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CLINICAL STUDY OF FACTORS INFLUENCING THE OUTCOME OF TYPHOID ILEAL PERFORATION

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Abstract

Background: - Typhoid fever is a disease caused by salmonella typhi, a gram-negative bacillus. Ileal perforation is a common drawback seen in tropical countries. The commonest cause is typhoid fever. In western countries, the causes are malignancy, trauma, and mechanical ethology. Intestinal perforation is a common cause of the occurrence of peritonitis necessitating emergency surgical intervention.

Methods: - An observational study was conducted on 50 cases of typhoid ileal perforation admitted in the Department of Surgery, Rajendra Institute of Medical Sciences, Ranchi during the period of November 2019 to September 2021. The study aimed to find out the presentation, management, outcome, and factors influencing the outcome of patients admitted with ileal perforation

Results: - Typhoid ileal perforation commonly occurred in the second and third decades with 62% of cases in that age group. Abdominal pain, fever, and vomiting were the commonest symptoms. The commonest signs were dehydration, abdominal tenderness, guarding, and intra-abdominal free fluid. Pneumoperitoneum in the chest and erect abdominal X-ray was seen in 78% of patients. The Widal test was positive in 22 patients out of 40 tested (55%). The histopathological report was suggestive of typhoid in three patients (20% of tested). Ileostomy was the commonest procedure done (64%). Two-layer closure was done in 24% and resection and anastomosis in 8% of patients. The mortality rate was 14%.

Conclusion: - Typhoid is the most common cause of Ileal perforation with male preponderance. Widal serology has been proven to be a useful test in the diagnosis of typhoid fever. Typhoid perforations have a higher morbidity rate. The type of surgical procedure did not influence the outcome, either morbidity or mortality.

Key Words: - Typhoid ileal perforation, Salmonella typhi, Widal test, mortality.

INTRODUCTION

Typhoid fever is a disease caused by salmonella typhi, a gram-negative bacillus.

Ileal perforation is a common drawback seen in tropical countries. The commonest cause is typhoid fever.[1]In western countries the causes are malignancy, trauma, and mechanical etiology, in the order of frequency.[2,3]

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The common cause of peritonitis necessitating emergency surgical intervention is Intestinal perforation. Perforation of the bowel is a serious complication of typhoid fever. Although intestinal hemorrhage is the most common complication of typhoid fever, intestinal perforation continues to be the most frequent reason behind high morbidity and mortality.[4,5] Despite global scientific development, typhoid fever, and its complication continue to be a great health problem, especially in developing countries. It has emerged as a global health problem that can have a devastating impact on the resources of poor countries and estimated more than 33 million cases of typhoid fever occur annually causing more than 5,00,000 deaths.[6,7] The rates of perforation have been reported in the literature to vary between 0.8% and 18%.[8-12]

Regions of the world like West Africa have a high incidence of typhoid fever because of lacking clean and potable water supplies and inadequate waste disposal systems. The foremost fatal complication of typhoid fever is ileal perforation. The incidence of typhoid ileal perforation varies from 15 to 33% in the West African environment.[13]Over the years a definite changing trend has been observed in ileal perforations both in terms of causes, treatment, and prognosis. Better antibiotics, aggressive surgery and the elimination of conservative treatment, better preoperative and postoperative care have all significantly contributed to the improvement in patient outcome.[14]

Despite decades of improvement in patient care, the morbidity and mortality of typhoid perforation remain high, and this is related to multiple variable factors. The factors influencing the outcome of typhoid ileal perforation are late presentation, delay in operation, multiple perforations, and drainage of copious quantities of pus and fecal material from the peritoneal cavity.[15]

Outcomes have indeed improved but still cases of ileal perforation cause significant morbidity and mortality that persists despite the significant changes in healthcare over the years.

AIMS AND OBJECTIVES

- To study the presentation and management of patients admitted with ileal perforation
- To study the outcome and factors influencing the outcome in thesepatients.

MATERIALS AND METHODS

This hospital-based prospective, observational, and descriptive study was conducted in the Department of General Surgery, Rajendra Institute of Medical Sciences (RIMS), Ranchi from November 2019 to September 2021. 50 patients, admitted with abdominal pain, fever, and vomiting in the surgical ward, were included in the study. Prior approval from the Institutional Ethics Committee was taken and informed consent from the patients was also taken.

Inclusion criteria*:*

- Patient has been admitted to the surgical ward with abdominal pain and distension, fever, vomiting, and shock.

Exclusion criteria:

- Patient otherwise unfit for radiological studies.
- Patient has no decision-making capability due to a mental illness or due to other medical conditions.

METHODS OF MEASUREMENT OF OUTCOME OF INTEREST:

- History with special reference to the presence of fever, pain, vomiting, abdominal distension, constipation, and treatment before admission was taken. Vital signs, hydration, abdominal distension, tenderness, guarding, and presence of free fluid were noted. Systemic examination of the cardiovascular, respiratory, and central nervous system was done.

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- The subsequent investigations were done as a routine:
  - Hemoglobin
  - Bleeding and Clotting times
  - Blood sugar and urea and Serum creatinine
  - Chest X-Ray
  - Electrocardiogram
  - Peritoneal fluid culture
  - Pus culture in case of wound infection

In all ileal perforations, the following additional investigations are required:

  - Widal test
  - Blood Culture

- All patients were resuscitated preoperatively with intravenous fluids and antibiotics. Patients unfit for surgery were initially treated with flank drains under local anesthesia as a temporary measure before definitive laparotomy. Most cases received cefotaxime or ciprofloxacin with metronidazole. In case of gross peritoneal contamination, aminoglycosides will be added.
- All patients underwent laparotomy under general anesthesia. The amount and type of peritoneal contamination, number, site, size of perforations, and procedure utilized were noted. The choice of procedure was based on the surgeon's preference or unit policy. The following procedures were employed.
  - Simple two-layer closure or extra mucosal single-layer repairs
  - Closure with free or pedicled omental patch
  - Resection and anastomosis or ileostomy
- Antibiotics were routinely given for 10 days.
- A diagnosis of typhoid was made only if the Widal test was positive, or Salmonellae was isolated from blood or urine, and if histopathological evidence of typhoid perforation was found.
- Postoperative complications to be noted. The factors influencing mortality and morbidity and outcome were assessed.

With regards to statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analyzed by SPSS (version 24.0; SPSS Inc., Chicago, IL, USA). The various tests used for statistical analysis were Chi-square and ANOVA.

RESULTS

Fifty patients with typhoid ileal Perforation admitted between November 2019 to September 2021 were included in this study.

Table 1: age and sex incidence

Age group (years)	Male	Female	Total	Percent
10 – 20	2	0	2	4%
20 – 30	15	4	19	38%

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30 – 40	9	3	12	24%
40 – 50	9	1	10	20%
50 – 60	4	1	5	10%
60 – 70	1	0	1	2%
70 – 80	0	0	0	0%
80 – 90	0	1	1	2%
Total	40	10	50	100

The distributions of age and sex in all cases are shown in Table 1. The age of patients ranged from 15 to 84. Typhoid ileal perforation commonly occurred in the second and third decades with 62% of cases in that age group. The male-to-female ratio was 3.8:1.

Table 2: Symptoms and signs

Symptoms	**Number**	**%**
Abdominal Pain	50	100
Fever	31	62
Vomiting	29	58
Constipation	23	46
Diarrhea	3	6
Signs	**Number**	**%**
Dehydration	33	66
Tenderness	50	100
Guarding	44	88
Distention	27	54
Free Fluid	31	62
Shock	6	12

Symptoms and signs are shown in Table 2. Most of the patients presented with symptoms and signs of peritonitis. The commonest symptoms were abdominal pain, fever, and vomiting. The commonest signs were dehydration, abdominal tenderness, guarding, and intra-abdominal free fluid. Most patients who suffered from typhoid gave a history of fever. 12% of patients were in shock.

Investigations

X-Ray: Pneumoperitoneum in the chest and erect abdominal X-ray was seen in 78% of patients. Features of intestinal obstruction, including dilated bowel loops with air-fluid levels in erect abdominal X-rays were seen in 24% of patients.

Hematology and Biochemistry: Hemoglobin was less than 8 g/dL in 17 (34%) of patients and Albumin of <3.5

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g/dL was seen in 13 (26%) of cases. Azotemia is defined as a Blood Urea of >52 mg/dL and/or Serum Creatinine >2 mg/dL was seen in 40% of patients.

Microbiology: Blood cultures were done in 30 patients and growth was obtained in 4. Salmonella typhi was found in 3 patients and pseudomonas in 1. The typhoid growths were sensitive to ciprofloxacin, cefotaxime, ceftriaxone, and amikacin. The peritoneal fluid culture was done in all patients and cultures obtained in 19. E. coli and Klebsiella spp. was found in 9 patients each and one patient had Proteus vulgaris. The Widal test was positive in 22 patients out of 40 tested (55%).

Histopathology: Pathological examination of either resected specimens or scrapings from the edge of the ulcer was done in all patients. The histopathological report was suggestive of typhoid in three patients.

Table 3: Lag period

Lag period (in hours)	Typhoid Ileal Perforation n = 50	%
<24	14	30
24 – 48	27	54
49 – 72	7	12
> 72	2	4
Total	50	

The above table shows that the time between the onset of pain and the surgical intervention was between 8 and 72 hours with an average of 32.64.

Table 4: Surgical procedure

Procedure	Typhoid Ileal Perforation n = 50	
Ileostomy	32	64.0%
Two-layer Closure	12	24.0%
Resection/Anastomosis	6	12.0%
Total	50	

Ileostomy was the commonest procedure done (64%). Two-layer closure was done in 24% and resection and anastomosis in 8% of patients.

Table 5: Number of perforations

Number of perforations	No. of patients
1	40
2	8
3	1
4	1
Total	50

The above table shows that multiple perforations occurred in 20% of patients. Over 90% of perforations were within 2 feet (60 cm) from the ileocaecal junction and 62% within 30 cm.

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Table 6: Surgical procedures and their complications

Complications	Ileostomy n = 32	Two-layer closure n = 12	Resection/ Anastomosis n=6	Total n = 50
Wound Infection Wound Dehiscence Abd. Collection	9 (28%)	4 (33%)	3 (50%)	16 (32%)
Fecal Fistula Reperforation	9 (28%)	3 (25%)	0 (0%)	12 (24%)
Respiratory				
Mortality	3 (9.4%)	3 (25%)	1 (16.7%)	7 (14%)
	7 (22%)	4 (33.3%)	2 (33.3%)	13 (26%)
	2 (6.3%)	1 (11%)	1 (16.7%)	4 (8%)
	8 (25%)	1 (11%)	1 (16.7%)	10 (20%)
	5 (15.6%)	1 (8.3%)	1 (16.7%)	7 (14%)
Patients with Complications	22 (68.8%)	8 (66.7%)	4 (66.7%)	34 (68%)

Complications occurred in 34 (68%) of all cases (Tables 6). The common complications seen were wound infection, fecal fistula, would dehiscence, intraabdominal collection, and respiratory complications. The fecal fistula was seen in 13 (26%) of cases. The cause was reperforation in 4 patients.

The highest complication rate was seen with simple closure and the least with resection and anastomosis though this difference was not statistically significant (p=0.857). Pus culture from patients with wound infection was done in all 16 cases and yielded growth in 12 cases. Of these 5 had Staphylococcus aureus, 2 had E. coli and Proteus and 3 had normal skin commensals.

Table 7: Surgical procedure and hospital stay

Procedure	Mean hospital stay (days)
Ileostomy	23.78
Two-layer closure	23.92
Resection Anastomosis	21.83
Total	23.58

$p > 0.05$

The average operating time was 106 minutes. Resection and anastomosis took a longer time than the other procedures but the difference was not statistically significant ($p > 0.05$). The median hospital stay was twenty days. There was no significant difference in the hospital stay of patients undergoing different surgical procedures.

Table 8: Surgical procedures and morbidity and mortality

	Ileostomy n = 32	Two-layer closure n = 12	Resection/ Anastomosis n=6	Total n = 50
Mortality	5 (15.6%)	1 (8.3%)	1 (16.7%)	7 (14%)
Patients with	22 (68.8%)	8(66.7%)	4 (66.7%)	34 (68%)

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complications				

Complication p > 0.05; Mortality p > 0.05

The mortality rate was 14%. Septicemia, fecal fistula, and respiratory complications were the commonest causes of death.

Table 9: Cause of death

Cause of death	No. of patients (n=7)
Fecal fistula	2 (28%)
- Anastomotic Leak	1 (14%)
- Reperforation	-
- Indeterminate	1 (14%)
Septicemia	2 (28%)
CVS/RS	3 (43%)

PROGNOSTIC FACTORS

Surgical Procedure

The type of surgical procedure did not influence the mortality or morbidity in typhoid ileal perforations. The morbidity was higher in patients who underwent ileostomy as compared to patients who underwent primary repair or resection and anastomosis in our study.

Repair of perforation and RA should be the initial choice of treatment in typhoid enteric perforation in CAT I, since this is simple, quick, with the lowest complication rates, and cost-effective. In CAT II, ileostomy should be preferred due to less complication, early discharge, and lifesaving procedure. Resection anastomosis is the less preferred procedure and should be avoided due to its higher complication rate, more chances of fecal fistula formation, which overall increases the hospital stay, morbidity, and mortality. An ileostomy is a lifesaving procedure and should be the procedure of choice in CAT III patients. Despite this, complication rates are higher in CAT III, this shows the high septicemic load and debilitating condition of the patient in CAT III.

Patients who suffered ileal perforations during the course of

typhoid fever had significantly higher levels of CRP than those with uncomplicated infection.

A high APACHE II score is associated with high mortality but did not predict morbidity rate in the typhoid ileal perforation.

In patients with typhoid, two-layer closure had the highest mortality and resection anastomosis the highest complication rate but not statistically significant (p > 0.05).

Table 10: Relation of the lag period to mortality and complications

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Lag Period (hours)	Number of cases	Complications	Death
<24	14 (30%)	6 (42.9%)	0
24 – 48	27 (54%)	19 (70.4%)	2 (7.4%)
49 – 72	7 (12%)	7 (100%)	4 (57.1%)
> 72	2 (4%)	2 (100%)	1 (50%)
Total	50	34 (68%)	7 (14%)

Complications $p < 0.05$; Death $p < 0.05$

Most patients presented with peritonitis of greater than 24 hours duration. An increasing lag period was associated with increased mortality and complication rate. The relationship of the increasing lag period to both mortality and morbidity in typhoid ileal perforations was found to be significant with $p < 0.05$.

Table 11: Risk factors for morbidity

Risk Factor	Morbidity n = 34	No Morbidity n = 16	p
Age > 50 years	**7**	**0**	**< 0.05**
Female sex	7	3	> 0.05
Male sex	27	13	> 0.05
Shock	6	0	> 0.05
Hb < 8 gm%	13	4	> 0.05
Alb < 3.5 g/dl	**13**	**0**	**< 0.05**
Azotemia	16	14	> 0.05
Multiple Perforation	8	2	> 0.05
Fecal Peritonitis	20	7	> 0.05

Table No. 11 shows the other risk factors for morbidity in ileal perforations and their statistical significance. For morbidity age >50 years, reduced serum albumin and an etiology of typhoid were associated with significantly high morbidity. Hemoglobin levels, sex, presence of shock or azotemia, multiple perforations, or fecal peritonitis did not affect the complication rate.

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Table 12: Risk factors for mortality

Risk Factor	Mortality n = 7	Survivor n = 43	p
Age > 50 years	**3**	**4**	**< 0.05**
Female sex	1	9	> 0.05
Male sex	6	34	> 0.05
Shock	**3**	**3**	**< 0.05**
Hb < 8 gm%	2	15	> 0.05
Alb < 3.5 gm/dl	3	10	> 0.05
Azotemia	5	15	> 0.05
Multiple Perforation	3	7	> 0.05
Fecal Peritonitis	6	21	> 0.05
Fecal Fistula	3	10	> 0.05

Table No. 12 shows the other risk factors for mortality in ileal perforations and their statistical significance. Mortality was affected significantly only by age and the presence of shock on admission. Fecal fistula and the etiology of typhoid showed a trend towards significance. Sex, biochemical parameters, number of perforations, and type of peritoneal fluid were not statistically significant.

DISCUSSION

Typhoid fever is the commonest cause of ileal perforation in tropical countries. Typhoid fever accounted for 56.6% of cases of ileal perforation in the series by Karmakar.[1] Mechanical causes and malignancy is the commonest causes of small bowel perforation in the western world. Mechanical causes and lymphomas accounted for 40.7% of perforations in the series by Dixon.[2] Malignancy was the commonest cause in the series by Orringer.[3] There were no cases of typhoid perforations in either series.[2,3]

There was a male preponderance with the male: female ratio in this study being 3.8:1. Published literature also shows a similar finding with reported ratios from 2.3:1 to 6.1:1.[16,17] Typhoid perforations as reported by Eggleston occurred in the second and third decades of life.[18] In this study 62% of cases were in a similar age group.

Most patients presented with features suggestive of peritonitis. Patients with typhoid perforation had a fever, abdominal pain, and vomiting. Examination revealed tenderness, guarding, distension, and intraperitoneal free fluid. 6 patients were in shock on admission. Eggleston reported that most patients had a fever, malaise, and sudden increase in abdominal pain in typhoid perforation. Examination revealed signs of toxemia and acute abdomen.[18] Gibney and Gilati reported pneumonia, cholecystitis, gastrointestinal bleeding, osteomyelitis, and intestinal perforation in patients with typhoid perforation.[19,20] Perforation was commonly seen to occur in the second week following the onset of illness.[21,17,22] Keenan reported that 88% of patients perforated in the second week.[21] Lizzaralde reported that 54.2% of patients perforated in the second week.[23] In this series the perforation was earlier with a

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majority occurring within a week of the onset offever.

Chest X-ray is a helpful investigation to discover hollow viscus perforation. Free gas was seen under the diaphragm in 78% of perforations. Abdominal X-ray revealed gas of features suggestive of ileus. Pneumoperitoneum has been reported in 52% to 82% in studies by Keenan, Archampong, and Vaidyanathan.[21,24,25]

Widal was positive in 55% of tested cases. Widal was reported positive in 30% of patients with typhoid perforation by Kaul and in 46.1% of patients by Santillana.[26,17] It was reported positive in 73% by Vaidyanathan.[25] Four-fold increase in titers is considered more significant.[27]

Salmonella typhi was grown in 3 (10% of tested) patients with typhoid ileal perforation in whom blood cultures were done. All cultures were sensitive to ciprofloxacin, cefotaxime, and ceftriaxone. Keenan reported positive cultures in 22.2% and Santillana in 48% of patients.[21,17] Prior antibiotic therapy was probably responsible for the low isolation of the study.[21,24,27] Another cause may be a delay in plating the samples.

Histopathology was suggestive of typhoid in three patients. The presence of erythrophagocytosis virtually confirms the diagnosis of typhoid perforation.[28] Two cases had both Widal and histopathology confirming the diagnosis whereas one did not have Widal positivity. Though all the tests are complementary in the diagnosis of typhoid, Widal is the most useful. It is easily available and is less susceptible to prior therapy when compared to blood culture. This usefulness was confirmed by Kim.[29]

In this study, most patients of confirmed typhoid were treated with ciprofloxacin and metronidazole. The rest had a third-generation cephalosporin (cefotaxime) and metronidazole.

In the management of typhoid perforation, some authors advocated conservative management.[30-32] Presently there is no such controversy in the treatment of typhoid perforation with the current recommendation being surgical management.[33] The various methods in use are local drains, simple closure, closure with the omental patch,wedge resection, resection and anastomosis, intertransverse anastomosis, and ileostomy.[19,23]Inthisstudypatientsunderwentileostomy,two-layer closure, and resection anastomosis. No patients were treated by conservative measures, wedge resection, or intertransverse anastomosis. Resection was employed in typhoid perforations wherein multiple perforations were found on laparotomy.

The overall complication rate for all patients in this series was 68%. Typhoid perforations are associated with a high morbidity rate with literature reports between 28.5% and 81%.[17,18, 21,22] Santillana[17] in his series reported a rate of 71.9% in 96 patients. In this series, typhoid perforations had a complication rate of 83.3%. The common complications were wound infection, wound dehiscence, fecal fistula, and respiratory complication compare with published reports.[17,21] Fecal fistula was seen in 26% of these patients (13 out of 50). Literature reports a rate of between 3% and 10%.[17,21] The high fistula rate may be due to the later presentation of patients in this study since most patients presented late. Ihekwaba and Shittu recommended early closure of the fistula, especially in developing countries where resources were low.[34]The mortality rate of patients with fistula is improved with total parenteral nutrition and better antibioticcover.

The mortality in this series was 14%. Though this rate has been on the decline, reported rates are between 3% and 60%. This difference should trend towards significance in statistical analysis.

The surgical procedure did not influence either the morbidity or the mortality in patients irrespective of etiology.

In moribund cases of ileal perforation peritonitis, Temporary de- functioning protective ileostomy is a lifesaving procedure. Apart from reducing mortality, it plays a vital role in decreasing the incidence of complications

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like fecal fistula. In an Indian setting where mostly the patients have low BMI and often present late with severe sepsis and generalized peritonitis, an ileostomy may be a more prudent alternative. Whereas some prefer anastomosis as a method of source control in these cases. An emergency surgeon must be well versed in all the techniques of source control in such cases and choose the appropriate source control measure.

Two-layer closure was found to have a higher complication rate but this was not statistically significant. Eggleston reported that the procedure is done did not influence the outcome.[18] Talwar and Sharma reported that mortality was least with early primary closure and Ameh et al found mortality was highest with wedge resection and least with resection and anastomosis.[35,36]

It is difficult to make a statement, whether ileostomy is better than primary repair of perforation because of the small incidence of these complications and the small size of our study and it needs to be evaluated further with a large number of patients; however, for a single perforation, primary closure of the perforation was the procedure of choice where there is a low volume of peritoneal contaminant.

Both mortality andmorbidity are influenced by the lag period.Regression analysiss how edthatmortality and morbidity increased with increasing lag period. This association wasa lso found in patients with typhoidpe rforations.An increasing lagperiod was associated with increased mortality in series by Archampong, Eggleston, andTalwar.[24,18,35] In patients of typhoid ileal perforation the significant factors influencing mortalityareage greaterthan50,femalesex,feculentperitonitis,raisedbloodurea,orcreatinineasperthe Manheimperitonitisindex.Inthisstudyage,greaterthan50andshockatpresentation were significant factors influencing mortality. Trends were seen with fecal fistula formations, etiology of typhoid, and preoperative azotemia. Sex, hemoglobin or albumin levels, several perforations, and the type of peritoneal contamination were not found to be significant.

Acheampong reported that urine output before surgery, blood urea, and serum potassium affected survival in patients with typhoid perforation. Survival was independent of hemoglobin level, shock, sickling status, and several perforations.[24] Mock reported that increasing the number of perforations, generalized contamination of the peritoneal cavity, and single-layer closure influenced survival.[37] Eggleston in his series of 78 patients reported that shock, uremia, encephalopathy, fecal peritonitis, and postoperative fecal fistula were predictors of mortality.[18]

CONCLUSION

- The most common cause of Ileal perforation is Typhoid.
- Patients have a male preponderance and are usually in the second andthird decades of theirlives.
- Widal serology is a useful test in the diagnosis of typhoid fever. Histopathologyis useful in the diagnosis of tubercular perforations but not very useful in the diagnosis oftyphoid.
- Typhoid perforations have a higher morbidity rate.
- In the absence of facilities for total parenteral nutrition, fecal fistulae shouldbe surgically closed early with resection and anastomosis orbypass.
- The type of surgical procedure didn't influence the outcome, either morbidity or mortality.

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