



CODEN [USA]: IAJPBB

ISSN : 2349-7750

**INDO AMERICAN JOURNAL OF  
PHARMACEUTICAL SCIENCES**

SJIF Impact Factor: 7.187

<http://doi.org/10.5281/zenodo.4395415>Available online at: <http://www.iajps.com>

Research Article

**TO REVEAL FREQUENCY OF FATTY LIVER IN PAKISTAN  
COHORT WITH RHEUMATOID ARTHRITIS**Dr Amir Hussain<sup>1</sup>, Dr Iqra Jamil<sup>2</sup>, Dr Usman Raza<sup>3</sup><sup>1</sup>Medical Officer at Imran Idrees Teaching Hospital, Cantt, Sialkot<sup>2</sup>Central Park Medical College Lahore<sup>3</sup>King Edward Medical University Lahore

Article Received: October 2020 Accepted: November 2020 Published: December 2020

**Abstract:****Objective:** To determine the frequency of fatty liver in Pakistan cohort with rheumatoid arthritis.**Study Design:** Cross-Sectional**Place and Duration:** This study was conducted at Mayo Hospital, Lahore for a duration of ten months from 1<sup>st</sup> November, 2019 to 31<sup>st</sup> August, 2020.**Methods:** 200 patients were included in this study. Patients detailed demographics age, sex, body mass index, smoking habits were recorded after taking written consent. The abdominal ultrasound scan was carried out by a radiologist. On the next day, 10 ml of blood was taken by the phlebotomist for lipid profile and fasting blood sugar levels, and 10-year Framingham cardiovascular risk score was calculated after results were available. Complete data was analyzed by SPSS 24.0 version.**Results:** Total 165(82.5%) were females presented in this study with mean age of 43.2 years. Fatty liver was observed in 45(22.5%) patients. Frequency of metabolic syndrome was in 33(73.33%) patients, diabetes mellitus was in 15(33.33%) patients, hypertension was in 26(57.8%), FRS score at high in 16(35.5%), previous history of desi medication was in 24(53.33%), While all study parameters except DMARDs were significantly associated with fatty liver during regression analysis ( $p < 0.05$ ).**Conclusion:** We concluded that non-alcoholic fatty liver disease is very prevalent in rheumatoid arthritis patients. As in the general population, it is multifactorial in origin, and needs careful monitoring and treatment.**Keywords:** MeTs, MARD's, FRS, Fatty liver, RA.**Corresponding author:****Dr. Amir Hussain.,**

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Please cite this article in press Amir Hussain et al, To Reveal Frequency Of Fatty Liver In Pakistan Cohort With Rheumatoid Arthritis., Indo Am. J. P. Sci, 2020; 07(12).

**INTRODUCTION:**

Rheumatoid arthritis is the most common inflammatory arthritis affecting 0.5 to 1 percent of the world's general population.[1] Nonalcoholic liver fat disease (NAFLD) is characterised as excessive fat accumulation (liver fat > 5-10 percent of liver weight), primarily in the form of triglycerides in those who use about 20 g ethanol/d daily alcohol), the spectrum of diseases ranges from simple steatosis to fibrosis, scarring, steato-hepatitis, ultimately leading to cirrhosis, with a worldwide prevalence of (10-40 percent).[2,3 ]

Liver injury is not considered a major extra-articular feature of RA, but abnormal liver tests that fluctuate with disease activity, mainly elevated alkaline phosphatase, have been seen in 18 to 50 percent of cases.[4] In a retrospective study on 188 autopsy cases of RA, 65 percent of unselected RA patients had abnormal liver biopsies, half of whom had mild portal chronic inflammatory infiltration .[5]

In their 846 RA observational study, Shunshuke Mori et al presented 42 methotrexate patients had persistent elevation of transaminase, while ultrasound showed fatty liver disease and histological results showed that non-alcoholic steato-hepatitis was the most prevalent pattern of liver injury, with no significant impact on the histological severity of the dose and duration of methotrexate. [6] Increased levels of transaminases (ALT, AST) are the second most common adverse effects after gastrointestinal problems with methotrexate therapy identified by Salliot and van der Heijde systematic review (20.2 percent).[7] Methotrexate therapy has long been associated with either imaging or biopsy diagnosed fatty liver disease (NAFLD). [10-8]

In their observational study, Rajalingham S, et al, found that the prevalence of MTX-associated

NAFLD was 4.7 percent and that the MTX dose was only an independent predictor of MTX-associated NAFLD associated with transaminitis.[11] Our objective was to determine the frequency of fatty liver (non-alcoholic) disease in rheumatoid arthritis patients.

**MATERIAL ANND METHODS:**

This cross-sectional study was conducted at Mayo Hospital, Lahore for a duration of ten months from 1<sup>st</sup> November, 2019 to 31<sup>st</sup> August, 2020 and comprised of 200 patients. Patients detailed demographics age, sex, body mass index, smoking habits were recorded after taking written consent. Patients with acute liver disease, chronic liver diseases like cirrhosis and malignancy, chronic hepatitis and those were not agree were excluded from this study.

An expert sonographer with 10 years of experience has classified all participants in the study with abdominal ultrasonography for NAFLD detection according to radiological criteria (bright hepatic echoes, increased hepato-renal echogenicity and vascular blurring of the portal or hepatic vein as unique sonographic features of NAFLD, participants in the study were asked to return the following morning with 14 hours of fasting, 5 ml of blood was taken by a trained aseptic phlebotomist, samples were sent to the laboratory on the COBAS-III machine for FBS, lipid profile, and liver enzyme levels. Complete data was analyzed by SPSS 24.0 version.

**RESULTS:**

Total 165(82.5%) were females presented in this study with mean age of 43.2 years, and rest of the patients 35 (17.5%) were males. Mean age of the patients were 43.2years and the patients with age group 31-40 years were 72(36%) patients was higher in numbers. Fatty liver was observed in 45(22.5%) patients. (Table 1)

Table 1: Baseline detailed demographics of enrolled patients

Variables	Frequency	% Age
<b>Age group</b>		
20-30 years	42	21
30-40 years	72	36
40-50 years	68	34
>50years	18	9
<b>Gender</b>		
Females	165	82.5
Males	35	17.5
Mean age(years)	43.2	
Fatty Liver	45	22.5

Patients with fatty liver were 45 in numbers in which 30(66.7%) were females and 15(33.3%) were males. Frequency of metabolic syndrome was in 33(73.33%) patients, diabetes mellitus was in 15(33.33%) patients, hypertension was in 26(57.8%), FRS score at high in 16( 35.5%), previous history of desi medication were in 24(53.33%), while on regression analysis all study parameters except DMARD's had significant association with fatty liver ( $p < 0.05$ ). (table 2)

Table 2: Classification of fatty liver with different parameters

Variables	Frequency of fatty liver (n=45)	% Age
<b>Sex</b>		
Females	30	66.7
Males	15	33.3
Desi Medication	24	53.33
Smoking	13	28.9
MeTS	33	73.33
Hypertension	26	57.5
DM	15	33.33
FRS	16	35.5

### DISCUSSION:

In patients with RA, there is insufficient understanding of how NAFLD develops. Folate deficiency, high cell turnover, purine deficiency, pyrimidine thymidine, methionine, and MTX polyglutamate accumulation with genetic polymorphisms such as C677T polymorphism in the MTX metabolism increase the chances of their toxicity.[12-15] The prevalence of NAFLD was 22.5% (n=45) in our study, while it was (4.7%) in the Rajalingham et al study, but MTX and other associate was not created.

The prevalence of NAFLD was found in a very recent study by Ursini et al (25 percent) and complement factor C3 was suggested as a potential biomarker for NAFLD.[16] PPAR $\gamma$  Pro12Ala polymorphism was associated with East NAFLD susceptibility in a meta-analysis conducted by Young-Ho lee et al on the genetic association of RA NAFLD and psoriatic arthritis. [18]

It is well known that metabolic syndrome precedes NAFLD development and is considered to be the hepatic manifestation of metabolic syndrome, but A. Lonardo et al found that the reverse is true that NAFLD precedes the metabolic syndrome, because in most cases insulin resistance is present, but only minorities develop metabolic syndrome, and it is strongly associated with type 2 diabetes mellitus, whereas these subjects are 1.6 times more likely to develop diabetes than NAFLD free cases.[20] In our

NAFLD po study, the prevalence of meta-like diabetes

In our study FRS score was at high in 16( 35.5%), previous history of desi medication were in 24(53.33%), frequency of metabolic syndrome was in 33(73.33%) patients, diabetes mellitus was in 15(33.33%) patients but studies conducted by Sombat Treeprasertsuk et al [19] has been reported that the Framingham cardiovascular risk score is higher in NAFLD patients than in the general population.

### CONSLUSION:

Fatty liver disease may increase the risk of cardiovascular events which are already high in RA by increasing conventional dmards and introducing biological dmards, in addition to hampering ongoing efforts to achieve remission. Regular monitoring with LFTs and ultrasonography is needed at the start of treatment and during follow-up.

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