# **Typhoid Intestinal Perforation Prognostic Score in Poor-Resource Settings**

#### Abstract

Background: Mortality from peritonitis due to typhoid intestinal perforation (TIP) in sub-Saharan Africa is high. Objectives: This study aimed to determine the predictive factors of mortality, propose a prognostic score, and determine the appropriate surgical treatment for TIP in low-resource settings. Materials and Methods: This was a retrospective data collection of peritonitis due to TIP admitted at Zinder National Hospital from 2014 to 2021. To build a typhoid intestinal perforation prognostic score (TIPPS), patients were randomised into two groups: a score-building group and a validation group. Univariate and multivariate analyses were performed to identify risk factors of mortality. The value of P < 0.05 was assigned significant for all analyses. **Results:** TIP accounted for 52.4% (n = 1132) of all cases of peritonitis (n = 2159). The median age was 12 years. Rural provenance represented 72.2% (n = 817). Deaths accounted for 10.5% (n = 119). The factors influencing mortality were respiratory rate  $\geq 24/\min$  (odds ratio [OR] = 2.6, P = 0.000), systolic blood pressure <90 mmHg (OR = 0.31, P = 0.002), serum creatinine >20 mg/L (OR = 2.6, P ≤ 0.009), haemoglobin (OR = 2.1, P = 0.000), comorbidity (OR = 3.5, P = 0.001), the American Society of Anesthesiologists score IV&V (OR = 3.3, P = 0.000), admission and management delay > 72 h (OR = 3.2, P = 0.001), and a number of perforations (OR = 2.4, P = 0.0001). These factors were used to build a "TIPPS" score, which ranged from 8 to 20. The risk of mortality was associated with increased TIPPS. The performance of this score was good in the two groups (area under receiver operating characteristic > 0.83). According to the severity and mortality risk of TIP, we classified TIPS into four grades: grade I (low risk: 8–10), grade II (moderate risk: 11–13), grade III (high risk: 14–16) and grade IV (very high risk: 17–20). Conclusion: The TIPPS is simple. It can describe the severity of the disease and can predict the risk of death. The study highlights the importance and impact of timely and adequate perioperative resuscitation in more complicated cases.

Keywords: Intestinal, perforation, peritonitis, prognosis, scoring, typhoid

#### Introduction

In sub-Saharan Africa and other lowincome-countries, typhoid fever (TF) is a severe endemic infectious disease caused by the Gram-negative bacillus, Salmonella enterica serovar Typhi. TF still remains a major public problem health of poor countries, due to poor living conditions and lack of access to safe water and sanitation.[1-3] Worldwide, there is an estimated 12–24 million cases of TF, including 75,000-600,000 deaths per year.<sup>[1,4-6]</sup> In Africa, a very variable annual incidence is described ranging from 13 to 8092 per 100,000.[1,7] Most of the global burden of TF occurs in low- and middle-income countries (LMICs) such as the Niger Republic.<sup>[1,3,7-9]</sup> The risk of intestinal perforation during TF can reach 40% in poor countries.<sup>[3,4,7]</sup> These statistics perforation in the aetiology of secondary acute peritonitis in rural sub-Saharan areas with a frequency of 40% to more than 60%of cases, whereas this cause has disappeared in the developed countries.<sup>[3,10,11]</sup> Peritonitis due to typhoid perforation is associated with a high mortality, which ranges from 5% to 80%.<sup>[1-4,10,12]</sup> The poor prognosis of peritonitis due to typhoid perforation in developing countries such as Niger Republic is linked to many factors.<sup>[4,8-10,12-14]</sup> The predictive value of prognostic factors and several severity scoring systems of peritonitis has been previously described.[15-21] However, the use of these scoring systems is not always easy and adaptable to typhoid intestinal perforations (TIPs) in our context and other LMICs. Also, we asked ourselves the question of the usefulness of a prognostic score that can help assess the severity of intestinal typhoid perforation, a common

explain the preponderance of typhoid

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surgical condition in our poor-resource settings. This study aimed to determine the predictive factors of mortality, propose a prognostic score, and determine the appropriate surgical treatment for TIP in low-resource settings.

#### **Materials and Methods**

#### Study design and setting

This was a retrospective data collection of cases of peritonitis due to TIP admitted at Zinder National Hospital (ZNH) in Niger Republic (West Africa). Data were collected over an 8-year period (from January 1, 2014, to December 31, 2021). ZNH is a third referral-level hospital with an 850-bed capacity located in Zinder City, Niger Republic. The surgical emergency department receives patients with acute abdominal conditions such as peritonitis due to typhoid perforation. Preoperative preparation was carried out before surgery. The peritoneal syndrome was clinically confirmed.

#### **Inclusion criteria**

The study included patients of both sexes and varying ages, who underwent an emergency operation for acute peritonitis, who had recovered or died and whose intraoperative diagnosis confirmed one or more typhoid perforations of the ileum. The typhoid origin of peritonitis was based on epidemiological criteria (typhoid endemic area, poor hygiene, and low socioeconomic levels), history, clinical examination, and the intraoperative macroscopic aspects of perforation (it is an oval and regular perforation on the antimesenteric edge of the intestine [Figure 1]) and regularly found on the distal part of the ileum. Isolation of *Salmonella typhi* and histological examination of samples were not systematic in our context because of technical insufficiency. The exclusion criteria were insufficient documentation.

#### Variables

Mortality was the dependent variable. The independent variables were chosen based on the physiological parameters for prognosis in abdominal sepsis F score,<sup>[17]</sup> quick sequential organ failure assessment score,<sup>[19]</sup> Jabalpur prognostic score (JPS),<sup>[21]</sup> peritonitis severity score (PSS),<sup>[16]</sup> Mannheim peritonitis index (MPI),<sup>[22]</sup> and acute physiology and chronic health evaluation II scoring system.<sup>[15]</sup> The following parameters were collected: age, sex, area of residence, admission delay (AD), heart rate, respiratory rate (<24 or  $\geq$  24 breaths/min), systolic blood pressure ( $\geq$ 90 or < 90 mmHg), temperature ( $\geq$ 39°C or < 36°C), serum creatinine ( $\geq$ 20 mg/L or <20 mg/L), haemoglobin level (<9 g/dL), comorbidity, number of perforations, and physical status score of the American Society of Anesthesiologists (ASA score).<sup>[23]</sup>

Comorbidity was defined as the presence of another underlying disease other than TF. Admission and management delay (AMD) was estimated through the clinical history, which reported the patient's infectious status, functional symptoms of an acute abdomen, but also the waiting time before surgery.

The Clavien-Dindo classification was used to classify postoperative complications. It was divided into five grades ranging from I to V, with grade V representing death.<sup>[24]</sup>

#### Treatment and surgical technique

All patients had undergone perioperative resuscitation with intravenous fluids to correct electrolyte and hemodynamic disorders. Bladder and nasogastric tubes were used. Initial antibiotic therapy was prescribed based on beta-lactams or quinolones combined with metronidazole. Blood transfusion was routinely administered to patients with blood haemoglobin of less than 9g/dL. General anaesthesia

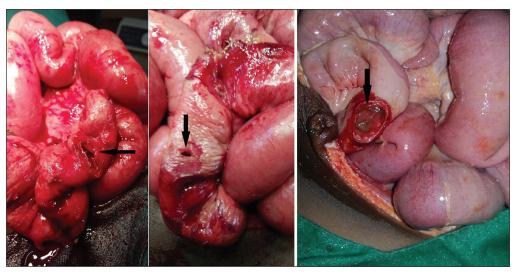


Figure 1: Intraoperative macroscopic aspects of intestinal perforation of typhoid origin (black arrows)

was given to all patients. Abdominal exploration was done via a midline incision under general anaesthesia with endotracheal intubation. The intraperitoneal collections were quantified. Peritoneal cavity was irrigated, and drains were placed. The surgical procedures performed were: excision and closure, resection and anastomosis, or ileostomy with or without intestinal resection. In our hospital, the standard surgical procedures that were applied by surgeons can be described as follows:

- The simple closure was performed in patients with single or double perforation, an abdominal contamination considered less dirty (nonfecal, nonpurulent) and with an ASA score of ≤3.
- Resection and anastomosis were performed in cases of several close perforations and in patients with an ASA score of ≤3.
- The ileostomy was systematically indicated for a dirty abdominal cavity, a patient in bad general status, or undernutrition whatever the number of perforations. It was made ahead of the most proximal perforation to protect distal closure, or a perforation not suitable for closure is brought out to the skin as an ileostomy. The ileostomy was also performed to protect a closure less than 2–5 cm from the ileocecal junction (anatomical turbulence zone).
- In some cases, these ileostomies were performed as part of damage control surgery. Damage control operations by abridged laparotomy were indicated for patients in poor general condition (severe sepsis, malnutrition, respiratory distress, etc.). The principle of this procedure is simple, borrowed from the management of abdominal trauma. In this case, it consists of opening the abdominal cavity quickly, in order to wash, to externalise the perforation(s) in the form of an ileostomy to the skin. It is also necessary to ensure a "resuscitation" of the patient (vascular filling with fluids to correct hypovolemia transfusion, antibiotics, cardiotonics, warming, oxygen therapy, etc.). Finally, the patient can be reoperated for a "second look" in 48-72h if necessary. Those who improved were taken back later to restore digestive continuity.

#### Statistical analysis

These data were collected on a pre-established survey sheet and saved with Microsoft Excel 2013. Data were exported to Epi-info7<sup>TM-CDC</sup> for statistical analysis. Quantitative variables were calculated as mean  $\pm$  standard deviation or median with interquartile range (Q1–Q3). Categorical variables were presented in absolute numbers or percentages, and Chi-square ( $\chi^2$ ) test was used to estimate associations between independent variables and mortality.

Patients were randomised into two groups: a score-building group (SBG), comprising 2/3 of the patients (67%), and a validation group (VG), comprising 1/3 (33%) of the

remaining cases. Independent variables were dichotomised for the purposes of univariate and multivariate analyses in logistic regression in the SBG. The odds ratio (OR) with confidence interval (CI) (95%) was used, and the value of P < 0.05 was assigned significant for all analyses. We considered significant factors in univariate and multivariate analyses to develop a typhoid intestinal perforation prognostic score (TIPPS) in the SBG. Model discrimination was assessed using the area under curve of receiver operating characteristic (ROC); it shows how well the model can distinguish cases in the two groups (alive and dead). Significant factors only in univariate analysis scored 2 points if present and 1 point if not. When the factor considered in the scoring system was significant in the multivariate logistic regression, it was between 1 and 3 points. The risk score of the patients was calculated in the SBG and the VG to test the predictive power of the TIPPS. The good fit of the relationship between the TIPPS and the mortality was compared between the SBG and the VG using the coefficient of determination  $R^2$ .

## **Ethical considerations**

This study was conducted in conformity with the Helsinki Declaration, and other instruments related to ethical principles applicable to medical research. Ethical approval was obtained by the joint decision of the Scientific Board of the Faculty of Health Sciences of the University of Zinder and the Advisory Technical Advisory Council of ZNH (number: FSS-UZ&CTC-HNZ-MSP-0023/11/2019).

## Results

#### **Characteristics of patients**

During the study period, of 2159 patients with acute peritonitis, 1132 were operated for TIPs (i.e., 52.43%). There were 758 males (67%) and 374 females (33%). Their ages ranged from 2 to 79 years with a median of 12 years (Q1–Q3: 8–20 years). The paediatric population, aged 2–15 years accounted for 55.74% (n = 631). Patients who came from rural areas accounted for 72.2% (n = 817). Geographic accessibility to the hospital was difficult for most of them (561/817).

Patients were classified as ASA III in 43.11% (n = 488). Haemoglobin levels in the blood ranged from 3.8 to 16 g/dL, with an average of  $10.37 \pm 2$  g/dL. The serum creatinine level ranged from 7 to 75 mg/L with an average of  $16.61 \pm 10.7$  mg/L. The general characteristics of all patients are shown in Table 1.

#### Intraoperative findings, surgical procedures, and outcomes

Laparotomy was performed for all patients. Peritonitis was generalised for 96.46% (n = 1092) and localised in 3.54% (n = 40). The mean number of perforations was 2.26 ± 1.29 (range: 1–13). In 38.3% (n = 434) of cases, there was at least one perforation located less than 5 cm from the

	Table 1: Characteristics of patients (n = 1132)				
Variables	Number (%)	Death $(n = 119)$			
	an age $(IQ) = 12 (8-20)$				
≤15 years	631 (55.74)	64			
>15 years	501 (44.26)	55			
Gender					
Female	374 (33)	48			
Male	758 (67)	71			
Area of residence					
Urban	315 (28.2)	37			
Rural	817 (72.2)	82			
Heart rate (/min)					
<110	785 (69.35)	76			
≥110	347 (30.65)	43			
Respiratory rate (	/min)				
<24	941 (83.1)	83			
≥24	191 (16.9)	36			
Systolic blood pre					
<90	407 (36)	71			
≥90	725 (64)	48			
Temperature					
<39	855 (75.5)	84			
≥39	277 (24.5)	35			
Serum creatinine	. ,				
<20 mg/L	893 (78.9)	67			
≥20 mg/L	239 (21.1)	52			
	el in the blood, mean $\pm$ Sl	D: $10.37 \pm 2 \text{g/dL}$			
<9g/dL	346 (30.6)	62			
≥9 g/dL	786 (69.4)	57			
ASA score groups	3				
II	178 (15.72)	7			
III	488 (43.11)	26			
IV	450 (39.7)	76			
V	16 (1.4)	10			
Comorbid illness					
Yes	129 (11.4)	84			
No	1003 (88.6)	35			
Admission and m	anagement delay (AMD)				
≤48 h	748 (66.1)	45			
>48 h	384 (33.9)	74			
	( )				

IQ: interquartile range, SD: standard deviation

ileocecal valve. The ileostomy with or without intestinal resection was performed in 60.6% (n = 686), excision and primary closure in 35.15% (n = 398), and resection with anastomosis in 4.24% (n = 48). Surgical findings and procedures are listed in Table 2. Among these cases of ileostomies, 36.9% (n = 418) were performed as part of damage control surgery.

According to the Clavien-Dindo classification, we recorded 49.11% (n = 556) postoperative complications. These were septic complications in the majority of cases (30.56%; n = 346). The distribution of postoperative complications was given in Table 3. Grade V of the Clavien-Dindo classification represented the number of deaths in this study, 10.51% (n = 119).

Table 2: Surgical features of patients (n = 1132)			
Operative aspects	Number (%)		
Number of ileal perforations			
1	471 (41.6)		
2	235 (20.75)		
3	214 (18.9)		
≥4	212 (18.72)		
Distance between perforation and ileocecal junction (cm)			
<2 cm	200 (17.66)		
2–5 cm	234 (20.67)		
>5 cm	698 (61.66)		
Surgical procedures			
Ileostomy	686 (60.6)		
Without resection $(n = 575)$			
With resection $(n = 111)$			
Excision and sutures	398 (35.16)		
Bowel resection with anastomosis	48 (4.24)		

The average length of stay was  $13.20 \pm 5.11$  days.

# Prognostic factors of mortality and building prognostic score

After the randomisation of the patients in two groups, the SBG constituted 2/3 of the cases (n = 755) and the VG represented 1/3 of patients (n = 377).

Univariate analysis of the results was adjusted in a multivariate unconditional logistic regression. The final model included eight prognostic factors: (1) comorbidity, (2) systolic blood pressure, (3) respiratory rate, (4) AD, (5) ASA score, (6) serum creatinine level, (7) haemoglobin levels, and (8) number of perforations.

The respiratory rate, haemoglobin level, presence of comorbidity and number of perforations greater than 2 were statistically associated with mortality in univariate analysis (P < 0.05). Thus, each of these variables was rated 2 points in the prognostic score.

Multivariate analysis showed that the factors influencing mortality were as follows: systolic blood pressure at admission <90 mmHg (OR = 0.29, P = 0.002), serum creatinine >20 mg/L (OR = 3.54, P = 0.000), ASA score IV&V (OR = 3.69, P = 0.000), and AMD >72 h (OR = 3.2, P = 0.001). Table 4 shows the univariate and multivariate analyses in the SBG.

Each of the variables statistically associated with mortality in multivariate analysis scored 3 points.

The proposition of the TIPPS with the scoring of predictive factors is shown in Table 5. For each patient, the score varies from 8 to 20, and the higher it is, the higher the risk of mortality. According to the severity and mortality risk, we classified peritonitis due to TIP into four grades of increasing severity:

- Grade I: low risk (score: 8–10), simple closure of the perforation or ileostomy is recommended.

Outcomes			Number
Without complications			576
Complications (Clavien-Dindo	Grade I; 12.98% ( <i>n</i> = 147)	Superficial surgical site infection	131
grade), $n = 556$		Postoperatoire bowel obstruction	16
	Grade II; $6.62\%$ ( <i>n</i> = 75)	Anaemia with transfusion	47
		Severe malnutrition	28
	Grade III; 12.72% ( <i>n</i> = 144)	Deep surgical site infection	73
		Ostomy necrosis	4
		Postoperative peritonitis without organ failure	67
	Grade IV; $6.27\%$ ( <i>n</i> = 71)	Postoperative peritonitis with renal failure	10
		Sepsis	61
	Grade V; 10.51% ( <i>n</i> = 119)	Death	119
	Total		1132

# Table 3: Distribution of Postoperative Complications

# Table 4: Univariate and multivariate analyses of prognostic factors affecting mortality in the score-building group (n = 755)

(n = 755)   Variables Number Deaths (%) Univariate Multivariate						
Number	Deaths (%)	Univariate	Univariate			
		ORna (95% CI)	Р	ORa (95% CI)	Р	
419	41 (9.79)					
185	39 (11.61)	1.21 (0.76–1.92)	0.418			
247	33 (13.36)					
508	47 (9.25)	0.66 (0.41-1.06)	0.085			
520	51 (9.81)					
235	29 (12.34)	1.29 (0.79-2.1)	0.295			
		. ,				
624	54 (8,65)					
131	26 (19.85)	2.61 (1.2-4.8)	0.0001	2.16 (1.20-3.89)	0.09	
	· · · ·	· · · · ·				
489	32 (6,54)					
266	48 (18.05)	0.31 (0.19-0.51)	0.0000	0.29 (0.17-0.50)	0.002	
	· · · ·	~ /				
564	57 (10.11)					
191		1.21 (0.5-2.2)	0.452			
L)	· · · ·	· · · · ·				
	45 (7.53)					
		3.52 (2.17-5.71)	0.0000	3.54 (2.05-6.12)	0.001	
		~ /				
518	37 (7.14)					
		0.34 (0.21-0.55)	0.0000	0.39 (0.23-0.67)	0.061	
399	20 (5.01)					
		3.84 (2.26-6.51)	0.0000	3.69 (2.12-6.41)	0.000	
665	55 (8.27)					
90		4.26 (2.49-7.30)	0.0000	3.69 (2.12-6.41)	0.0709	
ement delay (h)		(				
• • • /	36 (7.19)					
		2.7 (1.69-4.32)	0.0000	3.2 (1.6-6.3)	0.001	
	35 (7.37)					
		2.4(1.50-3.84)	0.0001	2.06 (1.19-3.55)	0.087	
	419 185 247 508 520 235 624 131 489 266 564 191 L) 598 157 518 237 399 356 665	$\begin{array}{c} 419 & 41 (9.79) \\ 185 & 39 (11.61) \\ 247 & 33 (13.36) \\ 508 & 47 (9.25) \\ 520 & 51 (9.81) \\ 235 & 29 (12.34) \\ 624 & 54 (8,65) \\ 131 & 26 (19.85) \\ 489 & 32 (6,54) \\ 266 & 48 (18.05) \\ 564 & 57 (10.11) \\ 191 & 23 (12.04) \\ L \\ 598 & 45 (7.53) \\ 157 & 35 (22.3) \\ 518 & 37 (7.14) \\ 237 & 43 (18.14) \\ 399 & 20 (5.01) \\ 356 & 60 (16.85) \\ 665 & 55 (8.27) \\ 90 & 25 (27.78) \\ ement delay (h) \\ 501 & 36 (7.19) \\ 254 & 44 (17.32) \\ 18 \\ 475 & 35 (7.37) \\ \end{array}$	NumberDeaths (%)Univariate ORna (95% CI) $419$ $41 (9.79)$ $185$ $39 (11.61)$ $1.21 (0.76-1.92)$ $247$ $33 (13.36)$ $508$ $47 (9.25)$ $0.66 (0.41-1.06)$ $520$ $51 (9.81)$ $235$ $29 (12.34)$ $1.29 (0.79-2.1)$ $624$ $54 (8.65)$ $131$ $26 (19.85)$ $2.61 (1.2-4.8)$ $489$ $266$ $32 (6.54)$ $266$ $0.31 (0.19-0.51)$ $564$ $157$ $57 (10.11)$ $191$ $1.21 (0.5-2.2)$ $598$ $157$ $45 (7.53)$ $3.52 (2.17-5.71)$ $518$ $37 (7.14)$ $237$ $43 (18.14)$ $0.34 (0.21-0.55)$ $399$ $20 (5.01)$ $356$ $60 (16.85)$ $3.84 (2.26-6.51)$ $665$ $90$ $25 (27.78)$ $4.26 (2.49-7.30)$ ement delay (h) $501$ $254$ $36 (7.19)$ $254$ $2.7 (1.69-4.32)$	NumberDeaths (%)Univariate ORna (95% CI)41941 (9.79) 18539 (11.61) $1.21 (0.76-1.92)$ $0.418$ 24733 (13.36) 508 $47 (9.25)$ $0.66 (0.41-1.06)$ $0.085$ 52051 (9.81) 23529 (12.34) $1.29 (0.79-2.1)$ $0.295$ 62454 (8,65) 13126 (19.85) $2.61 (1.2-4.8)$ $0.0001$ 48932 (6,54) 26648 (18.05) $0.31 (0.19-0.51)$ $0.0000$ 56457 (10.11) 19123 (12.04) $1.21 (0.5-2.2)$ $0.452$ L)59845 (7.53) 35 (22.3) $3.52 (2.17-5.71)$ $0.0000$ 51837 (7.14) 237 $43 (18.14)$ $0.34 (0.21-0.55)$ $0.0000$ 39920 (5.01) 356 $60 (16.85)$ $3.84 (2.26-6.51)$ $0.0000$ 66555 (8.27) 90 $2.5 (27.78)$ $4.26 (2.49-7.30)$ $0.0000$ 66555 (8.71) 90 $2.7 (1.69-4.32)$ $0.0000$ 1847535 (7.37) $2.7 (1.69-4.32)$ $0.0000$	Number     Deaths (%)     Univariate ORna (95% CI)     Multivariate P     Multivariate ORa (95% CI)       419     41 (9.79)     1.21 (0.76-1.92)     0.418       247     33 (13.36)     0.66 (0.41-1.06)     0.085       508     47 (9.25)     0.66 (0.41-1.06)     0.085       520     51 (9.81)     1.29 (0.79-2.1)     0.295       624     54 (8.65)     2.61 (1.2-4.8)     0.0001     2.16 (1.20-3.89)       489     32 (6.54)     0.31 (0.19-0.51)     0.0000     0.29 (0.17-0.50)       564     57 (10.11)     1.21 (0.5-2.2)     0.452     0.452       598     45 (7.53)     3.52 (2.17-5.71)     0.0000     3.54 (2.05-6.12)       518     37 (7.14)     0.34 (0.21-0.55)     0.0000     0.39 (0.23-0.67)       399     20 (5.01)     3.84 (2.26-6.51)     0.0000     3.69 (2.12-6.41)       665     55 (8.27)     90     25 (27.78)     4.26 (2.49-7.30)     0.0000     3.69 (2.12-6.41)       ement delay (h)     501     36 (7.19)     2.7 (1.69-4.32)     0.0000     3.2 (1.6-6.3)       18 </td	

ORa: odds ratio adjusted, ORna (95% CI): odds ratio nonadjusted with 95% confidence interval, SBP: systolic blood pressure. Hosmer and Lemeshow test: Chi-square 8.956, P = 0.346.

<sup>a</sup>Comorbidity: comorbid illness recorded in our study were: malaria (n = 33), HIV infection (n = 6), diabetes mellitus (n = 4), and tuberculosis (n = 2)

Table 5: Proposition of the typhoid intestinal perforation prognostic score (TIPPS) with the scoring				
Predictive factors	Score <sup>a</sup>			
	1	2	3	
Comorbidity	No	Yes		
Mean systolic blood pressure (mmHg)	≥90	-	<90	
Respiratory rate (/min)	<24	≥24		
Admission and management delay (hours)	≤72	-	>72	
ASA score	I–II–III	-	IV&V	
Serum Creatinine level (mg/L)	≤20	-	>20	
Haemoglobin (g/dL)	≥9	<9		
Number of perforation	≤2	3 and more	-	

According to the severity and mortality risk of TIP, we classified patients into four grades of increasing severity: Grade I: low risk (score: 8–10), suture of the perforation or ileostomy is recommended; Grade II: moderate risk (score: 11–13), ileostomy is recommended with a normal operating time for the treatment of peritonitis; Grade III: high risk (score: 14–16), ileostomy by damage control surgery is recommended; and Grade IV: very high risk (score: 17–20), ileostomy by damage control surgery is recommended.

<sup>a</sup>Total score "TIPPS" varies from 8 to 20 = Respiratory rate + mean systolic blood pressure + serum creatinine level + haemoglobin + comorbidity + ASA score + admission and management delay + number of perforation

TIPPS	Score-buildi	Score-building group ( $n = 755$ )		Validation group $(n = 377)$	
	Number (%)	$\frac{\text{Specific mortality}}{n(\%)}$	Number (%)	$\frac{\text{Specific mortality}}{n(\%)}$	
Grade I: 8–10	256 (33.9)	9 (3.5)	161 (42.7)	5 (3.1)	
Grade II: 11–13	326 (43.2)	22 (6.7)	163 (43.2)	12 (7.4)	
Grade III: 14–16	142 (18.8)	31 (21.8)	35 (9.3)	10 (28.6)	
Grade IV: 17–20	31 (4.1)	18 (58.1)	18 (4.8)	12 (66.7)	
Total	755	80	377	39	

- Grade II: moderate risk (score: 11–13), ileostomy is recommended with a normal operating time for the treatment of peritonitis.
- Grade III: high risk (score: 14–16), ileostomy by damage control surgery is recommended.
- Grade IV: very high risk (score: 17–20), ileostomy by damage control surgery is recommended.

Table 6 gives us the distribution according to the different grades of severity. The ROC curves of the SBG and VG are shown in Figure 2A and B. The performance of the prognostic score and discriminant ability was good in SBG (area under ROC = 0.834; 95% CI, 0.777-0.892;  $P \le 0.001$ ) and VG (area under ROC = 0.878; 95% CI, 0.777-0.892;  $P \le 0.001$ ). The coefficient of determination was high ( $R^2 = 0.9569$ ), indicating a good fit of relationship between the TIPPS and the mortality both in the building and VGs [Figure 2C]. This "TIPPS" score can be established before surgery (scored at 18/18) and after surgery (scored at 20/20).

# Discussion

The management of TF is a real burden for the health system in these countries, as many patients are diagnosed with lethal complications such as intestinal perforation or bleeding.<sup>[1,3,4,10,12]</sup> Vaccination against TF still does not exist in the Expanded Program on Immunisation in Niger. However, the 2018 World Health Organization guidelines recommend the addition of the typhoid vaccine to the vaccination program in typhoid-endemic countries. Implementation of this measure would reduce the frequency of this disease.<sup>[6]</sup> The incidence of typhoid perforation varies from one country to another, but a high rate of 10%–33% has been reported in West Africa with high mortality.<sup>[4,5,8-10,12,25]</sup> In our Nigerian context, as in most African countries, TIP is a burden for the predominantly rural population, and its management is a daily activity of the surgeon.<sup>[1-5,9,12,14,25-28]</sup>

Surgical treatment of TIP must be prompt after an appropriate resuscitation. In this study, ileostomy was the main surgical procedure. Some of our patients were admitted in a bad general state, some even moribund (ASA IV or V). In these cases, surgical treatment will consist of a damage control, a rapid toilet of peritoneal cavity, and creation of an ileostomy. The patient could possibly benefit from a second look 24–48 h after resuscitation. Many are unanimous in favouring the option of an ileostomy and not performing primary closure in a septic environment.<sup>[2,3,9,25-27]</sup> Based on our experience and existing literature, we recommend the creation of a stoma in the cases of TIPs seen late. Moreover, to improve the prognosis, the damage control, formerly used in the context of trauma surgery, is nowadays an option used in the management of

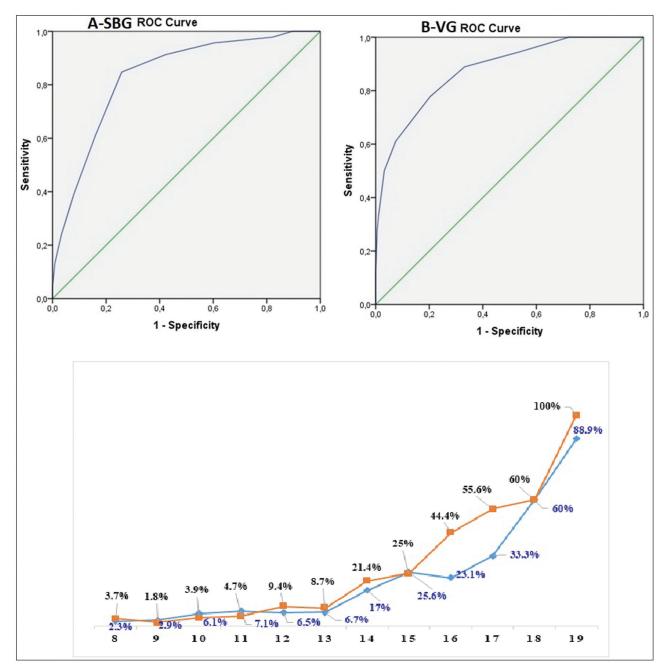


Figure 2: Performance of the prognostic score—(A) SBG (AUC =0.834) and (B) VG (AUC = 0.878). (C) The relationship between the TIPPS and the mortality both in the building and validation groups (coefficient of determination  $R^2$  = 0.9569). AUC: area under curve

significantly physiologically deranged patients with intraabdominal sepsis.<sup>[29]</sup>

The mortality recorded in this study (10.5%) is comparable to other African studies.<sup>[4,8,12,25,28]</sup> As part of the prognostic evaluation of intra-abdominal sepsis, several scores and many predictive factors have been reported.<sup>[15-18,20-22]</sup> According to Biondo *et al.*,<sup>[16]</sup> to be useful, a classification and scoring system must be compatible with the concepts of physiopathology, aetiology of the disease, and surgical results. However, the use of these scores is not always easy especially in sub-Saharan Africa and other lowincome countries.<sup>[20]</sup> This is due to the lack of sophisticated equipment, difficulties in data collection, and methodological problems.<sup>[2,17,20,21]</sup> Faced with these handicaps, the JPS system, established in the context of peptic perforation, is a simple prognostic score, feasible and adapted for poor countries.<sup>[20]</sup> Our study was inspired by several prognostic scores. Our experience and the high frequency of TIP in our context led us to propose this new prognostic score for TIP, reproducible in a situation of limited resources: "TIPPS." Indeed, in our study, the results show eight factors, all significantly associated with postoperative mortality. This allowed us to develop the TIPPS with scores from 8 to 20. According to the severity of the disease and

risk of mortality, we classified peritonitis due to TIP into four grades of increasing severity: grade I: low risk (score: 8-10), grade II: moderate risk (score: 11-13), grade III: high risk (score: 14-16), and grade IV: very high risk (score: 17-20). The prognosis progressively worsens with mortality of 3.1%-3.5% for grade I, 6.7%-7.4% for grade II, 21.8%-28.6% for grade III, and 80%-100% for grade IV.

The TIPPS score that we suggested has some similarities to the JPS, which predicts the prognosis of peritonitis due to peptic perforation.<sup>[20]</sup> Moreover, Singh et al.<sup>[21]</sup> had demonstrated that JPS can be easily used on TIPs by making minor modifications. However, in our study, unlike that of Mishra et al.<sup>[20]</sup> and Singh et al.,<sup>[21]</sup> age was not considered a statistically significant prognostic factor. In this study, we have also added other significant prognostic factors in the building of our score: respiratory rate, ASA score, haemoglobin levels in the blood, and number of intestinal perforations. This proposed TIPPS score is easier to use than the acute physiology and chronic health evaluation II score<sup>[15]</sup> and the MPI,<sup>[22]</sup> particularly in sub-Saharan Africa where there is a lack of diagnostic equipment. The PSS score proposed by Biondo et al.[16] is better adapted to assess the prognostic value of specific factors in patients with left colon perforation.

This proposed score, far from making the claim of universal validity, or even challenging previous scores, is a contribution to the evaluation of the prognosis of peritonitis due to TIP that is still endemic and fatal in poorresource settings.<sup>[24,7,8,10,25]</sup> Prospective studies in hospitals in the Republic of Niger and other regions of Africa could be considered for a better evaluation and validation of this "TIPPS" score.

Limitations of the study are as follows: retrospective data are characterised by the loss of patient information. Also, our context of limited resources does not allow to carry out all biological exams (such as blood culture, coproculture, and ionogram). It is the same problem for imaging such as computed tomography. These limitations did not prevent building of this "TIPPS" score, which is easy to reproduce in other hospitals with limited resources.

# Conclusion

TIP is the main cause of peritonitis in Niger. Ileostomy was the main surgical procedure. TIP continues to have a persistently high mortality. The proposal of this TIPPS, rated 8–20, is a contribution to the management of this disease. This TIPPS score allowed us to divide the TIP into four increasing severity grades: grade I (low risk), grade II (moderate risk), grade III (high risk), and grade IV (very high risk). Indeed, the TIPPS is simple. It can describe the severity of the disease and, thus, predict the risk of death. Improving the prognosis requires early diagnosis. The study highlights the importance and impact of timely and

adequate perioperative resuscitation in more complicated cases. However, a better prevention policy, through access to drinking water, the promotion of personal hygiene, the use of sanitation facilities, and vaccination campaigns against TF will reduce this burden in sub-Saharan Africa.

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#### **Conflict of interest**

There are no conflicts of interest.

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