PriMera Scientific Surgical
Research and Practice
Volume 4 Issue 4 October 2024
DOI: 10.56831/PSSRP-04-140
ISSN: 2836-0028

PriMera Scientific Publications

Pathogenesis and Management Modalities of Typhoid Perforation: A Review of Literature

Type: Review Article
Received: September 16, 2024
Published: October 03, 2024

Citation:
Kefas John Bwala., et al. "Pathogenesis and Management Modalities of Typhoid Perforation: A Review of Literature". PriMera Scientific Surgical Research and Practice 4.4 (2024): 15-19.

Kefas John Bwala[1]*, Ballah AM[2], Kirfi AM[3], Ogunleye OO[1], Adamu A[3], Baffah AM[4], Essien OB[5], Abdul MM[6], Dauda MM[7] and Duke R[8]

[1]*Surgery Department, University of Calabar/Abubakar Tafawa Balewa University, Nigeria*

[2]*Department of Anaesthesiology, Abubakar Tafawa Balewa University Bauchi, Nigeria*

[3]*Department of Otorhinolaryngology, Abubakar Tafawa Balewa University Bauchi, Nigeria*

[4]*Department of Obstetrics and Gynaecology, Abubakar Tafawa Balewa University Bauchi, Nigeria*

[5]*Department of Chemical Pathology, University of Calabar, Calabar, Nigeria*

[6]*Department of Ophthalmology, Abubakar Tafawa Balewa University Bauchi, Nigeria*

[7]*Department of Surgery, Ahmadu Bello University, Zaria, Nigeria*

[8]*Department of Ophthalmology, University of Calabar, Calabar, Nigeria*

***Corresponding Author:** Kefas John Bwala, Surgery Department, University of Calabar/Abubakar Tafawa Balewa University, Nigeria.

Abstract

Typhoid fever has been a recognized infectious disease for centuries, with historical accounts of outbreaks dating back to ancient times. However, it was not until the late 19th and early 20th centuries that the association between typhoid fever and intestinal perforation was fully elucidated. Pioneer works by Widal, Wilson, and Ganière provided early insights into the pathogenesis of typhoid intestinal perforation. Transmission is through feco-oral route. Virulence and dose of the organism as well as the host resistance play pivotal role in the pathogenesis. Adequate resuscitation, prompt surgical intervention, with repair of the damaged bowel as well as copious peritoneal lavage are key to favourable outcome.

Keywords: pathogenesis; management; typhoid perforation

Introduction

Typhoid fever is a septicaemic illness caused predominantly by the bacterium Salmonella enterica serovar Typhi, a gram-negative facultative anaerobe.

It is a multi-systemic infection which is transmitted through the feco-oral route by ingestion of contaminated food and/or water [1]. A similar but often less severe disease is caused by Salmonella enterica serovar Paratyphi A and less commonly by serovar Paratyphi B. Although its primary mode of transmission is feco-oral, hematogenous and lymphatic transmission have also been identified [2].

There are estimated seventeen million cases of typhoid fever worldwide ,with mortality rates ranging from 500,000 to 600,000 annually [3]. Incidence in Africa is estimated at 10-1000 cases per 100,000. The true incidence in Nigeria is difficult to estimate due to lack of coordinated epidemiological surveillance system, however, researchers have reported 0.071% in Oyo, 47.1% in Osun [4] and 4.8% in Bauchi [5].

It is a disease of significant global health concern, particularly in regions with limited resources and inadequate sanitation. It is associated with substantial morbidity and mortality, particularly among children [6]. Immunization against typhoid fever was developed as early as 1896 using a whole-cell vaccine consisting of heat-killed Salmonella typhi preserved in phenol but this vaccine had a very high incidence of side effects and was not universally acceptable. The infection is endemic in many developing countries, such as Nigeria, due to poor sewage disposal systems, inadequate water supply and unhygienic environment [7]. There are newer vaccines : injectable typhi Vi and oral Ty 21a vaccine which are potent as well as quite safe . Vi polysaccharide conjugate vaccines, (Linked to the diphtheria and the tetanus toxoid proteins), mutant strains 541 Ty and 543 Ty by genetic engineering techniques are in progress.

Despite considerable progress in sanitation and the availability of effective vaccines, typhoid fever continues to afflict millions of people annually, with a disproportionate impact on children [8-10].

Typhoid intestinal perforation, a severe complication of typhoid fever, occurs when the infection leads to the perforation of the intestinal wall, resulting in life-threatening conditions. The resultant fulminant generalized peritonitis, intraperitoneal abscesses, septicaemia, imbalance in serum electrolytes and severe malnutrition are the usual causes of death in this condition.

Typhoid intestinal perforation is a surgical emergency, that is associated with high morbidity and mortality, especially in paediatric populations [11]. Despite advances in surgical techniques and perioperative care, its management in children remains challenging, and outcomes vary. Intestinal perforation is a common cause of peritonitis necessitating emergency surgical intervention. Although intestinal haemorrhage is the most common complication of typhoid fever, ileal perforation continues to be the most frequent cause of its high morbidity and mortality [3].

Pathogenesis of Typhoid Intestinal Perforation

Three important factors are crucial for the development of the disease: dose of infecting salmonella (inoculum), virulence of the organism, and host resistance [12, 13]. It is transmitted faeco-orally. Following the ingestion of contaminated food or water, gastric acid kills some of the bacteria, but if the number of bacteria is large, some escape the effects of gastric acid and go down to the terminal ileum where intraluminal multiplication takes place. Translocation of the bacteria occurs through Payer's, this leads to bacteremia followed by immune sensitization. Intracellular multiplication within the reticuloendothelial cell system continues leading to septicaemic phase affecting various parts of the body such as bone marrow, lungs, kidney, heart etc. some of the bacteria will be secreted from the liver through bile while some remain in the gall bladder. With release of bile into the duodenum, some re-enter the intestinal lumen for the second time and can be seen in stool in the second week of infection. Typhoid intestinal perforation involves a complex interplay of factors. The bacteria invade the intestinal mucosa and induces an inflammatory response. This inflammation can weaken the intestinal wall, leading to ulceration and subsequent perforation. The ileum is the most common site of perforation, likely due to its thin walls and high bacterial load [11]. By third week of infection, there will be hyperplastic changes in the mesenteric lymph nodes leading to necrosis, haemorrhage and perforation [14].

Immunological Factors that lead to tissue damage

The host's immune responses; both innate and adaptive also play a crucial role in the pathophysiology.

Immune mechanisms are activated in response to the infection, contributing to tissue damage and systemic manifestation. Deregulated immune responses can exacerbate the inflammatory process, increasing the risk of perforation. The pathogenicity of Salmonella typhi stems from its ability to survive and replicate within macrophages. The ensuing immune response aimed at eliminating the bacteria contributes to tissue damage, particularly in the Peyer's patches of the terminal ileum. The interaction among the bacterium, the

host's immune system, and the surrounding tissue microenvironment is central to the pathology of typhoid perforation. The organism possesses Vi antigen which imparts virulence to human host [15, 16].

It also produces invasin, a protein which allows it invade macrophages where it lives and replicates [17].

The bacterium expresses some resistance to gastric acid via an acid inducible tolerance mechanism.

It invades and colonizes the Peyer's patches in small intestine particularly the ileum. It multiplies therein and organisms get disseminated via lymphatics and blood to reticuloendothelial system (RES) of the liver,spleen and bone marrow.

Second phase bacteremia occurs from (RES) by shedding of the organism into the blood stream. The organism injects effector proteins into the macrophages thereby provoking pro and anti-inflammatory responses. The severe inflammatory response may result in bowel necrosis and perforation or haemorrhage particularly in the Peyer's patches (Schwarzman's reaction) [11, 18].

Pathologically, four [4] stages are described; hyperplasia, necrosis, ulceration and perforation. Organisms in bile may infect the gallbladder causing acute acalculous cholecystitis. Other complications include; osteomyelitis, typhoid soft tissue abscesses, septic arthritis, hepatic/splenic abscesses, orchitis, otitis media, parotitis etc.

Formation of Ulcers

The on-going immune response and tissue damage leads to the formation of ulcers on the intestinal mucosa. These ulcers represent weakened areas in the intestinal wall that are highly susceptible to perforation. They are shallow irregular oval ulcers disposed longitudinally on the antimesenteric border of the ileum especially terminal ileum along the distribution of payer's patches.

Perforation may be small or wide up to 2.5cm. Most within 45cm from the ileocecal junction. They are multiple in 20% of patients. The aetiology of typhoid perforation is intimately connected to the development and progression of these ulcers, as their size and extent can influence the likelihood of perforation [19].

Microbial Load and Virulence

The severity of the infection, as indicated by the bacterial load and the virulence of the Salmonella typhi strain, plays a critical role in the typhoid intestinal perforation. Higher bacterial loads are often associated with more extensive inflammation and tissue destruction, increasing the likelihood of perforation [5].

Host Factors

Beyond the infection itself, typhoid intestinal perforation is influenced by host-related factors. The age of the affected child, their nutritional status, and overall immune competence can impact the course and outcome of the disease. Malnutrition, which is prevalent in many typhoid-endemic regions, weakens the host's defences and contributes to the severity of typhoid perforation.

Understanding the aetiology of typhoid perforation in children involves a multifaceted exploration of the primary causative factors that lead to this condition. It encompasses the intricate interplay between the infecting bacterium, the host's immune response, tissue damage, and the overall microbial and host factors.

Operative Management

The goals of operative management are to correct the anatomic problem, correct the cause of peritonitis and to remove any foreign material in the peritoneal cavity.

Correction of fluid and electrolyte imbalance as well as correcting anaemia is crucial. Extracellular fluid losses are replaced by colloids or crystalloids that have electrolyte composition similar to plasma. Nasogastric suction to empty the stomach and reduce the risk of further vomiting, urinary catheterization to monitor urinary flow and adequacy of fluid replacement. Broad spectrum antibiotics

and analgesics are also administered.

Operative management

Surgical management of typhoid perforation is the most important component of its management. Once the patient has been resuscitated, an abdominal exploration will be required. In some instances, operation is part of the resuscitative measures. Usually there will be gush of air with a characteristic putrefactious smell from /the peritoneal cavity and then feculent peritonitoneal fluid that need to be drained out. There are also fibrinoid adhesions. The perforated portion needs to be identified. There may be single or multiple perforations. The most proximal perforation to the ileocecal valve needs to be considered. If the perforation is within 10cm from the ileocecal valve (ICJ), a limited right hemicolectomy and ileocolic anastomosis will be indicated. For perforations far away from ICJ, excision and repair of the defect is done. For multiple perforations closed to each other, segmental resection and ileo-ileal anastomosis should be done. In some situations when the patient is physiologically unstable, or there is gross contamination or unhealthy bowel with severe oedema, an ileostomy will suffice and reversal will be done at a later day when the patient stabilises. Bedside flank peritoneostomy drain and conservative management is a non-target oriented technique in patients with poor general condition, who cannot withstand anaesthesia but once the patient is resuscitated, patient should have surgical intervention [19].

Copious peritoneal lavage with warm normal saline is done, usually about 6 litres or more ''solution to pollution is dilution''. Both subphrenic spaces and paracolic gutters as well as pelvic area are to be cleaned thoroughly. Head up position of the operating bed may be useful.

Post-operative complications include superficial surgical site infection, to deep infections. abdominal wound dehiscence and enterocutaneous fistula. Reperforation or missed perforation may result in recurrent generalized peritonitis which may require re-exploration [20]. Mortality may occur due to septicaemia, electrolyte derangement or severe malnutrition. Early or late post-operative adhesive intestinal obstruction may also occur. The wound may heal by secondary intention with an ugly scar.

Early presentation, early intervention and optimal resuscitation may reduce the risk of morbidity and mortality.

Conclusion

Typhoid intestinal perforation remains a dreaded disease especially in low and middle income countries where there are poor sanitation, poor hygiene and poor water supply. Understanding the pathogenesis and pathophysiology of the disease is key to adequate preoperative resuscitation and subsequent surgical management.

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