e-ISSN 2830 5442



# APGHN

Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

Volume 3 / No. 2 May 2024


www.apghn.com

Published by
Indonesian Society of Pediatric Gastroenterology, Hepatology, and Nutrition

e-ISSN 2830 5442

Volume 3, No. 2, May 2024

APGHN

Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

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e-ISSN 2830 5442

Volume 3, No. 2, May 2024

APGHN

Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

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Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

Original Article

# Coagulation Parameters as a Prognostic Factor for Mortality in a Neonate with Duodenal Obstruction

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**e-ISSN: 2830-5442**

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**Published:**
31st May 2024

**DOI:**
https://doi.org/10.58427/apghn.3.2.2024.1-7

**Citation:**
Desdwianto D, Setiawan A, Hariastawa A, Budiman SP, Coagulation parameters as a prognostic factor for mortality in a neonate with duodenal obstruction. *Arch Pediatr Gastr Hepatol Nutr.* 2024;3(2):1-7.

**Abstract:**

***Background***: Although the mortality cases of duodenal obstruction are only about 5%, this abnormality remains a burden in pediatric surgery. Several conditions can worsen a patient's outcome, and a proper understanding of the coagulation parameters is vital for a good result.

***Methods:*** This is a descriptive-analytic study. Data on duodenal obstruction in neonate patients were taken from medical records from 2016 to 2020. The data were then processed using SPSS 26.0

***Results:*** From 59 samples of neonates with duodenal obstruction, most of them were born full term 38 (64%), with 32 male patients and 27 female patients. The number of neonates who died based on complete obstruction were 12 (20.3%), and there was no significant difference between neonates who died with low birth weight and normal birth weight. The most commonly performed surgical procedure was the kimura procedure (43 patients), with a mortality rate of 14%. In the analysis of coagulation parameters including platelets, prothrombin time (PT), and activated partial thromboplastin time (APTT), only APTT demonstrated significant correlation with mortality with the p- value of 0.016, OR 3.98.

***Conclusion:*** There was a significant correlation between activated partial thromboplastin time (APTT) and mortality, with abnormal APTT had 3.98 times higher risk of dying.

**Keywords:** duodenal obstruction, neonates, prognostic factor

## Introduction

Duodenal obstruction is one of the most common congenital anomalies in neonates; the incidence occurs in 1 per 5.000 – 10.000 live births, affecting boys more commonly than girls.[1] Although the mortality cases of duodenal obstruction are only about 5%, this abnormality remains a burden in pediatric surgery.[2]

Duodenal obstruction is anatomically classified as complete and incomplete obstruction. An incomplete obstruction due to a fenestrated web or diaphragm is considered a stenosis. Complete obstruction includes atresia, which may be accompanied by an annular pancreas. Those two types of obstruction have different mortality rates.[3,4]

Other factors that are thought to influence mortality in cases of congenital duodenal obstruction are gestational age and birth weight.[5,6] In addition, various congenital disorders also often accompany congenital duodenal obstruction, such as congenital heart defects, Down syndrome, and other congenital intestinal anomalies.[7,8]

Perioperative coagulation management has a significant impact on the perioperative journey of patients.[9] Anaesthesia providers play a critical role in the surgical setting. Various tests are available to identify coagulation abnormalities in the perioperative period, such as platelets, APTT and PT. A proper understanding of the interpretation of the coagulation parameters is vital for a good outcome.[10,11]

This study aims to identify prognostic factors for mortality in a neonate with duodenal obstruction. The results of this study are expected to be used as a reference regarding the prognostic factors for mortality in patients with duodenal obstruction so that it can be used in clinical practice to reduce mortality in cases of congenital duodenal obstruction.

## Methods

This study was a descriptive-analytic study with a retrospective cohort design to identify prognostic factors for mortality in a neonate with duodenal obstruction. The target population is all neonate patients with duodenal obstruction from 2016 - 2020. This study used secondary data by looking at medical records at Dr. Soetomo General Hospital Surabaya. The inclusion criteria were all cases of duodenal obstruction in neonates, which were proven through clinical examination and babygram imaging, and who underwent surgery at RSUD Dr. Soetomo Surabaya from 2016 to 2020, while the exclusion criteria in this study were incomplete medical record data and patients aged more than 28 days. Once the diagnosis is made, appropriate resuscitation with correction of fluid balance and electrolyte abnormalities is required in addition to

gastric decompression. At our institution, all neonates diagnosed with duodenal obstruction receive a complete metabolic profile, complete blood count, coagulation studies, and radiology plain photographs. Emergency surgery is only performed in cases where malrotation with concomitant volvulus cannot be excluded. Depending on the pathology, the operative techniques performed are duodenoduodenostomy, web excision duodenoplasty, or Ladd's procedure.

The data obtained were analysed using the SPSS version 23 application. Approval and informed consent for this study was granted by the Research Ethical Committee of Soetomo Hospital Surabaya under a Letter of Approval No. 1304/LOE/301.4.2/V/2023.

## Results

From 59 samples of neonates with duodenal obstruction, most of them were born aterm pregnancy 38 (64%) patients, with 32 male patients and 27 female patients. In this study, the minimum operating age was 6 days and the maximum was 46 days with an average operating age of 18 days. Based on demographic data, we excluded data based on exclusion criteria and analysed variables based on outcomes. From Statistically for risk outcome, Birth weight had OR=2.23 for Low birth weight (LBW) with P value= 0.149, Gestation had OR=1.63 for Aterm with P value 0.404, Type of obstruction had OR 2.77 for complete with P value 0.709, and surgical procedure Kimura procedure had OR 1.4 with P value 0.493 (**Table 1**). Based on laboratory data statistically from ROC curve analysis, we got Hemoglobin with a cutoff point of 9.8 g/dL, white blood cells (WBC) 13.600 g/dL, Platelets 259.000, Protrombine time (PT) 12.2, and Activated partial thromboplastin time (APTT) 41. There was no significant correlation between blood count and mortality. Coagulation parameters platelets, PT, and APTT, only APTT there was a significant correlation with P- value (0.016), OR 3.98, 95% CI (1.294-12.294).

## Discussion

Several modalities were studied to be used as predictors of outcome in infants with duodenal obstruction, including gestational age, low birth weight, surgical technique, type of obstruction, and blood coagulation function. Several other studies also assessed other variables, such as the presence or absence of coexisting congenital anomalies, age and weight at the time of surgery, and others.[12]

In this study, it was found that Low birth weight had a 2.3 times higher risk of dying than normal birth weight, but there was not a significant correlation between birth weight and outcome. In addition to being an adverse factor for duodenal obstruction,

**Table 1.** Data analysis on outcomes

| Variable | Total (Outcome%) | OR | 95% CI for OR | P |
|---|---|---|---|---|
| **Birth weight** | | | | |
| LBW | 13 (44.8%) | 2.23 | 0.750-6.653 | 0.149 |
| Normal | 8 (26.7%) | 1.00 | | |
| **Gestation** | | | | |
| Preterm | 6 (28.6%) | 1.00 | | 0.404 |
| Aterm | 15 (39.5%) | 1.63 | 0.517-5.142 | |
| **Type obstruction** | | | | |
| Incomplete | 6 (23.1%) | 1.00 | | 0.790 |
| Complete | 15 (45.5%) | 2.77 | 0.888-8.694 | |
| **Surgical Procedure** | | | | |
| Kimura | 18 (41.9%) | 1.4 | 0.593-3.336 | 0.493 |
| Duodenoplasty | 2 (18.2%) | 1.00 | | |
| Ladds | 0 (0%) | | | |
| Others | 1 (50%) | | | |
| **Hb** | | | | |
| Anemia | 2 (60%) | 3.00 | 0.459-19.592 | 0.251 |
| No | 18 (33%) | 1.00 | | |
| **WBC** | | | | |
| No | 13 (31.7%) | 1.00 | | 0.349 |
| Leukocytosis | 8 (44.4%) | 1.72 | 0.552-5.382 | |
| **Thrombocyte** | | | | |
| Thrombocytopenia | 12 (36.4%) | 1.01 | 0.344-2.996 | 0.977 |
| No | 9 (36%) | 1.00 | | |
| **Electrolyte imbalance** | | | | |
| Yes | 13 (39.4%) | 2.76 | 0.493-0.4336 | 0.493 |
| No | 8 (30.8%) | 1.00 | | |
| **PPT** | | | | |
| Normal | 3 (20%) | 1.00 | 0.682-11.227 | 0.154 |
| Abnormal | 18 (40.9%) | 2.76 | | |
| **APTT** | | | | |
| Normal | 8 (22.9%) | 1.00 | | 0.016 |
| Abnormal | 13 (54.2%) | 3.98 | 1.294-12.294 | |

low birth weight is also at risk for other events that require surgery, such as necrotising enterocolitis, intestinal perforation, and meconium ileus. Of the 443 babies with very low birth weight studied by Okuyama, it was found that 150 babies (34%) needed surgery because they suffered from necrotising enterocolitis, intestinal perforation, and meconium ileus taken from 2003 – 2012. LBW male infants were more likely to have a more significant body weight than LBW female infants of the same gestational age. However, the morbidity and mortality rates for LBW boys are higher than for LBW girls. LBW male infants born at gestational age > 27 weeks are more at risk of experiencing respiratory disorders. Meanwhile, LBW male infants born at a gestational age between 23-25 weeks are more likely to experience gastrointestinal disturbances.[13]

Low birth weight has a negative impact on morbidity and mortality, including in patients with duodenal obstruction.

In congenital duodenal obstruction, several conditions can worsen the patient's prognosis, such as prematurity. Babies with a history of premature birth also experience more complex problems during treatment, especially postoperative care. Several studies have shown that prematurity (gestational age) has a poor prognostic value in patients with duodenal obstruction. This includes not only morbidity and mortality but also its management, both before surgery and after surgery.[14] In this study, it was found that full term babies had a 1.63 times higher risk of dying than preterm, but there was not a significant correlation between birth age and outcome.

In this study, it was found that complete or total obstruction had a 2.77 times higher risk of dying than incomplete or partial obstruction. This was supported by previous research. Estiarla found that 60% of the samples were of the total obstruction type, and as many as 55% of patients with duodenal obstruction died.[15] Brantberg et al. conducted a study with 29 newborns with duodenal obstruction, in which 18 (62%) died (prenatal or postnatal) or had substantial developmental impairments. A total of 10 of the 21 children alive (48%) had substantial developmental disabilities. Of 11 newborns with total duodenal obstruction, five (45%) died or had substantially impaired neurological development.[16] The correlation between birth age and the type of obstruction to prognostic factors still needs to be studied more deeply. In its development, coagulation levels were not only used to determine coagulation status but were also used to predict the outcome of a disease. The use of Prothrombin time (PT) and Activated Partial Thromboplastin Time (APTT) as predictor variables, including duodenal obstruction, is still being developed. In this study, it was found that there was a significant correlation between Activated Partial Thromboplastin Time (APTT) and mortality with a P value of 0.016, and abnormal APTT had a 3.98 times higher risk of dying than normal APTT.

The weakness of this study is that it was conducted in one tertiary referral hospital, which may under-represent the population and the quality or standard of health services in Surabaya or Indonesia; another thing is that there is no additional information about the initial treatment in the previous hospital which causes bias in the results of laboratory tests. Secondly, some preoperative variables or risk factors were not included, such as congenital anomalies, as such data are not routinely recorded and/or examined.

## Conclusion

The research results can be concluded as follows: there was a significant correlation between Activated Partial Thromboplastin Time (APTT) and mortality, with

abnormal APTT having a higher mortality rate than usual. Complete duodenal obstruction type had a higher mortality rate than incomplete duodenal obstruction type, and low birth weight had a higher mortality rate than normal birth weight. The correlation between the type of obstruction, birth weight and surgical procedure with mortality needs to be studied more deeply.

This data may not represent the wider population. Hence, a study with a larger number of samples is needed. Therefore, the research results can be more representative of the population.

## Acknowledgements

The authors extend their sincere gratitude to the Faculty of Medicine, Universitas Airlangga, and Dr. Soetomo Regional Public Hospital for their invaluable support in conducting this research.

## Funding

This research was a self-funded study.

## Conflict of Interest

None declared.

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APGHN
Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

Original Article

# Umbilical Venous Catheter Position in Hasan Sadikin General Hospital: Overview of the Time Required

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**Published:**
31st May 2024

**DOI:**
https://doi.org/10.58427/apghn.3.2.2024.8-14

**Citation:**
Suryaningrat FR, Primadi A, Kadi FA, Hudayari D, Ediwan NA, Yuniati T. Umbilical venous catheter position in hasan sadikin general hospital: overview of the time required. Arch Pediatr Gastr Hepatol Nutr. 2024;3(2).8-14

**Abstract:**

***Background:*** An umbilical venous catheter (UVC) is one of the most frequently used access in neonates. In developed countries, bedside ultrasonography (USG) is used in assessing the position of the UVC catheter's tip. However, this is difficult to be implemented in developing countries. In Indonesia, which categorized as a middle-income developing country, the evaluation of UVC mainly used chest radiographs. However, this procedure would take time. The delay in ascertaining UVC positioning through chest radiography among neonatologists in Indonesia remains unstudied, despite its potential on the clinical efficacy. Therefore, this study aimed to determine the time required for the installation of the UVC and the interval from the completion of UVC insertion until the release of the chest radiography result.

***Method*:** In this prospective observational cohort study, neonates requiring UVC access were examined in Dr. Hasan Sadikin Hospital in Bandung, West Java. Patients underwent anthropometric measurements and UVC installation. Duration required for UVC installation and the interval between the completion of UVC insertion and the release of the chest radiography result were documented. Descriptive data were shown in percentage, mean and standard deviation.

***Result:*** 127 neonates were studied. The average time taken for UVC insertion was 31 minutes and the average time taken from the completion of UVC insertion until the release of chest radiography results was 6 hours.

***Conclusion*:** The long wait for chest radiography results significantly delayed the administration of fluids, medications, and parenteral nutrition in this study. Therefore, we need alternative tools to evaluate the UVC location that can be used bedside right after the installation.

**Keywords:** chest radiography, neonates, umbilical venous catheter

## Introduction

The use of UVC is essential for newborns, particularly those at high risk. Some of the main indications for using UVC are hemodynamic monitoring, volume resuscitations, parenteral nutrition, and administration of medications.[1] UVC is one of the most frequently used central venous access in neonates due to its ease of use and affordability.[2]

After installation, it is important to ensure the correct positioning of the UVC. Misplacement of the catheter may lead to problems such as venous thrombosis, as well as liver and heart issues. The correct tip location is at the junction between the inferior vena cava (IVC) and the right atrium (RA), which can be reached after entering the umbilical vein and passing through the ductus venosus (DV).[3] This position is considered to be associated with the lowest incidence of complications.[3,4]

The rapid evaluation of UVC is essential for the prompt administration of nutrition and fluids. In developed countries, bedside USG is frequently used to evaluate UVC, particularly for determining the position of the catheter's tip. However, in developing countries such as Indonesia, this procedure is not applicable as the availability of bedside USG is still limited. Majority of the hospitals in Indonesia rely on radiograph examinations to assess the position of the catheter's tip. However, this procedure is time-consuming as immediate radiograph examination may not be possible due to the inavailability of portable X-ray machine, requiring transfer of the baby to the radiography room for examination.

In Indonesia, the delay in evaluating UVC positioning through chest radiography among neonatologists has not been studied. Therefore, this study aimed to determine the time required for the installation of the UVC and the interval from the completion of UVC insertion until the release of the chest radiography result.

## Method

This prospective observational cohort study was conducted from January to June 2023 in Dr. Hasan Sadikin Hospital, Bandung, West Java. This study employed a consecutive sampling method. The inclusion criteria were all neonates indicated for UVC access insertion. All neonates underwent UVC installation immediately within 0-1 hour age after birth. Neonates with major gastrointestinal or abdominal congenital anomalies were excluded.All study participants were inserted a polyurethane 4Fr catheters UVC. The Shukla and Ferrara method was used to estimate the optimal length of UVC insertion (Lenght (cm) = [(3 * BW in Kg + 9) / 2 +1]). Upon insertion, the UVC first entered the umbilical vein, then passed through the medial part of the left portal vein and ductus venosus, eventually reaching the junction of IVC and RA.

After the UVC were inserted, all participants then underwent a chest radiography examination. The UVC tip should be visualized at or just above the diaphragm (within 0.5–1.0 cm) on the anteroposterior chest and abdominal radiograph. The time taken for UVC installation, as well as the duration between the completion of UVC until the release of chest radiography results, were recorded.

This study was approved by the Research Ethical Committee Hasan Sadikin General Hospital, Bandung, West Java. Data were analyzed using SPSS statistical software version 25.0. Descriptive data were shown in percentage, mean and standard deviation.

## Result

A total of 127 were included in this study. male neonates (47.8%) highlighting a balanced gender distribution within the study. Subjects mean birth weight was 1699.8 gram and mean body length was 40.9 cm. The demographic characteristics of subjects are shown in **Table 1**.

In this study, it was found that the average time taken for UVC installation was 31 minutes. The time required for installation ranged from a minimum of 5 minutes to a maximum of 60 minutes. We discovered the average time taken from the completion of UVC insertion until the release of chest radiography results was 6 hours. The time required from a minimum of 39 minutes to a maximum of 24 hours. The details are shown in **Table 2**.

## Discussion

In this study, prematurity was the main indication of UVC insertion, with a mean gestational age of 33 weeks. Consequently, preterm birth leads to low birth weight.[5] The average birth weight was also markedly low at 1699.8 gram, with the majority of neonates weighing less than 2500g. Only six neonates were observed to have a birth weight exceeding 2500g. A previous study in Singapore mentioned that 108 neonates who underwent UVC insertion had an average birth weight of 1536.2 g.[6] Low birth weight, very low birth weight and extremely low birth weight infants are special among neonates, with high treatment needs and high mortality.[7] They also have high nutritional requirements to match postnatal growth during hospitalization.[8] With advances in enteral nutrition, UVC has become a common channel for nutrition and fluid delivery in the early postnatal period.[9]

The second most frequent underlying cause in this study is respiratory distress syndrome (RDS), which was found in 82 neonates (64.6%). A previous study on 100

neonates revealed that RDS (56%) was the most frequently observed condition requiring UVC insertion.[10] Another study on 82 neonates highlighted RDS (82%) as

**Table 1.** Characteristics of Subjects

| Characteristics | n (%) |
|---|---|
| **Gender** | |
| Male | 60 (47.2) |
| Female | 67 (52.8) |
| **Birth weight (g) – Mean ± SD** | 1699.8 ± 482 |
| **Body length (cm) – Mean ± SD** | 40.9 ± 4.2 |
| **Gestational age (weeks) – Mean ± SD** | 33 ± 2.8 |
| **Head Circumference (cm) – Mean ± SD** | 30.3 ± 2.2 |
| **Chest Circumference (cm) – Mean ± SD** | 25.2 ± 4.2 |
| **Indication for UVC insertion** | |
| Prematurity | 115 (90.5) |
| Low Birth Weight | 74 (58,3) |
| Very Low Birth Weight | 43 (33.9) |
| Extremely Low Birth Weight | 4 (3.2) |
| Respiratory Distress Syndrome | 82 (64.5) |
| Transient Tachypnea of Newborn | 13 (10.3) |
| Sepsis | 6 (4.8) |
| Pneumonia | 1 (0.9) |

**Table 2.** Time required for neonatologists to insert and determine UVC position using chest radiography

| Time Required | n =127 |
|---|---|
| **Insertion of the UVC (minutes) - Mean ± SD** | 31.4 ± 10 |
| **From the completion of UVC insertion until chest radiography result were released (hour) – Mean ± SD** | 6,3 ± 5,8 |

the most frequent condition found in neonates with UVC insertion.[11] RDS primarily affects preterm and low birth weight neonates due to a deficiency of surfactant. Optimal fluid and electrolyte management is critical in the initial course of RDS. Some neonates may require volume resuscitation using crystalloids and vasopressors to manage hypotension. Furthermore, these patients often exhibit high nutritional requirements due to low birth weight. The umbilical vein is the easiest and most-used

access during neonatal resuscitation.[12]. Therefore, UVC has become a channel for the treatment of the RDS.

Our study found that the average time for UVC installation was 31 minutes, which are in line with previous studies. Prior study on 100 neonates showed the median duration of the UVC procedure was 30 minutes.[10] Another study on 144 neonates also highlighted the mean time needed for UVC insertion was 28.31 minutes.[13] Furthermore, the average time taken from the completion of UVC insertion to the release of chest radiography results was 6 hours, with times ranging from a minimum of 39 minutes to a maximum of 24 hours in our study. A study conducted by Gerdina on 100 neonates mentioned that the duration from the start of the procedure until the catheter was used (including waiting time for the chest radiography to be performed and time needed to reposition catheters if necessary) was 74 (57–110) min.[10]

In this study, UVC was installed as soon as possible, within the 0–1-hour age after birth, with the average time for UVC installation was 31 minutes. According to NICE guidelines, when a baby qualifies for UVC insertion or parenteral nutrition, initiation should occur as soon as possible, and at the latest within 8 hours.[14] For subjects who had not yet received parenteral nutrition due to awaiting chest X-ray results, temporary peripheral access was provided while waiting for the results.

The long wait for chest radiography results significantly delayed the administration of fluids, medications, and parenteral nutrition in this study. This delay was due to the process that depended on the coordination of many people, including nurses, operators, and radiologists. Another imaging method useful to confirm the positioning of UVC is USG. USG bedside is increasingly used in developed countries and has been suggested in several papers as an alternative to chest radiography as it seems more reliable, faster, and without side effects.[15] Limiting the duration of the procedure may be very useful to enhance the treatment of neonates; therefore, we need an alternative tool to evaluate the UVC location that can be used bedside right after the installation.

## Conclusion

In conclusion, our study revealed that the time taken from the completion of UVC insertion until the release of chest radiography results was 6 hours. The long wait of chest radiograph result significantly impacts patient management. Thus, alternative tool that can be used in directly after installation is needed to enhance treatment for neonates.

## Conflict of Interest

None declared

## Funding Statement

The authors received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

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APGHN
Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

Case Report

# Cholelithiasis Diagnosis and Management in Thalassemia

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**e-ISSN: 2830-5442**

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**Published:**
31st May 2024

**DOI:**
https://doi.org/10.58427/apghn.3.2.2024.15-25

**Citation:**
Damayanti EL, Gayatri P. Cholelithiasis diagnosis and management in thalassemia. *Arch Pediatr Gastr Hepatol Nutr.* 2024;3(2):15-25

**Abstract:**

***Background:*** Cholelithiasis, while infrequently found in children, carries a significant risk for those with underlying conditions like thalassemia compared to the general population. This study aimed to describe the manifestations of cholelithiasis in thalassemic children.

***Case:*** A 12-year-old girl with beta-thalassemia major presented with recurrent right upper quadrant abdominal pain and vomiting. Imaging revealed cholelithiasis and choledocholithiasis. Due to complications related to her thalassemia, she underwent endoscopic retrograde cholangiopancreatography (ERCP) for gallstone removal followed by laparoscopic cholecystectomy. Post-operative management addressed post-ERCP pancreatitis and bleeding concerns. The patient recovered well and is scheduled for follow-up.

***Discussion:*** Increased bilirubin production, iron overload, and altered bile properties in beta-thalassemia contribute to cholelithiasis risk. The patient presented with typical symptoms and underwent successful laparoscopic cholecystectomy after initial management with ERCP, which led to post-ERCP pancreatitis.

***Conclusion:*** This case underscores the elevated risk of cholelithiasis in thalassemic children and the importance of early diagnosis and intervention for optimal outcomes.

**Keywords:** beta-thalassemia major, cholecystectomy, cholelithiasis, endoscopic retrograde cholangiopancreatography

## Introduction

Cholelithiasis, also known as gallstones, is uncommon in children. The prevalence between boys and girls during pre-puberty ranged similarly at 0.13% and 0.2%, respectively.[1] However, the increased use of ultrasound imaging since 2000 has led to a higher detection rate of cholelithiasis compared to previous years.[1]

Risk factors of cholelithiasis in children differs from adults. In children, the most common cause of cholelithiasis is thalassemia (20 – 30%), followed by factors such as obesity, total parenteral nutrition, ileal resection, congenital hepatobiliary disease, antibiotic use (e.g., ceftriaxone), metabolic syndrome, progressive familial intrahepatic cholestasis (PFIC), choledochal cysts, and idiopathic causes.[1] Children with thalassemia showed a 10 – 20% higher risk of cholelithiasis compared to the general population. However, it often remains asymptomatic for many years.[2]

Management for non-thalassemic patients with cholelithiasis is usually conservative unless signs of cholecystitis or cholangitis were found. However, due to the increased risk of complications, a tailored approach is required for managing cholelithiasis in thalassemia patients.[2] This case report illustrated the manifestations of cholelithiasis presenting in a thalassemic child, with the aim to increase the recognition of cholestasis signs and symptoms in children.

## Case

### Case Illustrations

A 12-year-old girl with beta-thalassemia major presented to the emergency department with a chief complaint of severe, stabbing pain in the right upper quadrant of her abdomen for three days. The pain was constant, radiated to her back, and worsened after consuming fatty foods. She also reported vomiting more than five times a day. Her appetite significantly decreased, resulting in a 3 kg weight loss. Presence of fever, cough, abdnormal bowel habit, or dark-colored urine were denied.

The patient had experienced recurrent abdominal pain for two years prior to this presentation. Previous abdominal ultrasound performed two years earlier revealed small gallstones, which were deemed not to require surgery at that moment. She was treated with pain medication and discharged for follow-up. Four months before admission, the pain intensity worsened. Re-evaluation using ultrasound was subsequently performed, revealing cholelithiasis with multiple, sand-like stones, signs of cholecystitis, common bile duct dilation containing multiple stones and splenomegaly. Due to limited resources, patient was referred to tertiary hospital for definitive management.

Patient was diagnosed with beta-thalassemia major at one year of age. She currently receives regular blood transfusions (every 2-3 weeks) and iron chelation therapy. There was no significant family history of similar conditions, but both her brother and sister are asymptomatic carriers of the thalassemia trait. Her development was with her age, and she had not yet begun menstruating.

Upon physical examination, she appeared generally ill with Cooley facies. Her anthropometric status indicated underweight with normal stature. Her abdominal examination displayed tenderness in the right upper quadrant (positive Murphy's sign) with a significant pain score (VAS 6-7). The liver was palpable (5 cm below costal margin) and the spleen mildly enlarged (Schuffner's grade 1-2), indicating complications related to the thalassemia. Vital signs and other examination were within normal limits, except for pale conjunctiva.

Laboratory workup revealed microcytic anemia (hemoglobin 9.6 g/dL, hematocrit 26.7%) and elevated ferritin (4515.37 ng/mL). Magnetic Resonance Cholangiopancreatography (MRCP) with intravenous contrast performed prior to admission demonstrated cholecystolithiasis with choledocholithiasis and dilation of the common bile duct and common hepatic duct, mild dilation of the right and left hepatic ducts and narrowing of the distal common bile duct. The results suggested a stricture due to passing gallstones in the distal common bile duct, bile sludge, decreased liver parenchymal homogeneity (which might also caused by hemosiderosis), and splenomegaly. Abdominal ultrasound results confirmed cholecystolithiasis, cholelithiasis, and choledocholithiasis, with dilation of the common bile duct, common hepatic duct, cystic duct, and right and left hepatic ducts. The ultrasound findings are shown in **Figure 1**.

**Case Management**

Based on clinical findings, the patient was diagnosed with multiple cholelithiasis, cholecystolithiasis, and beta-thalassemia major with hemosiderosis. Initial management included paracetamol for pain control, supplemented with ketoprofen as needed. Additionally, ursodeoxycholic acid and a red blood cell transfusion were given. Deferiprone was administered as iron chelation therapy due to concerns of hemosiderosis.

The patient was referred to gastroenterology for endoscopic retrograde cholangiopancreatography (ERCP) and pediatric surgery for a planned cholecystectomy. Due to the repeated episodes of severe pain (VAS 6-7) despite the administration of analgesics, patient was also referred to the pain management team. The regimen was adjusted to include ketorolac and increased-dose paracetamol. This effectively reduced pain, with a VAS score of 2-3.

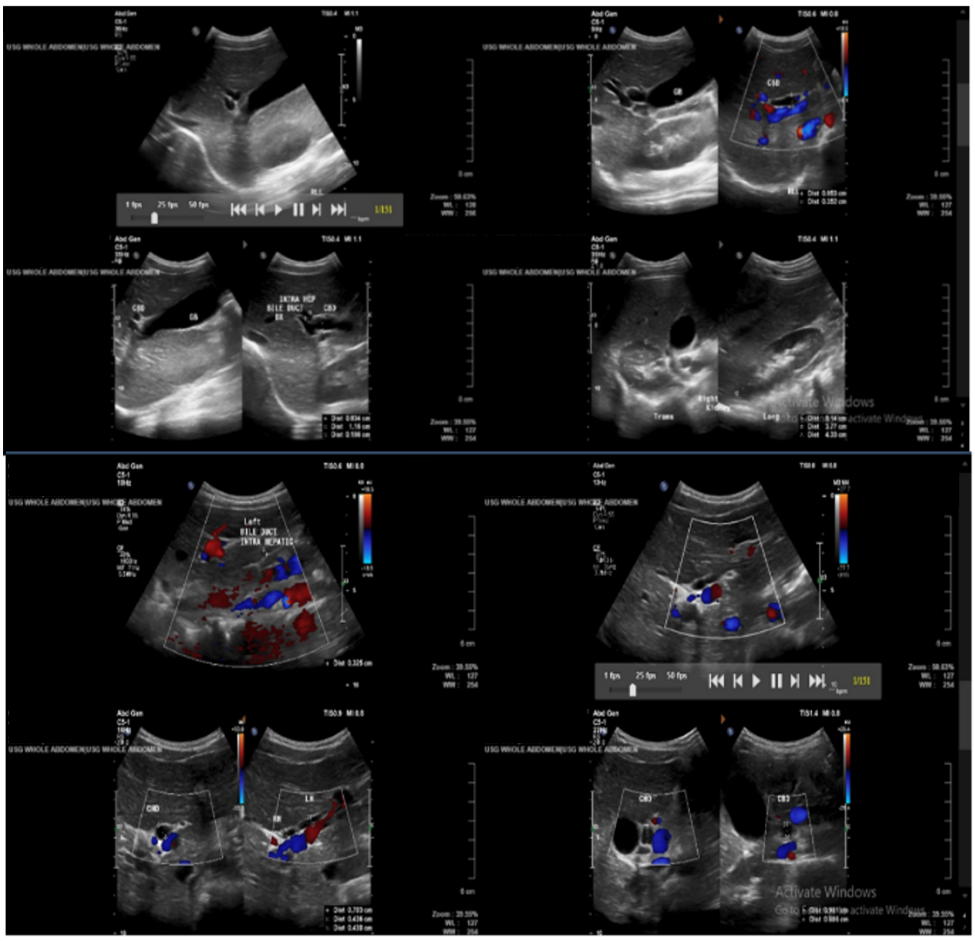

**Figure 1.** Abdominal ultrasound findings

On the 8th day, ERCP were conducted and revealed multiple mobile gallstones within the common hepatic duct. A successful gallstone extraction and biliary duct cleansing procedure were also performed (results shown in **Figure 2**).

Following ERCP procedure, the patient was placed on nil per os (NPO) status and received intravenous fluids. A prophylactic antibiotic regimen of cefoperazone-sulbactam was administered for seven days.

Additionally, she received vitamin K, tranexamic acid for bleeding prophylaxis, omeprazole for gastric acid suppression, sucralfate syrup for gastrointestinal protection, and ketoprofen suppositories for pain management. Somatostatin was administered as a bolus followed by a continuous infusion for five days to prevent post-ERCP pancreatitis. Frozen blood plasma was also administered. Six hours after ERCP, the patient developed severe right upper quadrant pain radiating to her back (VAS 6-7) with nausea and vomiting, which were managed with increased-dose of

paracetamol. Elevated amylase (954 U/L) and lipase (1378 U/L) confirmed post-ERCP pancreatitis. Laboratory evaluation on the 9th day of treatment revealed persistent mild anemia (hemoglobin 9.7 g/dL) requiring a red blood cell transfusion.

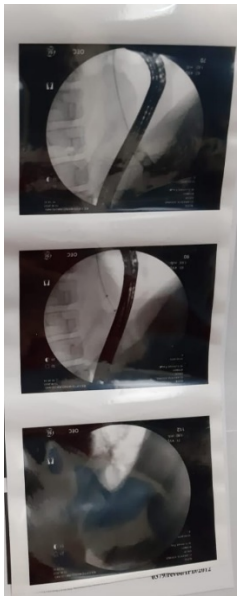

**Figure 2.** Endoscopic retrograde

On the 10th and 11th days of treatment, the pain further reduced to a VAS score of 1, with no fever, nausea, or vomiting. Hemodynamic parameters remained stable, and bowel function normalized. Oral fluid intake was gradually reintroduced and tolerated well.

By the 14th day of hospitalization, the patient's abdominal pain had significantly subsided. She was discharged on the 15th day with a prescription for ursodeoxycholic acid for continued gallstone dissolution, paracetamol for pain relief, and omeprazole) for gastric acid suppression.

One month later, the patient returned for follow-up. Examination revealed intermittent right upper quadrant pain (VAS 3-4) managed with analgesics, with no other significant symptoms. The patient was then scheduled for a definitive laparoscopic cholecystectomy. Pre-operative physical examination revealed a moderately ill but alert, with normal vital signs. Pre-operatively, the patient received a packed red blood cells transfusion due to severe anemia (Hb: 7.4) as well as frozen plasma transfusion and vitamin K due to prolonged APTT (1.9 times).

The patient underwent a successful laparoscopic cholecystectomy on the 3rd day of treatment. Post-cholecystectomy bile duct images are shown in **Figures 3.** Post-operatively, the patient experienced minimal pain, but developed diarrhea without blood or mucus, which resolved within 4 days. By the 7th day, her condition was stable, and she was discharged with follow-up instructions.

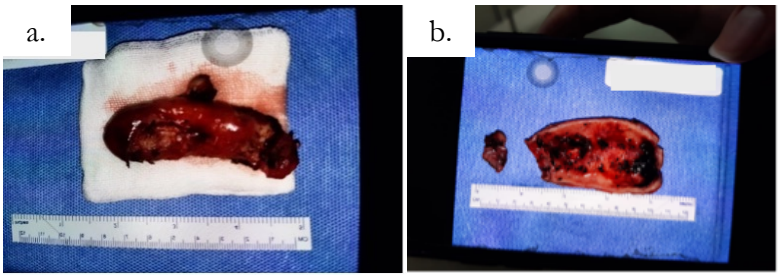


**Figure 3.** Post-cholecystectomy bile duct images. a. Intact bile duct; b. Incised bile duct

At a one-week follow-up appointment, the patient reported no new complaints. Examination revealed a well-healing surgical site, and she had resumed a normal diet. Surgical wound image is shown in **Figure 4.**

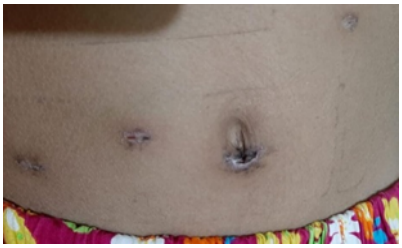

**Figure 4.** Post-cholecystectomy surgical wound

The patient's prognosis are *bonam* for *ad vitam*, *dubia ad bonam* for *ad functionam,* bonam for *ad sanationam.*

## Discussion

Cholelithiasis, the presence of gallstones, is a well-known issue in adults, but uncommon in children.[1] It is more prevalent in females compared to males. This sex disparity is attributed to the influence of estrogen, which binds to receptors in the liver and upregulates cholesterol secretion into bile, promoting gallstone formation.[3] In this case, although the patient, a 12-year-old girl, had not yet reached menarche, her gender placed her at a higher risk for developing gallstones.[3]

A summary of various causes and risk factors for cholelithiasis is presented in **Figure 5**.[4] Children with thalassemia have a 10 – 20% higher risk of cholelithiasis compared to the general population, often remains asymptomatic for many years.[2] This was the

case for this patient, whose underlying beta-thalassemia major likely contributed to her condition.

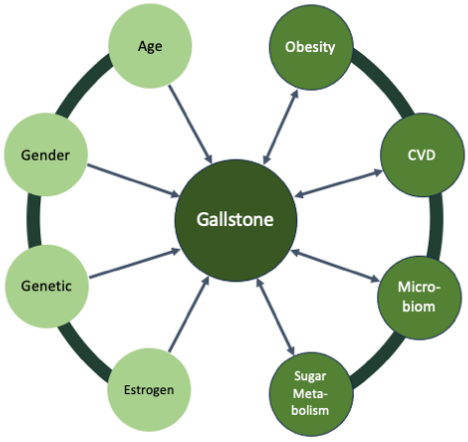


**Figure 5.** Influencing factors occurrence of cholelithiasis[4]

**Cholelithiasis Pathogenesis in Thalassemia**

Thalassemia is a genetic blood disorder affecting hemoglobin production. Iron overload and the underlying hemolytic process in beta-thalassemia, which this patient has, contribute to cholelithiasis development through several mechanisms.[5] First, ineffective erythropoiesis and increased hemolysis in these patients lead to elevated bilirubin production, a potential precursor for gallstone formation.[6, 7] Secondly, iron overload, a complication of chronic transfusion therapy in thalassemia, may contribute to gallbladder dysfunction and stone formation.[8] Thirdly, studies have shown that bile in patients with thalassemia major exhibits altered properties compared to healthy individuals. It demonstrates increased motility but reduced contractility, leading to slower gallbladder emptying, higher residual bile volumes, and potentially promoting cholesterol precipitation and stone formation.[9]

**Clinical Presentation and Differential Diagnosis**

Approximately 60% of children with cholelithiasis experience symptoms, primarily due to blockage in the biliary system.[10, 11] This blockage can cause right upper quadrant abdominal pain (biliary colic) and inflammation of the gallbladder (cholecystitis).[11] Common presenting features include pain in the right upper quadrant upon inspiration (Murphy's sign), nausea, vomiting, and sometimes fever, with these symptoms becoming more prevalent in teenagers compared to younger children.[1, 6, 11, 12] Notably, the patient in this case presented with right upper quadrant pain radiating to the shoulder, nausea, vomiting, and weight loss, but without fever.

It's crucial to differentiate cholelithiasis from other conditions presenting with similar symptoms. Peptic ulcer disease typically causes epigastric pain on an empty stomach or after meals, and is diagnosed through endoscopy revealing ulcers in the stomach or

duodenum. Acute cholecystitis presents with right upper quadrant pain and tenderness, often with fever and elevated inflammatory markers in blood tests. Additionally, ultrasound reveals a thickened gallbladder wall. Cholangitis presents with Charcot's triad (fever, jaundice, and right upper quadrant pain), and is confirmed with MRCP and abdominal ultrasound to detect bile duct stones.[1]

In this case, the absence of fever and leukocytosis in laboratory tests, coupled with the ultrasound findings of multiple gallstones, pointed towards cholelithiasis. A comprehensive history, physical examination, and imaging studies like ultrasound are essential for an accurate diagnosis.[1]

**Diagnostic Workup**

While no single laboratory test definitively diagnoses cholelithiasis, several blood tests are crucial for determining the underlying cause and preventing complications. These tests may include: Complete blood count, liver function tests to evaluate for potential liver damage, lipid profile, reticulocyte count, hemoglobin electrophoresis, genetic tests (if a genetic predisposition to gallstones is suspected), serum amylase, and lipase levels to rule out co-existing pancreatitis.[1]

Ultrasound is the imaging modality for diagnosing cholelithiasis, offering high accuracy with a sensitivity of 84% and specificity of 99%. It can detect gallstones as hyperechoic structures within the gallbladder lumen, often accompanied by distal acoustic shadowing. Biliary sludge, a precursor to gallstone formation, can also appear hyperechoic on ultrasound but lacks the acoustic shadow.[1] In cases where ultrasound findings are inconclusive, MRCP offers a detailed visualization of the biliary and pancreatic tree. ERCP serves a dual purpose, providing both diagnostic and therapeutic capabilities in situations of bile duct obstruction. [1, 13] If ERCP is unavailable, intraoperative cholangiography can be performed during surgery, followed by cholecystectomy, the definitive treatment for cholelithiasis.[13]

**Management Strategies**

Management of cholelithiasis can be broadly categorized into approaches for symptomatic and asymptomatic stones.[6] Patients experiencing recurrent abdominal pain are typically recommended for prompt surgical intervention (cholecystectomy) to prevent complications.[13] In this case, the patient initially responded to pain medication, but due to increasing pain frequency, cholecystectomy became necessary. Currently, laparoscopic cholecystectomy remains the gold standard for treating symptomatic cholelithiasis, offering advantages like shorter hospital stays, reduced postoperative pain, and faster recovery compared to traditional open surgery.[14]

Ursodeoxycholic acid (UDCA) therapy is an option for patients with asymptomatic cholesterol gallstones in adults.[1] By inhibiting cholesterol absorption in the intestine, UDCA can decrease cholesterol saturation by 40-60%.[14, 15] However, the role of UDCA in treating pediatric cholelithiasis is less established due to limitations like the need for long-term use, high recurrence rates, and potential side effects such as diarrhea and liver dysfunction.[1] In this case, the patient's history of frequent fatty food consumption prompted a trial of UDCA therapy, suggesting a possibility of cholesterol gallstones.

**Complications**

While asymptomatic in some cases, gallstones can lead to complications in up to 50% of patients within five years of diagnosis.[1] These complications include cholecystitis, choledocholithias, and acute pancreatitis. The reported incidence rates for these complications are approximately 27.7%, 10.6%, and 23.4%, respectively.[14]

It's important to note that pancreatitis can also occur as a post-ERCP complication (PEP). This can happen due to mechanical obstruction, such as edema or trauma to the papilla from excessive instrument manipulation during the procedure, or hydrostatic injury caused by contrast agents or irrigation fluids leading to local inflammation. PEP typically presents with abdominal pain and a significant elevation in pancreatic enzymes (amylase or lipase levels exceeding three times the upper limit of normal), which is what found in this patient.[16]

Some patients (10 – 40%) experience post-cholecystectomy syndrome (PCS), causing ongoing upper right abdominal pain due to alterations in bile flow patterns. The exact cause of PCS remains unclear, although it is thought to be linked to either organic or functional disorders of the digestive system.[17]

The prognosis for this patient is generally favorable (prognosis *ad vitam*) as it is uncomplicated cholelithiasis and does not pose a life threat.[6] However, the prognosis regarding overall function (prognosis *ad functionam*) can be guarded (*dubia ad bonam*) due to the potential development of post cholecystectomy syndrome (PCS).[17] Fortunately, the prognosis for complete recovery (prognosis *ad sanationam*) is excellent, with a very low recurrence rate of less than 1% following cholecystectomy.[6]

## Conclusion

This case report describes a 12-year-old girl with beta-thalassemia major who presented with recurrent right upper quadrant abdominal pain. Ultrasound confirmed cholelithiasis, and MRCP revealed choledocholithiasis with common bile duct dilatation. ERCP facilitated gallstone removal, and the patient subsequently underwent a successful laparoscopic cholecystectomy.

This case highlights the increased risk of cholelithiasis in children with beta-thalassemia major. Early identification and intervention are crucial to prevent complications. The prognosis for patients with uncomplicated cholelithiasis treated with cholecystectomy is excellent, with a very low recurrence rate.

## Acknowledgment

The authors would like to thank the patient and their parents for consenting to the inclusion of her medical data in this report.

## Funding Statement

This study was not supported by any external funding.

## Conflict of Interest

None declared.

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Case Report

# Outcome of Abdominal Tuberculosis Complicated by Portal Hypertension, Pulmonary Tuberculosis, and Severe Acute Malnutrition

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**e-ISSN: 2830-5442**

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**Published:**
31st May 2024

**DOI:**
https://doi.org/10.58427/apghn.3.2.2024.26-34

**Citation:**
Pattinasarany LC, Widowati T, Setyati, A. Outcome of abdominal tuberculosis complicated by portal hypertension, pulmonary tuberculosis, and severe acute malnutrition. *Arch Pediatr Gastr Hepatol Nutr.* 2024;3(2):26-34

**Abstract:**

***Background:*** Abdominal tuberculosis (TB) is a form of extrapulmonary TB that can present with or without involvement of the lungs. The diagnosis is difficult to establish, which may lead to diagnostic delays. Effective management of adolescent TB requires a holistic approach from various medical disciplines and interventions. This case presented a rare case 13-year-old girl diagnosed with abdominal TB

***Case:*** A 13-year-old girl presented with seven-months history of subfebrile fever, lymph node enlargement, abdominal distention, pallor, and severe weight loss. She was diagnosed with abdominal TB. The diagnosis was further complicated by portal hypertension, pulmonary TB, and severe acute malnutrition. To address these challenges, a multidisciplinary treatment plan was implemented and closely monitored for a period of 12 months

***Discussion:*** Multiple factors are significantly contributing to the successful outcome of the treatment for abdominal tuberculosis, including good adherence to the prescribed anti-tuberculous medications, absence of side effects from the drugs, the patient's positive knowledge, attitude and health behaviours, and housing and environmental health.

***Conclusion:*** This case highlights the importance of factors influencing disease outcomes of abdominal TB. Proper management of the factors would lead to significant clinical and nutritional status improvement, reduce TB transmission, and improved the overall quality of life.

**Keywords:** abdominal tuberculosis, adolescent, malnutrition, portal hypertension

## Introduction

Tuberculosis is one of the disease that significantly contributing to the mortality and morbidity of children worldwide. According to World Health Organization (WHO), pediatric tuberculosis (particularly age < 15 years old) accounts for approximately 12% of the estimated total case of tuberculosis and 16% all tuberculosis-related deaths.[1] Abdominal tuberculosis (TB) is a form of extrapulmonary TB that can occur with or without pulmonary focus. Establishing the diagnosis of abdominal TB is often difficult due to the unclear symptoms, non-specific signs, and a lack of definitive diagnostic tests, leading to the delay of diagnosis.[2] This study presented a longitudinal case of a patient diagnosed with confirmed bacterial pulmonary TB, abdominal TB complicated by esophageal varices secondary to portal hypertension, and severe acute malnutrition.

## Case

### Case Illustrations

A 13-years-old-girl presented with seven-months history of persistent subfebrile fever, a progressively enlarging lump on the right side of the neck, abdominal distention, pallor, reduced appetite and significant weight loss (body weight dropping 9 kilogram in 5 months). Laboratory results revealed hypochromic microcytic anemia, hypoalbuminemia and positive IGRA. Both acid-fast bacilli (AFB) staining and GeneXpert sputum examination results were positive, confirming the diagnosis of tuberculosis. Lymph node biopsy revealed necrotizing granulomaotous lymphadenitis, supported the clinical diagnosis. Abdominal ultrasound and Doppler showed acute inflammation of the liver parenchyma, ascites, splenomegaly, and decreased portal vein velocity with dilation of the splenic vein indicating early signs of portal hypertension. Subsequent abdominal CT scan revealed ascites and multiple lymphadenopathies in the mesentery and peritoneal nodules. Gastroscopy with biopsy demonstrated Grade II esophageal varices, esophagitis, and erosive gastritis. Additionally, ascitic fluid analysis revealed transudate impression, results (SAAG) 1.25 with interpretation SAAG >1.1, protein 2.78 (>2.5), PMN 2%, MN 99%, indicating portal ascites.

Patient was diagnosed with abdominal TB complicated with esophageal varices due to portal hypertension, confirmed bacterial pulmonary TB, and marasmic malnutrition. A 12-months ATD regimen was then initiated with rifampicin(R), isoniazid(H), pyrazinamide(Z), and ethambutol(E) were given during the intensive phase for 2 months. Prednisone was also administered in the first 2 weeks of therapy and subsequently tapered off. The regiment was continued with RH for 10 months in the continuation phase. Clinical responses and side effects were closely monitored during the period of therapy. Patient never had gastrointestinal bleeding episode during the course of therapy. However, during the first two weeks of therapy, patient experienced

nausea without vomiting. Patient close contacts were also identified during treatment, and her 3-years old younger sibling, presenting with no TB symptoms, were given TB prevention therapy (TPT). No side effects from TPT or development of TB symptoms were observed during therapy. Both parents were also examined and presented with no indications for TB.

Patient successfully completed the 12-month anti-tuberculosis drug (ATD) regiment. Abdominal distention stabilized and showed no further progression. Ascites was also completely resolved in the fourth month. Furthermore, weight gain was observed particularly during the intensive care and nutritional status was significantly improved in the end of therapy course. However, due to the COVID-19 pandemic, follow-up examination were unable to be conducted. For the pulmonary TB outcome, patient was classified as "completed treatment" as the post-treatment bacteriological examination were not feasible to be conducted. Meanwhile, patient was considered as clinically cured from abdominal TB as all pre-treatment signs and symptoms improved, despite the limitations of performing a follow-up abdominal CT scan due to the COVID-19 pandemic.

Besides pharmacological therapy, several evaluation and non-pharmacological intervention to the risk factors were also conducted to improve patient condition. Patient compliance was assessed in two aspects: regular medication intake and appointment attendance. Interventions to promote adherence included education, providing Drug Swallowing Control (DSC) techniques, and tracer method via messages. Patients regularly attending visits every two weeks during the intensive phase and monthly during the continuation phase. Patient also took her medicine regularly during the intensive phase. However, during the continuation phase, patient reported missed doses over consecutive days as she forgot to bring her medicine during travelling. Despite the missed dosages, patient therapy adherence observed using MMAS-8 (Medication Morisky Adherence Scale) questionnaire exhibited high level of adherence, with the total score of 8.

Patient and her family's knowledge and health behavior regarding TB were assessed using a questionnaire similar to one employed by the Indonesian Ministry of Health in 2004. The result exhibited a lower level of knowledge on several aspects of TB during the initial assessment. However, after further education, improved knowledge upon the disease were observed. Furthermore, the patient family sought medical attention from the beginning and utilized appropriate healthcare facilities, indicating positive health attitudes and behaviors. Based on home visits and evaluation using indicators established by the National Socioeconomic Survey, several environmental factors were identified and resolved through educational intervention. At the end of the observation period, several improvements were established, including sufficient

sunlight and air circulation to the patient's room, and elimination of cigarette smoke exposure from patient's father. Patient's quality of life using the PedsQL 4.0 score were also assessed, revealing a score lower than 70, indicating low quality of life. However, the result improved during treatment.

## Discussion

This paper described the prognostic factors and disease outcomes contributing to a patient presenting with pediatric abdominal TB with complication of Esophageal Varices secondary of Portal hypertension, Pulmonary TB and severe acute malnutrition. The prognostic factors analysed include medication adherence, patient behavior, attitude, and knowledge, house and environmental health, and the risk of transmission. Meanwhile, the outcome evaluated in this study include the treatment results, complications, side effects, nutritional status, and quality of life.

### Prognostic Factors

#### Medication Adherence

Overall, the patient demonstrated good compliance to the treatment regimen. Based on the MMAS-8 (Medication Morisky Adherence Scale) questionnaire, the patient showed a high level of adherence. Furthermore, the patient followed the recommended appointment schedule, as per the 2016 Indonesian Ministry of Health guidelines.[3] Despite the high level of overall compliance, patient did miss to take several medical doses during the continuation phase as she forgot to take her medicine during traveling. This finding aligns with research by Adane et al., which identified forgetting medication (34%), experiencing vomiting (24%), and traveling (17%) as the most common reasons not to take the medicine.[4]

#### Behavior, Attitude, and Knowledge

Patient and her family exhibited lower level of knowledge on the initial assessment. Similar results were obtained on the TB prevalence survey held by the Ministry of Health in 2024. The survey showed that despite 85% of the respondent were aware that TB is curable, only 26% of them able identify TB signs and symptoms correctly, and only 19% knew that anti-tuberculosis drugs (ATD) are free.[5] However, a significant improvement on the assessment were seen after educational interventions, indicating better understanding upon TB.

The patient's family also displayed positive health attitudes and behaviors by seeking medical attention promptly and utilizing appropriate healthcare facilities, despite their initial knowledge gap. These behaviors contrasts with national data from the Health Research and Development Agency, which indicated that 26% of respondents with suspected pulmonary TB symptoms did not go to a health professional.[6]

### Housing and Environmental Health

The quality of housing and surrounding environment can significantly influence TB outcomes. Several environmental issues were detected in patient household, particularly cigarette smoke exposure for patient's father. The issue of indoor air pollution from cigarette smoke is a major concern highlighted by the World Health Organization's 2016 housing health guidelines. Cigarette smoke exposure posed a significant health risk to all occupants, as it is linked to various diseases.[7] Furthermore, research suggests that exposure to cigarette smoke can impair the ability of alveolar macrophages to express cytokines, potentially disrupting TB treatment effectiveness.[8]

### Risk of Transmission

According to Indonesian Ministry of Health Regulation No. 67 of 2016, tuberculosis preventive therapy (TPT) is recommended for children under five who are in close contact with active TB patients, individuals living with HIV patient without TB diagnosis, and other specific populations.[3] However, challenges such as low adherence and completion rates to the therapy are commonly associated with TPT. In this case, TPT were given to patient's younger sibling for six months. Both parents also received examination for TB. This is aligned with the regulation established by the Ministry of Health regarding the identification and prevention protocol for potential transmission of TB.

## Disease Outcomes

### Treatment Outcome

Patient demonstrated a positive clinical response in all treatment phases. In the end of treatment, gastrointestinal symptoms such as abdominal distention and ascites were subsided. Nutritional status, a known predictor to treatment efficacy, also improved significantly, with weight gain observed during the intensive phase, as reported in other studies.[9] Given the favorable clinical response, surgical intervention was not needed, which aligns with research by Mandavdhare et al. where surgery was only necessary in 8.6% of abdominal TB cases.[10]

The outcome of abdominal TB was classified as clinically cured as all pre-treatment signs and symptoms were improved despite the limitations of performing a follow-up abdominal CT scan due to the COVID-19 pandemic. This positive response reflects the generally good response to anti-TB drug (ATD) observed in pediatric abdominal TB cases.[11]

Meanwhile, the result of pulmonary TB were classified as "completed treatment" due to the absence of a post-treatment bacteriological examination. This result aligns with data from the Indonesian Ministry of Health's TB treatment evaluation, where majority of cases achieved positive outcomes: 43.1% completed treatment, 42.0%

recovered, disappeared from observation 5.4%, moved 4.0%, died 2.5%, not evaluated 2.7%, and failed 0.4%.[12]

**Complications of Abdominal TB**

The complications anticipated and observed in this patient were directly attributable pulmonary and abdominal tuberculosis. Initially, patient presented with portal hypertension and esophageal varices as complications of abdominal TB. Other complications, including those resulting from the infection or as a consequence of the anatomic lesions, may also occur.

Abdominal ultrasound and Doppler revealed signs suggestive of early portal hypertension. While abdominal TB can lead to various complications, portal hypertension with esophageal varices complication is rarely reported, particularly in children. A search of literature identified one case report by Li Feng describing a 33-year-old man with abdominal TB and portal hypertension who required splenectomy, surgical porta-azygous devascularization, and splenorenal shunt to manage the complications. Two years post-surgery, patient was symptom-free, with CT showing transformation of the portal cavernous vein and esophagogastroduodenoscopy revealing the loss of varices and portal hypertensive gastroenteropathy.[13] This treatment could be an alternative choice for portal hypertension with esophageal varices in abdominal TB. However, its efficacy and safety in children still require further observation.

The gastroscopy of our patient revealed grade II esophageal varices, esophagitis, and erosive gastritis. These findings are likely due to the portal hypertension itself, where increased blood flow within the portal vein and resistance to portal blood flow can lead to these complications.[14] Unfortunately, due to the surge in COVID-19 cases at the end of the treatment period, planned follow-up evaluations with Doppler ultrasound and gastroscopy could not be performed. However, patient complication did not worsen until the end of treatment course, indicating appropriate management.

This case report is believed to be the first to document esophageal varices as a complication of abdominal TB in a child. Even in the adult population, only six cases have been reported, one of which was a case of a 30-year-old woman presenting with hematemesis and melena due to esophageal varices secondary to abdominal TB.[2]

**Side Effects of ATD**

During observation, side effects occurred in the intensive phase, consistent with findings from a study by Abdusalomova M. et al. This study identified gastrointestinal complaints as the most frequent side effects in children.[15] In this case, our patient exhibited nausea without vomiting during the first two weeks of therapy. Taking ATD

at night, as described in the same study, can be a helpful strategy to manage these gastrointestinal side effects, which often improve without medication.[3]

One important side effect to watch for is hepatotoxicity, which can be caused by ATD medications like isoniazid, rifampicin, or pyrazinamide. Previous studies have shown that isoniazid is associated with hepatitis, with a reported incidence of hepatotoxicity ranging from 0.8% to 16.2% in children.[16] Fortunately, this patient did not exhibit any signs of hepatotoxicity during treatment. It's important to note that, while less common than in adults, ATD side effects can still occur in children. To support the safety profile, Naude et al. conducted a prospective study in South Africa, observing no adverse effects in 306 children. Similarly, a prospective study in United States reported only 1% of patients experiencing delays of ATD due to vomiting and skin rashes.[9]

**Nutritional Status**

A study by Téllez-Navarrete N. et al. found an association between malnutrition and a higher rate of TB relapse.[17] Consistent with these findings, our patient experienced significant weight loss (25%) since the illness onset. As reported by Kant S. et al., weight loss or malnutrition in TB patients is often attributed to several factors, including inadequate protein intake, catabolism due to inflammatory responses during infection, and gastrointestinal symptoms caused by the body's acute-phase proteins.[18] Fortunately, the patient's nutritional status improved alongside her TB treatment. By the end of the observation period, she achieved a normal nutritional status with a healthy diet and good intake.

**Quality of Life**

Tuberculosis (TB) can negatively impact a patient's quality of life across various domains, including physical, psychological, financial, and social aspects. The initial PedsQL 4.0 score of our patient indicated a decreased overall quality of life, with a score lower than 70. This finding aligns with research by Lusmilasari et al., who reported that 80% of children and adolescents diagnosed with TB experience a decline in quality of life.[19] Several factors contribute to this decline, such as the lengthy treatment duration, potential side effects of anti-tuberculosis drugs (ATD), social stigma, and social isolation.

While Lusmilasari et al. identified social function as the most affected domain in their study population of children and adolescents, the primary domain affected in this case was physical function.[19] This discrepancy could be attributed to the patient's age (teenager), where physical appearance may hold greater significance.

The quality of life of TB patients improved as treatment began, signs and symptoms of TB began to disappear.[20] This case study further demonstrates that the patient's quality of life score improved alongside the treatment progression.

## Conclusion

The patient achieved a good overall outcome at the end of the observation period, demonstrating significant clinical improvement and improved nutritional status. Due to limitations imposed by the COVID-19 pandemic, a final treatment outcome classification of "completed treatment" was assigned, as neither a follow-up sputum smear nor an abdominal CT scan could be performed. Despite the lack of these evaluations, the patient's complications of portal hypertension and esophageal varices showed no clinical signs of worsening. Hepatic Doppler ultrasound and gastroscopy follow-up were also postponed due to the pandemic.

Transmission prevention efforts were successful. Contact tracing identified the patient's sister, who received preventive treatment with TPT. The patient's quality of life also improved concurrently with their clinical recovery.

## Acknowledgment

The authors would like to thank the patient and their parents for consenting to the inclusion of her medical data in this report.

## Funding Statement

This study was not supported by any external funding.

## Conflict of Interest

None declared.

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APGHN
Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

Literature Review

# Functional Abdominal Pain in Children

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**e-ISSN: 2830-5442**

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**Published:**
31st May 2024

**DOI:**
https://doi.org/10.58427/apghn.3.2.2024.35-51

**Citation:**
Ermaya YS. Functional abdominal pain in children. *Arch Pediatr Gastr Hepatol Nutr.* 2024;3(2):35-51.

**Abstract:**

***Background:*** Functional abdominal pain (FAP), often affecting girls and those with mental health issues, is a prevalent pediatric disorder characterized by persistent symptoms without a clear identifiable organic pathology. The Rome IV Criteria classify it into subtypes, which have distinct symptoms and required tailored management approaches.

***Discussion:*** Subtypes classified by the Rome IV Criteria include irritable bowel syndrome (IBS), functional dyspepsia, abdominal migraine, and FAP - not otherwise specified (NOS). The pathophysiology involves gut hypersensitivity, hyperalgesia, genetic predispositions, and psychosocial triggers. Diagnosis relies on medical history, physical examination, the presence of alarm signs, and the characteristic of pain. Treatment strategies encompass dietary modifications, psychological interventions, pharmacology treatment including proton pump inhibitors, prokinetics, and antidepressants like amitriptyline.

***Conclusion:*** Recognizing the specific subtypes, as defined by the Rome IV Criteria, allows healthcare professionals to implement individualized care strategies for optimal outcomes.

**Keywords:** functional abdominal pain, pediatric disorder, rome IV criteria

## Introduction

Functional abdominal pain is a disorder frequently found in children, typically diagnosed following a comprehensive medical evaluation, with manifestations that cannot be attributed to other medical conditions and the absence of clinical evidence indicating an organic disease.[1] The prevalence among children globally is 13,5% with a higher occurrence observed among girls and children with accompanying mental health conditions.[2]

The subtypes of functional abdominal pain were classified based on the Rome IV Criteria, consisting of Irritable Bowel Syndrome (IBS), Functional Dyspepsia, abdominal migraine, and functional abdominal pain - not otherwise specified (functional abdominal pain – NOS).[1,3] Functional abdominal pain disorder in children and adolescents have varying classifications with different diagnosis, approaches, and treatments. Therefore, a clinician must be able to understand and determine the proper evaluation and monitoring needed to care for patients with such functional abdominal pain.[1]

## Pathophysiology

Functional abdominal pain occurs due to changes in gut hypersensitivity and hyperalgesia, resulting from previous medical disturbance such as abdominal distention, gut motility disorders, inflammation (due to infection or allergy), and genetic predisposition that occurs in early life or is triggered by psychosocial factors including depression, anxiety, family-related stress, adapted lifestyle, secondary changes due to puberty, history of abuse, or stress. These factors lead to the abdominal pain and digestion disorder (**Figure 1**).[1]

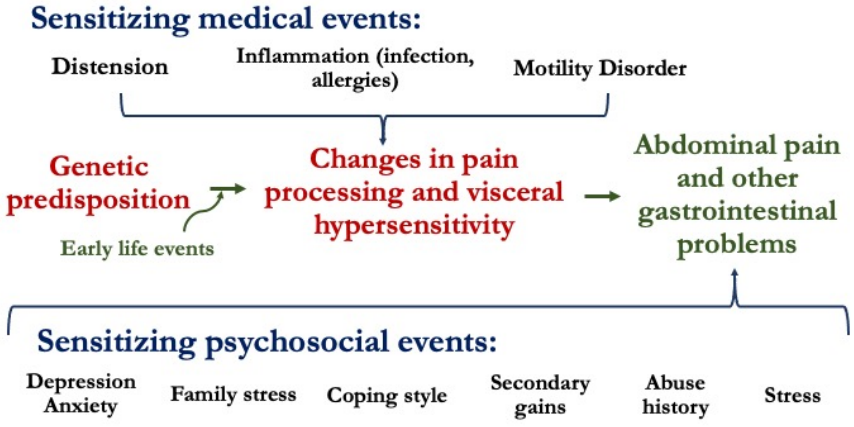


**Figure 1.** Pathophysiology of Functional Abdominal Pain[1]

## Classifications of Functional Abdominal Pain

Below is the classification of Childhood Functional GI Disorders (FGID) in children or adolescent as described in **Table 1**, Abdominal Pain Classification Based on FADP Criteria and its approach depicted in **Figure 2**, and **Table 2** shows potential alarm signs in children with Chronic Abdominal Pain.[1]

**Table 1.** The classification of childhood Functional GI Disorders (FGID) in Child/Adolescent[4]

| |
|---|
| H1. Functional nausea and vomiting disorders |
| H1a. Cyclic vomiting syndrome (CVS) |
| H1b. Functional nausea and functional vomiting |
| H1b1. Functional nausea |
| H1b2. Functional vomiting |
| H1c. Rumination syndrome |
| H1d. Aerophagia |
| H2. Functional abdominal pain disorders (FADP) |
| H2a. Functional Dyspepsia |
| H2a1. Postprandial distress syndrome |
| H2a2. Epigastric pain syndrome |
| H2b. Irritable Bowel Syndrome (IBS) |
| H2c. Abdominal migraine |
| H2d. Functional abdominal pain – NOS |
| H3. Functional defecation disorders |
| H3a. Functional constipation |
| H3b. Non-retentive fecal incontinence |

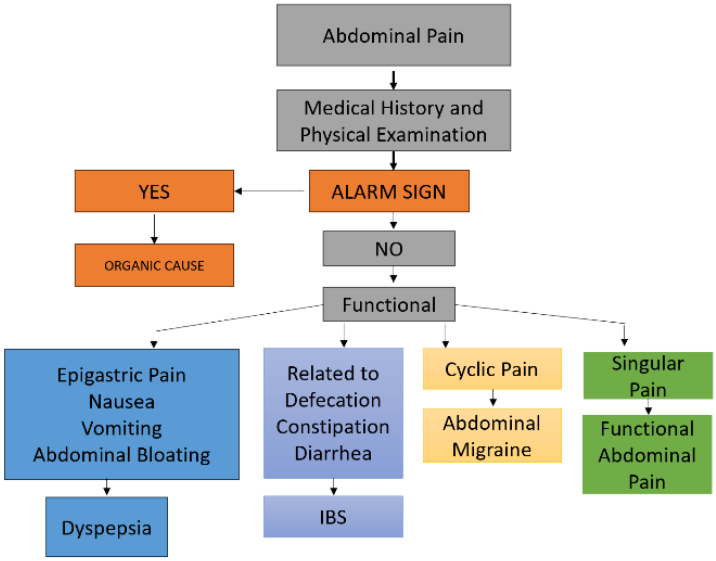


**Figure 2.** Abdominal Pain classification based on FADP criteria[5]

**Table 2.** Potential alarm signs in children with Chronic Abdominal Pain[1]

| |
|---|
| Family history of bowel inflammation, IBD, Celiac disease, or peptic ulcer disease |
| Persistent upper-right quadrant or lower-right quadrant pain |
| Dysphagia |
| Odynophagia |
| Persistent vomiting |
| Gastrointestinal blood loss |
| Nocturnal diarrhea |
| Joint inflammation |
| Perirectal diseases |
| Unexplained weight loss |
| Slow linear growth |
| Delayed puberty |
| Fever of unknown origin |
| Uveitis, oral lesions, skin rash, anemia, hepatosplenomegaly, icterus |
| Family history of bowel inflammation, IBD, Celiac disease, or peptic ulcer disease |
| Persistent upper-right quadrant or lower-right quadrant pain |
| Dysphagia |

## Pediatric Functional Abdominal Pain (Rome IV)

### Irritable Bowel Syndrome

Irritable Bowel Syndrome is a medical condition characterized by chronic, recurrent abdominal pain and discomfort, along with changes in defecation habit that are not influenced by other organic gastrointestinal diseases. While IBS often manifests in childhood, its prevalence peaks during early adulthood. Women are 2 times more likely diagnosed with IBS than men. The prevalence of IBS ranges from 10 – 20%, with an occurrence rate of 1 – 2 % per year. Studies conducted on school children in Colombia shows a prevalence of 4,9%, while in Sri Lanka the prevalence rate was 5.4%, and in the United States, it ranges from 1.2 – 2.9%.[6]

IBS does not have a specific etiology, but several probable causes include visceral hypersensitivity, stressful periods especially if occurring in early life, genetic factors, food intolerance, mental health conditions, such as depression and anxiety, microbiological factors such as SIBO (small intestinal bacterial overgrowth), inflammation, post-infection, gut motility disorder, or heavy metal poisoning.[7]

The pathophysiology of IBS is often considered to involve a disorder between the gut-brain axis, characterized by symptoms such as diarrhea versus constipation, severe pain, and psychosocial distress. While several children with IBS exhibit rectal hyperalgesia but not gastric disorders, the reverse can also occur with some children with functional abdominal pain with no organic causes (FAPNOS).[8, 9]

Visceral hypersensitivity occurs during psychological stress, including anxiety, depression, impulsivity, anger, and emotional management problems.[10] Pro-inflammatory cytokines in the mucosa can be induced by acute/post-infectious IBS, as well as changes in the gut microbiome.[11, 12]

The history of noxious events in early life such as past surgeries is also linked with the risk of childhood functional abdominal pain, including IBS.[13]

IBS can be suspected in patients experiencing recurrent abdominal pain occurring on average at least one day per week, with symptom onset typically occurring 2 months before diagnosis.[1]

The diagnosis of IBS is based on the Rome IV criteria, which include:[1]

1. Abdominal pain occurring at least four days per month, accompanied by one or more of the following symptoms:
   a. Related to defecation;
   b. Changes in defecation frequency;
   c. Changes in stool shape;
2. Pain does not subside after treatment of constipation;
3. Not related to other medical conditions.

The Bristol Stool chart is depicted in **Figure 3**. There are 4 categories in IBS:[1]

1. IBS-C, characterized by predominantly constipation, is defined as having more than 25% of stools with Bristol type 1 or 2 stool shape and less than 25% with Bristol type 6 or 7 stools;
2. IBS-D, characterized by predominantly diarrhea, is defined as having more than 25% of stools with Bristol type 6 or 7 shape and less than 25% Bristol type 1 or 2 stools;
3. IBS-M, which involves alternating diarrhea or constipation, is defined as having more than 25% defecation with Bristol type 1 or 2 stools and more than 25% with Bristol type 6 or 7 stools;
4. IBS-U, classified as unclassified IBS, occurs when a patient's defecation habits cannot be categorized into one of the three previous criteria.

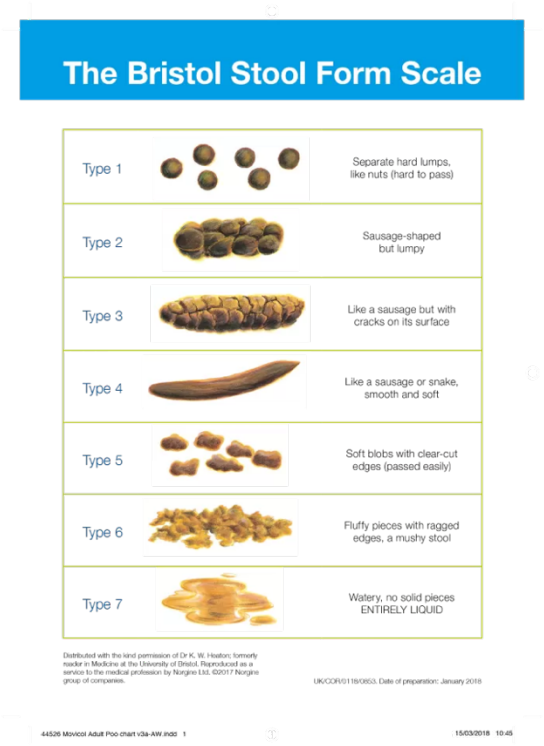


**Figure 3.** The Bristol Stool Chart[14]

Common symptoms of IBS in children and adolescents consist of abdominal pain and changes in defecation habits. Other symptoms may include bloating with or without abdominal distention, excessive gaseous abdominal bloating, and nausea (**Figure 4**).[15]

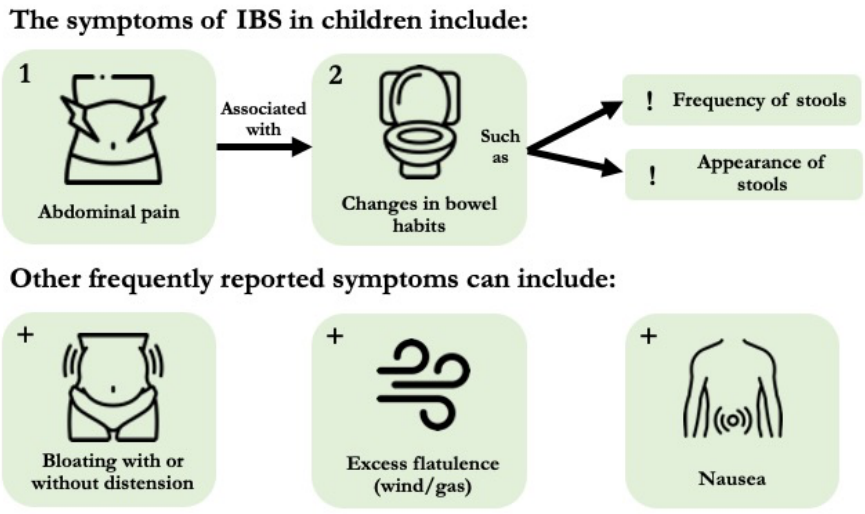


**Figure 4.** Pediatric IBS Symptoms[15]

Clinical evaluations of IBS consist of thorough history-taking and physical examination. Tests are performed to determine the presence of functional constipation, diarrhea, infection, Celiac disease, carbohydrate malabsorption, and inflammatory bowel disease (IBD). The more alarm symptoms discovered, the more likely it is to be an organic disease. Non-invasive testing such as stool calprotectin is preferable over C-reactive proteins to determine the presence of mucosal inflammation or IBD.[16] Several studies have demonstrated that probiotics can reduce bloating symptoms in IBS and improve the patient's quality of life.[17]

Treatments of IBS prioritizes functional treatments over specific therapeutic options. This includes encouraging FAPD diet and several studies also suggests the administration of other remedies such as probiotics and peppermint oil.[1] Additionally, there are additional options, such as amitriptyline, fibers, and hypnotherapy.[18-20]

1. FODMAP

In all IBS subtypes, dietary elimination by reducing intake of fermentable oligosaccharide, disaccharide, monosaccharide, and polyol (FODMAP) is highly beneficial. FODMAP is a category of foods containing short-chain carbohydrates that are difficult to digest for many people (**Table 3**). All FODMAP substances in food can trigger IBS symptoms by drawing excess water to the small intestines and subsequently to the large intestines, where they are fermented by bacteria, potentially mimicking the symptoms of IBD.[21, 22]

**Table 3.** FODMAP Diet Treatment for IBS[23]

| | |
|---|---|
| Initial Therapy | Avoiding foods that can produce intestinal gas, lactose avoidance, and following a FODMAP diet are recommended. Once symptoms are controlled, patients can gradually introduce new foods (1-2 new foods per week). If symptoms reappear with newly added foods, the patient will need to avoid those foods long-term. |
| Avoiding sources of bowel gas | The patient needs to avoid beans, pork, cabbages, broccoli, Brussel sprouts, wheat, high-carbohydrate foods, fructose, and dietary gluten.<br>Patients who avoid gaseous foods demonstrate alleviation of symptoms. |
| Lactose avoidance | The patient is subjected to a lactose breath test. If lactose intolerant, the patient will then limit their lactose intake. If lactose tolerant, the patient can reduce their lactose intake when all other therapeutic approaches fail.<br>FODMAP refers to food that increases the amount of gas in the intestines which can cause abdominal discomfort.<br>Patients who follow low FODMAP diet demonstrates score improvements for abdominal pain, bloating, and stool consistency. |

The FODMAP limitation approach is effective in adults, but more data is needed to assess its efficacy in children. Furthermore, this diet does not support the limitation of lactose.[22]

**Table 4.** The types of FODMAP[23]

| | Consume foods with low FODMAP | Avoid foods with high FODMAP |
|---|---|---|
| Fruits | Bananas, berries, melons (except watermelons), cranberry, grapes, oranges. | Apples, mangoes, pears, dried fruits, canned fruits, watermelon, peaches, prunes, plums |
| Vegetable | Bok Choy, beansprouts, red bell pepper, lettuce, spinach, carrots, green onions, cucumber, eggplants, mung beans, tomatoes, potatoes, chestnuts. | Artichoke, asparagus, sweet peas, cabbages, onions, shallots, scallions, garlic, cauliflower, mushroom, pumpkin, green bell pepper |
| Milk Products | Milk: almond, coconut, nutmeg, flaxseed milk, rice, lactose free milk, kefir, ice cream, butter, cream cheese, cheeses (cheddar, Swiss, brie, blue cheese) | Milk: cow, sheep, lamb, soy, evaporated milk, sweetened and thickened yogurt, cottage cheese, ricotta, mascarpone, ice cream, frozen yogurt, sherbet |
| Grains | Red Rice, oats, quinoa, corn, gluten free bread, cereals, pastas, and flours. | Wheat, barley |
| Legumes | Tofu, nuts | Peas, hummus, red bean, baked beans, edamame, soy milk, lentils |
| Seeds | 1-2 tablespoons of almond, macadamia, pecans, pine nuts, walnuts, pumpkin seeds, sesame seeds, sunflower seeds | Pistachios |
| Sweeteners | Sugar, glucose, pure maple syrup, aspartame | Honey, agave, high fructose corn syrup, sorbitol, mannitol, xylitol, maltitol, Splenda. |
| Proteins | Fish, chicken, turkey, eggs, meat | |
| Oils | Olive and Canola oil, olive, avocado | |

2. Peppermint Oil

Peppermint Oil (PO) is a natural carminative mixture, containing L-menthol compound, which blocks calcium channels in smooth muscles, thereby producing antispasmodic effects on antimicrobial channels, anti-inflammatory properties, antioxidant effects, immunomodulation, and anesthesia.[24]

In various meta-analyses, PO has been proven to be a safe and effective therapy for pain and common symptoms in adults with IBS. Other studies have demonstrated that PO acts as an antispasmodic fiber, and its administration is superior to placebo.[24] Studies on children measuring the motility effect of PO demonstrate an average decrease in intestinal contraction, alleviating IBS pain, but it does not significantly effect of gastrointestinal transit time. Peppermint oil is usually well tolerated at commonly suggested doses.[24]

However, Peppermint Oil is contraindicated on patients with hiatal hernia or Gastroesophageal Reflux Disease (GERD) due to its deleterious effect on reflux symptoms and its effect on lower esophageal sphincter function.[25]

3. Amitriptyline

Tricyclic antidepressants, known for their good safety profile, operate by blocking the reuptake of norepinephrine (NE) and serotonin (5-HT), while also acting as antagonists of H1, M, and 1 receptors. They play a crucial role in altering gastrointestinal sensors, motor functions, and brain-gut plasma peptide concentration. At doses ranging from 0.5 – 1 mg/Kg body weight, Amitriptyline (AMT) demonstrates clinically and statistically significant efficacy in controlling symptoms of irritable bowel syndrome. Additionally, low-dose AMT has been shown to reduce gastric sensitivity, making it a recommended option for managing functional gastrointestinal disorders.[18]

4. Fibers

A systematic review has revealed no evidence supporting the use of fiber supplementation in the treatment of functional gastrointestinal disorders (FGID) in children.[19]

5. Hypnotherapy

Hypnotherapy can be recommended to alleviate functional abdominal pain disorder or IBS. Typically, it involves six sessions over a three-month period. During these sessions, children and parents are advised not to discuss pain, and to engage in breathing exercises, along with progressive relaxation techniques.[20]

Positive suggestions provided during hypnotherapy sessions aid in reducing discomfort, anxiety, and stress. Consequently, hypnotherapy proves beneficial in treating chronic functional abdominal pain or IBS.[20]

**Functional Dyspepsia**

Functional Dyspepsia is a functional gastrointestinal disorder that occurs in children and is a chronic condition. Symptoms often manifest in upper abdominal pain as in

epigastric pain or discomfort, with no organic, systemic, or metabolic disorders that can explain the symptoms. The prevalence of Functional Dyspepsia in developing countries are 1.8 – 3.5%, while in developed countries, it ranges from 5 – 10%.[26]

The Rome IV criteria are utilized to determine the diagnosis of Functional Dyspepsia when there are complaints about the following symptoms occurring approximately four times a month within the span of 2 months before diagnosis:[1, 26]

1. Feeling of fullness after eating;
2. Initial sensation;
3. Epigastric pain that is not related to defecation disorders;
4. Not related to other medical conditions.

Functional Dyspepsia is divided into two subtypes:

1. Postprandial Distress Syndrome. This involves early or debilitating postprandial fullness, leading children to eat less than they used to. It also includes symptoms, such as upper abdominal bloating, postprandial nausea, or excessive burping episodes.[1]
2. Epigastric Pain Syndrome. This subtype includes debilitating localized epigastric pain or a burning sensation. The pain is not generalized or localized to other abdominal regions, and it does not subside with flatulence and/or defecation. Criteria for Epigastric Pain Syndrome include:
   a. Burning pain quality with no involvement of retrosternal components.
   b. Pain is usually induced or relieved by swallowing food, but can occur during fasting.[1]

The pathogenesis of Functional Dyspepsia includes the presence of gastroduodenal motility disorder, visceral hypersensitivity, psychosocial factors, gastric acid, *Helicobacter pylori* infection, post-infection, genetic factors, as well as food and lifestyle factors.[27]

The treatment of Functional Dyspepsia involves an integrated approach that considers physiological, biological, psychological, and social factors. Clinicians need to exclude organic factors and perform tests to determine the presence of *Helicobacter pylori* infection, subsequently eradicating the infection if detected.[1] **Figure 5** presents an algorithm for uninvestigated dyspepsia, systematic approach to diagnosis and treatment of Functional Dyspepsia.[27]

Patients are advised to avoid dietary triggers that can exacerbate dyspeptic symptoms, such as foods and drinks rich in caffeine, spices, and fat, as well as the use of Non-Steroidal Anti-Inflammatory Agents (NSAIDs). Psychological factors contributing to symptom exacerbation should also be addressed. For patients experiencing

accompanying pain symptoms, acid blockade with histamine receptor antagonist and proton-pump inhibitors can be prescribed.[28]

The use of proton pump inhibitors (PPI) is effective to alleviate symptoms of Functional Dyspepsia. Additionally, the administration of prokinetics has also demonstrated effectiveness in symptom relief. Successful treatment of Functional Dyspepsia is defined as symptom reduction after 4 weeks of medical treatment. Administration of 0.4 – 1 mg/KgBW Omeprazole with a frequency of 1 – 2 oral dose is superior to the administration of oral Ranitidine given at 2 – 5 mg/KgBW given 2 – 3 times orally, Famotidine 0,5 – 1 mg/KgBW 1 – 2 times orally, and Cimetidine 5 – 10 mg/KgBW 2 times orally.[29]

In children with more difficult-to-treat symptoms, such as nausea, bloating, and early fullness, PPIs and prokinetic agents such as Cisapride 0.2 mg/KgBW (up to a maximum dose of 10 mg) given 3 – 4 dose orally, along with oral Domperidone 0.2 – 0.5 mg/KgBW given 3 times, can be considered. A retrospective, open-label study has shown that Cyproheptadine with a dose of 0.1 mg/KgBW given 3 times orally is safe and effective in treating dyspeptic symptoms in children.[30]

Other research has investigated the administration of the extract of the Ikkunshito herbs (TJ-43). In addition, low-dose tricyclic antidepressants, such as Amitriptyline and Imipramine can be considered in severe cases, despite the lack of available data.[1]

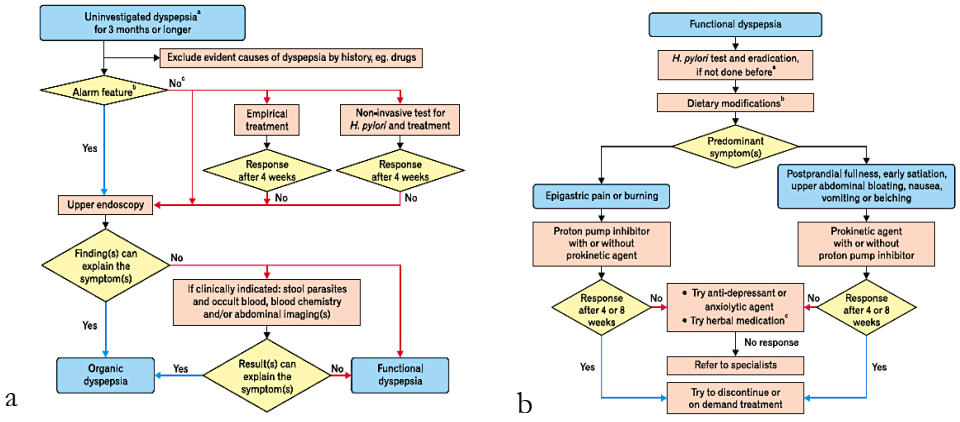


**Figure 5.** Algorithm. a. Algorithm for uninvestigated dyspepsia; b. Functional Dyspepsia diagnostic and its treatment algorithm.[27]

**Abdominal Migraine**

Abdominal migraine is classified as a functional abdominal pain disorder, with a prevalence rate ranging from 0.2 – 4.1% among children. Its symptoms typically include recurrent paroxysmal abdominal pain that may manifest in the midline, periumbilical region, or other areas, often occurring in acute episodes. These episodes

are accompanied by symptoms, such as pallor, nausea, vomiting, anorexia, headache, and photophobia. Between episodes, patients may return to a symptom-free state. Diagnosis of abdominal migraine is based on the Rome IV criteria and International Classification of Headache Disorders III.[31]

The highest incidence of abdominal migraine is observed between the ages of 5 and 10 years old. The presence of parents with migraines increases the likelihood of developing abdominal migraine, with a probability ranging from 65 – 75%. Abdominal migraine can persist until the end of adolescence, with 38 – 70% of patients experiencing migraine headaches.[31]

Various triggers can precipitate acute episodes of abdominal migraine, including:[31]

- Stress related to school and/or familial life
- Insufficient sleep or irregular sleep patterns
- Prolonged fasting
- Dehydration
- Travel
- Exercise
- Consumption of foods rich in amine (such as citrus fruits, chocolate, cheese, vegetables such as eggplants and mushrooms, and meat: salami and ham)
- Foods containing taste and colour additives, and Monosodium Glutamate (MSG)
- Exposure to flashing lights.

The diagnostic criteria for abdominal migraine must encompass all of the following features at least twice:[1]

1. Acute paroxysmal periumbilical episode: Intense, midline or diffuse abdominal pain, lasting for 1 hour or more (must be the most severe or debilitating symptom).
2. Episodes are separated by intervals from weeks to months.
3. Pain significantly interferes with daily activities.
4. Presence of stereotypical patterns and symptoms in the individual.
5. Pain is accompanied by two or more of the following symptoms:
    a. Anorexia
    b. Nausea
    c. Vomiting
    d. Headache
    e. Photophobia
    f. Pallor
6. Following a thorough evaluation, symptoms cannot be explained or attributed to other medical conditions.

These diagnostic criteria must be present at least six months before a diagnosis can be made.[1]

The treatment of abdominal migraine is shown in **Table 5**.[1]

**Table 5.** Abdominal Migraine Treatments[1]

| |
|---|
| Non-pharmacologic Treatment: STRESS Mnemonic |
| • S: (stress) stress management ± Cognitive Behavioral Therapy |
| • T: (Travel) traveling tips |
| • R: (Rest) rest and adequate sleep hygiene |
| • E: (Emergency) monitoring for emergency symptoms |
| • S: (Sparkling) avoid bright and flashing lights; rest in dark and quiet places |
| • S: (Snacking) snack often – avoid long fasting periods and foods high in amines |
| Preventive Medications |
| • Propranolol: 10-20 mg BID or TID |
| • Cyproheptadine: 0.25-0.50 mg/kgBW daily, syrup: 0,1 mg/kg/times 2 – 3 times |
| • Flunarizine: 5,0-7,5 mg per day |
| • Pizotifen: 0,25 mg BID; syrup |
| Abortive Medications |
| • Analgesics: Ibuprofen 10 mg/kg, acetaminophen 15 mg/kg |
| • Sumatriptan: 10 mg intranasal |

**Functional Abdominal Pain with No Specific Cause**

Functional Abdominal Pain - Not Otherwise Specified Epidemiology (FAPNOS) is a disorder that accounts for approximately one-third of children diagnosed with the Rome Criteria for Functional Abdominal Pain Disorders (FAPD). According to the Rome III criteria, the prevalence of FAPNOS is reported to be 2.7% in Colombia and 4.4% in Sri Lanka among school-age children.[6, 32] Studies relying on parental reports have found that the prevalence of FAPNOS are 1.2% in the United States and 2% in Germany among school-age children.[6, 33]

The difference between FAP-NOS and IBS lies in the fact that children with FAP-NOS typically do not exhibit rectal hypersensitivity, unlike children with IBS.[8, 9]

Previous studies indicate that children with FAP-NOS exhibit lower antral contractions and slower emptying of liquid food compared to healthy controls. However, the clinical significance of this characteristic remains unclear.[33] Evidence suggests a correlation between psychological stress and chronic abdominal pain in children and adolescents.[11, 34, 35] Stressful life events such as parental divorce, hospitalization, bullying, and childhood abuse also contribute to the development of FAP-NOS.[32, 36, 37]

The diagnostic criteria for FAP-NOS stipulate that symptoms must occur at least four times a month and include the following:[1]

1. Episodic or continuous abdominal pain occurring during physiological activities (such as meals or menstruation);
2. Insufficient criteria to diagnose IBS, Functional Dyspepsia, or abdominal migraine;
3. Following a thorough examination, abdominal pain cannot be attributed to a specific medical condition.

Symptoms must be present for at least 2 months before the time of diagnosis. Clinical examination of children with FAP-NOS often reveal somatic and non-specific findings, and extraintestinal symptoms do not typically necessitate laboratory testing or imaging studies.[1]

The coping mechanisms employed by children and their families in response to FAPD pain can significantly impact their ability to manage and accommodate the pain. The scoring of pain episodes experienced by a child plays a crucial role in this regard. When a child is unable to address the risk factors or when protective factors prove ineffective, it can lead to the development of maladaptive response, resulting in chronic abdominal pain for those with FAP-NOS.[38]

While small-scale studies have shown that administration of amitriptyline can have beneficial effects, large multi-center studies have not demonstrated a clinically significant effect.[39, 40] Studies on the use of citalopram have demonstrated its effectiveness compared to placebo in treating children with FAP.[41] Additionally, parental support is important in the management of FAP and can be facilitated through the use of hypnotherapy and cognitive behavioral therapy (CBT), both of which have demonstrated long and short-term effects for patients with FAP.[42, 43]

## Conclusion

In conclusion, functional abdominal pain (FAP) is a common disorder among children, diagnosed following a thorough medical evaluation when symptoms cannot be attributed to other medical conditions. The recognition and timely management of functional abdominal pain (FAP) in children are important. Subtypes of FAP, delineated by the Rome IV Criteria, encompass various disorders such as Irritable Bowel Syndrome (IBS), Functional Dyspepsia, abdominal migraine, and functional abdominal pain - not otherwise specified (FAPNOS), each demanding tailored diagnostic and therapeutic approaches.

## Acknowledgment

The authors would like to thank Awliya, M.D. and Nielda Kezia Sumbung, M.D. for their contribution in preparing this manuscript, Prof. Dwi Prasetyo PhD., Pediatrics Gastrohepatology as promotor Doctoral Program.

## Funding

Unpad Doctoral Dissertation Research (RDDU) Yudith Setiati Ermaya MD (grant number: 2203/NU6.3.1/PT.00/2022) from Universitas Padjadjaran.

## Conflict of Interest

None declared.

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# APGHN

Archives of Pediatric Gastroenterology, Hepatology, and Nutrition

www.apghn.com

Volume 3 / No. 2
May 2024

ISSN 2830-5442

Published by
Indonesian Society of Pediatric Gastroenterology, Hepatology, and Nutrition