16.23 % in secondary health-care facilities (Tehsil headquarters and district headquarter hospitals), 1.32 % in basic health units (providing primary health care services including health protection and promotion services) and 14.65 % were from private clinics. Of the total prescribers 31.68 % were house officers, 41.62% medical officers, 15.96% specialists and 10.74% general practitioners. Regarding the experience of the prescribers, 43.72% had working experience of < 1 year, 36.13% had 1–5 years, 8.11% had 6–10 years and 12.04% had > 10 years (Table 1).

**Table 1 Background characteristics of the sample of prescribers (n = 382)**

Variable	n (%)
<b>Gender</b>	
Male	223 (58.38)
Female	159 (41.62)
<b>Sector</b>	
Public	234 (61.26)
Private	148 (38.74)
<b>Type of health facility</b>	
Tertiary hospital	259 (67.80)
Secondary hospital	62 (16.23)
Basic health unit	5 (1.32)
Private clinic	56 (14.65)
<b>Profession</b>	
House officer	121 (31.68)
Medical officer	159 (41.62)
Specialist	61 (15.96)
General practitioner	41 (10.74)
<b>Experience (years) in treating arthritis</b>	
< 1	167 (43.72)
1–5	138 (36.13)
6–10	31 (8.11)
> 10	46 (12.04)

#### Opinions regarding management of arthritis in Pakistan

The results highlighted that 48.42 % of the prescribers were satisfied with the currently available drugs for the treatment of arthritis and 48.17% agreed that prescribing anti-arthritis drugs before performing a diagnostic test was beneficial in the management of arthritis. More than half of the respondents 61.78% agreed that prescribing from the STGs was cost-effective. The great majority of prescribers (90.32 %) agreed that there was a need for more educational programs to increase knowledge and awareness about the available treatment guidelines for arthritis (Table 2).

**Table 2 Prescribers' opinions regarding management of arthritis in Pakistan**

Item	Prescribers' opinions (n = 382)		
	Strongly disagree + disagree n (%)	Neutral n (%)	Strongly agree + agree n (%)
Rheumatoid Arthritis in patients is well controlled with current available medicine in Pakistan health care system. What is your opinion on the statement?	96 (25.14)	101 (26.44)	185 (48.42)
In your opinion, do you think prescribing medicine before performing diagnostic test is beneficial in the management of early arthritis?	158 (41.36)	40 (10.47)	184 (48.17)
Do you agree that prescribing medicine for rheumatic arthritis according to the guidelines is cost effective?	68 (17.80)	78 (20.42)	236 (61.78)
In your opinion, there is a need for more educational programs to increase knowledge & awareness on the available guidelines?	11 (2.88)	26 (6.80)	345 (90.32)
Do you think methotrexate besides a lot of side effect, is effective in treatment of rheumatoid arthritis?	17 (4.45)	52 (13.61)	313 (81.94)

**Factors affecting lack of adherence to standard treatment guidelines**

A majority of prescribers were of the view that patient-related factors (63.62%), availability of STGs for reference (19.12%), lack of awareness of prescribers regarding STGs (68.07%), prescribers' experience (62.06%) and lack of enforcement of STGs (65.4.5%) were the main factors contributing towards lack of adherence to STGs in the management of rheumatoid arthritis in Pakistan (Table 3).

**Table 3 Prescribers' perceptions about factors affecting adherence to standard treatment guidelines (STGs) in management of rheumatoid arthritis in Pakistan**

Factor	Prescribers' opinions (n = 382)		
	Strongly disagree n (%)	Neutral n (%)	Strongly agree n (%)
Patient related factors	66 (17.28)	73 (19.10)	243 (63.62)
Availability & accessibility of the guidelines for reference	233 (60.99)	76 (19.89)	73 (19.12)
Lack of awareness on guideline availability	64 (16.75)	58 (15.18)	260 (68.07)
Prescribers experience/ personal preference	64 (16.76)	81 (29.58)	237 (62.06)
Lack of guidelines enforcement	63 (16.49)	69 (18.06)	250 (65.45)

**Effectiveness of different available NSAIDs and disease modified anti rheumatoid drugs and steroids for treatment of rheumatoid arthritis**

Most of the prescribers were of the view that indomethacin (76.43%) and ibuprofen (68.84%) were the most effective NSAID and methotrexate (82.72%) and prednisolone (77.48%) disease modified anti rheumatoid drugs and steroids in management of rheumatoid arthritis. While aspirin (38.21%) and paracetamol (41.09%) were considered as the least effective NSAID and chloroquine phosphate (48.69%) as least effective disease modified anti rheumatoid drugs and steroids in management of rheumatoid arthritis (Table 4).

**Table 4 Prescribers' perceptions about effectiveness of different NSAIDs and disease modified anti rheumatoid drugs and steroids in management of rheumatoid arthritis in Pakistan**

Drugs	Effective n (%)	Least Effective n (%)
<b>NSAIDS used in the treatment of Rheumatic arthritis</b>		
Aspirin	146 (38.21)	236 (61.79)
Aspirin +cimetidine	163 (42.67)	219 (57.33)
Paracetamol	157 (41.09)	225 (58.92)
Ibuprofen	263 (68.84)	119 (31.16)
Indomethacin	292 (76.43)	90 (23.57)
<b>Disease Modifying Anti Rheumatic Drugs and steroids used in the treatment of Rheumatic arthritis</b>		
Chloroquine phosphate	186 (48.69)	196 (51.31)
Methotrexate	316 (82.72)	66 (17.28)
Azathioprine	247 (64.65)	135 (35.35)
Prednisolne	296 (77.48)	86 (22.52)
Methyl prednisolone acetate	274 (71.72)	108 (28.28)

**Prescribers' knowledge about standard treatment regimens**

Nearly half of the prescribers were aware of the correct standard treatment regimens for NSAIDS and disease modifying anti rheumatic drugs and steroids used in the treatment of rheumatic arthritis. Fifty percent of the prescribers were aware about the correct regimen for aspirin and 72.25 % knew the correct regimen for ibuprofen. On the other hand, 79.31% knew the correct regimen for methotrexate and 59.68 % were aware about the regimen for chloroquine phosphate used for treatment of rheumatoid arthritis (Table 5).

**Table 5 Prescribers' knowledge about standard treatment regimens for rheumatoid arthritis**

Drugs	Correct n (%)	Incorrect n (%)
<b>NSAIDS used in the treatment of Rheumatic arthritis</b>		
Aspirin 600-1200mg TID	192 (50.26)	190 (49.74)
Aspirin +cimetidine 600+200 mg TID	204 (53.40)	178 (46.60)
Paracetamol 500-1000 mg TID	193 (50.52)	189 (49.48)
Ibuprofen 400-800 mg TID	276 (72.25)	106 (27.75)
Indomethacin 25-50 mg TID	244 (63.87)	138 (36.13)
<b>Disease Modifying Anti Rheumatic Drugs and steroids used in the treatment of Rheumatic arthritis</b>		
Chloroquine phosphate 150-300 mg P.O daily	228 (59.68)	154 (40.32)
Methotrexate 7.5 mg P.O weekly	303 (79.31)	79 (20.69)
Azathioprine 100-150 mg/day	224 (58.63)	158 (41.37)
Prednisolne 30-40 mg P.O.QD	252 (65.96)	130 (34.04)
Methyl prednisolone acetate 20-80 mg intra-articular	264 (69.10)	118 (30.90)

The composite scores for knowledge were taken into account when assessing the knowledge of prescribers for the whole therapeutic regimen. The median score for overall knowledge of prescribers regarding the rheumatoid arthritis treatment regimen was 14 (range 10-20), for the NSAID treatment regimen it was 7 (range 5-10) and for disease modifying anti rheumatic drugs and steroids regimen it was 7 (range 5–10). Significant differences ( $P < 0.05$ ) were found among the knowledge scores of different professions of prescribers, while no significant differences ( $P < 0.05$ ) were found between the genders, city, sector, different level of experience. Prescribers working as GP had significantly better knowledge than other professionals (Table 6).

**Table 6 Comparison of prescribers’ knowledge scores about standard treatment regimen for rheumatoid arthritis by demographic characteristics**

Variable	Group 1				Group 2				Group 3			
	n	Median knowledge score	Test Statistics	P-value	n	Median knowledge score	Test Statistics	P-value	n	Median knowledge score	Test Statistics	P-value
<b>Gender</b>												
Male	222	7	16382.50	0.221	222	7	16911.50	0.431	222	14	17343.00	0.771
Female	159	7			159	7			159	14		
<b>Sector</b>												
Public	233	7	17038.50	0.842	233	7	16677.50	0.533	233	14	16918.00	0.755
Private	148	7			148	7			148	14		
<b>City</b>												
Islamabad	126	7	14847.50	0.218	126	7	15456.00	0.497	126	14	14787.00	0.203
Rawalpindi	255	7			255	7			255	14		
<b>Location</b>												
Tertiary	259	7			259	7			259	14		
Secondary	62	7	2.634	0.451	62	7			62	14		
Primary	5	8			5	7	1.326	0.723	5	14	1.367	0.713
Clinic	56	7			56	7			56	13.50		
<b>Profession</b>												
Specialist	61	7			61	7			61	14.50		
Medical Officer	159	7	2.192	0.534	159	7	8.186	0.042	159	14	5.549	0.136
House Officer	121	7			121	7			121	13		
GP	41	7			41	6			41	14		
<b>Experience (years)</b>												
< 1	167	7			167	7			167	13		
1–5	138	7	2.406	0.492	138	7	3.887	0.274	138	14	4.211	0.240
6–10	31	7			31	7			31	14		
> 10	46	7			46	7			46	14		

a. Mann–Whitney test; b. Kruskal–Wallis test.

#### IV. Discussion

Most of the medical practitioners in developing countries including Pakistan are often slow to incorporate standard treatment guidelines into their daily practices that might lead to inapt treatment of disease. The results of the present study showed that majority of prescribers believed that patient-related factors, unavailability of STGs for reference, lack of awareness of prescribers regarding STGs, prescribers’ experience and lack of enforcement of STGs as the main factors contributing towards lack of adherence to STGs in the management of rheumatoid arthritis in Pakistan. The results of the present study are in line with the other studies which showed similar findings highlighting unavailability of information to doctors and the public about disease and drugs, the content and context of guidelines, the format of the guidelines, inertia of past experience, the doctor- patient relationship, lack of staff support and practical related issues as few of the barriers towards lack of adherence to guidelines in the management of arthritis (14-16).

The results of the present study showed that nearly half of the prescribers were satisfied with the currently available drugs for the treatment of arthritis. Most of them agreed that prescribing anti-arthritis drugs from STGs and early treatment could be cost-effective and beneficial in the management of arthritis. Similarly findings from other studies highlighted that early detection and treatment of disease can improve functional outcomes and reduce long term joint damage (9). Early treatment of rheumatoid arthritis with DMARDs can decrease disease progression, however, only few months delay to institution of therapy can result in low response of the single-drug strategy (17). Awareness regarding early diagnosis and treatment guidelines must be promoted among prescribers.(18).

Indomethacin and ibuprofen were considered as the most effective NSAIDs while methotrexate and prednisolone as the most effective disease modified anti rheumatoid drugs and steroids for the management of rheumatoid arthritis in Pakistan according to most of the study respondents. The results of the present study are in line with other studies which showed effective predominant use of ibuprofen and methotrexate for improved patient outcomes (19). The current study reported that aspirin and chloroquine phosphate were considered as the least effective NSAID and disease modified anti rheumatoid drug and steroid by most of the respondents in the management of rheumatoid arthritis. The results are in line with the findings of the studies which reported that aspirin and bed rest were effective treatment for arthritis in the past but during the mid-1980s it was recognized from clinical cohorts that most patients experienced severe functional declines, work disability radiographic

progression and mortality later as aspirin possess short-term efficacy in management of rheumatoid arthritis (20-23).

The overall knowledge of prescribers regarding standard treatment regimens for NSAIDs and disease modifying anti rheumatic drugs and steroids was moderate in Pakistan. More than half of the prescribers were aware regarding the correct regimen for NSAIDs and DMARDs. The results of the study are in line with the findings of the study conducted in Germany which showed that most of the German rheumatologists were fully aware and were following the recent standard treatment guidelines. However, they were not well acknowledged in managing non pharmacological care like occupational therapy and patient counseling in order to reduce the hospital admission rates (13).

The present study reported no differences among the knowledge of different genders of prescribers, working in different cities, healthcare facilities and with different level of experiences. However, prescribers working as GP had significantly better knowledge than their counterparts. This might be due to the fact that most of the specialists are working as general practitioners running their own private clinics in the evening in Pakistan. General practitioners are usually the main prescribers of anti-rheumatic drugs due to the ease of access to their services and affordability for a large proportion of the population. The study findings are in line with another study which highlighted the need for training of GPs for early diagnosis skills and introduced them to shared care model of RA between primary care doctors/nurses and rheumatologists to prevent patient disability (24).

Almost all of the prescribers in the present study were of the view that there is a need for more educational programs to increase knowledge and awareness about the available treatment guidelines for arthritis. Only educational programs designed to fill the gaps in knowledge for improving adherence to guidelines are not enough. Intervention are also required that include increased continuing education programs for the standardization of rheumatologist care with respect to early referral, regular check-up, adjustment of treatment, and filling of prescriptions to prevent patient disability.

## V. Conclusion

The overall knowledge of prescribers regarding standard treatment regimens for rheumatoid arthritis in the 2 cities of Pakistan was moderate. More than half of the prescribers were aware of correct standard treatment regimens of NSAIDs and DMARDs used in the management of arthritis. Prescribers working as general practitioners possessed comparatively better knowledge. This indicates the potential of general practitioners to be engaged in the model of 'shared-care' of rheumatoid arthritis between primary care and rheumatologists in order to overcome the problem of shortage of rheumatologists in the country. This can lead to better cost-effective practices for the management of rheumatoid arthritis in Pakistan.

## Limitations

The study was conducted in only 2 cities of Pakistan and the results of the study may not be generalizable to other parts of the country. Financial and logistic constraints and political turmoil in the country were some of the problems faced during the conduct of the study.

## Conflict of interest

The authors declare no conflict of interest.

## References

- [1]. Mathers DSC, Pflieger B. The global burden of rheumatoid arthritis in the year 2000. *Criterion*.1(2).
- [2]. Hui M, Ding T, Deighton C. Anti-TNF therapy in rheumatoid arthritis: the role of primary care. *Prescriber*. 2010;21(9):48-52.
- [3]. Smolen JS, Aletaha D, Bijlsma JW, Breedveld FC, Boumpas D, Burmester G, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. *Annals of the rheumatic diseases*. 2010;69(4):631-7.
- [4]. Westhoff G, Schneider M, Raspe H, Zeidler H, Runge C, Volmer T, et al. Advance and unmet need of health care for patients with rheumatoid arthritis in the German population—results from the German Rheumatoid Arthritis Population Survey (GRAPS). *Rheumatology*. 2009;48(6):650-7.
- [5]. Sokka T, Kautiainen H, Pincus T, Verstappen SM, Aggarwal A, Alten R, et al. Work disability remains a major problem in rheumatoid arthritis in the 2000s: data from 32 countries in the QUEST-RA study. *Arthritis research & therapy*. 2010;12(2):R42.
- [6]. Kamal KM, Madhavan SS, Hornsby JAA, Miller L-A, Kavookjian J, Scott V. Use of tumor necrosis factor inhibitors in rheumatoid arthritis: a national survey of practicing United States rheumatologists. *Joint Bone Spine*. 2006;73(6):718-24.
- [7]. Clarke AM, Symmons DP. The burden of rheumatic disease. *Medicine*. 2006;34(9):333-5.
- [8]. Roberts L, Cleland L, Thomas R, Proudman S. Early combination disease modifying antirheumatic drug treatment for rheumatoid arthritis. *Medical journal of Australia*. 2006;184(3):122-5.
- [9]. Suter LG, Fraenkel L, Holmboe ES. What factors account for referral delays for patients with suspected rheumatoid arthritis? *Arthritis care & research*. 2006;55(2):300-5.
- [10]. Kitamura CR, Rohekar G, Bykerk VP, Carette S. Are the 2002 American College of Rheumatology guidelines for the management of rheumatoid arthritis being followed in Canada's largest academic rheumatology center? *The Journal of rheumatology*. 2007;34(11):2183-92.

- [11]. Kalla AA, Tikly M. Rheumatoid arthritis in the developing world. *Best Practice & Research Clinical Rheumatology*. 2003;17(5):863-75.
- [12]. Wall GC, Koenigsfeld CF, Hegge KA, Bottenberg MM. Adherence to treatment guidelines in two primary care populations with gout. *Rheumatology international*. 2010;30(6):749-53.
- [13]. Zink A, Listing J, Niewerth M, Zeidler H. The national database of the German Collaborative Arthritis Centres: II. Treatment of patients with rheumatoid arthritis. *Annals of the rheumatic diseases*. 2001;60(3):207-13.
- [14]. Ansari M, Shlipak MG, Heidenreich PA, Van Ostaeyen D, Pohl EC, Browner WS, et al. Improving Guideline Adherence A Randomized Trial Evaluating Strategies to Increase  $\beta$ -Blocker Use in Heart Failure. *Circulation*. 2003;107(22):2799-804.
- [15]. Lugtenberg M, Burgers JS, Besters CF, Han D, Westert GP. Perceived barriers to guideline adherence: a survey among general practitioners. *BMC family practice*. 2011;12(1):98.
- [16]. Lugtenberg M, Zegers-van Schaick JM, Westert GP, Burgers JS. Why don't physicians adhere to guideline recommendations in practice? An analysis of barriers among Dutch general practitioners. *Implement Sci*. 2009;4(54):5908-4.
- [17]. Möttönen T, Hannonen P, Korpela M, Nissilä M, Kautiainen H, Ilonen J, et al. Delay to institution of therapy and induction of remission using single-drug or combination-disease-modifying antirheumatic drug therapy in early rheumatoid arthritis. *Arthritis & Rheumatism*. 2002;46(4):894-8.
- [18]. Aletaha D, Eberl G, Nell V, Machold K, Smolen J. Practical progress in realisation of early diagnosis and treatment of patients with suspected rheumatoid arthritis: results from two matched questionnaires within three years. *Annals of the rheumatic diseases*. 2002;61(7):630-4.
- [19]. Puolakka K, Kautiainen H, Möttönen T, Hannonen P, Korpela M, Julkunen H, et al. Impact of initial aggressive drug treatment with a combination of disease-modifying antirheumatic drugs on the development of work disability in early rheumatoid arthritis: a five-year randomized followup trial. *Arthritis & Rheumatism*. 2004;50(1):55-62.
- [20]. Singh JA, Furst DE, Bharat A, Curtis JR, Kavanaugh AF, Kremer JM, et al. 2012 Update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis care & research*. 2012;64(5):625-39.
- [21]. WHO. standard treatment guideline for primary hospital. First edition ed2010.
- [22]. WHO. Standard Treatment Guidelines for Primary Hospital. Third edition ed2014.
- [23]. Yood RA. Guidelines ACoRSORA. Guidelines for the management of rheumatoid arthritis: 2002 update. 2002.
- [24]. Feldman DE, Bernatsky S, Haggerty J, Leffondre K, Tousignant P, Roy Y, et al. Delay in consultation with specialists for persons with suspected new-onset rheumatoid arthritis: A population-based study. *Arthritis Care & Research*. 2007;57(8):1419-25.