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## BIOCHEMICAL EVALUATION IN NON-MALIGNANT AND MALIGNANT ASCITES

Md.Khaleel Pasha<sup>1</sup>, Qamar Ayesha<sup>1</sup>, M.Lakshmi Narasu<sup>3</sup>, SK. Jaffar<sup>5</sup>, Md. Ibrahim<sup>6</sup>, B.Prabhakar<sup>1</sup>,  
M.Srinivasulu<sup>4</sup>, M.Gopal Reddy<sup>2</sup>

<sup>1</sup>Dept. of Gastroenterology, Osmania General Hospital, Hyderabad, AP. India.

<sup>2</sup>Dept. of Bio-chemistry, Osmania General Hospital, Hyderabad, AP India.

<sup>3</sup>Professor and HOD, Dept. of Biotechnology, JNTU, Kukatpally, Hyderabad A.P. India.

<sup>4</sup>Professor & HOD, Dept. of Surgical Oncology, M.N.J.Institute of Oncology Regional Cancer Centre,  
Red Hills, Hyderabad, A.P. India.

<sup>5</sup>Dept. of Biochemistry, Acharya Nagarjuna University, Guntur, A.P, India.

<sup>6</sup>Dept. of Biochemistry, Shadan Institute of Medical Science, Hyderabad, A.P. India.

*Email: [kpkhaleel6@gmail.com](mailto:kpkhaleel6@gmail.com)*

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### Abstract

Early diagnosis of peritoneal metastases from cancer patients provides better management and treatment aspects. In the present study biochemical investigations such as albumin, total proteins, lactate dehydrogenase and cholesterol in the serum and ascitic fluid aspirates were done in 46 ovarian malignant (46 females mean age 49.47±12.64 yrs) and 70 non-malignant ascites patients (54 males and 16 females mean age 49.1±10.78 yrs). The results in the fluid showed that lactate dehydrogenase, total proteins and cholesterol levels were drastically increased, while SAAG is reduced in malignant ascites when compared to non-malignant ascitic patients. The present study thus emphasizes that SAAG is still useful in the differential diagnosis of ascites.

**Key Words:** Ascites, Differential diagnosis, Malignancy, Biochemical markers.

### Introduction

Ascitic fluid proteins and lactate dehydrogenase (LDH) concentration as well as ascitic fluid to serum ratio of proteins and lactate dehydrogenase have been used earlier to classify ascites into exudate and transudate categories<sup>1</sup>.

A serum ascites albumin gradient (SAAG) is now considered a useful parameter in ascites<sup>2,3</sup>. Several studies were published earlier to assess the causative factors of ascites<sup>4,5</sup>. Ascitic cholesterol and lactate dehydrogenase were also assayed earlier as the discriminative parameters of malignant ascites from cirrhosis and hepatocellular carcinoma-

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associated ascites<sup>6</sup>. The diagnostic limitations of biochemical evaluation of peritoneal effusions in differentiating malignant and non-malignant pathologies were indicated earlier<sup>7</sup>. In the present study we have evaluated serum and ascitic fluid albumin, total proteins, lactate dehydrogenase and cholesterol levels in the patients with non-malignant and malignant ascites.

## **Materials and Methods**

Paired ascitic fluid and blood samples were obtained from the ascitic patients within 24 hrs of admission preferably before doing any interventions over a period of 8 months from Oct-2011 to May-2012 from the departments of Biochemistry and Gastroenterology, Osmania General Hospital and M.N.J. Institute of Oncology and Regional Cancer Centre, Red Hills, Hyderabad. Blood samples were collected in plain tubes and ascitic fluid in sterile containers. Blood samples were centrifuged for 10 minutes at 3000 rpm within one hour of collection. Serum and ascitic fluid samples were stored immediately at  $-20^{\circ}\text{C}$  till analysis was done within a period of 48 hours.

A total number of 46 female patients with ovarian malignancy (mean age  $49.47 \pm 12.64$  yrs) and 70 patients with cirrhosis of liver (non-malignant group) (54 males 16 females, mean age  $49.12 \pm 10.78$  yrs) and 60 healthy controls (paramedical staff & police recruitment constables) were included in the study.

The patient's history was recorded in the specific proforma approved by the Ethical Committee of Osmania Medical College. After thorough clinical examinations of the patients all the basic and routine investigations were done.

The specific biochemical parameters such as total proteins were measured by Biuret method, albumin measured by Bromo Cresol Green (BCG) dye binding method, lactate dehydrogenase was done by DGKC kinetic method and cholesterol by CHOD-PAP enzymatic method by using the kits from Erba Mannheim in auto analyzer.

The values of all these parameters from healthy controls and ascitic patients (both malignant & non-malignant groups) were expressed as mean  $\pm$ SD.

Statistical Evaluation: The results are given as mean, standard deviation. Statistical analysis was performed by One way analysis of Variance (ANOVA) followed by student unpaired "t" test for significance. Results were analyzed separately for the two groups.

## Results

The results of albumin, total proteins, lactate dehydrogenase and cholesterol in the serum sample of various groups are presented in table-1, while the results of the same parameters in ascitic fluid are presented in table-2. The results in the serum samples did not show major variations in malignant & non-malignant groups when compared to that of controls except for a drastic increase of lactate dehydrogenase levels in malignant group. Interestingly all these parameters i.e. albumin, total proteins, lactate dehydrogenase and cholesterol were significantly increased ( $P < 0.05$ ) and SAAG is significantly decreased ( $p < 0.05$ ) in the ascitic fluid samples of the malignant group, as depicted in graph 1 to 4.

**Table-1: Comparison of total proteins, albumin, lactate dehydrogenase and cholesterol in serum samples of non-malignant and malignant ascites with healthy controls.**

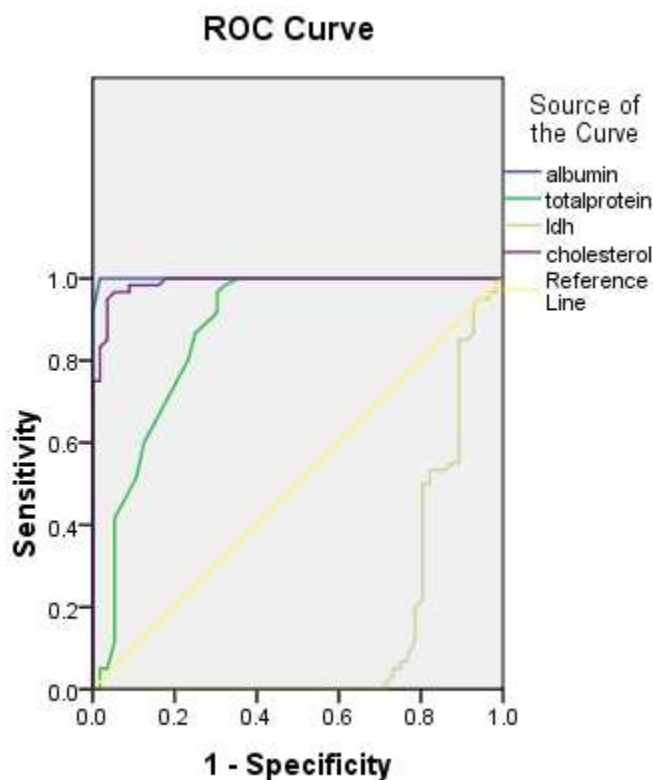
SERUM SAMPLES	HEALTHY CONTROLS n = 60	MALIGNANT ASCITES n = 46	NON- MALIGNANT ASCITES n=70	DIFFERENCES
Total proteins*	6.960±0.345	6.80 ±0.601	5.85 ± 0.819	P < 0.05
Albumin*	4.123 ±0.276	3.878 ±0.622	2.48±0.394	P < 0.05
Lactate dehydrogenase**	246.9 ±47.0	1496.2 ±138	469.2±165.3	P < 0.05
Cholesterol***	163.3±25.4	157.4±30	94.64±20.5	P < 0.05

Values are expressed as mean +/- S.D ; \* values are expressed as gm/dl, \*\* values are expressed as U/L, \*\*\* values are expressed as mg/dl.

**Table-2: Comparison of total protein, albumin, lactate dehydrogenase, cholesterol and SAAG in Ascitic Fluid samples of non- malignant and malignant Ascites.**

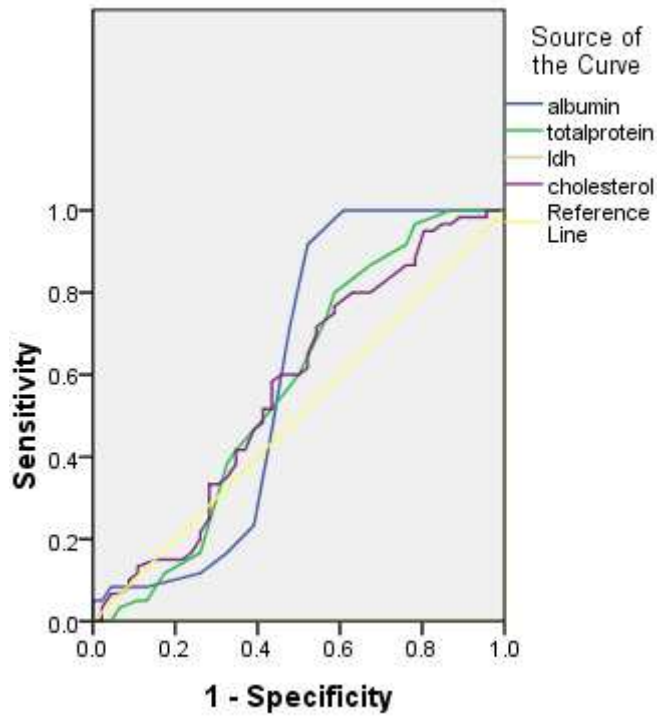
ASCITIC FLUID	MALIGNANT n = 46	NON- MALIGNANT n = 70	DIFFERENCES
Total proteins*	5.01±0.784	1.43 ±0.80	P < 0.05
Albumin*	3.278 ±0.64	0.5 ± 0.37	P < 0.05
Lactate dehydrogenase**	475 ±78.25	104 ±58.46	P < 0.05
Cholesterol***	90.89 ±12.0	13.57 ±4.85	P < 0.05
SAAG	0.60 ±0.163	1.92 ±0.44	P < 0.05

Values are expressed as mean ± S.D ; \* values are expressed as gm/dl, \*\* values are expressed as U/L, \*\*\* values are expressed as mg/dl.



**ROC Curve-1: Serum samples healthy and non-malignant group.**

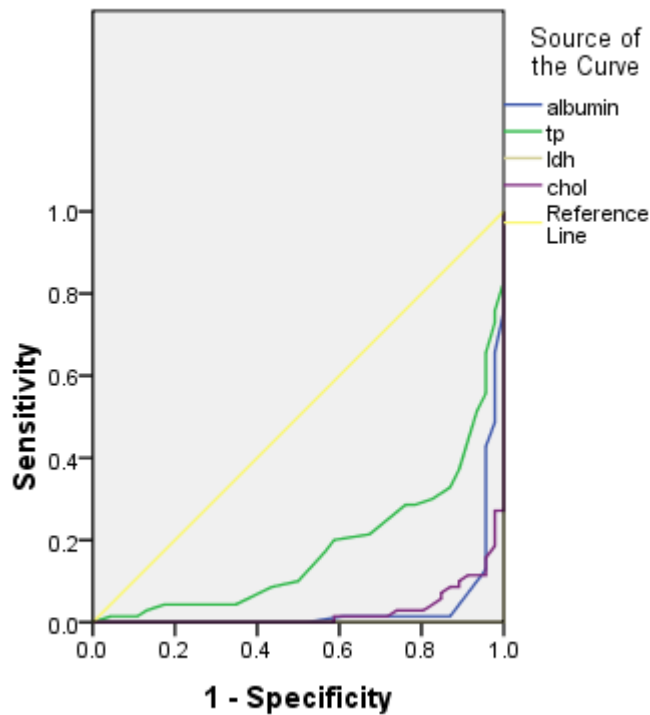
### ROC Curve



Diagonal segments are produced by ties.

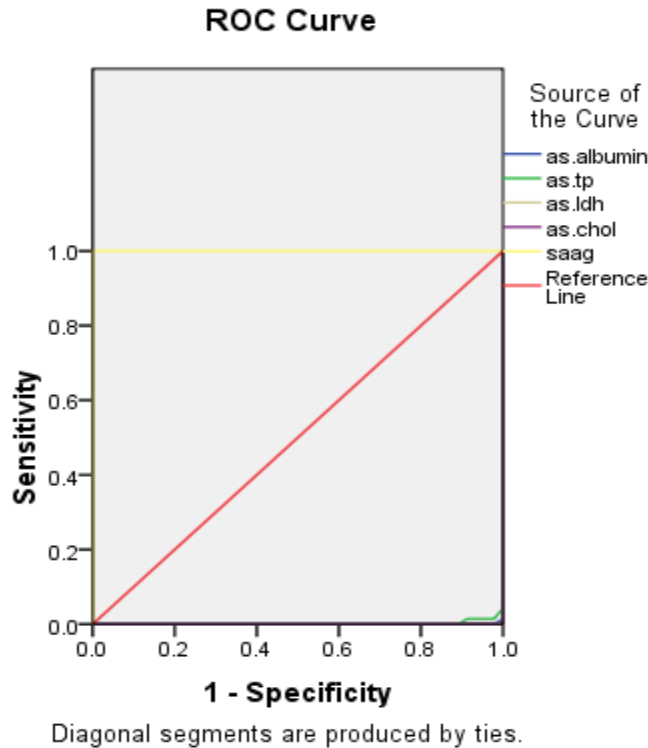
**ROC Curve-2: Serum samples healthy and malignant group.**

### ROC Curve



Diagonal segments are produced by ties.

**ROC Curve-3: Serum samples non-malignant and malignant group.**



**ROC Curve-4: Ascitic fluid non-malignant and malignant group.**

## Discussion

Distinction between malignant and other causes of ascites has important therapeutic and prognostic implications. Apart from routine cytology and microbiology, biochemistry of both serum and peritoneal effusion fluid may help in the differentiation of benign and malignant ascites. In the present study we have evaluated the levels of albumin, total proteins, lactate dehydrogenase, cholesterol in serum and ascitic fluids from 70 patients with cirrhosis of liver and 46 patients with ovarian malignancies. It is observed that lactate dehydrogenase, total proteins and cholesterol levels in peritoneal fluids are drastically increased and SAAG is reduced in malignant ascites. Jangst et al (1996) have evaluated the value of ascitic fluid lipids in the differentiation of cirrhotic and malignant ascites and concluded that ascitic fluid cholesterol determination offers an excellent, cost-effective discrimination of ascites due to the cirrhosis versus ascites caused by malignancies<sup>9</sup>. Castaldo et al (1994) showed a test association of ascitic cholesterol and lactate dehydrogenase discriminate between malignant and benign ascites with an efficiency of 100%<sup>6</sup>. Aksoy et al (1998) evaluated sialic acid, fibronectin, cholesterol, lactate dehydrogenase, total proteins in malignant and non-malignant ascites and found that fibronectin is the most efficient parameter for the differential diagnosis of ascites<sup>8</sup>. Bielakovic et al (2001) confirmed that biochemical, cytological and microbiological examinations are very helpful in differential

diagnosis of ascites and reported significantly higher total protein and cholesterol concentrations in malignant ascites<sup>10</sup>

.However the diagnostic limitations of biochemical evaluation of peritoneal effusion in different malignant and non-malignant pathologies are recently discussed by Cretu et al (2010) and they reported the accuracy of total cholesterol (90%), LDH(85%), and SAAG (85%)<sup>7</sup>.

## **Conclusion**

As success of treatment depends on the diagnostic accuracy, biochemical investigation of both serum and peritoneal fluids can be successfully employed for an initial diagnosis of malignant transformation and a better evaluation of progress of neoplasia and can be helpful in the therapeutic treatment. The present study emphasizes that SAAG is still useful in the differential diagnosis of ascites.

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**Corresponding Author:**

**Md.khaleel pasha\*,**

**Email: [kpkhaleel6@gmail.com](mailto:kpkhaleel6@gmail.com)**