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Tertiary Peritonitis, Severe Sepsis Needs Early Diagnosis and Treatment in Countries with Limited Resources: A Case Series

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Abstract

Background: Tertiary Peritonitis (TP) is defined as a severe recurrent or persistent intra-abdominal infection after adequate surgical source control of Secondary Peritonitis (SP). The aim of this study was to clarify the value of routinely used diagnostic parameters and early outcome after re-laparotomy in patients with tertiary peritonitis.

Patients and Methods: A retrospective study was conducted from 2018 to 2021. Baseline characteristics of admission, outcomes, laboratory results, and antibiotic therapy were recorded for analysis.

Results: Among 25 patients with secondary peritonitis, 8 (32%) developed tertiary peritonitis. Almost two-thirds (62.5%) were female; mean age was 32 years, 12.5% were with hypertension and 37.5% of patients were on steroids. Retroperitoneal abscess was the most frequent cause of intra-abdominal infection in 37.5%, in-hospital mortality was 25% and 37.5% of patients had a length of hospital stay more the 50 days.

Conclusion: It is desirable to have timely, diagnosis of TP and subsequent initiation of an appropriate therapy to improve outcome. Understanding and recognizing risk factors, may potentially help to identify patients with SP at risk for development of TP and possibly prevent it from happening.

Keywords: Case series; Tertiary peritonitis; Literature review; Severe sepsis; Diagnosis and treatment

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Abbreviations

TP: Tertiary Peritonitis; MDR: Multi Resistant Drug; SP: Secondary Peritonitis; APACHE: Acute Physiology and Chronic Health Evaluation; MPI: Mannheim Peritonitis Index

Introduction

The latest Intensive Care Unit (ICU) consensus conference guideline defines tertiary peritonitis as intra-abdominal infection that persists or recur ≥ 48 h following successful and adequate surgical source control. Tertiary peritonitis is poorly defined, misunderstood, and potentially historical [1]. Various definitions have emphasized on failed surgical source control or inadequate antibiotic therapy of secondary peritonitis or even impaired host response to peritoneal infection [2]. Peritonitis can be classified as primary, secondary, or Tertiary Peritonitis (TP) [1]. Peritonitis, as a major consequence of hollow visceral perforation, anastomotic disruption, ischemic necrosis, or other injuries of the gastrointestinal tract, often drives acute care in the emergency department, operating room, and the ICU [3].

However, there is a consensus that secondary peritonitis and TP exist in a continuum and the transition between both may be quite subtle [4]. It has been recognized that appropriate surgical and antimicrobial therapy does not result in full resolution of all cases of peritonitis, particularly in the most gravely ill patients [4].

Multiple scoring systems predicting the development of severe, life-threatening abdominal sepsis

have been established but have frequently failed to prognosticate the early onset of peritonitis and therefore miss the ideal time for intervention [4,5]. These scoring systems have been designed and used to grade the severity of acute peritonitis like, Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sepsis Severity Score (SSS), Ranson score, Imrie score, Mannheim Peritonitis Index (MPI) [6]. An important subset of chronic critically ill patients are those who have survived an emergency abdominal operation, but who subsequently require prolonged open abdomen management complicated by persistent peritoneal space infection [3].

Clinically, it is most often suspected in cases of prolonged systemic inflammatory response syndrome and shock following effective management of the inciting pathology causing secondary peritonitis [1,7,8]. In Pennsylvania, patients who suffered from tertiary peritonitis were comorbid, malnourished, and metabolically deranged [9]. Often, the diagnosis is made following repeated trips to the operating room on the suspicion of failed management of secondary peritonitis [8]. In Brazil, ultrasound examination and computerized tomography are often used and have satisfactory performances in the diagnosis/screening of intra-abdominal acute infections, with the latter having a higher potential for this purpose. Both methods aid in the detection and drainage of abdominal fluid collections [10]. The effective treatment of tertiary peritonitis is multifaceted, although it has been described as representing the limit of surgical treatment of severe secondary peritonitis [7,8].

The anesthesia consideration in tertiary peritonitis focuses on evaluation of cardiopulmonary stability, airway access history, and vascular access [11].

It was found that overall length of stay in ICU admission was 21 ± 14.9, frequency of TP of 27.3% at surgery and males were 80%. The clinical sequelae of tertiary peritonitis are grave and often deadly, with a mortality rate quoted at 30% to 64% in some populations [7,8].

Physiologic support often entails intensive care unit admission, administration of broad-spectrum antibiotics and ensuring source control [9]. Despite ideal management, non-resolving organ failure in TP patients results in mortality rate of about 30% to 64% [8,12].

The morbidity is associated with severe complications such as abscess, fistulas, bleeding, wound infection, dehiscence and ventral hernias [13]. However, there is lack of recent studies done on Tertiary peritonitis in Africa.

The aim of this retrospective study was to clarify the value of routinely used diagnostic parameters and early outcome after re-laparotomy in patients with tertiary peritonitis. We report a case series of 8 patients who developed tertiary peritonitis following management for secondary peritonitis [14,15].

Patient and Methods

This study included patients managed from January 1st, 2018 to December 31st, 202. Records of patients who were treated for secondary peritonitis were reviewed. Out of 25 patients with secondary peritonitis, 8 patients developed tertiary peritonitis.

Inclusion criteria for case selection was: 1) Patients with confirmed collection using ultrasound scan after initial laparotomy, 2) clinical signs indicating peritonitis after a successful surgical treatment of the secondary peritonitis [6].

Treatment consisted of intravenous fluid resuscitation, nasogastric tube and urinary catheterization, intravenous antibiotics (ceftriaxone 2 gm, metronidazole 500 mg, Meropenem 1 gr), omeprazole and intra-abdominal lavage with 5 to 10 liters of normal saline before closure.

Mannheim Peritonitis Index (MPI) is a scoring system with prognostic value among patients with peritonitis [4]. The MPI (Table 1) was applied along with other clinical and parameters recorded. Prediction was categorized into 3 groups: i) score ≤ 20 ii) Score 21-29 iii) score ≥ 30. Further resuscitation and ICU care was given as and when was necessary [16]. Patients were followed up postoperatively till the outcome i.e., mortality, morbidity or discharge [17-19]. The MPI takes into account age, gender, organ failure, cancer, duration of peritonitis, involvement of colon, and extent of spread and character of the peritoneal fluid. Patients with a score exceeding 26 are defined as having a high mortality rate. Outcome and clinical course of those studied patients were reviewed and analyzed.

Discussion

Tertiary peritonitis is a major cause of death among patients with secondary peritonitis, the aim of this study was to exhibit the risk factors, complications and the dilemma in treatment.

The frequency of TP in our study was 32% among 25 patients with secondary peritonitis. This finding is similar with the study of Bader et al. in Germany who reported an incidence between 30% to 42% [5], and almost similar to the study of Evans HL et al. in USA who reported an incidence of 27.27% [12]. However, in opposite, the study done by Ballus et al. showed a higher incidence of 53.93% [18] and a study done by Nathens showed 74% [7]. On the other hand, a study done by Formin in Ukraine showed a lower incidence of 18.3% [20].

The result of this study reflects that complications are now much more easily managed than previously, especially intra-abdominal sepsis, which can be successfully treated with lavage and antibiotic therapy [5]. Peritoneal lavage is employed in an attempt to "wash out" not only peritoneal contaminants, but also dilute and remove peritoneal cytokines [5,21-23].

Mortality in severe peritonitis depends in part on patients' age; delay in intervention beyond 24 h; and the extent of peritonitis [24]. In the study of Ballus, two-thirds (64.4%) were male; mean age was 63.7 ± 14.3 years [25]. In our results the predominance of female sex is explained by the fact that the majority of initial interventions were obstetrical-gynecological.

The mortality rate related to TP is a burden in our area; as to what was found by Clement et al. [21] and Ross et al. with 20% [26] but was greater than the study of Thirumalagiri et al. who found 8% of mortality [27]. However, many studies conducted in Canada, USA, found the mortality rate between 30% to 64% [1,2,21,25,28]. Specific peritonitis scores do exist, one example being the Mannheim Peritonitis Index (MPI). At least four prospective studies have confirmed that not only the MPI was as efficient in predicting the short-term risk of mortality of a patient with peritonitis, but as well, this is one, is the easiest scoring systems to apply and it can be calculated during operation [19].

Our result reflects that patients with TP have higher rates of multiple organ failure, and a higher mortality rate than patients with SP [13,29], besides, they are at a higher risk of developing severe sepsis and death [18]. Patients with transition to TP had significantly

Table 1: Mannheim peritonitis index.

Risk factor	Weightage, if any
Age >50 years	5
Female gender	5
Organ failure*	7
Malignancy	4
Preoperative duration of peritonitis >24 h	4
Origin of sepsis not colonic	4
Generalized peritonitis	6
Exudates	
Clear	0
Cloudy, purulent	6
Fecal	12

*Definition of organ failure: Kidney: Creatinine >117 µmol/L, urea >167 µmol/L, oliguria <20 ml/h, for lung po_2<50 mmHg, pCO_2>50 mmHg

Table 2: Demographic characteristics of patients with TP.

Variables	Numbers of Patients (n=8)
Mean age in years (range)	32.37% (16-55)
Sex female (%)	5 (62.5%)
Transfer from other hospitals (%)	2 (25%)
Co- morbidity (%)	
None	4 (50%)
Corticosteroids	3 (37.5%)
Hypertension	1 (12.5%)

Female predominance (62.5%) with a mean age of 32 years, 25% of patients was transferred from other hospitals and 37.5% of patients were on steroids but 12.5% were with hypertension.

Table 3: Causes of tertiary peritonitis at re-laparotomy.

Causes (diagnostic)	Patients (n=8)
Ileal perforation	2 (25%)[a]
Visceral gangrene	1 (12.5%)
Leakage of anastomose	2 (25%)
Retro peritoneal abscess	3 (37.5%)

"a" indicates percent

In this series of eight patients, Retro-peritoneal abscess was the most frequent cause of intra-abdominal infection at 37.5%

higher MPI at initial operation [30].

In America, tertiary peritonitis was found to be 27.3% [12]. In our study, retro-peritoneal abscess was frequent with 37.5% but there was no difference between the four causes of TP in our study. The same result was founded by Nathens who reported a postoperative peritonitis rate of 30% [5,7,25]. Patients with localized peritonitis were less prone to TP [25]. However, for others authors the causes for peritonitis in the postoperative peritonitis group were as follows: Anastomotic leakage 50.9%, perforations 22.8%, mesenteric ischemia 11.4% and others 14.9% [5]. While an intestinal perforation on its own leads to mortality of about 14%, a septic clinical progress is associated with an increase in mortality rate to 30% [17].

In our study, every patient had a high C reactive protein, and for some of them, leukocytes were elevated. TP generally demonstrate a hypercatabolism driven inflammatory profile marked by a high C-reactive protein concentration [3,20].

Complementarily, laboratory parameters and routine

Table 4: Clinical presentation and outcomes.

Outcome Variables	Patients (n=8)
Mortality rate	2 (25%)
Degree of MPI >26	3 (37.5%)
Average or Mean ASA score (range)	3.12 [2-5][b]
Surgical site infection	2 (25%)
Intra-abdominal collection	8 (100%)
Time taken to decide operation	
48 h-96 h	4 (50%)
<48 h	2 (25%)
>96 h	2 (25%)
Average or Mean BMI (range) kg/m^2	20.87[16-27]
<18.5	3 (37.5%)
18.5-25	4 (50%)
>25	1 (12.5%)
Length of hospital stay in days	
<30 days	3 (37.5%)
30-50 days	2 (25%)
>50 days	3 (37.5%)

"a" indicates percent, "b" indicates average or mean range and "n" is the number of patients. In our series of TP, two (25%) patients with tertiary peritonitis died after operation in the ICU, and was associated with a high degree of MPI>26 (defined as having a high mortality rate), BMI were under 18.5 in 37.5% and the operation was decided after 96 h (25%). The average of ASA was 3 with range between 2 to 5. Three patients were operated four times and 37.5% of patients had more than 50 days in-patient stayed.

Table 5: Baseline laboratory parameters and culture of patients with TP.

Patient	CRP (<10 mg/L)	WBC count (4 µL-10.5 µL)	Culture
1	12	14.56	*E. coli*
2	48	15.01	NA
3	36	14.31	*E. Coli*
4	114	15.09	*E. Coli*
5	72	NA	NA
6	24	9.92	NA
7	96	NA	*E. coli*
8	96	13.65	NA

NA: Not Available; CRP: C-Reactive Protein; WBC: White Blood cell; *E. coli*: *Escherichia Coli*. *E. Coli* was the most cultured microorganism and CRP was elevated in every patient

microbiological monitoring play pivotal roles in the diagnosis of the TP [10,31-33]. There have been 33 studies exploring CRP as a marker for abdominal infection or complications after surgery. Four reports suggest a persistent threshold of greater than 100 mg/L might indicate septic complications [30,34]; however other studies have refuted this conclusion, leaving uncertainty for clinical utility [18,30].

According to the diagnosis, peritonitis is supported by clinical signs, and we found intra-abdominal collection (located or generalized) in all our patients. Ultrasound may be positive in up to 72% for confirmation, CT in up to 82% [5,19]. Clinical suspicion of peritonitis can be elucidated with complementary data from imaging exams. In our settings, ultrasound examinations are often used and have satisfactory performances in the diagnosis of intra-abdominal acute infections, having a higher potential for this purpose [2]. Ultrasound and computed tomography scan have been used to

Table 6: Parameters of treatment.

Parameters	Patient (n=8)
Volume of fluid in Peritoneal lavage per op (litter)	6-10 L
Peritoneal lavage	8 (100%)
Antibiotic associations	
Ceftriaxone and metronidazole	7 (87.5%)
Meropenem and metronidazole	1 (12.5%)

All patients received antibiotics, 87.5% received "Ceftriaxone and metronidazole" and 12.5% received "meropenem and metronidazole", this difference of antibiotics is because of sensitivity results. Peritoneal lavage using a fluid volume between 6 liters to 10 liters to all patients

complete the clinical assessment of patients with intra-abdominal infection [35-38].

Regarding antibiotic used in our study, the most frequent use of ceftriaxone and metronidazole may be explained by their use as initial empiric therapy. They both provide optimal activity and, in combination with a better peritoneal lavage, may contribute to improving outcomes and preventing the appearance of MDR germs [5,7,32,38-40]. However, in the settings with a high incidence of extended-spectrum beta-lactamases producing Enterobacteriaceae, the extended use of cephalosporins should be discouraged and should be limited to pathogen-directed therapy because of its selective pressure resulting in emergence of resistance [38,39]. The higher microbiologic resistance rates of gram-negative bacteria such as *E. coli* to standard antibiotic therapy make the use of broad-spectrum antibiotic (such as meropenem) regimens mandatory [40].

In our study, patient stayed in the hospital more than 4 to 7 weeks, they were at a greater risk of colonization by MDR bacteria, and in these cases, the approach in TP is more complex, we used meropenem in combination with metronidazole [40]. Regarding the surgical treatment, our data shows that timely relaparotomy provided the only option that improves outcome [40,41]. All patients who underwent relaparotomy after 96 h of diagnosis died. However, later surgical treatment has reached its limit in patients whose source of infection could not be controlled at the initial operation [39].

Limitations

The most important being the absence of results of laboratory for some patients especially the culture were lost, and no TPN. Although the prognosis of TP is theoretically worse [2], we observed a difference in management between the primary and the TP but there was difficult to assess APACHE score, which should help us to assess the mortality rate. Culture was not considered as inclusion criteria because only 4 patients had cultures.

Strengths of Our Study

This was among the first studies in the region to study TP and show issues and challenges in assessment and treatment of the TP. Even with regard to the occurrence of septic shock or the death rate. We also found a high rate of TP development from SP. This is probably because of the severity of SP, the high death and morbidity rates characteristic of patients with peritonitis even with better management [18]. Also, ultrasound scan was done for all patients. Further, this study was conducted at a large teaching referral university hospital with a high level of complexity, over a four-year period.

Conclusion

Tertiary peritonitis remains a primordial cause of hospital mortality mainly with associated risk factors. Rapid diagnosis, which can be made easier with the use of clinical scores as MPI score may improve outcome. Immediate therapy should be instituted to control infectious focus and prevent new recurrences. In this case series, treatment was based on initial antimicrobial therapy and well performed peritoneal lavage during laparotomy. Antimicrobial therapy of TP can never be standardized and should always be thoroughly based upon regular and proper peritoneal and blood sampling.

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