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Pulmonary Function Assessment in Non-Alcoholic Fatty Liver Disease Patients - A Comparative Cross-Sectional Study

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ABSTRACT

Introduction: Non-communicable diseases have become a major global health burden. Metabolic syndromes, such as diabetes mellitus and hypertension account for a large proportion of non-communicable diseases. Non-alcoholic fatty liver disease (NAFLD) is considered the hepatic manifestation of metabolic syndromes. Numerous studies have shown that individuals with metabolic syndromes experience impaired respiratory function.

Objectives: This study aimed to determine respiratory function in patients with different grades of NAFLD by assessing forced vital capacity (FVC) and forced expiratory volume in 1s (FEV1).

Materials & Methods: This comparative cross-sectional study was conducted on 50 NAFLD patients in a tertiary care hospital in South India. These patients were divided into three severity groups. Severity was assessed and graded by the ultrasound examination. Then the pulmonary function was assessed by measuring FVC and FEV1 using Spirometer. Statistics were done for assessing the correlation between pulmonary function and three different grades of NAFLD.

Results: The measured FVC and FEV1 is significantly lower in NAFLD grade III when compared with NAFLD grade I patients.

Conclusion: This study shows that impairment of respiratory function is more pronounced in patients with increased severity of NAFLD.

Keywords: Non-alcoholic Fatty Liver Disease, Metabolic Syndrome, Respiratory Function Tests, Forced Expiratory Volumes, Spirometry.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is now considered as the most common cause of end-stage liver disease. It is estimated that over 25% of the world's population is suffering from NAFLD with the highest prevalence was reported from South America and Middle East countries [1]. In India, the overall pooled prevalence among the adults in India is 38.6%, with similar rates among males and females [2]. NAFLD is diagnosed when there is evidence of excessive accumulation of fat in the liver, either through histology or by imaging methods such as Ultrasonography, and there is no history of any other secondary causes

for fatty liver, such as the history of alcohol consumption or taking any steatogenic medication [3].

NAFLD is considered as the hepatic manifestation of Metabolic syndrome [4]. The metabolic syndrome is defined by the presence of the aggregation of metabolic disorders including central obesity, increased low density lipoproteins level, hypertriglyceridemia, hypertension and increased fasting blood sugar [5]. Insulin resistance is considered as the pathology behind metabolic syndrome. Accumulation of fat in the liver is thought to be caused by an imbalance in any of the processes in pathways of formation, transport, storage and oxidation of triacylglycerol. Several cross-sectional studies show the link between impairment in respiratory function and the individual components of metabolic syndrome. Some studies showed respiratory function impairment by different methods in NAFLD patients. In this study, we propose to assess respiratory function in patients with different NAFLD severity by measuring forced vital capacity (FVC) and forced expiratory volume in 1 sec (FEV1).

MATERIALS & METHODS

This is a comparative cross - sectional study conducted at a tertiary care hospital in Southern India after obtaining Institutional ethical committee clearance and written informed consent from all the participants. Patients aged 18 – 60 years of both genders who were diagnosed nonalcoholic fatty liver disease by clinical and ultrasonogram examination were selected from the institution's Internal medicine outpatient department by consecutive sampling method.

Inclusion Criteria:

Both males and females aged 18 – 60 years who were diagnosed with NAFLD by clinical evaluation and ultrasonography were included in the study.

Exclusion criteria:

Patients with history of alcohol consumption, Smoking, Metabolic disorders such as Diabetes Mellitus, Hypertension, Cardiac or pulmonary diseases, Recent surgery, Pregnancy, Prior history of any liver diseases, Chronic use of hepatotoxic drugs such as Valproate, Corticosteroids etc. were excluded from the study.

After applying the above inclusion and exclusion criteria, 50 eligible participants were enrolled in our study. Informed consent in both verbal and written form was obtained from the participants after explaining the objectives and procedures in detail.

Grading of NAFLD:

The fatty liver was graded based on severity in the selected participants by the experienced Radiologists in Radiology department by using ALOKA ultrasound machine equipped with a low frequency (3.5 MHz) convex array transducer. The severity of fatty liver was graded as I, II, III based on a visual assessment of the hepatic echo intensity [6].

Grade I: Mild, diffuse increase in liver parenchymal echoes with normal visualization of diaphragm and intrahepatic vessel borders.

Grade II: Moderate, diffuse increase in liver parenchymal echoes with slightly impaired visualization of intrahepatic vessel borders and diaphragm.

Grade III: Marked increase in liver parenchymal echoes with poor or non-visualization of the intrahepatic vessel borders, diaphragm, and posterior right lobe of the liver.

Pulmonary function assessment:

Pulmonary function assessment was done in Research lab in Physiology department. FVC and FEV1 were measured using EasyOne^{TM} portable Spirometer. The following set of instructions was given to the participants as per ATS/ERS task force. [7]

- Stop Smoking for at least 1 hour prior to testing.
- Avoid bronchodilators if is in use, before the procedure.

- Avoid consuming intoxicants within 8 hours before testing.
- Avoid performing vigorous exercise 30 min before testing.
- Avoid wearing clothing that restricts full chest and abdominal expansion.
- Avoid eating a large meal within 2 hours of testing.

Spirometry Procedure:

Tests were performed in sitting position. A sterilized spirette was fixed to the spirometer. Each participant was given instruction to keep the mouthpiece of the spirometer in the mouth so that there will be a good seal around the mouthpiece. Then the participants were asked to blow out as fast as possible for at least 6 seconds. This procedure was repeated three times until we get three acceptable man oeuvres and then the best of the three values was noted. Then obtained measurements were compared with the predictive values obtained from a study on Chennai subjects by Vijayan et al [8] in the year 1990.

STATISTICAL ANALYSIS

data were analyzed using Statical Package for the Social Sciences Software (SPSS) Version 26. Demographic data were summarized by descriptive statistics. ANOVA is used to compare FVC and FEV1 in the three grades of NAFLD.

RESULT

Based on ultrasonographic grading, 50 participants with non-alcoholic fatty liver disease (NAFLD) were distributed as: Grade I: (n=23) Grade II: (n=16) Grade III: (n=11).

The demographic characteristics of the study participants were shown in [Table 1].

Table 1: Demographic Characteristics

PARAMETERS	MEAN ± S. D
Age (Years)	44.86 ± 9.35
Height (Cm)	158.22 ± 8.19
Weight (Kg)	62.88 ± 8.21
FVC % predicted	73.26 ± 7.75
FEV1 % predicted	81.4 ± 8.37
FVC / FEV1 % predicted	118.98 ± 10.40

The mean FVC % predicted and the mean FEV1 % predicted of study participants is in decreasing order as the grades of NAFLD increases from I to III shown in Figure 1&2.

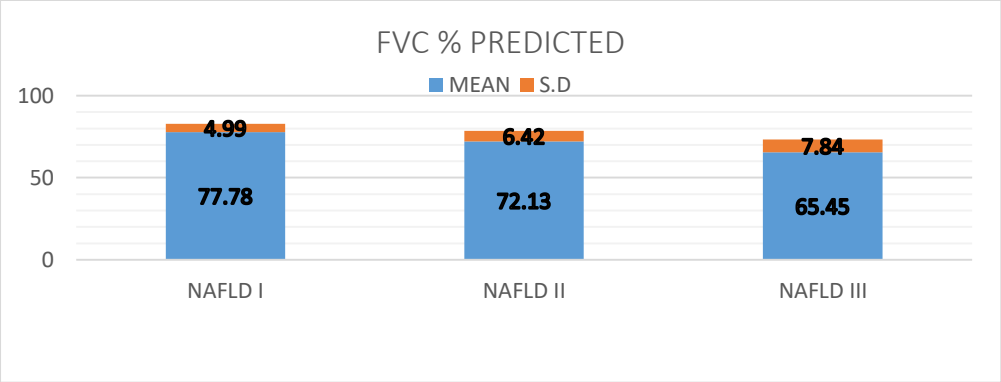

Figure 1: Comparison of mean FVC% Predicted among different NAFLD groups

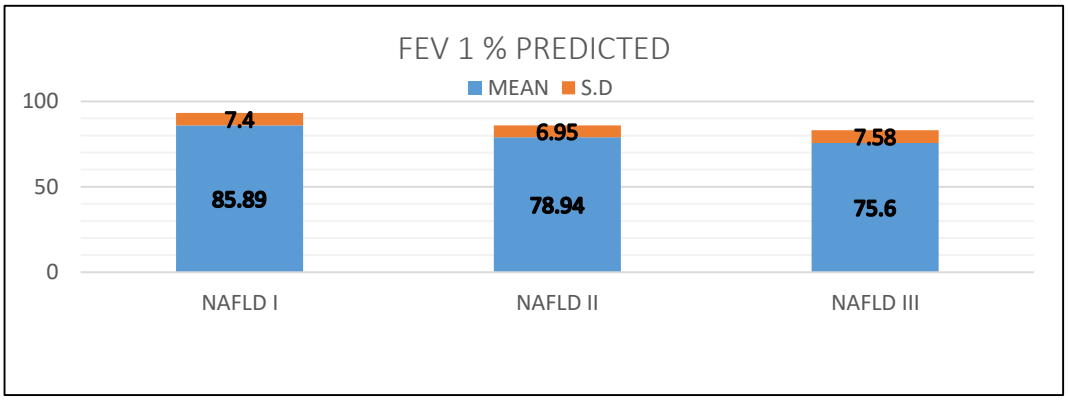

Figure 2: Comparison of mean FEV1% Predicted among different NAFLD groups

There is statistical significance (p <0.05) among FVC % and FEV1 % predicted of the study participants in different grades of NAFLD as show in Table 2&3.

Table 2: Mean FVC% Predicted Among Different Grades Of NAFLD

ANOVA					
FVC % Predicted					
	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between Groups	1161.127	2	580.564	15.323	.000
Within Groups	1780.748	47	37.888		
Total	2941.876	49			

Table 3: Mean FEV1% Predicted Among Different Grades Of NAFLD

ANOVA					
FEV1 % Predicted					
	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between Groups	931.345	2	465.672	8.748	.001
Within Groups	2502.030	47	53.235		
Total	3433.375	49			

Post hoc test shows that the mean FVC % and FEV1 % predicted between grade I NAFLD participants and grade III NAFLD participants is statistically significant (p <0.05). i.e FVC and FEV1 % predicted percentage is significantly lower in grade III NAFLD when compared to grade I NAFLD.

But mean FVC % and FEV1 % predicted of grade II NAFLD is not statistically significant with grade I or grade III NAFLD.

Mean FEV1/FVC % PRED % shown in Figure 3.

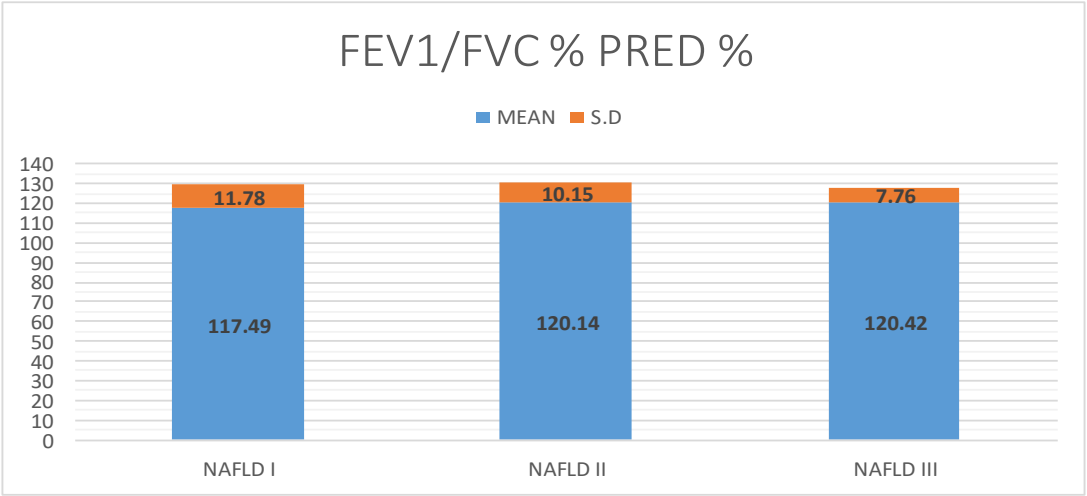

Figure 3: Comparison of FEV1/FVC % Pred % among different NAFLD groups

There is no statistical significance among the mean differences of % predicted FEV1/FVC % among the grades of NAFLD shown in Table 4.

Table 4: Mean FEV1/FVC % Pred % among different grades of NAFLD

ANOVA					
% FEV1/FVC % PRED					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	95.629	2	47.814	.432	.652
Within Groups	5199.092	47	110.619		
Total	5294.721	49			

DISCUSSION

Nonalcoholic fatty liver disease (NAFLD) is widely regarded as the hepatic manifestation of metabolic syndrome. NAFLD can be classified into three grades based on histopathological or ultrasonographic findings. This present study was aimed to assess respiratory function in patients in a South Indian city with different grades of NAFLD by assessing the FVC % and FEV1%. The study results shows that the study participants with higher degree of severity of fatty liver have lesser FVC % and FEV1%, which suggests a decrease in respiratory function with increasing hepatic steatosis severity.

Similar results were obtained in cross sectional study conducted by Peng et al., [9] in cross sectional analysis of the Third National Health and Nutrition Examination Survey (NHANES III) study. In their study, on examining the pulmonary function and hepatic steatosis relationship in 9976 adults participated in the study, they concluded that predicted FEV1% and FVC% were significantly and inversely associated with the increasing grades of steatosis. Their study also shows that the patients with moderate and severe steatosis have increased risk for restrictive lung pattern than obstructive lung pattern. In another study by Qin Li et al., [10] FVC and FEV1 predicted percentage were low in subjects with NAFLD when compared to non NAFLD subjects. But in this study, the subjects were middle and elderly Chinese males above 40 years. A study conducted on 7417 participants from the Korean National Health and Nutrition Examination Survey (KNHANES) by Kwak et al [11] showed NAFLD was significantly associated with reduced lung function and this relationship was more prominent among males. In this study, there were no statistically significant associations found between NAFLD and lung function among females and the criteria for NAFLD in this study was increased serum alanine amino transferase level.

Ozkarafakili et al [12] done a study on 94 nonsmoking males by evaluating steatosis degree by liver biopsy and obtained NAFLD activity score (NAS). In their study, the degree of steatosis was negatively correlated with FVC and FEV1. Also, they found out that FVC and FEV1 are also negatively correlated with insulin resistance. They concluded that insulin resistance in both liver and lungs is the probable mechanism for the results obtained.

A meta-analysis and systemic review were done by Mantovani et al [13]. Which included 133,707 middle aged individuals. Predominantly they were females and are of Asian ethnicity. From the meta-analysis done, they came to conclusion, NAFLD is significantly associated with reductions of both FEV1 and FVC in Asian and United states.

CONCLUSION

This study shows that FVC predicted % and FEV1 predicted % decreases as the grades of NAFLD increases and there is no change in predicted FVC/FEV1 % in NAFLD patients. So, it may be concluded that restrictive pattern of lung disease is seen in NAFLD patients and the decrease in lung

function is more when degree of steatosis increases.

Limitations of the Study

This study has few limitations. The sample size of the study was relatively small and study did not include a control group. Liver biopsy, the gold standard test for diagnosing NAFLD was done, as it is invasive. The restrictive lung pattern was not confirmed through the direct measurements such as total lung capacity and residual volume.

Declaration by Authors

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Conflict of Interest: The authors declare no conflict of interest.

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