

Original Research Article

Perceptions of primary care physicians about early diagnosis of rheumatoid arthritis and methotrexate monitoring

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ABSTRACT

Background: Current guidelines recommend the early recognition and diagnosis of rheumatoid arthritis and treatment with disease-modifying antirheumatic drugs (DMARDs). Methotrexate is the first drug of choice for most patients with rheumatoid arthritis, but this medication has contraindications and side effects that need monitoring. This survey analysis aims to explore the level of knowledge of primary healthcare physicians towards the early detection of rheumatoid arthritis and monitoring treatment with methotrexate.

Methods: A self-administered structured questionnaire was distributed to primary healthcare physicians in the region of Riyadh, Saudi Arabia. The survey consists of sections including the demographics of respondents, knowledge about rheumatoid arthritis, and methotrexate. Data were analyzed using SPSS version 22.

Results: In total, 249 physicians responded to the survey. Physicians with more years of experience showed a significantly higher level of knowledge about rheumatoid arthritis and methotrexate monitoring (p-value <0.001). The responses of physicians regarding knowledge about the disease were better than their responses about the drug.

Conclusions: The knowledge of primary healthcare physicians in Riyadh, Saudi Arabia, is considered satisfactory in regard to rheumatoid arthritis diagnosis, but the level of knowledge about methotrexate requires improvement.

Keywords: Knowledge, Methotrexate, Perceptions, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disorder that causes symmetrical polyarthritis of large and small joints. Typically, it presents between the ages of 30 and 50 years. It affects about 25 men and 54 women per 100,000 people and is responsible for 250,000 hospitalizations and 9 million physician visits in the US each year.¹⁻³ The causes of RA are not fully understood but include a complex interplay

of environmental and genetic factors. Genetics also plays a role in the severity of the disease. A triggering event, possibly an autoimmune or infectious event, initiate's inflammation of the joints.²

The diagnosis of RA is mainly clinical. The typical presentation is polyarticular with pain, stiffness, and swelling of multiple joints in a bilateral, symmetric pattern. A minority of patients present with oligoarticular asymmetric involvement.⁴ The attack is usually insidious,

with joint symptoms emerging over weeks to months and often accompanied by anorexia, weakness, or fatigue.⁵ Individuals usually suffer from morning stiffness that lasts for more than an hour.

Generally, the joints involved are the wrist, proximal interphalangeal, metacarpophalangeal, and metatarsophalangeal joints, while distal interphalangeal joints and spinal joints are usually spared.⁶ Typical examination findings include swelling, boggy, tenderness, and warmth of the joints involved, along with atrophy of the muscles near them. Weakness is out of proportion to tenderness.⁷ Rarely, RA patients may present with single joint involvement or severe systemic symptoms of fever, weight loss, lymphadenopathy, and multiple organ involvement such as lung or heart.⁸

There is no single test that confirms the diagnosis RA. Initial laboratory tests should include a complete blood cell count with the differential, rheumatoid factor, and erythrocyte sedimentation rate or C-reactive protein.⁹ Rarely, joint aspiration may also be required to rule out infectious or crystal-induced arthritis, especially with monoarticular presentations. Baseline renal and hepatic function tests are recommended to guide medication choices.¹⁰

Methotrexate is a synthetic Disease-Modifying Anti-Rheumatic Drug (sDMARD) that is recommended and widely used in many rheumatological diseases, such as RA, psoriatic arthritis, and systemic lupus erythematosus.⁷ Methotrexate is a relatively well-tolerated and effective drug for the treatment of RA. Early initiation of methotrexate can minimize joint deformities and functional disability, as well as decrease the incidence of cardiovascular events in RA patients.¹¹

The most common adverse effects of methotrexate are hepatotoxicity, gastrointestinal upset, and infections. These effects can be reduced with the administration of folic acid, which also reduces withdrawal from methotrexate therapy. Because of the potential toxicities of methotrexate, it should be monitored by regular blood tests and clinical follow-up. Therefore, the aim of this study is to estimate the perception of primary care physicians in the early diagnosis of RA and methotrexate monitoring in Riyadh, Saudi Arabia.

METHODS

This cross-sectional, qualitative, prospective study was carried out in Riyadh, Saudi Arabia. The study surveyed local primary care physicians to identify their perceptions and practices and to establish how RA patients’ diagnosis and treatment could be improved. A survey was administered and included socio-demographic data such gender, years of experience, and marital state. There were 21 questions regarding perception and knowledge about RA diagnosis, methotrexate use, and its side effects. We also asked about the frequency of lab checks and the

safety of methotrexate use during pregnancy. Only participants who filled out the survey completely were included in the analysis.

Data collection

There is a total of 792 registered primary care physicians with the ministry of health in Riyadh city, who serve a population of around 7 million.¹² A self-developed online questionnaire was distributed through email. Non-responders were emailed again after four weeks. The required sample size was calculated as 75.

Statistical analysis

Data are represented in terms of frequencies and valid percentages for categorical variables. ANOVA was used to compare means among different groups. p values <0.05 were considered statistically significant. IBM SPSS (Statistical Package for the Social Science version 21 for Microsoft Windows; IBM Corp, Armonk, NY, USA) was used to perform all statistical calculations.

Ethical considerations

Confidentiality was assured for all participants. The respondents were given a brief description of the study and its objectives.

RESULTS

There were 249 (31.4%) physicians who responded to the online questionnaire. The mean age of the participants was 32.73±10.489 years with a maximum age of 60 years. Males constituted 53.4% of the participants, while 46.6% were female. The years of experience were also evaluated: 47.8% had less than 4 years of experience, while 14.1% had 6 to 10 years of experience. All socio-demographic data are shown in detail in Table 1.

Table 1: Socio-demographic characteristics of participants.

		Frequency (N)	Percent (%)
Gender	Female	116	46.6
	Male	133	53.4
Experience	0-3	119	47.8
	4-6	43	17.3
	6-10	35	14.1
	>10	50	20.1
Marital status	Married	160	64.3
	Single	89	35.7

Participants were also asked questions about the diagnosis and presentation of RA. The physicians had to choose from three possible answers: “Yes,” “No,” and “I don’t know.” More than half of the physicians had

answers that reflect a good level of knowledge about the disease, as shown in Table 2.

Table 2: Responses of physicians on knowledge about RA as percentages.

	I don't know	No	Yes
RA may resemble other forms of inflammatory arthritis	1.6	16.5	81.9
No single test can confirm RA	2.4	2.8	41
To make a proper diagnosis, the rheumatologist will ask questions about personal and family medical history, perform a physical exam and order diagnostic tests	0	1.2	98
Examine each joint, looking for tenderness, swelling, warmth and painful or limited movement is important in the diagnosis of RA	4.4	6.8	87.1
The blood tests will measure inflammation levels and look for biomarkers such as antibodies (blood proteins) linked with RA	0	1.2	98.8
Erythrocyte sedimentation rate (ESR, or "sed rate") and C-reactive protein (CRP) level are markers of inflammation related to RA	5.6	24.1	70.3
A high ESR or CRP is not specific to RA, but when combined with other clues, such as antibodies, helps make the RA diagnosis	1.6	3.6	94
Rheumatoid factor (RF) is an antibody found in about 80 percent of people with RA during the course of their disease.	20.5	13.3	63.5
Anti-cyclic citrullinated peptide (anti-CCP) – occurs primarily in patients with RA	22.9	11.2	64.7
An X-ray, ultrasound, or magnetic resonance imaging scan may be done to look for joint damage, such as erosions – a loss of bone within the joint – and narrowing of joint space	6.4	10	81.9

Moreover, the physicians were asked about their knowledge of methotrexate use, its side effects, and monitoring. Again, physicians had to choose from three options: "Yes," "No," and "I don't know." Although physicians had good knowledge of the disease, almost

one-third of the physicians chose the response "I don't know" for more than half of the questions. This reflects a low level of knowledge about the drug, as shown in table 3.

Table 3: Responses of physicians on knowledge about methotrexate as percentages.

	I don't Know	No	Yes
Methotrexate is a toxic medication	13.3	10.8	73.5
Minor toxic effects include stomatitis, malaise, nausea, vomiting, diarrhea, headaches, and mild alopecia	14.5	6	79.5
Most minor toxic effects are associated with depletion of folate	16.1	5.2	78.7
Low-dose folate does not interfere with the efficacy of methotrexate	42.6	11.2	46.2
Rheumatoid nodules may also increase in size during methotrexate therapy	68.3	14.9	16.9
Monitoring of serum aspartate aminotransferase (AST) and Alanine transferase levels is recommended for all patients receiving methotrexate	20.9	2.8	76.3
Pulmonary abnormalities are emerging as the more common major toxic effects of methotrexate use	38.6	10.8	49
Monitoring signs of myelosuppression can reduce complications such as severe anemia, and sepsis	23.7	7.2	64.7
Is methotrexate safe in pregnancy?	8.4	85.5	4.4
The decision to use methotrexate should be made by the patient and the physician, who should weigh the risks and benefits of therapy	5.6	6	83.9
Should family physician stop methotrexate if a patient is on full remission?	31.7	54.2	14.1
Can a family physician start methotrexate in RA patients by himself?	13.7	69.1	17.3

Physicians were also asked about the frequency of checking lab investigations with methotrexate. The results revealed that 63.1% of the physicians mentioned that it should be checked every six months, while 1.2% of

the physicians mentioned that it should be checked every three months, as shown in Figure 1.

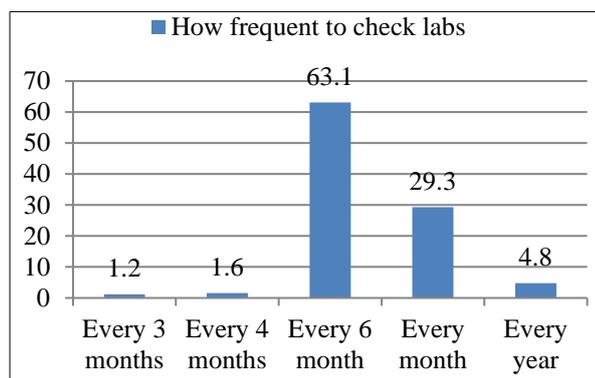


Figure 1: Responses regarding the frequency of checking lab investigations with methotrexate as percentages.

Physicians were also asked about the proper duration to stop methotrexate before pregnancy. As shown in figure 2, 53.8% of the physicians mentioned that it should be stopped at three months before pregnancy, while 5.6% mentioned that it should be stopped at nine months before pregnancy.

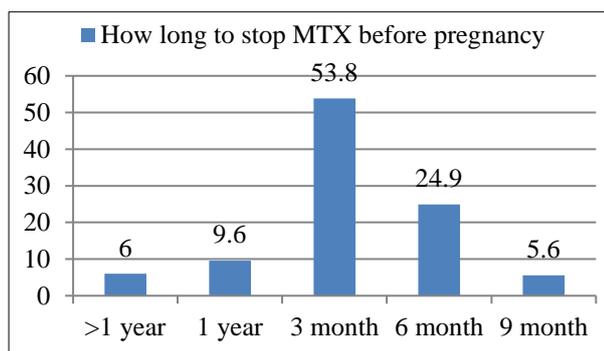


Figure 2: Responses regarding the duration to stop methotrexate before pregnancy as percentages.

Table 4: Comparison of the mean score for different years of experience using one-way ANOVA.

Years of experience	Mean	Standard deviation	p-value
0-3	13.08	3.261	<0.001*
4-6	13.51	2.806	
6-10	15.49	1.522	
>10	15.60	1.948	

Finally, the total score for the knowledge section was calculated and analyzed for all responses. The minimum reported score was 4, while the maximum score was 20, with an average score of 13.99±2.961. The mean score was then compared with respect to years of experiences of the participants using one-way ANOVA. A statistically significant difference was found between mean scores at

different levels of experience (p-value <0.001). Physicians with more years of experience showed significantly higher levels of knowledge about RA and methotrexate monitoring, as shown in Table 4.

DISCUSSION

Therapy for RA is multi-disciplinary and involves physicians, physiotherapists, occupational therapists, the patients themselves, and other medical staff. Professional care has become more serious in handling complex medication regimens. However, access to timely specialized care is not universally available.

The approach to the care of subjects with RA includes two groups. The first comprises people with early RA, which is defined as individuals who have had symptoms for a duration of less than three months. The second group comprises individuals with an established disease who have suffered from symptoms related to inflammation and joint damage.¹³ Methotrexate is the first-line treatment as an immunosuppressant therapy. The drug has various mechanisms of action to improve clinical symptoms and control the disease in individuals with RA, including repression of inflammatory cell proliferation, interference with T-cell activity and cytokine secretion, and augmented release of adenosine, which in turn activates receptors on macrophages and neutrophils to decrease the release of pro-inflammatory cytokines.¹⁴

The present study investigated the level of knowledge of primary care physicians about RA and methotrexate monitoring in Riyadh, Saudi Arabia. The results demonstrated that physicians with more years of experience had a significantly higher level of knowledge about RA and methotrexate monitoring (p-value <0.001). Notably, the responses regarding knowledge about the disease itself were better than their responses about the drug.

RA and methotrexate use have been evaluated in different settings. Byng-Maddick et al surveyed 86 general physicians, who all indicated that they repeated methotrexate prescriptions, but only 77.4% of them monitored it.¹⁵ Of those who did monitor it, 58.6% were aware of local guidelines, and only 48.4% were aware of national guidelines. Furthermore, 26.7% of general practitioners were monitoring and prescribing methotrexate but were not aware of any guidelines. Among this number, 37.5% did not feel that they needed further education. This study suggested that any doctor prescribing methotrexate should also be monitored according to guidelines.¹⁵

Similarly, the present study showed that family physicians in Saudi Arabia had good knowledge about RA, but their level of knowledge about methotrexate was unsatisfactory. Additionally, the present work included a larger sample size, which increases the reliability of the

results. However, the present investigation did not examine the attitude of physicians towards the disease in spite of examining their level of knowledge.

Nash et al performed a study using a questionnaire, which was answered by rheumatologists.¹⁶ They found that methotrexate was well used, well tolerated, and well perceived by rheumatologists. However, they suggested that rheumatologists should discuss methotrexate use with their patients and consider alternative strategies for some patients to ensure that methotrexate therapy is as effective as possible.¹⁶ Although the present study included family physicians, the results comply with those of Nash et al in the good level of knowledge about the disease diagnosis. Nevertheless, the level of knowledge about methotrexate is considered unsatisfactory.¹⁶

The present study had some limitations. First, the study was performed in one city only, which could affect the validity of the outcomes. Furthermore, the study only evaluated the level of knowledge without measuring its impact on the attitude of physicians' practice, which could decrease the reliability of the results. To our knowledge, this is the first study to evaluate the knowledge and attitude of analgesic use in the general population of primary care physicians in Saudi Arabia.

CONCLUSION

The knowledge of family physicians in Riyadh, Saudi Arabia, is considered satisfactory, but the level of knowledge about methotrexate requires improvement. This could be achieved through training programs and workshops for family physicians about the drug and its monitoring. Further studies are required in other areas in Saudi Arabia to determine the national level of knowledge in the Kingdom about RA and methotrexate. Furthermore, future studies should consider studying the attitudes of physicians towards prescribing methotrexate.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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