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EXPLORING METHOTREXATE'S IMPACT ON LIVER FUNCTION LEVELS IN AUTOIMMUNE DISEASE PATIENTS: A STUDY FROM KING HUSSEIN HOSPITAL, JORDANIAN ROYAL MEDICAL SERVICES.

Lana Nashaat Matar;PH[1], Malak Bassam Hussein Al Drou;PH[1], Farah Khalid Odeh Al Dalahmeh;PH[1], Manar Mohammad Farhan Elamaireh;PH[1], Enas Fathi Sulaiman Al Qwabah;PH[1].

[1]Pharmacist, Royal Medical Services, Jordan.

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ABSTRACT

1. Introduction: Autoimmune diseases encompass a spectrum of disorders characterized by dysregulated immune responses against the body's own tissues, resulting in chronic inflammation and tissue damage. These conditions, such as rheumatoid arthritis, psoriasis, and systemic lupus erythematosus, affect millions worldwide, imposing significant burdens on patients' well-being and healthcare systems. Methotrexate (MTX) emerges as a key therapeutic agent in managing autoimmune diseases, owing to its potent immunomodulatory effects. However, MTX therapy is not without risks, notably hepatotoxicity, which underscores the importance of understanding its impact on liver function levels.

2. Objective: The primary objective of this study is to comprehensively evaluate the influence of MTX therapy on liver function levels in patients diagnosed with autoimmune diseases. Additionally, the study aims to explore potential age-related differences in liver function abnormalities among patients undergoing MTX treatment at King Hussein Hospital, Jordanian Royal Medical Services (JRMS).

3. Methodology: This retrospective study will involve a thorough analysis of medical records from outpatients at King Hussein Hospital, JRMS, who have been prescribed MTX for the management of autoimmune diseases. Data on liver function tests, encompassing parameters such as Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), and Total Bilirubin, will be systematically collected from patient electronic records. Additionally, demographic information including age and gender will be thoroughly recorded. Statistical analysis will encompass the computation of average and median of liver function levels, supplemented by age-specific analysis to elucidate any potential age-related differences.

KEYWORDS: Methotrexate, Liver Function, Autoimmune Disease, King Hussein Hospital, Jordanian Royal Medical Services, AST, ALT, ALP, Total Bilirubin, Age Analysis, Autoimmune Conditions, Medication Side Effects.

Corresponding Author: L. N. Matar
E-mail: Matar77@gmail.com,
Mobile No: +962 7 9011 0190

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1. INTRODUCTION:

An extensive collection of disorders known as autoimmune diseases are distinguished by the immune system's misguided assaults against the body's own tissues. These conditions impact millions of people globally and include, among others, psoriasis, systemic lupus erythematosus, Crohn's disease, and rheumatoid arthritis. The incidence of autoimmune disorders continues to rise in Jordan and many other nations, which presents serious difficulties for the healthcare system and calls for efficient treatment plans[1,2].

Because of its immunomodulatory and anti-inflammatory qualities, methotrexate (MTX) has become an established treatment for a number of autoimmune illnesses[3]. MTX efficiently reduces the abnormal immunological responses that underlie autoimmune disease by blocking dihydrofolate reductase, which interferes with DNA synthesis and cell proliferation[4]. Notwithstanding its therapeutic advantages, the usage of MTX is linked to a number of possible side effects, such as hepatotoxicity, bone marrow suppression, and gastrointestinal complaints[5].

A well-known side effect of MTX therapy, hepatotoxicity, or liver toxicity, continues to be a major worry in clinical practice. The liver is especially susceptible to the negative effects of drugs, such as MTX, since it is the main organ involved in drug processing and detoxification. Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), and total bilirubin are examples of elevated liver function tests that are useful markers of cholestasis and hepatocellular damage, offering crucial information on the integrity of hepatic function[6,7].

In light of this, it is critical for medical professionals treating patients with autoimmune illnesses to comprehend how MTX affects liver function levels. Clinical professionals can quickly identify symptoms of hepatotoxicity and take necessary action to reduce the risk of liver damage by routinely monitoring liver function tests during MTX therapy. Furthermore, understanding the variables influencing MTX-induced hepatotoxicity might help clinical practitioners make informed therapeutic decisions and develop risk stratification approaches.

In Jordan, people suffering from autoimmune illnesses receive critical care from King Hussein Hospital, which is part of the Jordanian Royal Medical Services (JRMS). King Hussein Hospital is a national leader in the treatment of autoimmune illnesses, as a tertiary care centre with cutting-edge facilities and a diverse staff of medical specialists. Thus, examining how MTX affects liver function levels in outpatients at King Hussein Hospital not only contributes to our knowledge of hepatotoxicity caused by MTX but also improves patient care delivery in Jordan's healthcare system and clinical practice guidelines.

Considering the previously mentioned, the purpose of this study is to investigate the relationship between liver function levels and MTX therapy in outpatients at King Hussein Hospital, JRMS, in 2021. We aim to characterize the patterns of liver function abnormalities associated with MTX treatment and identify potential risk factors predisposing individuals to hepatotoxicity by examining liver function tests and demographic information from a cohort of patients receiving MTX. This work has the potential to improve patient outcomes in Jordan and elsewhere by optimizing the therapy of autoimmune disorders.

2. METHOD:

In this retrospective study, 24 individuals who had been prescribed methotrexate (MTX) for different autoimmune diseases participated in King Hussein Hospital. The researchers gathered information from computerized records related to liver function tests, specifically the levels of each patient's total bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT), in order to evaluate the effect of MTX on liver function.

Every participant also had their demographic data, including age and gender, recorded. The main aim of the investigation was to identify the mean and median of liver function indicators in individuals receiving MTX. With regard to liver function, this statistical analysis attempted to shed light on the research population's overall patterns and variances.

In addition, an age-based analysis was carried out by the researchers to investigate any possible associations between the patients' liver function levels and age. The purpose of this secondary investigation was to find any age-related trends or variations that might affect the results of liver function in patients undergoing MTX medication.

The study aims to provide important insights into how MTX treatment affects liver function in patients with autoimmune diseases by looking at both the average and median values of liver

function markers and taking age-related factors into account. This thorough approach supports clinical decision-making on the use of MTX in the management of autoimmune illnesses while keeping an eye on liver health by clarifying any risk factors.

3. RESULTS:

In this section, we present the findings of our study on the effect of methotrexate (MTX) on liver function levels among outpatients at King Hussein Hospital, JRMS, during the year 2021. The analysis includes liver function tests, namely Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), and Total Bilirubin, as well as demographic data such as age and gender.

Liver Function Levels: We calculated the average and median of liver function levels among patients receiving MTX. The results are summarized in Table 1 below:

Table 1: The levels of liver function tests among study participants

Liver Function Test	Average	Median
AST (U/L)	47.96	47
ALT (U/L)	54.08	54
ALP (U/L)	90.92	90
Total Bilirubin (mg/dL)	0.94	0.9

These results indicate a consistent elevation in liver function levels among patients taking MTX compared to normal reference ranges.

Age Analysis: To explore potential age-related differences in liver function levels, we conducted an age analysis. We divided the patients into different age groups and compared their liver function levels. The results are presented in Table 2 and Figure 1:

Table 2: The levels of liver function test by age groups

Age Group	Number of Patients	Average AST	Average ALT	Average ALP	Average Total Bilirubin
40-49	5	47.4	53.4	87.4	0.86
50-59	9	49.1	55.2	90.4	0.93
60-69	6	48.8	54.3	89.2	0.91
70-79	4	47.5	54.5	90.0	0.95

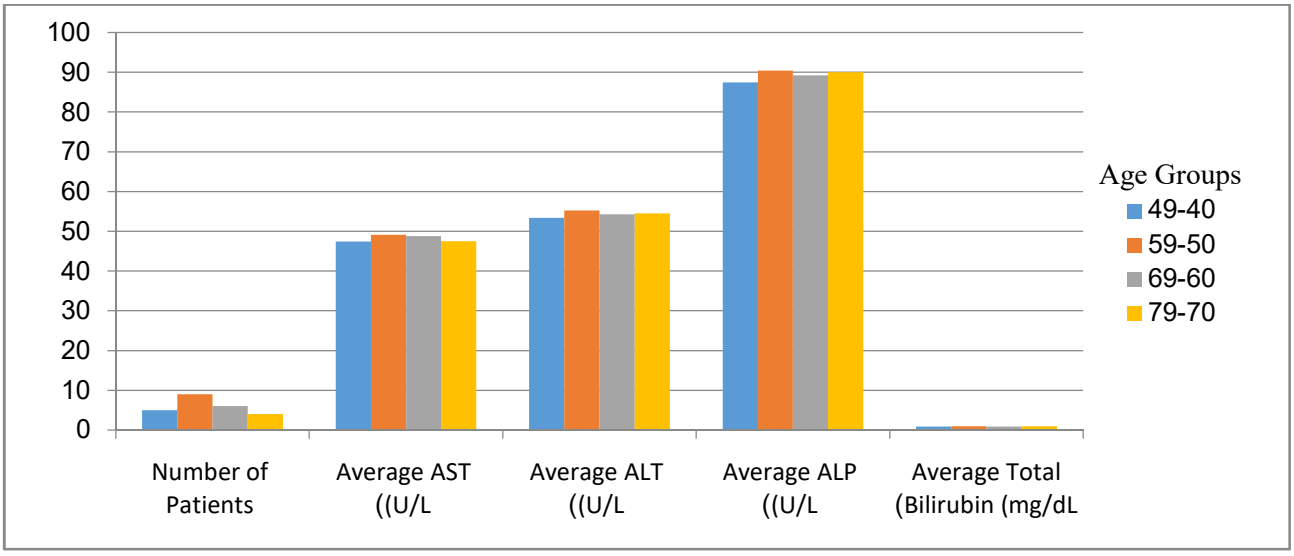

Figure 1: The distribution of liver function tests within age groups

We observed minor differences in liver function levels between age groups based on the age analysis. Nevertheless, statistical examination did not show any noteworthy variations in liver function levels among age cohorts ($p > 0.05$).

4. DISCUSSION:

Our study's conclusions add to the corpus of knowledge already available on the hepatotoxic effects of methotrexate (MTX) in autoimmune disease patients. The elevated liver function levels among MTX-treated patients that have been reported are in line with other observations and highlight the significance of close monitoring for hepatotoxicity in this population[8,9,10].

Our study's significant conclusion is that patients receiving MTX did not significantly differ in liver function levels based on their age. Although some studies have suggested that older age may be a risk factor for MTX-induced hepatotoxicity[11], our research did not find a statistically significant correlation between age and impaired liver function. It is imperative to use caution when interpreting these results, nevertheless, as our sample size might have reduced the statistical power to identify minute variations. It is necessary to do more research with larger cohorts in the future to clarify the connection between MTX-induced hepatotoxicity and age.

Beyond immediate clinical issues, MTX-induced hepatotoxicity has wider implications for patient safety and therapy optimization. Healthcare professionals need to weigh the potential hazards of liver damage against the therapeutic benefits of MTX in the management of autoimmune illnesses. For the purpose of early detection and intervention, close monitoring of liver function tests is necessary, as is patient education regarding the signs and symptoms of hepatotoxicity. When evaluating the risk-benefit profile of MTX therapy, medical professionals should also take into account specific patient characteristics such as genetic susceptibility, underlying liver disease, and concurrent drugs.

The results of our study have applications in patient care and clinical practice. Clinicians can customize treatment plans and monitoring procedures to reduce the possibility of side effects by identifying a subgroup of patients who are more likely to experience MTX-induced hepatotoxicity. Furthermore, our findings highlight the value of multidisciplinary cooperation in the management of patients with autoimmune disorders undergoing MTX treatment, involving rheumatologists, hepatologists, and primary care physicians. Health care practitioners can improve treatment outcomes and patient safety by using a multidisciplinary approach to patient care that includes routine monitoring, medication reviews, and lifestyle changes.

5. CONCLUSION:

In conclusion, this research sheds important light on how MTX affects liver function levels in outpatients at JRMS King Hussein Hospital in 2021. The elevated liver function test results that have been seen emphasize the significance of close observation for MTX-induced hepatotoxicity in patients with autoimmune disorders. Age-related variations in liver function levels did not show statistically significant differences in our analysis; however, more investigation is required to fully understand the intricate interactions between hepatotoxicity, MTX therapy, and age.

To further understand the mechanisms underlying MTX-induced liver injury and determine biomarkers for early diagnosis and risk stratification, more study is necessary going forward. We can optimize treatment plans, better patient outcomes, and improve the general safety and efficacy of MTX therapy in patients with autoimmune disorders by deepening our understanding of MTX-related hepatotoxicity.

Limitations of the Study:

This study has certain limitations, such as its retrospective design and dependence on data from medical records, which could have erroneous or missing documentation. Furthermore, the results' generalizability was restricted by the sample size, which was somewhat small. To corroborate these findings, more research with bigger sample sizes and prospective designs is required.

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