

Morbidity and Mortality of Typhoid Intestinal Perforation Among Children in Nigeria 2003 - 2023: A Scoping Review

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Abstract

Background: Typhoid intestinal perforation (TIP), 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 fulminating generalized peritonitis, intra-peritoneal abscess, septicaemia, imbalance in serum electrolytes and severe malnutrition are the usual causes of death in TIP.

Methods: This scoping review was conducted using the PRISMA-ScR checklist, the following databases were searched Science Direct, ProQuest, PubMed, AJOL and Google Scholar. Data was then extracted from the 15 studies that were found to have met the inclusion criteria.

Results: All the included studies were conducted in tertiary healthcare facilities, 13 of them were retrospective studies. The mortality rate ranged from 4.7% to 75%. SSI was the most commonly reported post-operative complication, ranging from 9.5% to 83.3%, others were ECF, wound dehiscence and intra-abdominal abscess.

Conclusion: TIP is a leading cause of morbidity and mortality among pediatric population in Nigeria. Late presentation, poor pre-operative preparation and presence of multiple intestinal perforations impact significantly on morbidity and mortality of patients. This can be prevented by provision of safe WASH facilities and improving access to healthcare.

Keywords: Complications, Morbidity, Mortality, Pediatrics, Typhoid intestinal perforation.

INTRODUCTION

Typhoid fever is a multi-systemic infection that is transmitted through the feco-oral route by ingestion of contaminated food and/or water. It is a disease of significant public health, particularly in regions with limited resources and inadequate sanitation.

Typhoid fever can present with several complications, of note is typhoid intestinal perforation (TIP). Other complications include intestinal bleeding, typhoid caditis, pneumonia, and arthritis.

TIP is a surgical emergency that is associated with high morbidity and mortality, especially in pediatric population. Surgical intervention is the main stay in the management of TIP. Surgical intervention helps in repairing the perforated area in the intestine and prevents further contamination of the peritoneal cavity with the intestinal content. It also removes the contaminant by cleaning the peritoneal cavity with copious normal saline.

The mechanism of intestinal perforation in typhoid fever has been attributed to hyperplasia of Peyer's patches that then causes extension of the lymphoid tissues from the lamina propria to the sub-mucosa. The resulting tissue damage leads to ulceration, bleeding, necrosis and finally full-thickness perforation of the affected segment of bowel^[1]. Where facilities are present, a plain abdominal radiograph may show air under the right hemi-diaphragm.

Early intervention is crucial to prevent further intra-peritoneal contamination from the perforated intestine and reduce its associated morbidity and mortality. Aggressive fluid resuscitation, broad spectrum antibiotics, correction of anemia and electrolyte derangements is essential for stabilization before surgery. Exploratory laparotomy should be expedited to assess extent of perforation and intra-peritoneal contamination and repairing the perforations.

The definitive treatment depends on the intra-operative findings, for single perforations, simple closure of perforation after refreshing the edge using interrupted sutures. Alternatively, removal of affected

bowel segments when there are multiple perforations or very wide perforation or unhealthy long segment of bowel with end-to-end anastomosis using vicryl sutures. If the patient is haemodynamically unstable, has severe malnutrition, severe bowel oedema or there is gross contamination of the peritoneal cavity, temporary diversion is done in form of ileostomy. Minimally invasive technique may also be used in some selected group of patients.

Following surgery for TIP the outcome may be uneventful but sometimes some complications may occur such as superficial or deep surgical site infection (SSI), residual intra-peritoneal abscess, burst abdomen and even development of entero-cutaneous fistula (ECF), pneumonia and septicaemia may also occur. The aim of the study therefore is to comprehensively review what had already been documented concerning morbidity and mortality following TIP in Nigeria between 2003 to 2023.

METHODOLOGY

This scoping review was conducted utilizing the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews” (PRISMA-ScR) checklist by Arksey and O’Malley^[2,3]. Our primary research question was to identify the currently available literature on morbidity and mortality rates of typhoid intestinal perforation in children, 15 years of age and below in Nigeria. We also reviewed reported morbidity rates and surgical complications when available.

Research questions

This review set out to answer the following questions:

- i. What is the available evidence on the mortality rate of typhoid intestinal perforation among children in Nigeria?
- ii. What is the available literature on the morbidity of typhoid intestinal perforation among children in Nigeria?

Eligibility Criteria

The following criteria were used to assess the existing literature on typhoid intestinal perforation among children in Nigeria:

Inclusion criteria:

- Studies which reported the morbidity and mortality of typhoid intestinal perforation
- Studies conducted among children aged 15 years and below
- Studies published between 1 January 1993 – 31 December 2023
- Studies conducted in Nigeria

- Studies whose full texts could be assessed.

Exclusion criteria:

- Studies reporting other causes of generalized peritonitis
- Studies conducted among adults
- Studies published before 1 January 1993 or after 31 December 2023
- Studies conducted outside Nigeria
- Studies where full-texts could not be retrieved

Search Strategy

A database search was conducted to retrieve relevant articles among the following databases – Science Direct, ProQuest, PubMed, AJOL and Google Scholar for articles published between 1993 to 2003. The database search was conducted using the following keywords – “typhoid intestinal perforation”, “morbidity”, “mortality”, and “paediatric”. Case reports were excluded as they generally only report on one or two patients, thus artificially inflating or deflating associated mortality rates.

Charting the Data

A data extraction form was designed using Microsoft Excel and was pre-tested. The author names, date of publication, place of study, study years, number of patients, age range, post-operative morbidity and mortality rates were extracted and filled in the form.

Collating, Summarizing and Reporting the Results

Collation and summarizing of the findings focused on the variables of interest - morbidity and mortality of typhoid intestinal perforation among children in Nigeria. Data extracted was thus arranged thematically and tabulated to summarize the findings of interest, as contained in the result section below.

RESULTS

The initial database search with the search filters delivered a total of 336 results. After the initial title screening and removal of duplicates 55 studies were assessed for eligibility. After screening the abstracts 24 were found to be eligible, but 15 studies in total were found to have met the inclusion criteria for this review and were included in the data extraction process (Fig. 1). The excluded studies were found to have reported on only the operative management of typhoid ileal perforation and not

the morbidity and mortality, other abdominal surgical pathologies and those whose full free texts could not be accessible.

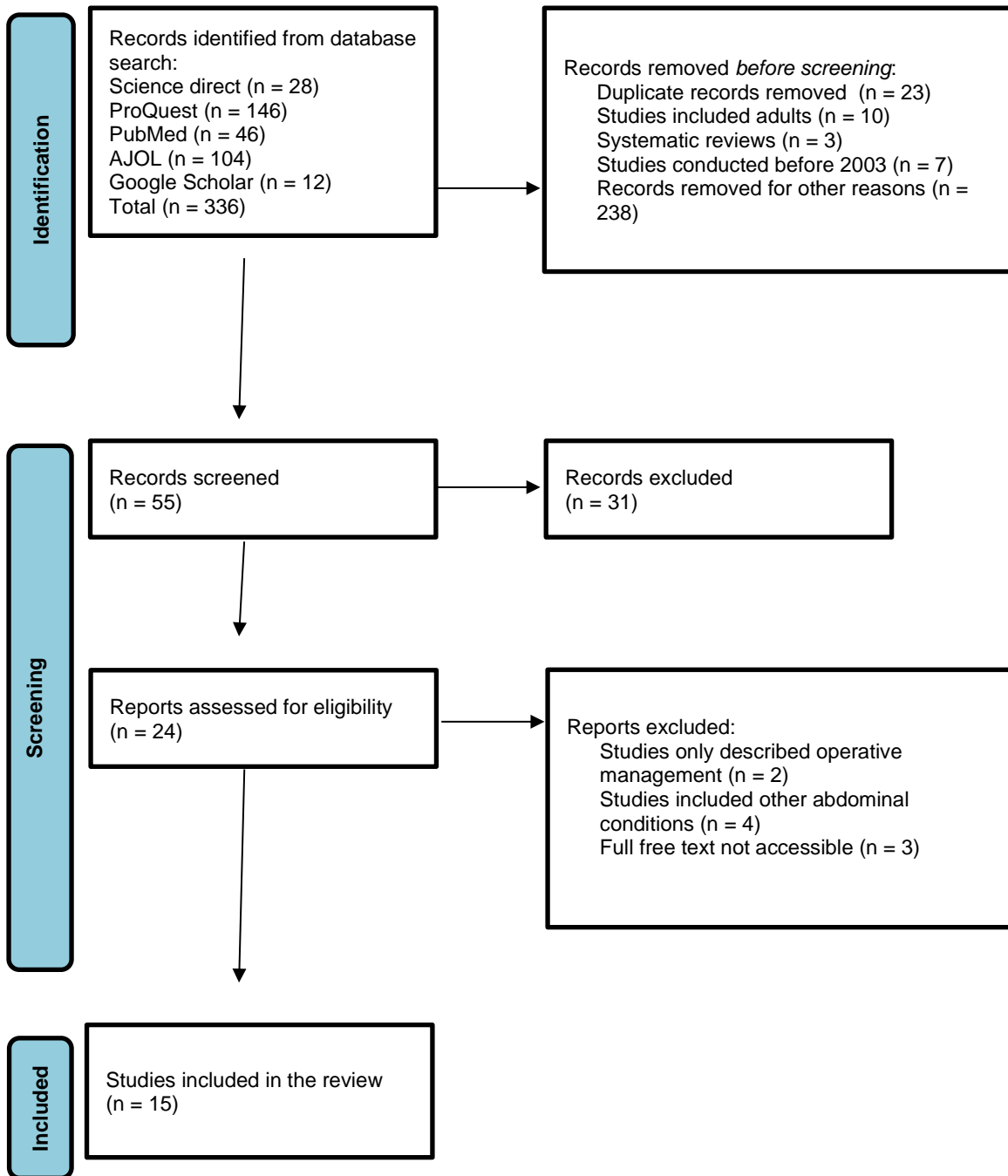


Fig 1: PRISMA 2020 flow diagram of studies screened and included in this review.

Out of the 15 papers, 13 were retrospective and only two from Abia State University Teaching Hospital and Murtala Specialist hospital Kano were prospective studies. Eight of the studies were conducted from the southern part of Nigeria and only 6 from northern Nigeria.

All of the studies were from tertiary healthcare centers, 12 from teaching hospitals, 1 from a federal medical center (FMC) and another from state specialist hospital. The number of patients included from the studies ranged from 12 to 902.

Table 1: Study characteristics and mortality rates

Authors	Place of Study	Study Years	Number of Patients	Age	Mortality n (%)
Uba et al (2006) ^[4]	Jos, Plateau State	1996 - 2005	320	4 - 15 years	42 (22.8%)
Ekenze and Ikefuna (2007) ^[5]	Enugu, Enugu State	2001 - 2006	83	< 5 years	21 (25.3%)
Ekenze et al (2008) ^[6]	Enugu, Enugu State	1995 - 2004	89	1 - 15 years	17 (19.1%)
Usang et al (2009) ^[7]	Ile-Ife, Osun State	1994 - 2004	38	3 - 15 years	6 (15.8%)
Nuhu et al (2010) ^[8]	Azare, Bauchi State	2004 - 2008	46	15 months - 15 years	13 (28.3%)
Osifo and Ogiemwonyi (2010) ^[9]	Benin City, Edo State	1993 - 2007	12	5 - 13 years	9 (75%)
Nasir et al (2011) ^[10]	Ilorin, Kwara State	2002 - 2009	147	5 - 13 years	15 (10.2%)
Ibrahim et al (2013) ^[11]	Kano, Kano State	2007 - 2012	902	3 - 14 years	42 (4.7%)
Talabi et al (2014) ^[12]	Ile-Ife, Osun State	2005 - 2013	87	2 - 15 years	9 (20%)
Anyanwu et al (2017) ^[13]	Kano, Kano State	2009 - 2013	129	3 - 13 years	14 (10.9%)
Usang et al (2017) ^[14]	Calabar, Cross River State	2006 - 2015	49	5 - 15 years	4 (8.2%)

Ekpemo, Eleweke (2018) ^[15]	Aba, Abia State	2016 - 2018	60	3 - 15 years	5 (8.3%)
Olori and Ukpoju (2019) ^[16]	Gwagwalada, Abuja	2008 - 2011	46	2 - 14 years	10 (21.7%)
Emeka et al (2022) ^[17]	Enugu, Enugu State	2016 - 2020	118	7 - 15 years	16 (13.6%)
Bwala et al (2023) ^[18]	Bauchi, Bauchi State	2017 - 2021	168	9.75 +/- 3.57	32 (19%)

Table 1 summarizes the study characteristics and mortality rates. The mortality rate across studies ranged from 4.7% in Kano to 75% in Benin City [9,11]. There was no clear decrease in the mortality rates across all the included studies and over time period of the included studies. However, studies from Enugu which had the highest number of studies (3) show a decrease in the mortality rate from 25.3% in 2007 to 19.1% in 2008 and 13.6% in 2022 [6,19]. Whereas in Kano where 2 studies were conducted the mortality rate increased from 4.7% in 2013 to 10.9% in 2017 [11,20]. This increase in mortality rate with time is similar to the findings in Ile-Ile, Northwestern Nigeria where 2 studies were also conducted and the mortality rate increased from 15.8% in 2009 to 20% in 2014 [7].

Table 2: Most common post-operative complications reported

Authors	Number of Patients	Postoperative morbidity n (%)						
		Surgical Site Infection	Chest Infection	Intra-abdominal abscess	Enterocutaneous Fistula	Wound Dehiscence	Incisional Hernia	Re-perforation
Uba et al (2006)	320	164 (51.3%)	98 (30.6%)	23 (7.2%)	46 (14.4%)	102 (31.9%)	5 (1.6%)	

Ekenze and Ikefuna (2007)	83	43 (51.8%)	12 (14.5%)	5 (6%)		10 (12%)	8 (9.6%)	6 (7.2%)
Ekenze et al (2008)	89	41 (46.1%)	21 (23.6%)	2 (2.2%)		7 (7.9%)		16 (21.3%)
Usang et al (2009)	38	17 (44.7%)		2 (5.3%)	2 (5.3%)	5 (13.2%)		
Nuhu et al (2010)	46	21 (45.6%)	4 (8.7%)	1 (2.2%)	4 (8.7%)	6 (13%)		9 (19.7%)
Osifo and Ogiemwonyi (2010)	12	3 (25%)			4 (33%)	2 (16.7%)	2 (16.7%)	
Nasir et al (2011)	147	97 (66%)		9 (6.1%)	12 (8.2%)	47 (32%)		
Ibrahim et al (2013)	902	306 (33.9%)			60 (6.7%)	41 (4.5%)		
Talabi et al (2014)	87				4 (4.6%)	6 (6.9%)		
Anyanwu et al (2017)	129	88 (68.5%)		16 (15.1%)	13 (11.8%)	44 (34.1%)		
Usang et al (2017)	49	20 (40.8%)	5 (10.2%)		5 (10.2%)			
Ekpemo, Eleweke (2018)	60	50 (83.3%)	30 (50%)	30 (50%)	5 (8.3%)			
Olori and Ukpoju (2019)	46	16 (34.8%)		3 (6.5%)				3 (6.5%)
Emeka et al (2022)	118	47 (39.8%)	6 (5.1%)	13 (11%)	9 (7.6%)	2 (1.7%)	1 (0.8%)	

Bwala et al (2023)	168	16 (9.5%)		3 (1.8%)	4 (2.4%)	9 (5.3%)		
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The most commonly reported morbidities were summarized in Table 2, not all the papers reported on all the complications listed in Table 2. Surgical site infection (SSI), intra-abdominal abscess, entero-cutaneous fistula and wound dehiscence were among the most reported post-op complications by the papers included in this review.

SSI was the most commonly reported post-op complication reported by 14 out of the 15 studies included in this review. The rate of SSIs ranged from 9.5% reported by Bwala et al in Bauchi to 83.3% reported by Ekpemo in Aba [15,18].

Enterocutaneous fistula was reported by 12 of the included studies and ranged from 33% reported by Osifo in Benin to 2.4% reported by Bwala et al in Bauchi [9,18]. Wound dehiscence was reported by 12 of the included studies and ranged from 34% reported by Anyanwu et al in Kano to 1.7% reported by Emeka et al in Enugu [19,20]. Intra-abdominal abscess was reported by 11 of the included studies and ranged from 50% to reported by Expemo in Aba to 1.8% reported by Bwala et al in Bauchi [15,18].



DISCUSSION

Typhoid fever is a major public health problem facing low and middle-income countries. Typhoid intestinal perforation (TIP) has been described as the most deadly complication of typhoid fever because of its associated high morbidity and mortality especially in developing countries [15,18].

The mortality rate across studies ranged from 4.7% in Kano to 75% in Benin City [9,11].

Those with lower mortality rates attributed them to early surgical intervention, adequate resuscitation prior to surgery and availability of more potent antibiotics [14,16].

Other authors have reported that the most significant patient factors affecting mortality are the age of the patient – mortality was reported to be higher among children less than 5 years of age, and development of burst abdomen [12]. In another study by Anyanwu et al post-operative mortality was more common in patients who had a peritoneal aspirate volume more than 1000 ml [13].

There was no clear reduction in the mortality rates with time across the included studies only studies conducted in Enugu showed a decrease in the mortality rate from 25.3% in 2007 to 19.1% in 2008 and 13.6% in 2022 [6,19]. Whereas in Kano the mortality rate increased from 4.7% in 2013 to 10.9% in 2017^[11,20]. This increase in mortality rate with time is similar to the findings in Ile-Ife where 2 studies were also conducted and the mortality rate increased from 15.8% in 2009 to 20% in 2014 [7].

The high morbidity rates seen across many of the included studies have been attributed to some pre-operative factors such as late presentation, delay in diagnosis, difficulty in accessing appropriate care in rural areas [12,21]. Other factors include the number of perforations present intra-operatively and lack of access to an intensive care unit post-operatively. There's also inadequate culture data to guide appropriate antibiotic therapy, which also contributes to poor outcomes [21].

All the studies included in this review were conducted in tertiary healthcare centers, this is similar to the findings in the scoping review by Birkhold et al who did a study in sub-Saharan Africa. The patients were reported to have presented to other clinics prior to their presentation to the tertiary healthcare facilities, which contributes to the prolonged perforation-to-surgery interval with the attendant sepsis and electrolyte derangements which require pre-operative resuscitation[21].

Surgical site infection (SSI) was the most commonly reported postoperative complication, the rates of SSI varied from 9.5% - 83.3%. The high rates of SSI were attributed to the fact that intestinal perforation leads to the spillage of gut bacteria into the peritoneal cavity leading to gross peritoneal contamination. In addition, the patients often from low socio-economic status and present very ill with low nutritional status and compromised immunity that impairs their ability to mount a response [19]. SSI may be superficial, deep or extending to organ or space, this can lead to partial or complete wound breakdown and in severe cases evisceration of small bowel requiring secondary wound closure. Intra-abdominal abscess can occur in deep SSI and was reported to range from 1.8% - 50%, this was been attributed to gross peritoneal contamination and improper cleaning of the peritoneal cavity during surgery[19].

Enterocutaneous fistula (ECF) is the most dreaded complication of surgery for TIP, with devastating consequences that can prove fatal to the patient. This was reported by most of the studies included in this review and ranged from 2.4% - 33% among the studies included. ECF is a result of a breakdown

of the repaired intestinal perforation site or a new perforation. The presence of fecal contamination is also thought to impair wound healing. To reduce the rate of occurrence of ECF, some authors have suggested that during surgery for TIP the whole ileum should be inspected for potential areas of reperforation[13,15,19].

The high morbidity rates have been attributed to late presentation, inappropriate antimicrobial therapy and extensive peritoneal contamination. The high post-operative morbidity rates results in prolonged hospitalization with its' attendant financial strain on families[14,21].

Typhoid fever and its' surgical complications can be prevented by immunization, improving access to clean water, improving sanitation, and educating individuals and communities on proper personal hygiene. Similarly, educating individuals as well as healthcare workers in the community on the symptoms and signs of typhoid fever, so as to present to a healthcare facility for proper treatment. Educating healthcare workers on the danger signs and complications of typhoid fever, in order to refer patients promptly, thereby reducing the delay from perforation-to-surgery, which is believed to be an important factor with a considerable impact on morbidity and mortality[21].

CONCLUSION

There's a high rate of morbidity and mortality of typhoid intestinal perforation mong children in Nigeria. Late presentation, inadequate pre-operative resuscitation, number of perforations, extent of peritoneal contamination have all been reported to have a significant effect on patients' prognosis. Improving water, sanitation and hygiene (WASH) facilities, use of vaccines, health education and improving access to healthcare can help in reversing this ugly trend.

References

- [1] Chalya P, Mabula J, Mbeta K, Kataraihya J, Hyasinta J, Mshana S, et al. Typhoid intestinal perforations at a University teaching hospital in Northwestern Tanzania. *World J Emerg Surg* 2012;7(4):1–11.
- [2] Arksey H, O'malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol [Internet]* 2005 [cited 2022 Jun 7];8(1):19–32. Available from: <https://www.tandfonline.com/action/journalInformation?journalCode=tsrm20>
- [3] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Ann Intern Med* 2018;169(7):467–73.
- [4] Uba AF, Chirdan LB, Ituen AM, Mohammed AM. Typhoid Intestinal Perforation in Children A Continuing Scourge in a Developing Country. *Int J Pediatr* 2007;23:33–9.

- [5] Ekenze SO, Ikefuna AN. Typhoid Intestinal Perforation Under 5 Years of Age. *Ann Trop Pediatr* 2008;28:53–8.
- [6] Ekenze SO, Okoro PE, Amah CC, Ezike HA, Ikefuna AN. Typhoid ileal perforation: Analysis of morbidity and mortality in 89 children. *Niger J Clin Pract* 2008;11(1):58–62.
- [7] Usang UE, Sowande OA, Ademuyiwa AO, Bakare TIB, Adejuyigbe O. Outcome of primary closure of abdominal wounds following typhoid perforation in children in Ile-Ife, Nigeria. *African J Paediatr Surg* 2009;6(1):31–4.
- [8] Nuhu A, Dahwa S, Hamza A. Operative management of typhoid ileal perforation in children. *African J Paediatr Surg* 2010;7(1):9–13.
- [9] Osifo OD, Ogiemwonyi SO. Typhoid ileal perforation in children in Benin city. *African J Paediatr Surg* 2010;7(2):96–100.
- [10] Nasir A, Abdur-Rahman LO, Adeniran JO. Is Abdominal Drainage Necessary After Laparotomy for Typhoid Intestinal Perforation. *J Pediatr Surg* 2012;7:355–8.
- [11] Ibrahim M, Getso KI, Yashuwa AH, Mohammad AM, Anyanwu LJC. Single-layer closure of typhoid enteric perforation: Our experience. *African J Paediatr Surg* 2013;10(2):167–71.
- [12] Talabi AO, Etonyeaku AC, Sowande OA, Olowookere SA, Adejuyigbe O. Predictors of Mortality in Children With Typhoid Ileal Perforation in a Nigerian Tertiary Hospital. *Int J Pediatr* 2014;30:1121–7.
- [13] Anyanwu L, Mohammad A, Abdullahi L, Farinayo A, Obaro S. Determinants of Post-operative Morbidity and Mortality in Children Managed for Typhoid Intestinal Perforation in Kano. *J Pediatr Surg* 2017;06:2–7.
- [14] Usang UE, Inyang AW, Nwachukwu IE, Emehute JC. Typhoid Perforation in Children An Unrelenting Plague in Developing Countries. *J Infect Dev Ctries* 2017;11(10):747–52.
- [15] Ekpemo S, *Pediatr NEAJ*, 2018 undefined. Childhood typhoid intestinal perforation in Aba, Nigeria. *ArticleAmjpediatrOrg* [Internet] 2018;4(4):110–3. Available from: <http://article.amjpediatr.org/pdf/10.11648.j.ajp.20180404.17.pdf>
- [16] Olori S, Ukpoju E. Typhoid ileal perforation in children: does clinical diagnosis alone justify laparotomy? *South Sudan med j* [Internet] 2019;12(1):9–11. Available from: <https://pesquisa.bvsalud.org/gim/resource/en/biblio-1272106>
- [17] Chukwubuike KE. Typhoid Intestinal Perforation in Children : Still a Persistent Problem in a Developing Country. *Clin Surg Res Commun* 2020;4(2):26–31.
- [18] Bwala KJ, Oloko NL, Akawu KS, Aminu UM, Adamu S, Yusuf S, et al. MANAGEMENT OUTCOME OF TYPHOID INTESTINAL PERFORATION IN CHILDREN. *Int J Curr Adv Res* 2023;12(11):2646–8.

- [19] Emeka CK, Unebike EW, Nnanyereugo OL. Post-operative Complications following Laparotomy for Typhoid Intestinal Perforation in Children : Experience in a Tertiary Hospital in Enugu , Nigeria. 2022;01(02):41–5.
- [20] Sheshe A, Anyanwu L, Mohammad A, Muhammad A, Obaro S. Typhoid Intestinal Perforation : Analysis of the Outcome of Surgical Treatment in Kano , Nigeria. Arch Med Heal 2018;6:59–63.
- [21] Birkhold M, Coulibaly Y, Coulibaly O, Dembélé P, Kim DS, Sow S, et al. Morbidity and Mortality of Typhoid Intestinal Perforation Among Children in Sub-Saharan Africa 1995–2019: A Scoping Review. World J Surg 2020;44(9):2892–902.