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Medicine

The Ascitic Fluid Fibronectin Level to Differentiate Malignant From Nonmalignant Ascites

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Abstract **Original Research Article**

Objective: In this study our main goal is to evaluate the ascitic fluid fibronectin level to differentiate malignant from nonmalignant ascites. ***Method:*** This observational, cross sectional type study conducted in Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka from September 2014 to February 2017. During the study period of total 60 patients (30 patients with malignant ascites and 30 patients with nonmalignant ascites) were enrolled for the study. ***Results:*** Mean ascetic fluid fibronectin was found 0.50±0.15µg/ml in malignant ascites group and 0.22±0.07µg/ml in nonmalignant ascites group. Mean ascitic fluid fibronectin was found 0.64±0.11 µg/ml in positive for malignant cell group and 0.45±0.17 µg/ml in negative for malignant cell group. The mean difference was not statistically significant (p>0.05) between two groups. Sensitivity of cut off value of ascitic fluid fibronectin ≥0.22 µg/ml was 82.86%, specificity 96.0%, accuracy 88.33%, positive and negative predictive values were 96.67% and 80.0% respectively. ***Conclusion:*** The present study revealed on the usefulness of fibronectin in the differential diagnosis of ascites and these data and findings suggest that fibronectin may have potential value to differentiate malignant from nonmalignant ascites.

Keywords: Ascitic fluid fibronectin, malignant ascites, nonmalignant ascites.

INTRODUCTION

Ascites is the pathologic accumulation of fluid in the peritoneal cavity [1]. It forms because of conditions directly involving the peritoneum (malignancy, infection), or diseases remote from the peritoneum (liver disease, heart failure, hypoproteinaemia). Cirrhosis is the commonest cause of ascites (85%), remaining 15% have a cause other than liver disease, including peritoneal tuberculosis, cancer, cardiac failure or nephrotic syndrome [2].

Differentiation between malignant and nonmalignant ascites is a common clinical problem because no single routine biochemical laboratory test can completely distinguish between them and, although cytological examination of ascitic fluid is highly specific, its diagnostic sensitivity is only about 40-60% [3, 4]. There are no distinctive features and no single diagnostic test is accurate in differentiating malignant and nonmalignant ascites [5]. There is a chance of false positive results in cytological examination as reactive mesothelial cells in the ascitic fluid are mimic of malignant cells [6]. Various tumor markers (CA 19-9, CEA, AFP, CA 125, CA 15-3) are used to diagnose primary site of malignancy. But these are too sensitive to diagnose. On the other hand, diagnostic performance of these tumor markers in malignant ascites is not conclusive.

In this study our main goal is to evaluate the ascitic fluid fibronectin level to differentiate malignant from nonmalignant ascites.

OBJECTIVE

General objective

- To evaluate the ascitic fluid fibronectin level to differentiate malignant from nonmalignant ascites.

Specific objective

- To detect relation of ascitic fluid fibronectin in malignant ascites with negative and positive for malignant cell
- To assess performance of diagnostic test in the patients.

METHODOLOGY

Study type

- This was an observational, cross sectional type study.

Place and period of the study

- This study was conducted in Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, and Dhaka from September 2014 to February 2017.

Study Population and sample size

- During the study period of total 60 patients (30 patients with malignant ascites and 30 patients with nonmalignant ascites) were enrolled for the study.

Study procedure

- Patients with ultrasonographic evidence ascites admitted in the Department of Hepatology, Oncology, Gynae Oncology and Internal Medicine of BSMMU were provisionally selected. Then proper history, clinical examination and some initial investigations like CBC, S. Albumin, Urine R/M/E, Ascitic fluid study (Cytology, total protein, SAAG, ADA, malignant cell) and Chest X-ray P/A view were done for matching of inclusion and exclusion criteria. Further investigations were done according to the study protocol like ECG, Echocardiography, AFP, CA 19-9, CEA, CA 125, CA 15-3, TVS, Endoscopy of UGIT, Colonoscopy, CT Scan of abdomen, FNA from primary site, Laparoscopy/ Laparotomy with biopsy. Patients who meet inclusion & exclusion criteria were informed in details about the study.

Data processing and data analysis

- The statistical analysis was carried out using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test was used to analyze the categorical variables, shown with cross tabulation. Sensitivity, specificity, positive predictive value and negative predictive value were calculated by using the area under the receiver operating characteristic (AUROC) curves. P value of <0.05 was taken as significant.

RESULTS

In figure-1 shows age distribution of the patients where in nonmalignant ascites group 9(30.0%) patients belonged to age 41-50 years and malignant ascites group majority 8(26.7%) patients belonged to age 51-60 years. The mean age was found 29.19±9.11 years were nonmalignant group and 32.80±9.20 years in malignant group. The following figure is given below in detail:

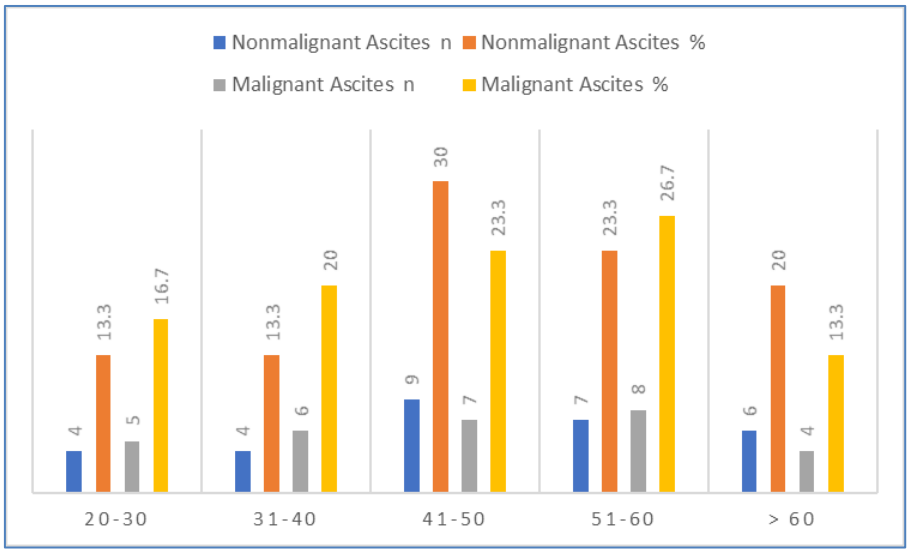

Fig-1: Distribution of age in years according to study groups (n=60)

In figure-2 shows gender distribution of the study patients, it was observed that male was found 22(73.3%) in nonmalignant ascites group and 13(43.3%) in malignant ascites group. The difference was statistically significant (p<0.05) between two groups. Female patients were more in malignant group compared to male. The following figure is given below in detail:

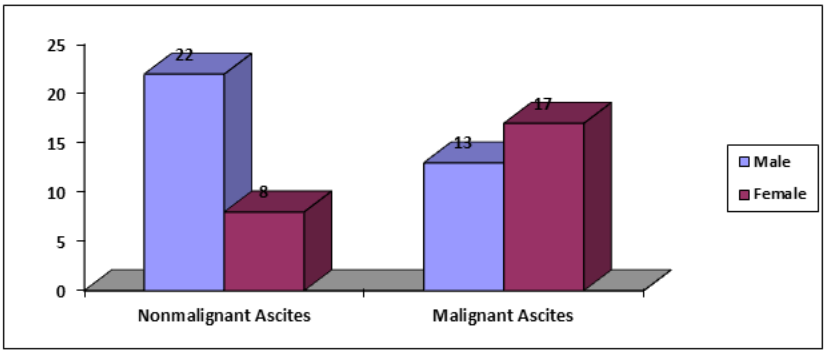

Fig-2: Gender distribution of the study patients

In table-1 shows relation between ascitic fluid fibronectin between malignant and nonmalignant ascites. Mean ascetic fluid fibronectin was found 0.50±0.15µg/ml in malignant ascites group and 0.22±0.07µg/ml in nonmalignant ascites group. The mean difference was statistically significant ($p<0.05$) between two groups. The following table is given below in detail:

Table-1: Relation between ascitic fluid fibronectin between malignant and nonmalignant ascites (n=60)

Variable	Nonmalignant ascites Mean(±SD)	Malignant ascites Mean(±SD)	p value
Ascitic fluid fibronectin (µg/ml)	0.22(±0.07)	0.50 (±0.15)	<0.001

p value reached from unpaired t-test.

In table-2 shows relation of ascitic fluid fibronectin with negative and positive for malignant ascitic cell. Mean ascitic fluid fibronectin was found 0.64±0.11 µg/ml in positive for malignant cell group and 0.45±0.17 µg/ml in negative for malignant cell group. The mean difference was not statistically significant ($p>0.05$) between two groups. The following table is given below in detail:

Table-2: Relation of ascitic fluid fibronectin in malignant ascites with negative and positive for malignant cell

Variable	Positive for malignant cell Mean(±SD)	Negative for malignant cell Mean(±SD)	p value
Ascitic fluid fibronectin (µg/ml)	0.54(±0.11)	0.45 (±0.17)	0.49

In figure-3 shows receiver–operator characteristics (ROC) curve of ascitic fluid fibronectin for performance of diagnostic test. The test result variable(s): Ascitic fluid fibronectin (0.951) has at least one tie between the positive actual state group and the negative actual state group. 95% Confidence Interval of the difference lower 0.884 and upper 1.0. Ascitic fluid fibronectin ≥0.22 µg/ml. The following figure is given below in detail:

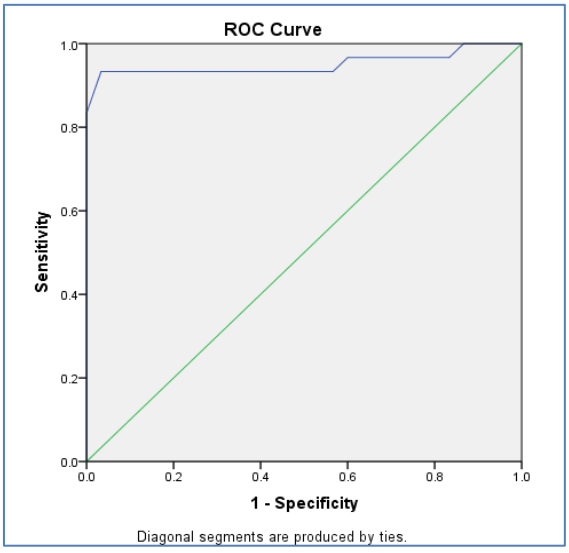

Fig-3: Receiver –operator characteristics (ROC) curve of ascitic fluid fibronectin for performance of diagnostic test

In table-3 shows performance of diagnostic test where table shows that sensitivity of cut off value of ascitic fluid fibronectin ≥0.22 µg/ml was 82.86%, specificity 96.0%, accuracy 88.33%, positive and negative predictive values were 96.67% and 80.0% respectively. The following table is given below in detail:

Table-3: Performance of diagnostic test

Variable	Sensitivity	Specificity	PPV	NPV	Accuracy
Cut off value of ascitic fluid fibronectin ≥0.22 µg/ml	82.86%	96.00%	96.67%	80.0%	88.33%

DISCUSSION

Regarding gender distribution of the study patients, it was observed that male was found 13(43.3%) in malignant ascites group and 22(73.3%) in nonmalignant ascites group. The difference was statistically significant (p<0.05) between two groups. In our study female patients were more in malignant group. Similar observations were found in different studies. One study showed that 25 (33.3%) were males and 50 (66.7%) females. Male was found 7 in malignant group and 18 in nonmalignant group. Female was 30 in malignant group and 20 in nonmalignant group. [6] Another report showed 55 was female and 52 were male [7].

In this study the mean ascitic fluid fibronectin was found 0.50±0.15 µg/ml in malignant ascites group and 0.22±0.07 µg/ml in nonmalignant ascites group. The mean difference was statistically significant (p<0.05) between two groups. One study showed that the mean ascitic fibronectin concentration in patients with malignant ascites was 97.54±17.73 µg/ml as against 47.76±13.32 µg/ml seen in nonmalignant ascites (p<0.001) [6]. Another study showed that concentrations of ascitic fibronectin were significantly higher in malignant ascites than in nonmalignant ascites. They also showed that there is a link between malignancy and fibronectin levels [8]. Another report showed that the mean values of ascitic fluid fibronectin, for malignant and nonmalignant group were 538±46 pg/mL and 60± 4.92pg/mL, respectively (p < 0.001) [9].

In our study showed that sensitivity of cut off value of ascitic fluid fibronectin ≥0.22 µg/ml was 82.86%, specificity 96.0%, accuracy 88.33%, positive and negative predictive values were 96.67% and 80.0% respectively. One study showed the diagnostic accuracy of fibronectin in ascitic fluid was found to be 94.7%, using a cut-off value of 73µg/ml. The sensitivity, specificity, and accuracy of fibronectin were 94.6%, 94.7% and 94.7% respectively [6]. This agrees with earlier studies done by other study who got an accuracy of 97.1% in their study and a sensitivity of 100%.

Another report also conducted similar studies and arrived at a diagnostic accuracy of 95.9% for ascitic fibronectin [10]. In a similar study showed 100% accuracy for fibronectin as against 78.7% for malignant cytology. This implies that fibronectin may be more sensitive for diagnosis of malignant ascites [11]. The specificity of ascitic fibronectin in this study (94.7%), is similar to that reported by other studies [13].

CONCLUSION

The present study revealed on the usefulness of fibronectin in the differential diagnosis of ascites and these data and findings suggest that fibronectin may have potential value to differentiate malignant from nonmalignant ascites.

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