

Factors Associated with Survival in Patients of Enteric Perforations; A Retrospective Analysis of 73 Patients

MALIK A.K.,¹ NOMANI A.Z.,² QURESHI A.U.,³ GONDAL K.M.⁴

Address for Correspondence: Department of Child and Family Psychiatry, Mayo Hospital, Lahore – Pakistan.

Objective: A retrospective study was conducted with 73 patients of enteric ileal perforation to determine the factors influencing survival.

Method: A 2 years retrospective analysis from March 2008 to March 2010 was carried out at South Surgical Unit of Mayo Hospital, Lahore (Pakistan) from admission and operation records taking into account multiple factors associated with survival in patients of enteric ileal perforation.

Results: A total of 73 patients presenting over two years in South Surgical Unit of Mayo Hospital were included in the study. An overall mortality rate of 10.96% was observed. Most common predictive factors for the mortality were perforations > 0.5 cm (15.9%, p 0.135*), peritoneal fluid recovered at laparotomy > 1,000 ml (13.3%, p 0.702*), with most significant factors being > 2 weeks pre-hospital symptoms of perforation (53.8%, p < 0.01*) and development of post-operative septicemia (80%, p < 0.01*).

Conclusion: Mortality rates from enteric perforations are still high in developing countries. Females are more prone with size of perforation > 0.5 cm, > 1,000 ml of peritoneal fluid (p-values > 0.05 for each), pre-hospital symptoms of perforation > 2 weeks (p-values < 0.05) and development of septicemia (p-values < 0.05). Most of deaths occur within first week of admission.

Key Words: Enteric Perforations, Ileal Perforations, Septicemia.

Introduction

Typhoid fever is a bacterial disease, caused by *Salmonella typhi*. It is transmitted through the ingestion of food or drink contaminated by the feces or urine of infected people¹. It is the fourth most common cause of death in Pakistan.² Up to 93% of global episodes occurs in Asia, where Southeast Asia has an estimated incidence of 110 cases / 100,000 population.³ Early diagnosis and treatment avoids extensive procedures and is associated with lower morbidity and mortality.⁴ Enteric perforations have a high mortality rate, up to 60% as shown in various studies of the East.⁵ However, Aggressive resuscitation, effective antibiotics and early surgery has significantly reduced the mortality rate and complications in these patients.⁵

Typhoid fever occurs predominantly in poor socio-economic areas with poor sanitary conditions.⁴ After ingestion of contaminated food, bacteria multiply in the reticuloendothelial system during an incubation period of 1–14 days.⁴ Clinical manifestations prior to perforation include malaise, headache, high fever with relative bradycardia, Rose spots, abdominal pain and altered bowel habits in the past few days along with signs of bacteremia and systemic sepsis with characteristic normal or low blood counts and anemia.^{4,6}

From the reticuloendothelial system, the bacteria become localized in Peyer's patches in the terminal ileum which undergo swelling and ulceration on the anti-mesenteric border of the intestine leading to capillary thrombosis

and necrosis.⁴ This may lead to secondary perforation of the terminal ileum usually occurring in 3rd week with signs and symptoms of generalized peritonitis like tenderness, guarding and absent bowel sounds.^{4,7}

There is an increase in titer of agglutinins against the somatic (O) and flagellar (H) antigens of *S typhi*.⁴ Flagellar (H) antigens are the basis of Widal test (not reliable).^{4,6} Other tests include Blood Cultures (first 10 days), urine / stool cultures (later), bone marrow culture (highest yield), DNA probes and PCR tests (not widely available).⁶

The aim of this study was to identify possible factors predictive of postoperative survival in patients presenting to a surgical unit at a tertiary care hospital with well equipped emergency and follow-up facilities, so that a comparison with similar studies carried out elsewhere can be made.

Subjects and Methods

Mayo Hospital, Lahore, Pakistan is a 1,800 bed largest tertiary care hospital in Punjab province of Pakistan. This retrospective analysis was carried out on patients presenting in South Surgical Unit at Mayo Hospital, Lahore, with typhoid ileal perforations during past two years, i.e. from March 2008 to March 2010. The data was retrieved from the admission and operation records and case files of the patients for analysis.

Diagnosis was done clinically on the characteristic findings of peritoneal irritation in emergency room along with history consistent with enteric fever. It was supported with

evidence of free air under the diaphragm on abdominal x-rays and elevated white cell counts (TLC and DLC). Only 4 (5.47%) patients had previously done Widal test for prolonged fever, before presenting in emergency room with clinical findings of perforation. A titer of 100 or more for O antigen and a titer in excess of 200 for H antigens were considered significant. However, there were no definitive confirmatory tests like serology and cultures done for the rest of the patients in emergency room to avoid unnecessary delays in emergency treatment.

Data was analyzed for various possible factors that might influence the survival of patients presenting with enteric perforations. Age and mean hospital stay were calculated. Gender of patients, type of operation done, exteriorization of gut via ileostomy done or not, duration of symptoms before presentation in emergency room, size and number of perforations, amount of peritoneal fluid recovered on opening the peritoneal cavity and development of post-op complications especially septicemia were evaluated for their effects on survival outcome. Evidence of septicemia was obtained via paired qualitative blood cultures with blood taken from a peripheral vein and associated elevated white blood cell counts.

Data was put in SPSS (Statistical Package for the Social Sciences) version 13.0, and actual numbers, percentages and P-Values for the results were obtained after applying various statistical tests.

Results

73 patients presented to South Surgical Unit of Mayo Hospital, Lahore (Pakistan) from March 2008 to March 2010. Out of these 73, 65 (89.04%) patients survived to recover completely while 8 died because of the development of complications giving a mortality rate of 10.96%. Mean age rank for survivors was found to be 34.6 years, while for the dead was found to be 56.5 years (Table 1).

Mean hospital stay in case of survival was 7.38 days (95% CI: 6.37 – 8.40) while in case of death was 3.88 days (95% CI: 1.00 – 6.75) (Table 3).

Table 2: Survival in various operative procedures for Enteric Gut Perforations.

Variable	Survived	Dead	P-value
1. Operation			
Simple Closure	26 (92.9%)	2 (7.1%)	0.702*
Resection and anastomosis	39 (86.7%)	6 (13.3%)	
2. Iliostomy			
Yes	14 (87.5%)	2 (12.5%)	1.000*
No	51 (89.5%)	6 (10.5%)	

*p-values are calculated through Fisher's Exact Test as Cell count was less than 5 in one or more of the results.

Male to female ratio was about 8:1. Out of 65 male patients, 59 (90.8%) survived while 6 (9.2%) males died. Whereas out of 8 females, 6 (75%) survived and 2 (25%) did not survive (p-value 0.210*) (Table 1).

In 28 patients done with Simple Closure, a mortality rate of 7.1% (n = 2) was obtained. Primary resection and anastomosis was done in 45 patients, 6 (13.3%) of these patients did not survive (p-value 0.702*) (Table 2).

57 patients underwent primary closure or resection and end – to – end anastomosis, Iliostomy was done in only 16 patients. 10.5% (n = 6) mortality rate was observed in former group, while of 12.5% (n = 2) was observed in latter (p-value 1.000*) (Table 2).

Table 1: Demographic data for 73 cases of Enteric Perforations.

Variable	Survived	Dead
1. Age		
Mean Rank	34.60	56.50

Variable	Survived	Dead	P-value
2. Gender			
Male	59 (90.8%)	6 (9.2%)	0.210*
Female	6 (75%)	2 (25%)	

*p-values are calculated through Fisher's Exact Test as Cell count was less than 5 in one or more of the results.

Duration from onset of symptoms of perforation to presentation in the emergency room was less than 2 weeks in 60 patients with a mortality rate of 1.7% (n = 1). Mortality rate was increased significantly (p-value < 0.01*) to 53.8% for patients presenting after 2 weeks of onset of symptoms of perforation as 7 patients died in this group while only 6 (46.2%) patients survived (Table 3).

Single and multiple perforations had mortality rates of 10.3% (n = 6) and 13.3% (n = 2) respectively (p-value 0.664*) (Table 3).

29 patients with perforations size less than 0.5 cm had 3.4% (n = 1) mortality rate whereas out of 44 patients with perforation size more than 0.5cm, mortality rate was raised to 15.9% (n = 7) (p-value 0.135*) (Table 3).

Amount of peritoneal fluid was less than 1000 ml in 28 patients having a mortality rate of 7.1% (n = 2). Mortality rate almost doubled to 13.3% (n = 6) in 45 patients with amount of peritoneal fluids recovered at laparotomy more than one liter

(p-value 0.702*) (Table 3).

Only 2 (20%) patients who developed septicemia post-operatively survived to full recovery while 8 (80%) patients developing post-operative septicemia died. All 63 other patients not developing septicemia post-operatively survived (p-value < 0.01*) (Table 3).

Discussion

Despite marked improvements in management of the patients presenting with Enteric Perforations to tertiary care hospitals in developing countries like Pakistan, there is a significant morbidity and mortality associated with them. A mortality rate of about 11% was obtained for 73 cases which was similar to mortality rates of 7.6 – 16% as reported by studies in other parts of the country.^{4,10}

Most of the deaths occurred within first week with a mean of 3.88 days (95% CI: 1.00 – 6.75) indicating a positive prognosis for those who survive at the end of first week. Mean stay in hospital for survivors was observed as 7.38 days (95% CI: 6.37 – 8.40). However, Edino ST et al¹¹ reported the duration of hospital stay for survivors as 8 – 57 days with a mean of 16.1 days. This probably indicates better availability of operative and post-operative care facilities in Mayo Hospital, Lahore (Pakistan) as compared to hospitals in other developing countries, reducing the hospital stay.

Mortality rate was more in females (25%, n = 2) as compared to males (9.2%, n = 6). (p-value 0.210*, Not Significant). This was probably due to confounding effect of many other variables like lack of proper nutrition, gender discrimination etc that were not explored in this retrospective study. Also, there was no reliable study found for comparison in this case.

Primary resection and anastomosis had almost double mortality rate (13.3%, n = 6) as compared to Simple Closure (7.1%, n = 2) (p-value 0.702*, Not Significant). This difference was probably due to the fact that primary resection and anastomosis was done in patients having greater contamination of peritoneal cavity and consequently, more severe peritonitis. This was also a non-significant factor in the study by Edino ST et al,¹¹ where mortality rate was 14.7% (n = 5) with simple closure and 15.8% (n = 3) with resection and anastomosis. (p-value = 0.96).

Iliostomy had a little, if any, impact on survival (p-value 1.000*, Not Significant). Perhaps, more ileostomies are done in more contaminated peritoneal cavities and hence, their benefit may be partially masked by patient selection for various operative procedures. On the contrary, marked difference in results was obtained in a study at Nishtar Medical College, Multan⁹ where 25% mortality rate was observed after primary closure and 10% after ileostomy / colostomy.

Greater than 2 weeks of symptoms of perforation prior to hospital admission has a significantly high mortality rate (53.8%, n = 7) (p-value < 0.01*) as compared to patients presenting within 2 weeks after start of symptoms (1.7%,

Table 3: Various operative and post-op factors in 73 patients of Enteric Perforations.

1. Duration of pre-hospital symptoms of perforation			
< 2 Weeks	59 (98.3%)	1 (1.7%)	0.000*
> 2 weeks	6 (46.2%)	7 (53.8%)	
2. Number of perforations			
Single	52 (89.7%)	6 (10.3%)	0.664*
Multiple	13 (86.7%)	2 (13.3%)	
3. Size of the perforation			
< 0.5 cm	28 (96.6%)	1 (3.4%)	0.135*
> 0.5cm	37 (84.1%)	7 (15.9%)	
4. Amount of peritoneal fluid recovered at laparotomy			
< 1000 ml	26 (92.9%)	2 (7.1%)	0.702*
> 1000 ml	39 (86.7%)	6 (13.3%)	
5. Development of post-op septicemia			
Yes	2 (20%)	8 (80%)	0.000*
No	63 (100%)	0 (0%)	
6. Stay at the hospital			
<i>Category</i>	<i>Mean</i>	<i>SD</i>	<i>95% CI</i>
Survivor	7.38	4.114	6.37 – 8.40
Dead	3.88	3.441	1.00 – 6.75

*p-values are calculated through Fisher's Exact Test as Cell count was less than 5 in one or more of the results.

n = 1). Similar results were obtained by Edino ST et al,¹¹ where 25% (n = 6) mortality was associated with greater than 2 weeks of pre-hospital symptoms of perforation as compared to 6.9% (n = 2) in patients presenting in less than 2 weeks time (p-value > 0.05).

Mortality rates appeared, however, less related to number of perforations (p-value 0.135*, Not Significant) in contrast to study by Edino ST et al,¹¹ where multiple perforation significantly affected the outcome with a mortality rate of 33.3% (n = 5) as compared to 7.9% mortality of single perforation (p-value 0.023). This might be due to the fact that multiple perforations with greater contamination are treated with either primary resection and anastomosis or ileostomy is done in these cases.

Perforations with size less than 0.5 cm, 1 (3.4%) patient died whereas mortality rates increased to 15.9% (n = 7) in patients with perforation size more than 0.5cm (p-value 0.135*, Not Significant). There was no reliable study found for comparison in this case.

Death rate almost doubled (13.3%, n = 6) as amount of

peritoneal fluids recovered at laparotomy became more than one liter as compared to in patients with less than 1 liter of peritoneal fluid recovered at laparotomy (7.1%, n = 2) (p-value 0.702*, Not Significant). Similarly, this factor was found more significant in study by Edino ST et al¹¹, where mortality rate increased from 8.9% (n = 4) in patients with less than 1 liter of peritoneal fluid to 50.0% (n = 4) in patients with more than 1 liter of peritoneal fluid recovered at laparotomy (p-value 0.027).

Many of the post-operative complications were considered for possible impact on survival but significant results were obtained only with post-operative septicemia in current study. All the deaths occurred due to development of post-operative septicemia. Mortality was significantly high (80%, n = 8) in patients developing septicemia post-operatively (p-value < 0.01*). Similarly, in study by Edino ST et al,¹¹ 100% (n = 2) mortality was found in patients who developed septicemia post-operatively (p-value < 0.05).

Conclusion

Mortality rates from enteric perforations continue to stay high (11%) despite good health care facilities. Most of the deaths occur within first week of admission to hospital. More prone are females, primary resection and anastomosis done as a primary operation, size of perforation > 0.5 cm and more than one liter of peritoneal fluid recovered at laparotomy, although the results were statistically not significant. Greater than 2 weeks of pre-hospital symptoms of perforation and the development of post-op septicemia were found to significantly (p value > 0.05) increase the mortality in cases of enteric ileal perforations.

Acknowledgments

The authors wish to thank Dr. Zeeshan Butt, *M.B.; B.S.* of Department of South Medicine, Mayo Hospital, Lahore (Pakistan) for immense help in statistical analysis of the data.

References

1. World Health Organization (WHO); Typhoid fever [Online] [Cited on 2010 June]. Available from URL: http://www.who.int/topics/typhoid_fever/en/.
2. GlaxoSmithKline Pakistan Website [Cited on 2010 June]. Available from URL: <http://www.gsk.com.pk/typhoid.html>.
3. Siddiqui FJ, Rabbani F, Hasan R, Nizami SQ, Bhutta ZA. Typhoid fever in children: some epidemiological considerations from Karachi, Pakistan. *International Journal of Infectious Diseases*. 2006 May; 10 (3): 215-22.
4. Wani RA, Parray FQ, Bhat NA, Wani MA, Bhat TH, Farzana F. Nontraumatic terminal ileal perforation. *World Journal of Emergency Surgery*. 2006; 1: 7. Available from <http://www.wjes.org/content/1/1/7>.
5. Gupta S, Kaushik R. Peritonitis – the Eastern experience. *World Journal of Emergency Surgery*. April 2006; 1: 13. Available from: <http://www.wjes.org/content/1/1/13>.
6. Longmore M, Wilkinson I, Turmezei T, Cheung CK. *Oxford Handbook of Clinical Medicine* (7th Ed.). New York: Oxford University Press Inc., 2007.
7. Ahmad T, Khan MI, Hussain N, Siddiqui E, Zia-Ul-Islam. Perforation operation interval as a prognostic factor in typhoid ileal perforation. *Journal of Surgery Pakistan (International)*. Jan – Mar 2009; 14 (1): 11-14.
8. Ansari AG, Naqvi SQH, Ghumro AA, Jamali AH, Talpur AA. Management of typhoid ileal perforation: A surgical experience of 44 cases. *Gomal Journal of Medical Sciences*. Jan – Jun 2009; 7 (1): 27-30.
9. Ali S, Sattar A, Amin MA. Typhoid Perforation; Primary Closure vs Ileostomy. *Professional Medical Journal*. Jun 2006; 13 (2): 269-273.
10. Ahmed HN, Niaz MP, Amin MA, Khan MH, Parhar AB. Typhoid Perforation still a common problem: Situation in Pakistan in comparison to other countries of Low Human Development. *Journal of Pakistan Medical Association*. May 2006; 56 (5): 230-232.
11. Edino ST, Yakubu AA, Mohammed AZ, Abubakar IS. Prognostic Factors in Typhoid ileal Perforation: A Prospective Study of 53 Cases. *Journal of the National Medical Association*. Sep 2007; 99 (9): 1042-1045.