RESEARCH ARTICLE

Six-minute walk distance, ECOG Performance Status, and Modified Borg Scale scores in a cohort of Pakistani patients with noncancerous end-stage liver disease selected for liver transplant

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Abstract

Objectives: To evaluate the functional status of Pakistani patients with non-cancerous end-stage liver disease selected for liver transplant and to compare results acquired through various assessment tools.

Methods: The study was conducted at the Rehabilitation Medicine Department, Shifa International Hospital Islamabad, Pakistan, from August 2017 to November 2019 and comprised end-stage liver disease patients of either gender who had been selected for liver transplant. Assessment tools included the Six-Minute Walk Distance, Eastern Cooperative Oncology Group Performance Status and Modified Borg Dyspnoea Scale across age, gender, ethnicity, primary aetiology, and Model for end-stage liver disease score. Data were analysed using SPSS 20.

Results: Of 172 patients, 143(83%) were males; 99(58%) hailed from the Punjab province; and 118(71%) had hepatitis C as the most common aetiology. The overall mean age was 46.1±10.5 years (range: 14-70 years). The mean Six-Minute Walk Distance was 291.9±67.2m. Model for end-stage liver disease score had a significant inverse correlation with Six-Minute Walk Distance ($p<0.01$) and a significant positive correlation with Modified Borg Dyspnoea Scale ($p=0.02$) and Eastern Cooperative Oncology Group Performance Status scores ($p<0.01$). Age and ethnicity had no correlation with the variables ($p>0.05$).

Conclusions: The Six-Minute Walk Distance was significantly low. The Model for end-stage liver disease score was inversely correlated with Six-Minute Walk Distance score, and positively correlated with Eastern Cooperative Oncology Group Performance Status and Modified Borg Dyspnoea Scale scores.

Keywords: Activities of daily living, End-stage liver disease, Liver transplantation, Patient acuity.

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Introduction

End-stage liver disease (ESLD) has profound detrimental effects on physical and psychosocial aspects of human life.[1] Eligibility for liver transplantation (LT) depends on several factors including physical ability. LT significantly improves survival, physical condition, and quality of life (QOL) in suitable patients with ESLD and thus is the treatment of choice. Physical activity of the human body involves integrating the musculoskeletal system with cardiac, pulmonary, and peripheral circulatory systems.[2]

Several clinical tools can be used to assess physical ability. These include the Six-Minute Walk Distance (6MWD), the Eastern Cooperative Oncology Group (ECOG) scale of Performance Status, and the Modified Borg Dyspnoea Scale (MBDS). The 6MWD is a simple hands-on test that evaluates how the body responds to physical activity, and has been used to assess functional status in patients with peripheral vascular disease, heart failure, fibromyalgia, and other conditions.[3] It also has been utilised to predict mortality in patients with heart failure, pulmonary arterial hypertension, chronic obstructive airway disease, and to assess liver and lung transplant candidates.[2,3]

The ECOG Performance Status is another tool to measure patients' ability to perform daily life activities.[4] ECOG developed this tool for use in clinical trials of cancer treatments, but it seems suitable to assess functional status in other patients as well. The ECOG Performance Status measures patients' ability to care for themselves in terms of their daily activities and physical abilities like walking and working.

The assessment of perceived exertion is another method that can be used to determine the maximum tolerated exercise or the maximum safe functional capacity of an individual. The MBDS is one such rating scale, and it is used routinely in cardiopulmonary rehabilitation programmes.[5]

The Model for ESLD (MELD) score is an excellent survival predictor in ESLD patients.[6] The MELD score incorporates three widely available laboratory variables: international normalised ratio (INR), serum creatinine, and serum bilirubin. The score can be calculated online.[7]

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Very few studies worldwide[2,8] have evaluated functional status in patients with ESLD selected for LT. So far, no study has been done in Pakistan in this regard. The current study was planned to evaluate the functional status of Pakistani patients with non-cancerous ESLD who were selected for LT, and to compare results acquired through various assessment tools.

Patients and Methods

This prospective study was conducted at the Rehabilitation Medicine Department, Shifa International Hospital Islamabad, Pakistan, from August 2017 to November 2019. After approval from the institutional ethics review board, the sample size was calculated using an online calculator[9] with known anticipated mean of 369±122 m,[2] power of the test as 95%, α = 0.05, and anticipated mean of the study group as 291.9 m. The sample was raised using consecutive sampling technique from patients of either gender aged >12 years with a medical diagnosis of ESLD who had been selected for LT. Patients with haemodynamic instability, hepatocellular carcinoma, advanced osteoarthritis of the knee or hip joints, and neuromuscular disorders were excluded.

After obtaining written consent, demographic data like age and gender were collected. Ethnicity was based on Pakistani provinces i.e. Punjab, Sindh, Khyber Pakhtunkhwa (KP), Balochistan, and Azad Jammu & Kashmir and Gilgit-Baltistan. They were subsequently evaluated for primary ESLD aetiology. INR and levels of serum creatinine, serum albumin, and serum bilirubin were evaluated in the clinical chemistry laboratory of the institution using an integrated system (ARCHITECTR ci8200; Abbott Diagnostics, Lake Forest, IL, USA). MELD[6] score was evaluated before estimating 6MWD.[3]

The 6MWD was estimated according to the published guidelines.[10] The test was conducted by trained physiotherapists. The patients did not undergo any training to perform the 6MWD test; thus, the first test attempt was the most reliable measure of functional capacity and only the first attempt was used for analysis. The patients were asked to walk as fast as possible in a straight line on a flat surface along the walls of a large hall for six minutes. Development of pain, dyspnoea or palpitations were recorded as drop-out points. The 6MWD was recorded in metres. After the test, the patients were instructed to rate their sensations of dyspnoea and lower-limb fatigue using MBDS from 0 to 10.[5]

The ECOG Performance Status score[4] was also noted. Data were analyzed using SPSS 20. For statistical analysis, the sample was divided into groups based on gender, ethnicity, and primary ESLD aetiology. Mean values were compared with previously reported values using one-sample t-test. Age and MELD score were correlated with 6MWD, ECOG Performance Status MBDS scores employing two-tailed Pearson's bivariate correlation analyses. Analysis of covariance (ANCOVA) using a univariate general linear model was employed to find association of the various tools with gender, ethnicity, and primary ESLD aetiology. The age and MELD scores were taken as covariates during ANCOVA analysis. $P \leq 0.05$ was considered significant.

Results

Of the 260 patients assessed, 172(66%)were included. Of

Table-1: Demographic and clinical profile.

Variables (n)	Mean ± SD (Range)	Variables	n (%)
Age in years (172)	46.1 ± 10.5 (14-70)	Gender	
		Male	143 (83.1)
		Female	29 (16.9)
Six-minute walk distance in meters (162)	291.9 ± 67.2 (70-500)	Primary etiology of chronic liver disease	
		Hepatitis-B Virus	23 (13.8)
		Hepatitis-C Virus	118 (70.7)
		Hepatitis-B and C Virus co-infection	3 (1.8)
		Non-B Non-C Hepatitis Virus	10 (6)
		Others	13(7.8)
Modified Borg Scale Score (162)	1.6 ± 1.2 (0-5)	Missing	5
Eastern Cooperative Oncology Group Performance Status Score (171)	1.6 ± 0.6 (1-3)	Ethnicity based on provinces	
		Punjab	99 (57.9)
		Sindh	31 (18.1)
		Khyber Pakhtunkhwa	21 (12.3)
		Balochistan	14 (8.2)
		Kashmir & Gilgit Baltistan	6 (3.5)
Model for End-Stage Liver Disease Score (172)	18.3 ± 7 (6-40)	Missing	1

SD: Standard deviation.

Table-2: Table showing correlation of 6MWD, ECOG Scales scores, and modified Borg Scales scores with age and MELD scores.

Evaluation tools	Age		MELD[3] Score	
	P-value	r^2	P-value	r^2
6MWD	0.1	-0.13	<0.01	-0.25
ECOG Performance Status Scores	0.14	0.12	<0.01	0.40
Modified Borg Scales scores	0.18	0.11	0.02	0.19

6MWD: Six-minute walk distance
ECOG: Eastern Cooperative Oncology Group
MELD: Model for end-stage liver disease.

them, 143(83%) were males; 99(58%) were from the Punjab province; and 118(71%) had hepatitis C as the noncancerous ESLD aetiology. The overall mean age was 46.1±10.5 years (range: 14-70 years). The mean MELD score was 18.3±7 (range: 6-40), mean ECOG Performance Status score, assessed in 171(99.4%) subjects was 1.6±0.6 (range: 1-3), mean MBDS score, assessed in 162(94%) subjects was 1.6±1.2 (range: 0-5), and mean 6MWD score assessed in 162(94%) subjects, was 291.9±67.2m (Table-1).

MELD score had a significant inverse correlation with 6MWD (p<0.01) and a significant positive correlation with MBDS (p=0.02) and ECOG Performance Status ((p<0.01). Age did not have a significant correlation with 6MWD, MBDS or ECOG Performance Status (Table-2).

Mean 6MWD score was significantly higher in male patients, while the variation for ethnicity and primary ESLD aetiology was not significant (p>0.05). The mean MBDS and ECOG Performance Status did not show significant variance (Table-3).

Discussion

The mean age of the sample in the current study was significantly lower than in studies done in Karachi and Peshawar.[11-13] These studies were done 8-9 years ago, which means that compared to the previous decade, ESLD patients in Pakistan are now selected for LT at significantly younger ages than in the past, when they were hospitalized only after developing complications. This finding indicates progress in healthcare facilities in Pakistan as well as improvement in awareness among patients.

The study participants were predominantly male, which is consistent with other studies from Pakistan exploring ESLD in the local population.[11-13] Pakistani Males may be affected more often than Pakistani females because of cultural and social values. The major cause of ESLD is hepatitis B or C virus infection, for which the primary modes of transmission are contaminated blades used by barbers and sharing of syringes by intravenous drug abusers. In both situations, males are mainly involved. Because the Pakistani government bans alcohol use, alcohol-induced ESLD is not frequent in Pakistan, nonetheless, alcohol-induced hepatitis is also more common in men because it is consumed mostly in settings like bachelor parties.

The most common cause of ESLD in the current study was hepatitis C infection. Other studies from Pakistan have also identified hepatitis C as the most common cause of the upsurge in ESLD in the past few decades.[11-13] Worldwide, the aetiology of ESLD has been changing. In the United States[14] and Brazil,[15] hepatitis C has surpassed alcoholic

Table-3: Variance of 6-minute walk distance (6MWD), Eastern Cooperative Oncology Group (ECOG) Performance Status Score, and Modified Borg Scale scores among genders, Pakistani provinces, and primary aetiology of end-stage liver disease (ESLD).

Variables	6MWD (n=162)	P-value	ECOG Performance Status Score (n=171)	P-value	Modified Borg Scale Score (n=162)	P-value
Gender						
Male	295.2 ± 66.4	0.04	1.6 ± 0.6	0.790	1.6 ± 1.3	0.08
Female	274.8 ± 70.1		1.6 ± 0.5		1.9 ± 1.1	
Ethnicity based on Pakistani provinces						
Punjab	292.7 ± 67.8	0.536	1.6 ± 0.6	0.328	1.6 ± 1.2	0.803
Sindh	301.4 ± 75.9		1.8 ± 0.6		1.8 ± 1.4	
Khyber Pakhtunkhwa	276.6 ± 56		1.4 ± 0.5		1.6 ± 1.3	
Balochistan	284.6 ± 73.5		1.6 ± 0.5		1.4 ± 1.1	
Kashmir and Gilgit Baltistan	305 ± 35.4		1.5 ± 0.5		2.2 ± 1.8	
Primary aetiology of end-stage liver disease						
Hepatitis-B Virus associated hepatitis	283.2 ± 73.7	0.391	1.8 ± 0.6	0.541	1.9 ± 1.6	0.234
Hepatitis-C Virus associated hepatitis	293 ± 65.2		1.6 ± 0.5		1.6 ± 1.2	
Hepatitis B & C co -infection	326.7 ± 64.3		1.3 ± 0.6		0.67 ± 0.6	
Non-A Non-B Hepatitis Virus infection	247.9 ± 73.3		1.7 ± 0.7		2.4 ± 1.4	
Others	324.1 ± 68.9		1.3 ± 0.5		1.6 ± 1.4	

liver disease as the leading cause of cirrhosis. In Europe, alcohol remains the top causative factor for ESLD.[16,17]

The predicted 3-month mortality risk of the sample in the current study was 2% on the basis of available literature.[18] Regrettably, the sampled patients could not be followed up for outcome. The mean MELD score of the sample was significantly higher than what was reported by two studies in Pakistan[19,20] and an American study.[2] However, it was significantly lower compared to another Pakistani study.[11]

A significant inverse correlation of MELD score with 6MWD score was observed, similar to an American study,[2] and a positive correlation was observed for ECOG Performance Status and MBDS scores. These correlations support the assumption that higher MELD scores and thus severe ESLD are associated with poor physical and functional performance. Another study[21] also found low functional capacity and survival rates among patients with severe ESLD before LT. This poor performance was attributed to multiple extra-hepatic complications including de-conditioning, malnutrition-associated muscle weakness, anaemia, cirrhotic cardiomyopathy, and hepato-pulmonary syndrome.[22]

The 6MWD score in our sample was significantly lower than those reported for healthy adults.[8] For patients with cirrhosis, the 6MWD in the current study was significantly shorter compared to a Brazilian and an American studies.[2,15] The male patients in the current study achieved a significantly higher mean 6MWD score than female patients. Several controlled studies have also shown that in healthy populations, males surpass females in 6MWD scores.[23-26] This difference can occur because males are generally taller and have higher levels of physical activity and greater muscle mass than do females.[23,26]

The current study could not establish a significant correlation of 6MWD, MBDS and ECOG Performance Status with ESLD aetiology or ethnicity. In addition, no relation was found of gender with MBDS and ECOG Performance Status. Worldwide, very few studies have found a significant correlation of 6MWD with ESLD aetiology like a Brazilian study[15] found a significantly shorter mean 6MWD for patients with alcoholic cirrhosis compared to patients with hepatitis B or C.

The current study has a few limitations. First, the waiting time for LT was not included which was a potential confounder in terms of altering functional status. Also, there were missing values that might have influenced the overall results. Finally, the patients were not followed-up to observe survival in the sample.

Conclusion

6MWD scores were significantly lower compared to healthy individuals and scores previously reported. The males had higher mean 6MWD scores than females. MELD scores inversely correlated with 6MWD scores and positively with the ECOG Performance Status and MBDS scores. The 6MWD, MBDS and ECOG Performance Status were not affected by age, ESLD aetiology or ethnicity.

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