

Original article

Prevalence of tuberculous peritonitis in the North of Iraq and sociodemographic comparison with pulmonary tuberculosis

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Abstract

Objective: Tuberculosis continues to be an important health problem in the world. Despite the widespread impression that abdominal tuberculosis is rare today, the disease is still endemic in developing world and is re-emerging in the West. The aim is to review our local experience with tuberculous peritonitis. **Methods:** Between January 2000 and December 2006, the case records of histologically documented tuberculous peritonitis (TBP) diagnosed and treated at the tuberculosis coordinating center in Erbil city, Iraq were reviewed. Comparisons were made with pulmonary tuberculosis patients regarding socio-demographic, clinical and laboratory findings. **Results:** Forty one cases of TBP were diagnosed during the study period. Their age range was 26-72 years (46 ± 17), with a male; female ratio of 1.5:1. The median duration of symptoms before diagnosis was 6 weeks (range; 10 days to 18 months.). Eleven patients (26.8%) had comorbid conditions and 6 patients (14.6%) had a history of positive contact with Tuberculosis (TB) case. Presenting symptoms were abdominal distension (70%), abdominal pain (65%), fever (68%), anorexia (65%) and weight loss (44%). Four patients had pulmonary symptoms: cough and/ dyspnoea ($n = 2$) and cough ($n = 2$). Chest X-ray changes consistent with pulmonary tuberculosis (PTB) were seen in 25%. Tuberculous peritonitis was diagnosed by laparoscopy ($n = 29$) and laparotomy ($n = 12$). Adverse effects of TB drugs occurred in nearly 40%, consisting of hepatitis ($n = 2$), nausea/vomiting ($n = 11$), rash ($n = 2$) and encephalopathy ($n = 1$). Hemoglobin and serum albumin levels were significantly lower in tuberculous peritonitis (TBP) TBP patients ($P = 0.027$ and 0.003 , respectively). There was a significantly greater occurrence of adverse effects ($P < 0.001$) in TBP patients. No significant differences between TBP and PTB were demonstrated in regard to age and sex distribution, non-specific symptoms (fever, weight loss, and anorexia) and erythrocyte sedimentation rate. All were treated with standard regimens and responded to treatment. **Conclusion:** Tuberculous peritonitis is prevalent in our population. Therefore, TBP should be considered in patients presenting with abdominal symptoms and non-specific constitutional symptoms, particularly in young patients. Laparoscopy and laparotomy with tissue biopsy was the specific diagnostic procedure.

Keywords: Tuberculous peritonitis; Pulmonary tuberculosis; Laparotomy; Laparoscopy; Treatment outcome

INTRODUCTION

The incidence of tuberculosis (TB) is sharply rising in the developing as well as in developed countries and tuberculous peritonitis is often diagnosed late in

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the course of the disease, resulting increased patient morbidity and mortality^[1, 2]. Despite the widespread impression that tuberculous peritonitis (TBP) is rare today, the disease appears regularly on the surgical services worldwide^[3, 4]. Its symptoms are insidious and non-specific and often simulate symptoms of carcinomatous peritonitis^[5]. It constitutes the third most common etiologic factor for ascites, after hepatic cirrhosis and neoplasm and it is the sixth most frequent cause of extra pulmonary tuberculosis (PTB) in the USA^[6], following lymphatics, genitourinary tract, bone and joint, miliary and meningeal tuberculosis^[6,7]. It may be associated with Human Immunodeficiency Virus, although the pattern of presentation seems to differ^[8]. It is often not considered in the differential diagnosis of abdominal pain and it is left untreated. Most often, especially in women with abdominal pain, ascites, obstruction or peritonitis, the diagnosis is ovarian cancer^[7, 9, 10].

In this article, we present a review of the local experience with tuberculous peritonitis, looking at the clinical characteristics, investigations and treatment outcomes. Comparisons were made with pulmonary tuberculosis regarding socio-demographic, clinical and laboratory findings.

MATERIAL AND METHODS

All cases of tuberculous peritonitis diagnosed and treated at the TB coordinating center, Erbil, Iraq between January 2000 and December 2006 were reviewed. All patients had histological diagnoses consistent with TB (positive for caseating granuloma with or without positive smear for acid-fast bacilli). The case records were analyzed and data on age, sex, ethnicity, clinical presentation, duration of symptoms before diagnosis, history of contact with TB case, co-morbid conditions particularly those associated with immunocompromised state (diabetes mellitus, renal failure, malignancies), blood investigations including hemoglobin and albumin levels, erythrocyte sedimentation rate (ESR), operative and histological findings, treatment outcomes, and adverse drug reactions were extracted. Immunocompromised and human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) patients were excluded.

All patients were treated with standard TB ther-

apies according to 2 standard regimes. In 20 patients, the first-choice regime was the SRIP (streptomycin 15 mg/kg/day, rifampicin 10 mg/kg/day, isoniazid 5 mg/kg/day and pyrazinamide 30 mg/kg/day). For the other 21 patients, treatment started with quadruple regime of RIPE rifampicin, isoniazid, pyrazinamide and ethambutol 20 mg/kg/day) for the first 3 months, followed by rifampicin and isoniazid for a further 6 to 12 months. Pyridoxine (vitamin B6) was routinely given to prevent peripheral neuropathy secondary to isoniazid.

Patients who were at risk of or had experienced adverse events were routinely followed more closely until events had settled. Patients and family members were advised to seek medical attention if patients experienced adverse symptoms. Side effects of TB drugs were considered if the events or symptoms had begun after anti-TB medications, other causes were absent and there was resolution of these side effects upon reducing or stopping the suspected medication. These ranged from non-specific gastrointestinal symptoms such as nausea, vomiting and abdominal pain, to known complications such as hepatitis. Significant hepatitis was considered when serum alanine aminotransferase rose to more than 2 times the baseline or 3 times the upper limit of normal. Patients were observed closely and treatment restarted either sequentially or altogether if patients' symptoms had not resolved. Alternative regimes were used if a particular medication could not be restarted. Ophthalmologic and otological evaluations were done for patients treated with ethambutol and streptomycin, respectively. After the completion of treatment, patients were followed up for a further 12 months to exclude the possibility of relapse.

Datas on the number of cases of pulmonary TB diagnosed and treated at the TB center between January 2000 and December 2006 were collected. The case records of 159 patients of them diagnosed and treated in 2002 were reviewed and information on age, sex, ethnicity, clinical presentation, co morbidities, laboratory findings, and adverse drug reactions were collected.

For statistical analysis, the Chi-square and Student *t*-test were used, *P* value ≤ 0.05 was considered as statistically significant.

RESULTS

A total of 41 cases of tuberculous peritonitis were diagnosed during the study period. All patients were local Kurds, their age ranged between 26 and 72 years (46 ± 17 years); 25 were males and 16 females giving a male: female ratio of 1.5:1. The median duration of symptoms before diagnosis of tuberculous peritonitis was 6 weeks (range: 10 days-18 months). Six patients (9.8%) had a history of positive contacts with TB cases. All were negative for HIV serology. During the same period a total of 1521 cases of pulmonary tuberculosis were diagnosed, which indicates that the rate of tuberculous peritonitis was 2.6% of all cases of tuberculosis.

Eleven patients (26.8%) had commorbid conditions. They were diabetes ($n = 5$), hypertension ($n = 5$), and end-stage renal failure on dialysis ($n = 1$). Presenting complaints are shown in Table 1. Chest radiographic changes consistent with pulmonary tuberculosis were seen in 25% of patients; in the form of right upper zone fibrosis (20%) and pleural effusions (5%). Four patients had pulmonary symptoms; cough/dyspnoea ($n = 2$) and cough ($n = 2$); all had chest radiographic changes. Tuberculous peritonitis was diagnosed by laparoscopy and biopsy in 29 patients and by laparotomy and biopsy in 12 patients. Only 12 patients (29.3%) had clinical evidence of ascites. Ascitic fluid analysis is shown on Table 2.

All patients responded to treatment (median, 6 months, range: 6-12 months). Side effects of TB drugs were seen in 16 patients (39%) and these consisted of hepatitis ($n = 2$) nausea/vomiting ($n = 11$) rashes ($n = 2$) and encephalopathy ($n = 1$). The encephalopathy was attributed to isoniazid, as no other cause of encephalopathy would settle with withdrawal of isoniazid. Fortunately, these adverse effects were mild; medications needed to be altered in 6 patients. There were no deaths attributed to tuberculous peritonitis.

Around 70% of pulmonary tuberculous patients were Kurds which is significantly lower than the proportion of Kurds with TB peritonitis ($P < 0.001$). Tuberculous peritonitis patients had significantly lower hemoglobin levels ($P = 0.027$) and serum albumin ($P = 0.003$) than pulmonary tuberculous patients. They also had more comorbid conditions that can lead to immuno-compromising state, but this did not reach statistical significance ($P = 0.402$). There was a significantly greater occurrence of side

effects of tuberculous drugs in tuberculous peritonitis patients ($P < 0.001$). There were no differences in terms of age and sex distribution, prevalence of non-specific symptoms (fever, weight loss and loss of appetite) and erythrocyte sedimentation rate. These findings are shown in Table 3.

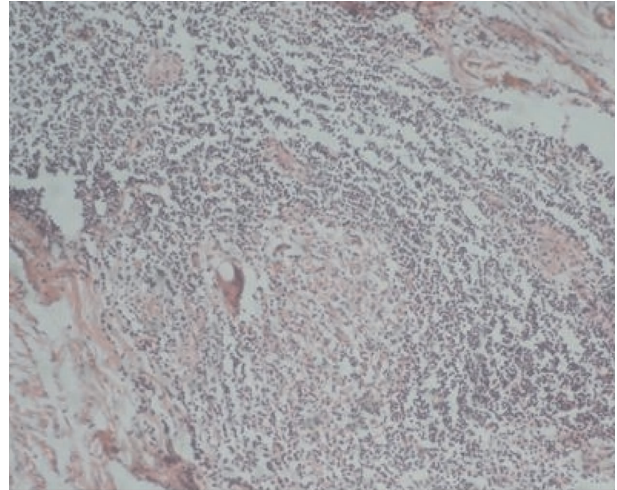


Figure 1 histopathological study showing epithelioid granuloma in the submucosa as well as in the muscle coat with nucleated giant cells and dense lymphocytic infiltration suggestive of tuberculosis of the ascending large bowel.



Figure 2 Plain radiograph of abdomen with diffuse calcified mesenteric lymphadenopathy in a patient with tuberculous peritonitis.



Table 1 Clinical presentation of tuberculous peritonitis patients ($n = 41$).

Presenting complaint	No. of patients (%)
Abdominal distention	29 (70.7)
Abdominal pain	21 (65.8)
Weight loss	18 (43.9)
Fever/ night sweats	28 (68.2)
Loss of appetite	27 (65.8)
Diarrhoea	19 (46.3)
Others (cough, weakness, dyspnoea)	10 (24.4)

Table 2 Laboratory analysis of ascitic fluid in 12 patients on admission.

Laboratory tests	Mean \pm SD
Protein	4.6 \pm 1.5 mg/dL
Glucose	60 \pm 15 mg/dL
LDH	442 \pm 36 U/L
Cholesterol	43 \pm 14 mg/dL
Leukocytes	175 \pm 75 cells/mL

Table 3 Sociodemographic, clinical, and laboratory findings of patients with tuberculous peritonitis ($n = 41$) and pulmonary tuberculosis ($n = 159$).

Variable	Tuberculous peritonitis	Pulmonary tuberculosis	P value
Mean age (yr)	46.0 \pm 17.0	41.2 \pm 17.3	0.312
Gender: Male	25	94	0.829
Female	16	65	
Ethnicity (Kurd)	100%	71.10%	<0.001
Comorbidities	26.80%	20.80%	0.402
Non-specific symptoms:			
Fever/night sweats	68.20%	56.00%	0.153
Weight loss	43.90%	47.80%	0.655
Loss of appetite	65.80%	60.40%	0.52
Blood investigations:			
Hemoglobin (g/dL)	10.4 \pm 2.0	11.8 \pm 2.5	0.027
ESR (mm/hour)	70 \pm 18	58 \pm 38	0.238
Albumin (g/dL)	26.4 \pm 4.2	32 \pm 3.8	0.003
Adverse drug reactions	41.50%	9.40%	<0.001

DISCUSSION

Although the incidence of tuberculosis has decreased over time, there has been a resurgence of this lethal infectious disease in recent years^[11]. In Europe and the USA, tuberculosis seems to be an increasingly important health issue with its vague clinical signs and nonspecific symptoms and has been growing in parallel to the increasing incidence of HIV^[12]. In developing countries including my country TB continues to be a common disease and one of its presentations is abdominal tuberculosis.

Tuberculous peritonitis is an easily treated in-

fection but remains the leading infectious cause of death worldwide, particularly in underdeveloped and developing nations^[13]. The infection route of the peritoneum by tuberculosis bacterium may occur by reactivation of a long-latent TB focus in the peritoneum from a primary focus in the lung or elsewhere, infected mesenteric lymph nodes, extension from tuberculous enteritis or a tuberculous salpingitis in the female^[8,14].

The frequency of TB peritonitis is estimated to range from 0.1-0.7% of all cases of TB, while it is 2.5% in this study^[8]. The frequency of TB peritonitis in our series in males is nearly 1.5 times that in

females, which is similar to the findings of other workers^[15, 16].

There are three forms of tuberculous peritonitis: the "wet" (with ascites), the "dry" (peritoneal involvement without ascites) and the "fibroid" type (with profound omental thickening and extensive adhesion formation)^[6, 9]. In our series, peritonitis was either of the wet or dry type. The "wet" (with free or loculated ascites) type was less common (29.2%) in comparison with other studies which reported that the "wet" type occurs in 55% to 75% of patients^[8].

Delay in the diagnosis of TB or misdiagnosis can lead to delay in treatment, leading to significant morbidity and even mortality^[4, 5, 17]. This is particularly true for extrapulmonary TB, which can be quite difficult to diagnose without a high level of suspicion^[16]. Pulmonary changes consistent with old PTB may be seen only in 20% to 30% and have been reported to occur less frequently in patients with active PTB and TB peritonitis^[18, 19]. Changes consistent with PTB were seen in 25% of our patients. Chest radiograph suggestive of PTB were seen in about 18% of Lisehora *et al.*^[5] study. The presence of pulmonary changes often heightens clinical suspicion and helps in making early diagnosis^[20].

As TB infection is known to affect almost any organ, it is possible that many patients with peritoneal involvement were not identified. This is because the treatment of TB is essentially the same; hence the identification of TB infections, particularly PTB or that occurring in another organ, often leads to treatment without further investigations being required unless indicated^[21].

Laparoscopy with biopsy is currently considered the gold standard for diagnosing tuberculous peritonitis, with low complications and a reported sensitivity of up to 100%^[16, 22-24]. All patients in our study showed matted bowels and dense adhesions, with typical white nodules representing granuloma involving the peritoneum which is characteristic of tuberculous peritonitis; there was no evidence of any overt perforation during surgery. Acid-fast bacilli can often be very difficult to isolate from pleural and ascitic fluids. The literature shows that the positive rates are disappointingly low but can be raised by increasing the amount of fluid analysed^[21]. The standard

culture positivity varies from 7.7% to 83%^[25]. Data on smear and culture positivity for AFB were not available in the case records in our study.

Often, the presence of TB infections indicates the presence of underlying conditions that compromise host immunity^[16]. This is true in developed nations, where most cases of TB are associated with conditions such as HIV infections, diabetes, and end-stage liver and end-stage renal diseases; however, in underdeveloped and developing nations, this may not be true, TB infections can occur even in patients without any significant comorbid conditions. Only 11 (26.8%) of our patients had comorbid conditions that could have contributed to infection or reactivation of previous infections.

In our study, tuberculous peritonitis patients have significantly lower serum albumin and hemoglobin levels comparing with PTB patients. These may indicate a more severe spectrum of TB infection compared to PTB. Non-specific symptoms are also common in patients with tuberculous peritonitis; however, these were not statistically significantly different from PTB cases. In addition, side effects of TB drugs were significantly more common in tuberculous peritonitis patients. These findings are similar to those reported by Chong and Rajendran^[16]. Despite most of these adverse events being self-limiting, it is important that they have to be recognized early to avoid any complications that may affect the outcomes of treatment.

The treatment of TBP is essentially the same as the treatment of active PTB, with standard triple or quadruple therapy for 3 months initially, followed by dual therapy for a further 3 to 6 months. Existing therapies are very effective and it is important to make an early diagnosis to avoid unnecessary delay in treatment^[11, 25].

The retrospective nature of this study is inherently associated with many limitations, particularly in assessing the prevalence of symptoms. However, our results are nearly comparable to those published in the literature.

CONCLUSION

Since the diagnosis of tuberculous peritonitis may be difficult and elusive, it is important to make an ac-



curate diagnosis as treatment is prolonged and associated with side effects. Therefore, TBP should always be considered in patients presenting with abdominal symptoms and non-specific constitutional symptoms, particularly in young patients. Although no data were available on radiographic and sonographic findings in the case records of our patients, it is important to emphasize the use of ultrasound and CT as diagnostic tools for TB peritonitis to avoid clinical mismanagement.

ACKNOWLEDGEMENTS

The authors would like to thank all doctors at the National Iraqi TB centre and local TB center in Erbil city for their assistance with data collection. Great thanks to departments of microbiology, pathology and biochemistry at the College of Medicine, Hawler Medical University for their kind help with laboratory investigations.

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