

## Low gradient ascites: A seven-year course review

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### Abstract

**AIM:** To study the patients with low gradient ascites in hospitals of Guilan Province (northern Iran).

**METHODS:** Patients admitted in hospitals of Guilan Province with low gradient ascites from 1993 to 2000 were enrolled in the study. Serum and ascitic fluid albumin levels were determined by biochemical reactions. The serum-ascitic albumin gradient (SAAG) less than 1.1 g/dL was considered low. Statistical analysis was performed with SPSS 9.0 software and  $P < 0.05$  was considered statistically significant.

**RESULTS:** Of the 148 patients enrolled in the study, 72 (48.6%) were males and 76 (51.4%) were females with a mean age of  $59.03 \pm 13.54$  years. Tuberculous peritonitis was the most frequent cause of low gradient ascites in 68 (45.9%). Other most frequent causes were cancer in 62 (41.9%), nephrotic syndrome in 9 (6%), pancreatitis in 6 (4%). Peritoneal cancer was found in 22 (35%), ovarian and gastric cancers were found in 14 (22.5%) and 12 (19.3%), respectively. All of which were the causes of ascites. The mean SAAG was  $0.68 \pm 0.19$  g/dL. The mean serum and ascitic fluid albumin concentrations were higher in tuberculous patients ( $P < 0.006$ ), but lactate dehydrogenase (LDH) level was higher in cancer patients ( $P < 0.0001$ ). In peritoneal tuberculosis, mean ascitic glucose concentration was significantly lower than other patients ( $P < 0.0001$ ).

**CONCLUSION:** Tuberculosis should be considered in all patients with low gradient ascites especially in developing countries (like Iran), as the first cause of ascites. In the approach to patients with low gradient ascites, ascitic fluid glucose, and LDH level are useful indicators for decision making.

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**Key words:** Ascites; Tuberculosis; Cancer; Albumin

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### INTRODUCTION

Pathologic accumulation of fluid in the peritoneal cavity (ascites) is an important clinical finding and its appropriate treatment depends on correct diagnosis, which can be made by diagnostic abdominal paracentesis, a simple and safe procedure, which can be done at bedside or in the office<sup>[1,2]</sup>.

Serum ascites albumin gradient (SAAG), cell count, bacterial culture, pH, glucose, lactate dehydrogenase (LDH) and amylase are useful in the differential diagnosis of ascites<sup>[3,5]</sup>.

Different diseases can cause different types of ascites. Some of the known low gradient ascites include tuberculous peritonitis-induced ascites, malignancy-induced ascites (for instance, peritoneal carcinomatosis, gastric and ovarian cancer metastases), pancreatic ascites, renal ascites, biliary ascites, bacterial peritonitis and serositis-induced ascites. On the other hand, high gradient ascites are uncomplicated cirrhosis-induced ascites, heart-failure-induced ascites, those induced by extensive liver metastases and other circumstances such as fulminant hepatic failure<sup>[4-7]</sup>.

Like wise, the measurement of SAAG is helpful in the determination of response to treatment of all types of ascites<sup>[8]</sup>.

In the present study, we determined the relative frequency of low gradient ascites in a 7-year period in Guilan Province, northern Iran.

### MATERIALS AND METHODS

This survey was done according to the data obtained from the records of admitted patients with primary diagnosis of ascites, from 1993 to 2000 in hospitals of Guilan Province. Serum and ascitic fluid samples were taken for determination of the levels of albumin (blue bromocresol procedure), LDH (LDH specific kits) and glucose (biochemical assays)<sup>[9]</sup>.

In this study, SAAG less than 1.1 g/dL was considered as low gradient ascites<sup>[4,6]</sup>.

Cytological study of ascites and peritoneal biopsy (blind peritoneal biopsy, biopsy with laparoscopy or laparotomy) were used for the diagnosis.

Malignancy-induced ascites included those caused by peritoneal carcinomatosis with unknown origin, ovarian cancer, extensive liver metastases, hepatocellular carcinoma (HCC), lymphoma and gastric cancer<sup>[10]</sup>.

The diagnosis of TB peritonitis required mycobacterial growth in the ascitic fluid culture or the presence of

**Table 1 Comparison of causes of low gradient ascites in age groups**

Causes Age (yr) group	TB		Malignancy		Other causes		Total	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%
35-45	3	11.1	13	48.2	11	40.7	27	100
46-55	11	38	13	44.8	5	17.2	29	100
56-65	21	51.3	19	46.3	1	2.4	41	100
>65	33	64.7	17	33.3	1	2	51	100
Total	68	45.9	62	41.9	18	12.2	148	100

$P < 0.0001$ ,  $\chi^2 = 39.3$ .

granuloma in the biopsy specimen of peritoneum, which was confirmed by laparoscopy<sup>[11]</sup>. The diagnosis of pancreatic ascites was based on clinical manifestations and at least more than twice the rise of ascitic fluid amylase in proportion to its normal serum level. The diagnosis of renal or nephrotic syndrome ascites was suspected when the patient developed ascites in the presence of nephrotic syndrome (it means urine protein excretion rate more than 3.5 g/1.73 m<sup>2</sup> per 24 h). Connective tissue diseases were considered as a cause of ascites when ascites developed in a known case of connective tissue diseases such as systemic lupus erythematosus, scleroderma, rheumatoid arthritis without other causes<sup>[4,5]</sup>.

Data were analyzed with SPSS 9.0 using Friedman's test, Student's *t* test and  $\chi^2$  test.

## RESULTS

One hundred and forty-eight patients with low gradient ascites admitted into hospitals of Guilan Province from 1993 to 2000 were enrolled in the study. There were 72 (48.6%) males and 76 (51.4%) females with a mean age of 56.03±13.54 years.

Tuberculous peritonitis was the most frequent cause of low gradient ascites in 68 (45.9%). Other frequent causes were cancer in 62 (41.9%), nephrotic syndrome in 9 (6%), pancreatitis in 6 (4%), serositis in 2 (1.3%) and spontaneous bacterial peritonitis (SBP) in 1 (0.7%).

Peritoneal cancer was found in 22 (35%), ovarian and gastric cancers were found in 14 (22.5%) and 12 (19.3%) respectively followed by lymphoma in 8 (12%) and HCC in 6 (10.2%), all of which were the causes of ascites.

Tables 1 and 2 show the frequency of low gradient ascites according to age group and sex.

Age groups had significant differences ( $\chi^2 = 39.3$ ,  $P < 0.0001$ ), but type of low gradient ascites did not show any significant difference between male and female groups.

The mean SAAG was 0.68±0.19 g/dL. The mean serum albumin concentration was 3.94±0.76 g/dL and that of ascitic fluid was 3.28±0.68 g/dL. The mean serum and

**Table 2 Comparison of causes of low gradient ascites in sex groups**

Causes Sex	TB		Malignancy		Other causes		Total	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%
Male	36	50	28	38.9	8	11.1	72	100
Female	32	42.1	34	44.7	10	13.2	76	100
Total	68	45.9	62	41.9	18	12.2	148	100

**Table 3 Comparison of the concentration of serum albumin (Alb), ascites Alb, SAAG, ascites, lactate dehydrogenase (LDH) and glucose in TB patients and cancer patients (mean±SD)**

Disease Parameter	TB	Malignancies	Differences
Serum Alb.	4.2±0.49	3.9±0.70	$P < 0.005$
Ascitic Alb.	3.5±0.47	3.30±0.50	$P < 0.006$
SAAG	0.68±0.17	0.69±0.22	Not significant
Ascitic LDH	327±113	409±106	$P < 0.0001$
Ascitic glucose	71±13.82	101.4±17.2	$P < 0.001$

ascitic albumin, LDH and glucose were compared between TB and cancer patients, all differences were significant ( $P < 0.006$ ). The mean SAAG did not differ significantly between cancer and TB patients (Table 3).

Moreover, the mean ascitic glucose concentration in TB patients was the lowest in comparison to all other causes of low gradient ascites and the differences were statistically significant ( $P < 0.001$ ).

When patients were divided into two groups according to their LDH concentration, the relative frequency of cancer group with LDH >250 u/mL was significantly higher than that of TB group ( $P < 0.0001$ ).

## DISCUSSION

In the present study, the causes of low gradient ascites were found as follows: TB peritonitis, peritoneal carcinomatosis and other malignancies, nephrotic syndrome, pancreatitis, serositis, and SBP.

In a study by Runyon in 1991<sup>[3]</sup>, low gradient ascites include malignancy-induced ascites (peritoneal carcinomatosis), TB peritonitis-induced ascites, pancreatic ascites, biliary ascites, nephrotic ascites, ascites induced by serositis, and intestinal obstruction or infarction.

In contrast, TB was the most frequent cause in our study. Since it is a treatable infectious disease and has a good prognosis, TB should always be considered as the first diagnosis in patients with low gradient ascites. In a survey in United States, 11 of 20 patients with liver cirrhosis died of TB peritonitis, without any suspicion to TB before death<sup>[12]</sup>.

Peritoneal cancer was most frequently found, usually without any evidence of its origin. Prognosis of different cancer-induced ascites was also different. For example, the survival of patients with ovarian cancer was 1-2 years, whereas with gastric cancer, the life span of patients usually was no more than 4 mo<sup>[10-13]</sup>.

In this study, the mean serum and ascitic fluid albumin concentrations were significantly higher in TB patients than in cancer patients.

Ascitic fluid LDH level in cancer patients was higher than that in TB patients, but glucose level was lower in ascitic fluid of TB patients. As reported in the literatures<sup>[8,14]</sup> measuring LDH and glucose in ascitic fluid would help in the differential diagnosis of low gradient ascites.

The mean SAAG was not significantly different between TB and cancer patients with low gradient ascites, indicating that although SAAG has a good diagnostic value in differential diagnosis of ascites, it does not give much help

in the differentiation of various types of low gradient ascites.

In spite of the moderate prevalence of tuberculosis in Iran<sup>[15]</sup>, more than 45% of low gradient ascites were caused by TB peritonitis followed by cancers. Therefore, we recommend that whenever the diagnosis in low gradient ascites is established by measuring SAAG, LDH and glucose level of ascitic fluid should also be measured as an adjunct for diagnostic approach. Low LDH (<250 u/mL) and glucose levels indicate TB, while high LDH and glucose levels suggest cancer as the major cause.

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