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Assessment of Osteoporosis with Aspartate Aminotransferase to Platelet Ratio Index Score in Patients of Chronic Liver Disease

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ABSTRACT

Objective: to assess Osteoporosis with APRI score (aspartate aminotransferase to platelet ratio index) in patients with chronic liver disease.

Study Design: Cross-sectional study.

Study Setting and Duration: Pak Emirates Military Hospital Rawalpindi, Pakistan from Jan to Dec 2021.

Methodology: All Adult patients aged 18 years and above with clinical and imaging features suggestive of chronic liver disease were included in the study. APRI score calculated as the ratio of aspartate aminotransferase to platelet based on the laboratory analysis of Aspartate aminotransferase (AST) and platelet levels was done. Furthermore, a bone density scan (DEXA scan) was also carried out for all the study participants.

Results: One hundred and sixty patients fulfilling the inclusion criteria were included. Of the total 160 cases, 53(33.1%) had normal bone density on DEXA scans, 43(26.9%) had Osteopenia and 64(40%) had Osteoporosis. Twenty-nine cases of chronic liver disease cases (25%) had APRI scores <0.3, 40(25%) had APRI scores>0.3 and<0.5, 37 cases (23.1%) had APRI scores>0.5 and <1.5, 30 cases (18.8%) had APRI score >1.5 and <2 and 24 patients (15%) had APRI score >2. The significant (p<0.001) association was observed between APRI score and bone density, showing bone density decreased with the progression of the disease.

Conclusion: Patients with chronic liver disease almost invariably develop Osteoporosis with the progression of the disease. Early recognition and treatment are pivotal to lessen morbidity and mortality associated with Osteoporosis.

Keywords: Aspartate aminotransferase, Chronic liver disease, Hepatitis C, Osteoporosis, Osteopenia, Platelet.

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INTRODUCTION

Osteoporosis is one of the most common complications reported in 12-15% of patients with chronic liver disease.[1] Its pathogenesis is multifactorial and caused by both decrease in bone formation and enhanced bone resorption due to either vitamin D deficiency, altered calcium metabolism, hormonal imbalance, vitamin K deficiency, or deficiency of insulin-like growth factor 1 (IGF-1).[2,3] The liver is involved primarily in the metabolism of vitamin D, where Vitamin D3 is hydroxylated to 25-hydroxy vitamin D (25-OH-vitamin D) followed by renal conversion to 1,25-hydroxyvitamin D. [4]

The primary causative agent in chronic liver diseases is hepatitis C virus infection, a condition that affects nearly 200 million people across the globe, mainly in low and middle-income countries.[5,6] Most of these patients develop chronic liver disease characterized by fibrosis of liver tissues. If untreated, these patients ultimately develop a fatal condition called cirrhosis or end-stage liver disease. Therefore, successful diagnosis, management and prognosis of the condition require an accurate assessment of the extent of hepatic fibrosis.[7] In this context, a biopsy of the hepatic tissue is the gold standard and most widely used method for assessing liver fibrosis. However, because of being an invasive procedure with associated complications and other limitations, it is not a practical tool for monitoring the progression of the disease.[8] An alternative, non-invasive and reliable choice is the APRI index based on the Aspartate aminotransferase to platelet ratio index that is also used across the world for assessing the extent of liver fibrosis, especially in chronic hepatitis C patients in chronic hepatitis C (CHC) patients. [9]

The current study has been carried out to assess the frequency of Osteopenia and Osteoporosis in cases of chronic liver disease and the association between the

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Aspartate aminotransferase to platelet ratio index (APRI) score and Osteoporosis.

METHODOLOGY

The cross-sectional study was conducted at Pak Emirates Military Hospital Rawalpindi from January to December 2021 after approval from the Hospital Ethical Committee. The sample size was calculated using the online Raosoft Sample size calculator taking global prevalence of chronic liver disease (cirrhosis) (Range: 4.5% to 9.5%).10. Non-probability consecutive sampling technique was used.

Inclusion Criteria: Patients presenting with clinical and imaging/radiological features of chronic liver disease were included in the study.

Exclusion Criteria: Patients who had a known history of established osteopenia/osteoporosis, bedridden cases, those on corticosteroids, patients who had knee or hip replacement surgeries, and cases with spontaneous bone fractures were excluded from the study.

The Aspartate aminotransferase to platelet ratio index (APRI) score was calculated for all the cases after getting laboratory results of Aspartate aminotransferase (AST) and platelet levels and putting the values in the calculator. APRI score was interpreted as follows; Stage 1=APRI <0.3: Unlikely cirrhosis or significant fibrosis, Stage 2=APRI index >0.3 but ≤0.5 indicate significant fibrosis possibility but cirrhosis is unlikely, Stage 3=APRIindex >0.5 and ≤1.5 indicating significant cirrhosis or fibrosis possibility, Stage 4= APRI index >1.5 and ≤2: likely significant fibrosis, cirrhosis possible, Stage 5 APR>2: likely cirrhosis.[11,12]

A bone density scan (DEXA scan) was carried out for all the patients who presented with chronic liver disease due to any aetiology and consented to the study. DEXA scan results were interpreted as follows; 1)T score of -1.0 or above=Normal bone density, 2) T score between -1.0 to -2.5=Osteopenia or decreased bone density, 3) T score of -2.5 or lower= Osteoporosis.[13]

All the data, including age, gender, APRI score, and DEXA scan findings, were entered in Statistical Package for Social Sciences (SPSS) version 21.00 and analyzed. Quantitative variables were expressed as mean±SD and qualitative variables were expressed as frequency and percentages. Inferential statistics were explored using the Chi-square and Independent sample t-test .The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

One hundred sixty patients fulfilling the inclusion criteria who consented to the study were recruited. There were 84 males (52.5%) and 76 females (47.5%). The age range was from 33 to 71 years, with a mean age of 52.77+9.61 years. Out of the total of 160 cases, 53(33.1%) had normal bone density on DEXA scans, 43(26.9%) had Osteopenia, and 64(40%) had Osteoporosis on the DEXA scan, as shown below in Table-I.

Table-I: DEXA Scan Result of the Study Participants (n=160)

DEXA Scan Results	n(%)
Normal	53(33.1%)
Osteopenia	43(26.9%)
Osteoporosis	64(40%)

Twenty-nine cases of chronic liver disease cases (25%) had APRI scores <0.3, 40(25%) had APRI scores >0.3 and <0.5, 37 cases (23.1%) had APRI scores >0.5 and <1.5, 30 cases (18.8%) had APRI score >1.5 and <2. Twenty-four patients (15%) had APRI scores >2, as shown in Table-II.

Table-II: Aspartate Aminotransferase to Platelet Ratio Index Score (APRI) distribution of the Cases (n=160)

APRI Score	n (%)
APRI <0.3	29(1.1%)
APRI>0.3 and <0.5	40(25%)
APRI>0.5 and <1.5	3723.1%)
APRI>1.5 and <2	30(18.8%)
APRI>2	24(15%)

There was a significant association between APRI score and bone density, (*p*-value<0.001), as shown below in Table-III.

Table-III: Comparison between DEXA Scan Results and APRI Score (n=160)

APRI Score	DEXA Scan Result/Bone Density			*p*-value
	Normal	Osteopenia	Osteoporosis	
APRI <0.3	23(43.4%)	6(13.9%)	0	<0.001
APRI>0.3 and<0.5	26(49.1%)	11(25.6%)	3(4.7%)	
APRI>0.5 and<1.5	4(7.5%)	21(48.8%)	12(18.8%)	
APRI>1.5 and<2	0	3(6.9%)	27(42.2%)	
APRI>2	0	2(4.6%)	22(34.4%)	
Total	53	43	64	

Out of a total of 29 cases of APRI stage 1 (APRI<0.3) majority (23) were normal, 6 cases had Osteopenia, and none had Osteoporosis. Out of a total of 40 cases with stage 2 APRI scores (APRI>0.3 and

<0.5) majority (26) had normal bone density, 11 had Osteopenia, and 3 had Osteoporosis. In cases of APRI stage 3 (APRI>0.5 and<1.5), only 4 had normal bone density, 21 had Osteopenia, and 12 were osteoporotic. In stage 4 disease (APRI>1.5 and <2), the majority (27 out of 30) had Osteoporosis. Similarly, in Stage 5 disease (APRI>2), almost all (22 out of 24) had Osteoporosis.

DISCUSSION

In our study, 40% of individuals had Osteoporosis, and 26.9% had Osteopenia. The frequency of Osteoporosis increased with the degree of liver fibrosis /severity of the chronic liver disease. Most cases with APRI stage 4 and APRI stage 5 had Osteoporosis.

In Pakistan, the progression of hepatitis C disease to cirrhosis is very high; approximately 41-52% of cases of hepatitis C develop cirrhosis and associated complications.[13] The additional morbidity and risk associated with Osteoporosis increase the disease burden.[14] Osteoporosis in chronic liver disease patients adds to the morbidity of patients and increases the risk of fractures which drastically affect the quality of life and mortality among these patients. It is generally recommended that all patients with chronic liver disease should undergo additional screening with bone densitometry. Management of associated Osteoporosis ideally comprises controlling risk factors like smoking, alcohol intake, regular adequate exercise, calcium and vitamin D supplementation, and limiting drugs that increase Osteoporosis, e.g. corticosteroids. Hormone replacement therapy (HRT) with estrogen is considered in postmenopausal women with chronic liver disease. It has significantly improved bone mass density (BMD) and reduced fractures.[10] However, clinicians should be careful and consider the hepatotoxicity related to this hormone therapy.[15,16] Bisphosphosphonates also increase bone mass density (BMD) and prevent bone resorption in liver patients. However, they are also associated with oesophagal ulcers, which are of serious concern in such patients.[17] However, calcium and vitamin D supplements and more advanced recent therapeutic options provide promising improvements in patients of chronic liver disease with Osteoporosis.[18]

We recommend, based on our findings, that all the cases of chronic liver disease who have APRI stage 3 or beyond should be immediately started treatment for imminent Osteoporosis. Increased awareness, early detection, and prompt early treatment of Osteoporosis in cases of chronic liver disease are of utmost importance to improve quality of life and decrease morbidity. This study is unique in associating APRI scores with Osteoporosis. Furthermore, APRI is a non-invasive and cost-effective method of measuring liver fibrosis. Therefore, it can be a useful method/modality to foresee impending osteoporotic complications.

CONCLUSION

Chronic liver disease patients almost invariably develop Osteoporosis with the progression of the disease. Therefore, early recognition and treatment are important to lessen morbidity and mortality associated with Osteoporosis.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

FS & RSAK: Critical review, concept, study design, drafting the manuscript, approval of the final version to be published.

SA & MAK: Data acquisition, drafting the manuscript, approval of the final version to be published.

QI:, FBH: & KH : Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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