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CONSERVATIVE MANAGEMENTS PRIOR TO SURGICAL INTERVENTION AMONG A SAMPLE OF 6 MONTHS – 4 YEARS CHILDREN WITH CHRONIC CONSTIPATION

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Abstract

Background: Constipation is a common and a long-term problem persisting for many monthsto years in children. Approximately 95% of childhood constipation is functional in nature. Hirschsprung disease is an important cause of constipation arising in infancy and requires a thorough diagnostic evaluation and surgical treatment. **Aim of the Study**: To identified how conservative treatments can help diagnose Hirschsprungillness in children aged six months to four years who have chronic constipation before undergoing rectal biopsy. **Patients and Methods:** A retrospective cohort study conducted at the department of pediatric surgery in Tikrit teaching hospital and one of privet clinic of pediatric surgery specialist in Tikrit city/Iraq for the period from the 15th of November 2022 to 15th of August 2023. A convenient sample of 120 children aged six months-four years diagnosed to have chronic constipation according to Rome IV criteria and having complete data were followed up for fourmonths to assess their response to conservative treatment (dietary, behavior, softener and stimulated peristalsis drugs) at their second visit after 40 days and third visit after 90 days. Those who have no response were exposed to contrast enema, only those who were suggestiveto have Hirschsprung disease, rectal biopsy was done for them. **Results:** The mean age of the included infants and toddlers was 26.8 (±15.3) months, the median age was 24 months and male: female ratio was 1.07: 1. Those who had good responseto conservative treatment on the second visit were 64.2% and reach to 87.5% on the third visit.The lowest rates of good response to conservative treatment both on the second and third visitswere among infants and toddlers of families of low economic status, history of delayed passageof meconium, age of onset of constipation of less than six months and those on breast feeding .Only 15 (12.5.%) children show no response to conservative treatment and the results of their contrast enema were suggestive for Hirschsprung disease and need rectal biopsy accordingly three children diagnosed to have Hirschsprung disease with prevalence of 2.5% among the studied group. Delayed passage of meconium and age of onset of constipation lessthan six months were the risk factors that significantly associated with Hirschsprung diseases. **Conclusions:** Most of Infants and toddlers with chronic constipation managed effectively withconservative treatment without the need for invasive interventions and just 15 of them requiredrectal biopsy to reach the final diagnosis. Only three children diagnosed to have Hirschsprungdisease and needed surgical treatment.

Keywords: Chronic Pediatric Constipation, Functional Constipation, Hirschsprung Disease, Conservative Treatment, Rectal Biopsy.

INTRODUCTION

Childhood functional constipation (FC) is a major health issue.[1] Even in young children, thecondition has a negative effect on health-related quality of life and results in significant healthcare costs.[2,3] It was shown that children under the age of one year had the greatest rate of emergency department visits in the United States for constipation and related symptoms, and that the expenditures of care had increased by (121%) between 2006 and 2011.[4]Childhood constipation frequently begins in infancy and early childhood. A retrospective record assessment of children with constipation found that the median age of onset was (2.3) years.[5]

According to an Italian birth cohort research, the prevalence/onset of constipation at three, six, and twelve months was (11.6 %), (13.7 %), and (10.7 %), respectively.[6] A representative community survey in the United States discovered that (4.7%) of babies and (9.4%) of toddlers had FC. [7] The shift from breastfeeding to formula feeding or theintroduction of solid foods during infancy is occasionally a trigger for the start of FC.[8] Another key risk factor for the development of constipation is poor toilet training during the toddler period.[9]

Hirschsprung disease (HD) is a gastrointestinal motor disease caused by the failure of neural crest cells to migrate entirely during fetal intestine development. This process begins in week four of pregnancy and end in week seven with the arrival of neural crest derived cells at the colon's distal end. If this process fails, some of a ganglionic segment of the colon fails to relax,resulting in a functional blockage.[10]

The majority of HD patients are identified during the newborn period, however, some appear later with persistent and severe constipation.[11] Failure to pass meconium within 48 hours of delivery is the most prevalent presentation (80-90%).[11,12] Other symptoms of intestinal obstruction include abdominal distention (76%), bilious vomiting (69%), and feeding intolerance.[13]

The global incidence of HD is estimated to be one to two cases per 10.000 live births (1-2.8%)With proper care, most persons have a normal adult life.[3]

In a statewide Japanese survey conducted over 30 years, HD was projected to occur in 1 in 5000 live births. Except even when the entire colon was included, the male-to-female ratio wasabout 1:1.[14]

The condition can cause neurological, cardiovascular, urologic, or gastrointestinal problems. The most frequent chromosomal defect associated with the condition is Down syndrome (trisomy 21), which affects roughly 10% of individuals. Early detection is critical to avoiding complications (such as enter colitis and colonic rupture).[15]

Functional constipation must be treated with an inter professional team approach for success. The patient, family members, and healthcare professionals must all work together to address functional constipation and avoid consequences like encopresis and recurring stomach discomfort. For kids with constipation, a typical level of physical activity is advised combinedwith a normal fiber and hydration consumption. Exercise that is appropriate for age and drinking adequate fluid are also crucial.[16]

Children who have completed toilet training should be encouraged to sit on the toilet and attempt to urinate for five to ten minutes after the same meal, at the same time of day, every day. By doing this, parents can take advantage of the gastrocolic reflex and lower the risk of constipation by "training" their children to urinate regularly. In one to three weeks, a scheduledfollow-up visits are needed to evaluate the effectiveness of conservative therapy so as to discussany adjustments that might be needed to the treatment schedule.[16]

Rectal biopsy is necessary for the diagnosis of HD. There is a lot of literature supporting the diagnostic potential of rectal biopsy, which is typically thought of as a safe procedure; yet, problems may happen, and occasionally with severe morbidity. Rectal biopsies can cause serious complications, including perirectal sepsis, limb gangrene, hemorrhage, and rectal perforation, which have been recorded (rates 1%) and can be serious causes of morbidity and mortality.[17, 18]

PATIENTS AND METHODS

Study Design

A retrospective cohort studies.

Study Setting and Duration

This study was carried out at the department of pediatric surgery in Tikrit teaching hospitaland at one of private clinic of pediatric surgery specialist in Tikrit city/Iraq for the period from 15th of November 2022 to 15th of august 2023.

Study Sample

A convenient sample of 120 infants and toddlers aged six months -four years presented to thedepartment of pediatric surgery in Tikrit teaching hospital or the privet clinic of pediatric surgeon in Tikrit city, diagnosed to have chronic constipation according to Rome IV [(44)] criteria and had completed the management protocol assigned for them for four months.

Inclusion Criteria

Infants and toddlers aged six months to four years with complete data were included, regarding the basic data and management information both at time of presentation at the first visit and that of follow up visits; the second and third visit

Exclusion Criteria

Infants and toddlers with other comorbidities and sever illness

Ethical Consideration

Initially the study was approved by the research ethics committee of the executive office of the Arab board of Health specializations (Appendix I). Tikrit director of health (DOH) and the administration of pediatric surgery department in Tikrit teaching hospital were informed about the scope and the nature of the study and a verbal agreement were taken from them. The parents of all the included infants and toddlers were informed by mobile about the purpose and the objectives of this study and were asked if they accept to utilize the data of their children, meanwhile a verbal consent was obtained from them after they assured thatthis information will be kept confidential and not be used except for the study purpose.

Data Collection

Source of Data

For infants and toddlers with chronic constipation, the official records that were already in use in Tikrit teaching hospital and the private clinic of the pediatric surgeon were used. The data were rearranged for this study's purpose, and a revised format was created to encompassall the information's needed to accomplish the study's goals. This form was subsequently divided into three parts (appendix II):

Part I: Cover the history of the participants including: age, gender, mode of delivery, history of delayed passage of meconium, economic status of the family; high (exceed daily needs) medium (enough for daily needs) or poor (not enough for daily needs), type of feeding (breastfeeding, bottle feeding, or mixed), age of introducing complementary food, Age of toilet training, and family history of chronic constipation (1st degree relatives)

Part II: Include the information related to the pattern of constipation: age of onset and duration of constipation, the clinical presentation related to Rome IV criteria for diagnosingpediatric chronic constipation at age six months -four years, the child should have two or more of the following happening at least once a week for at least one month duration [44].

- having two or less bowel motion per week
- having painful bowel motion
- having hard bowel motion
- having large diameter stool
- having at least one episode/week of stool incontinence

Part III: Related to the management protocol and follow up plan that usually applied at pediatric surgery department in Tikrit teaching hospital and at the private clinic of pediatric surgeon for patients diagnosed to have pediatric chronic constipation. Management protocol and follow up plan

All study participants were followed up for more than four months, during which three visitswere completed including:

First Visit: at initial visit all the infants and toddlers had received conservative treatment including three parameters; dietary, behavior, softener and stimulated peristalsis drugs, include the following:

1. Dietary management. Include:

- Avoiding or decrease the following:
  - Milk and dairy products
  - French fries and crispy food
  - All types of nuts
  - All drinks that contain caffeine
  - Pomegranate
- Encourage taking food rich with fibers, watery fruits and drinking large amounts of water

2. Behavioral management. Include:

- Daily toilet training
- Avoiding video games and electronic devices
- Encourage sports and interactive toys
- Good family support
- Encourage social interaction with siblings and other children

3. Medications. Include:

- Oral medications: two laxative is used:
    - Movicol sachets (laxative): Given single dose daily for 20 days
    - Senna tablet (stimulant laxative): Given twice daily, continuously to the next visit
- Lidocaine ointment: to be used twice daily, continuously to the next visit
- Glycerin suppositories (stool softener): is given on need

Second Visit: after 40 days the response for initial management is assessed for every participant which is either good, fair-weak or no response, accordingly the management planeis tailored for everyone.

1. If the response is good (patient passing one or more bowel motion per day without pain);the next step is to decrease the laxative (senna tab) and continue dietary and behavior life style and wait for the third visit.
2. If the response is fair- weak (patient passing 2-3 bowel motions per week with pain or lessthan two bowel motions per week without pain), the plan is to increase the dose or frequencyof laxative drug and continue dietary and behavioral life style and wait for the third visit.
3. If the response is poor (no bowel motion for more than one week) the patient will be prepared for contrast enema and rectal biopsy. If contrast enema is suggestive for HD, then rectal biopsy is done and if rectal biopsy result is negative for ganglion cell, then the patient is diagnosed as HD and surgery will be done for him, but if rectal biopsy result is positive forganglion cell the patient is diagnosed as functional constipation and continue on conservativemanagement.

Third Visit: After 90 days the child is assessed again, accordingly:

1. If the response is good, the diagnosis is functional constipation and the next step is taperingof medication then stop it.
2. If there is no response, the patient will be prepared for contrast enema and rectal biopsy andif rectal biopsy result is negative for ganglion cell the patient is diagnosed as HD and go on tosurgery

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 26). Chi-square test of association was used to compare proportions of two or more groups. Fisher's exact test was used when the expected frequency (value) was less than five of more than (20%) of the cells of the table. A p value of ≤ 0.05 was considered as statistically significant.

RESULTS

The total number of children was 120. Their mean age (±SD) was 26.8 (15.3) months, the median was 24 months, and the age range was 6-48 months. Around one third of the children (32.5%) were aged 6-17 months, and 28.3% were aged 42-48 months. Around half (51.7%) were males, and the male: female ratio was 1.07: 1. More than half (53.3%) of the families were of medium (enough for daily needs) economic status, and 41.7% of the children have been delivered by Cesarean section. Only 5% of the

children had history of delayed passage ofmeconium (Table 1).

Table 1: Basic Characteristics of the Studied Sample

	No.	(%)
Age (months)		
6-17	39	(32.5)
18-29	30	(25.0)
30-41	17	(14.2)
42-48	34	(28.3)
Gender		
Male	62	(51.7)
Female	58	(48.3)
Economic status		
Exceeds daily needs	42	(35.0)
Enough for daily needs	64	(53.3)
Mode of delivery		
Normal vaginal delivery	70	(58.3)
Cesarean section	50	(41.7)
Delayed passage of meconium		
Yes	6	(5.0)
No	114	(95.0)
Total	120	(100.0)

More than half (55.8%) of the children were on bottle feeding, 41.7% were on mixed feeding, while only 2.5% were on breast feeding. Regarding the age of introducing complimentary food, it was before six months of age among 65% of the children (Table 2).

Table 2: Feeding History

	No.	(%)
Feeding		
Breast	3	(2.5)
Bottle	67	(55.8)
Mixed	50	(41.7)
Age of introducing complimentary food		
Before six months	78	(65.0)
Six months and above	42	(35.0)
Total	120	(100.0)

Only 7.5% of the children had family history of constipation. The duration of constipation was less than six months in 25.8% of the children, and it was 30-36 months in 8.3% of children. The age of onset of constipation was 6-11 months in 54.2% of the children. Regarding the age of starting toilet training among children aged more than 30 months, it was 36 months in 54.2% of the children (Table 3).

Table 3: Pattern of Constipation

	No.	(%)
Family history of constipation		
Yes	9	(7.5)
No	111	(92.5)
Duration of constipation (months)		
< 6	31	(25.8)
6-11	20	(16.7)
12-17	27	(22.5)
18-23	11	(9.2)

24-29	21	(17.5)
30-36	10	(8.3)
Age of onset of constipation (months)		
< 6	8	(6.7)
6-11	65	(54.2)
12-17	14	(11.7)
≥ 18	33	(27.5)
Age of starting toilet training (months)(n= 48)*		
24	2	(4.2)
30	20	(41.7)
36	26	(54.2)
Total	120	(100.0)

*Among children aged >30 months

The criteria of chronic constipation of nearly all infants and toddlers in this study were: havingless than two bowel motion per week, painful bowel motion, having hard and large stool, whileonly 10(8.3%) of them have stool incontinence (Figure 1).

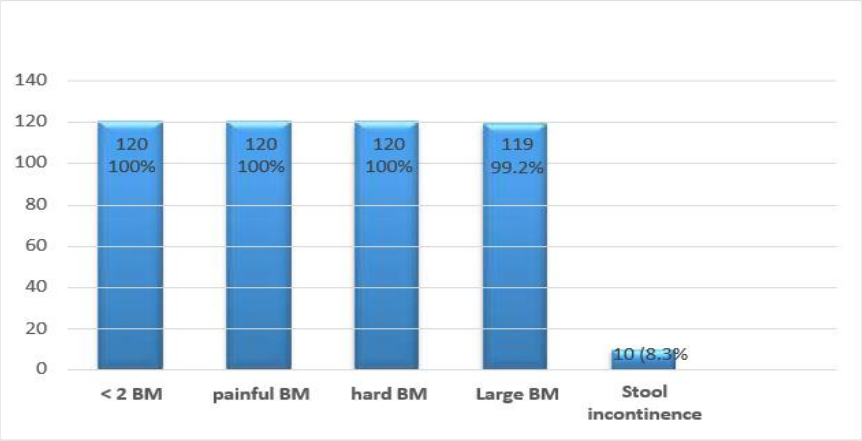

Figure 1: Criteria of Chronic Constipation of the Studied Sample

Good response to treatment was detected in the second visit in 64.2% of children, and only 3.3% had no response. The majority (87.5%) of the children had good response in the third visit, and only 12.5% had no response (Table 4).

Table 4: Response to Treatment in the Second and Third Visits

	No.	(%)
Second visit		
Good response	77	(64.2)
Weak-fair response	39	(32.5)
No response	4	(3.3)
Third visit		
Good response	105	(87.5)
No response	15	(12.5)
Total	120	(100.0)

There was no significant association between the response on the second visit and the followingvariables: age (p = 0.144), gender (p = 0.554), and mode of delivery (p = 0.564), while significant association was detected with economic status (p = 0.041), where it is evident in table 5 that the least rate of good response (35.7%) was found among those with poor economicstatus. When there is delayed passage of meconium, the rate of good response was significantly(p < 0.001) low (33.3%) as presented in

Table 5.

Table 5: Response on the Second Visit by the studied basic Characteristics

Respond on the second visit					
		Good	Weak-Fair	No response	
	N	No. (%)	No. (%)	No. (%)	P*
Age (months)					
6-17	39	25 (64.1)	12 (30.8)	2 (5.1)	
18-29	30	22 (73.3)	7 (23.3)	1 (3.3)	
30-41	17	14 (82.4)	3 (17.6)	0 (0.0)	
42-48	34	16 (47.1)	17 (50.0)	1 (2.9)	0.144
Gender					
Male	62	37 (59.7)	23 (37.1)	2 (3.2)	
Female	58	40 (69.0)	16 (27.6)	2 (3.4)	0.554
Economic status					
Exceeds daily needs	42	26 (61.9)	15 (35.7)	1 (2.4)	
Enough for daily needs	64	46 (71.9)	17 (26.6)	1 (1.6)	
Not enough for daily needs	14	5 (35.7)	7 (50.0)	2 (14.3)	0.041
Mode of delivery					
Normal vaginal delivery	70	42 (60.0)	25 (35.7)	3 (4.3)	
Cesarean section	50	35 (70.0)	14 (28.0)	1 (2.0)	0.564
Delayed passage of meconium					
Yes	6	2 (33.3)	1 (16.7)	3 (50.0)	
No	114	75 (65.8)	38 (33.3)	1 (0.9)	< 0.001
Total	120	77 (64.2)	39 (32.5)	4 (3.3)	

*By Fisher's exact test.

The highest rate of good response on the second visit was detected among those on mixed feeding (70%), while 33.3% of those on bottle feeding had good response (p = 0.006). No significant association (p = 0.877) was detected between the response and age of introducing complimentary food (Table 6).

Table 6: Response on the second visit by feeding history

Response on the second visit					
		Good	Weak-Fair	No response	
	N	No. (%)	No. (%)	No. (%)	p
Feeding					
Breast	3	1 (33.3)	0 (0.0)	2 (66.7)	
Bottle	67	41 (61.2)	25 (37.3)	1 (1.5)	
Mixed	50	35 (70.0)	14 (28.0)	1 (2.0)	0.006*
Age of introducing complimentary food					
Before six months	78	51 (65.4)	24 (30.8)	3 (3.8)	
Six months and above	42	26 (61.9)	15 (35.7)	1 (2.4)	0.877
Total	120	77 (64.2)	39 (32.5)	4 (3.3)	

*By Fisher's exact test.

It is evident in Table 7 that there was a significant (p = 0.010) association between response onthe second visit and age of onset of constipation, but this association was not consistent throughout the age of onset categories. The rate of good response was low among the categories'< 6 months' (37.5%) and '12-17' months' (50%), while it was high (69.2%) in the category '6-11' months and ≥ 18 months (66.7%). No significant association was detected with the other variables as follows: family history of constipation (p = 0.060), duration of constipation (p = 0.125), and age of toilet training (p = 0.292)

Table 7: Response on the second visit by pattern of constipation

Response on the second visit					
		Good	Weak- Fair	No response	
N		No. (%)	No. (%)	No. (%)	P*
Family history of constipation					
Yes	9	9 (100.0)	0 (0.0)	0 (0.0)	
No	111	68 (61.3)	39 (35.1)	4 (3.6)	0.060
Duration of constipation (months)					
< 6	31	19 (61.3)	10 (32.3)	2 (6.5)	
6-11	20	17 (85.0)	3 (15.0)	0 (0.0)	
12-17	27	18 (66.7)	9 (33.3)	0 (0.0)	
18-23	11	8 (72.7)	2 (18.2)	1 (9.1)	
24-29	21	11 (52.4)	10 (47.6)	0 (0.0)	
30-36	10	4 (40.0)	5 (50.0)	1 (10.0)	0.125
Age of onset of constipation (months)					
< 6	8	3 (37.5)	2 (25.0)	3 (37.5)	
6-11	65	45 (69.2)	19 (29.2)	1 (1.5)	
12-17	14	7 (50.0)	7 (50.0)	0 (0.0)	
≥ 18	33	22 (66.7)	11 (33.3)	0 (0.0)	0.010
Age of toilet training (months) (n = 48)					
24	2	2 (200.0)	0 (0.0)	0 (0.0)	
30	20	13 (65.0)	6 (30.0)	1 (5.0)	
36	26	13 (50.0)	13 (50.0)	0 (0.0)	0.292
Total	120	77 (64.2)	39 (32.5)	4 (3.3)	

*By Fisher's exact test.

Table 8 shows no significant association between the response on the third visit and the following variables: age (p = 0.429), and gender (p = 0.890). The rate of response to treatmentwas significantly (p < 0.001) low among those with poor economic status (50%). The rate of good response was significantly low (81.4%) among children who have been delivered vaginally, compared with 96% among those delivered by Cesarean section (p = 0.017). Significant low rate of response (50%) was detected among those with delayed passage of meconium, compared with 89.5% among those with normal passage of meconium (p = 0.025)

Table 8: Response on the Third Visit by the studied basic Characteristics

Response on the third visit				
		Yes	No	
	N	No. (%)	No. (%)	p
Age (months)				
6-17	39	36 (92.3)	3 (7.7)	
18-29	30	27 (90.0)	3 (10.0)	
30-41	17	15 (88.2)	2 (11.8)	
42-48	34	27 (79.4)	7 (20.6)	0.429**
Gender				
Male	62	54 (87.1)	8 (12.9)	
Female	58	51 (87.9)	7 (12.1)	0.890*
Economic Status				
Exceeds daily needs	42	40 (95.2)	2 (4.8)	
Enough for daily needs	64	58 (90.6)	6 (9.4)	
Not enough for daily needs	14	7 (50.0)	7 (50.0)	< 0.001*
Mode of delivery				
Normal vaginal delivery	70	57 (81.4)	13 (18.6)	
Cesarean section	50	48 (96.0)	2 (4.0)	0.017*
Delayed passage of meconium				
Yes	6	3 (50.0)	3 (50.0)	
No	114	102 (89.5)	12 (10.5)	0.025**
Total	120	105 (87.5)	15 (12.5)	

*By Chi square test. **By Fisher's exact test.

Nearly the same pattern was observed regarding the response to the third visit and type of feeding (p = 0.015). No significant association was detected with age of introducing complimentary food (p = 0.664) as presented in Table 9.

Table 9: Response on the Third visit by Feeding History

Response on third visit				
		Yes	No	
	N	No. (%)	No. (%)	p
Feeding				
Breast	3	1 (33.3)	2 (66.7)	
Bottle	67	62 (92.5)	5 (7.5)	
Mixed	50	42 (84.0)	8 (16.0)	0.015**
Age of introducing complimentary food				
Before six months	78	69 (88.5)	9 (11.5)	
Six months and above	42	36 (85.7)	6 (14.3)	0.664*
Total	120	105 (87.5)	15 (12.5)	

*By Chi square test. **By Fisher's exact test.

No significant association was detected between the response on the third visit with family history of constipation (p = 0.600), and age of toilet training (p = 0.426). Significant associationwas detected with the duration of constipation (p = 0.046), but the association was not consistent throughout the categories. The least rate of response (62.5%) was observed when the constipation starts before 6 months of age (p = 0.036) (Table 10).

Table 10: Response on the Third Visit by Pattern of Constipation

Response on the third visit				
		Yes	No	
	N	No. (%)	No. (%)	P*
Family history of constipation				
Yes	9	9 (100.0)	0 (0.0)	
No	111	96 (86.5)	15 (13.5)	0.600
Duration of constipation (months)				
< 6	31	28 (90.3)	3 (9.7)	
6-11	20	20 (100.0)	0 (0.0)	
12-17	27	22 (81.5)	5 (18.5)	
18-23	11	8 (72.7)	3 (27.3)	
24-29	21	20 (95.2)	1 (4.8)	
30-36	10	7 (70.0)	3 (30.0)	0.046
Age of onset of constipation (months)				
< 6	8	5 (62.5)	3 (37.5)	
6-11	65	61 (93.8)	4 (6.2)	
12-17	14	12 (85.7)	2 (14.3)	
≥ 18	33	27 (81.8)	6 (18.2)	0.036
Age of toilet training (months) (n = 48)				
24	2	1 (50.0)	1 (50.0)	
30	20	16 (80.0)	4 (20.0)	
36	26	22 (84.6)	4 (15.4)	0.426
Total	120	105 (87.5)	15 (12.5)	

*By Fisher's exact test.

The results of contrast enema of 15 children were all suggestive for Hirschsprung disease accordingly rectal biopsy was done for them. The histopathological results of rectal biopsy were negative for ganglion cells among only 3 (20%) of them and

diagnosed as Hirschsprung disease while the rest 12 (80%) were positive for ganglion cells and diagnosed as functional constipation (Figure 2).

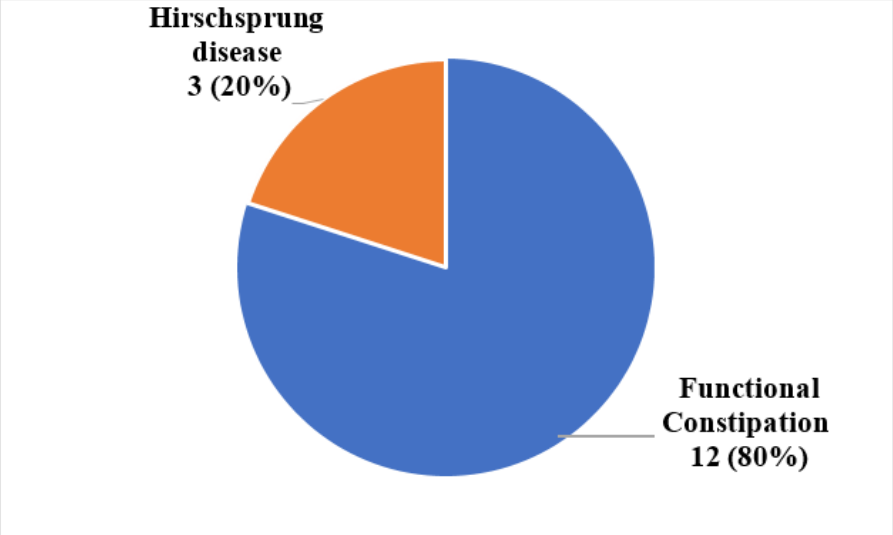

Figure 2: Results of Rectal Biopsy of Children whose Contrast Enema were Suggestion for Hirschsprung Disease

The prevalence of Hirschsprung disease among infants and toddlers with chronic constipationin this study was 2.5% while most of them 97.5% were consequently diagnosed as functional constipation (Figure 3).

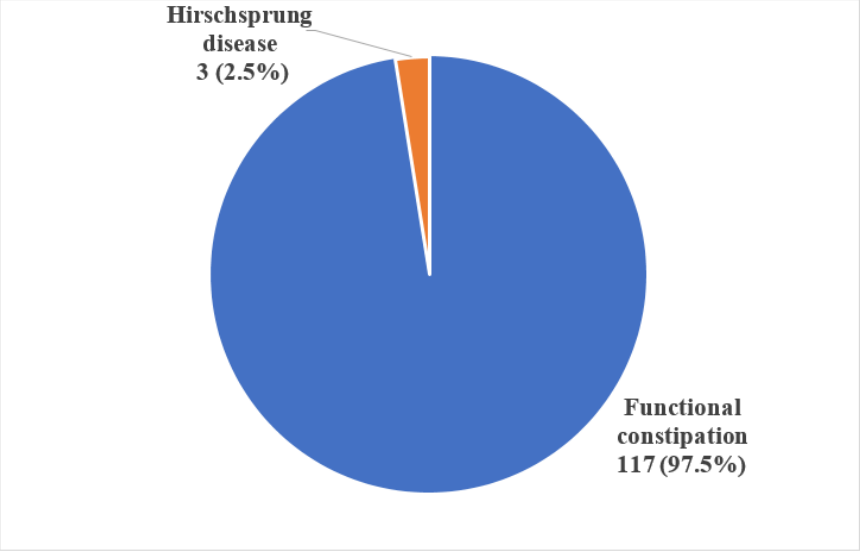

Figure 3: Prevalence of Hirschsprung Disease in the Studied Sample

The prevalence of Hirschsprung disease was 50% among children with history of delayed passage of meconium compared with 0% among those with normal passage of meconium ($p < 0.001$). No significant association was detected between the prevalence and the following variables: age ($p = 0.688$), gender ($p > 0.999$), economic status ($p = 0.354$), and mode of delivery ($p > 0.999$) as presented in (Table 11).

Table 11: Prevalence of Hirschsprung Disease by the studied basic Characteristics

Final diagnosis (prevalence)				
		Functional constipation	Hirschsprung disease	
	N	No. (%)	No. (%)	P*
Age (months)				
6-17	39	37 (94.9)	2 (5.1)	
18-29	30	29 (96.7)	1 (3.3)	
30-41	17	17 (100.0)	0 (0.0)	
42-48 GenderMale	34 62	34 (100.0) 60 (96.8)	0 (0.0) 2 (3.2)	0.688
Female	58	57 (98.3)	1 (1.7)	>0.999
Economic status				
Exceeds daily needs	42	41 (97.6)	1 (2.4)	
Enough for daily needs	64	63 (98.4)	1 (1.6)	
Not enough for daily needs	14	13 (92.9)	1 (7.1)	0.354
Mode of delivery				
Normal vaginal delivery	70	68 (97.1)	2 (2.9)	
Cesarean section Delayed passage of meconiumYes	50 6	49 (98.0) 3 (50.0)	1 (2.0) 3 (50.0)	>0.999
No	114	114 (100.0)	0 (0.0)	< 0.001
Total	120	117 (97.5)	3 (2.5)	

*By Fisher's exact test.

No significant association was detected between the prevalence of Hirschsprung disease and the following variables: feeding (p = 0.074), and age of introducing complimentary food (p > 0.999) (Table 12).

Table 12: Prevalence of Hirschsprung Disease by Feeding History

Final diagnosis (prevalence)				
		Functional constipation	Hirschsprung disease	
	N	No. (%)	No. (%)	P*
Feeding				
Breast	3	2 (66.7)	1 (33.3)	
Bottle	67	66 (98.5)	1 (1.5)	
Mixed	50	49 (98.0)	1 (2.0)	0.074
Age of introducing complimentary food				
Before six months	78	76 (97.4)	2 (2.6)	
Six months and above	42	41 (97.6)	1 (2.4)	>0.999
Total	120	117 (97.5)	3 (2.5)	

*By Fisher's exact test.

No significant association was detected between the prevalence of Hirschsprung disease and family history of constipation (p > 0.999), and duration of constipation (p = 0.265), while significant association was detected with the age of onset of constipation, where it is evident that the prevalence was 37.5% when the age of onset of constipation was less than 6 months, and 0% in the other categories (p < 0.001) (Table 13).

Table 13: Prevalence of Hirschsprung Disease by Pattern of Constipation

Final diagnosis (prevalence)				
	Functional constipation		Hirschsprung disease	
	N	No. (%)	No. (%)	P*
Family history of constipation				
Yes	9	9 (100.0)	0 (0.0)	
No	111	108 (97.3)	3 (2.7)	>0.999
Duration of constipation (months)				
< 6	31	29 (93.5)	2 (6.5)	
6-11	20	20 (100.0)	0 (0.0)	
12-17	27	27 (100.0)	0 (0.0)	
18-23	11	10 (90.9)	1 (9.1)	
24-29	21	21 (100.0)	0 (0.0)	
30-36	10	10 (100.0)	0 (0.0)	0.265
Age of onset of constipation(months)				
< 6	8	5 (62.5)	3 (37.5)	
6-11	65	65 (100.0)	0 (0.0)	
12-17	14	14 (100.0)	0 (0.0)	
≥ 18	33	33 (100.0)	0 (0.0)	< 0.001
Age of toilet training (months)(n = 48)				
24	2	2 (100.0)	0 (0.0)	
30	20	20 (100.0)	0 (0.0)	
36	26	26 (100.0)	0 (0.0)	NA**
Total	120	117 (97.5)	3 (2.5)	

*By Fisher's exact test.

**NA: Not applicable.

DISCUSSION

For parents, a child's persistent constipation is a source of worry since they are concerned thatit might be a sign of a serious illness. However, only a tiny percentage of children actually havea biological reason for their constipation. The most frequent cause of constipation beyond the neonatal period is functional (FC), also known as idiopathic constipation, functional fecal retention, and fecal withhold (16).

Constipation is a very common problem in children. Whether it's something temporary after an illness or diet change, or something more chronic, up to 20% of children suffer from it at one time or another. As much as it makes people uncomfortable to talk about poop, having trouble pooping is even more uncomfortable, luckily it is generally a very treatable problem.[19]

A large proportion of children with FC can be treated effectively with the conservative and therapeutic agents that are currently available. This study was carried out to declare the role ofconservative management as a first line measure in dealing with infants and toddlers with chronic constipation before any further invasive intervention is applied whether diagnostic or therapeutic.

In this study the follow up of infants and toddlers diagnosed to have chronic constipation andreceived initially a conservative treatment revealed a good response of nearly two thirds of them in the second visit and only 3.3% had no response. Meanwhile the majority (87.5%) of those infants and toddlers reported a good response in the third visit, and only 12.5% had no response. This finding is significantly higher than a study conducted by Pijpers et al.'s [20] who reported that within 6-12

months around 50% of children with functional constipation had recovered and did not require to remain on laxatives, furthermore, 10% were symptom free while on medication and 40% had no response to medication.

The relationship between constipation and socioeconomic status is still controversial. Variousstudies have reported that there is no association between low family income and child constipation.[21] However, in a Nigerian study it was reported that the prevalence of constipation was higher among children with low socioeconomic status.[22]

Only 11.7% of the children in our researcher who had chronic constipation were from familieswith low incomes. However, those with low socioeconomic level had the lowest rate of excellent response to the treatment in the second (35.7%) and third (50%) visits.

Any newborn with delayed meconium passage should be evaluated for Hirschsprung disease.[23] in this study the rate of good response to conservative treatment among infants and toddlerswith history of delayed passage of meconium was significantly low both in the second visit (33.3%) and in the third visit (50%), on the other hand 50% of those having this history finallyneed further interventions, so as contrast enema and rectal biopsy were done for them and diagnosed to have HD. Croaker et al.,[24] reported that delayed passage of meconium was morefrequent among children with slow transit constipation compared to general population.Meanwhile, in our study the prevalence of Hirschsprung disease among children with history of delayed passage of meconium was 50% compared to those with normal passage of meconium which was null. Bhatnagar reported that delayed passage of meconium in healthy term newborns is considered HD although this feature is found in only 50% in neonates with HD.[25]

The causes of functional constipation are multifactorial, the dysbiosis of the gut microbiota considered to be one contributing factor.[26] It is well known that the changes in the composition of baby gut microbiota depend on delivery mode.[27, 28]

Vertical transmission of maternal microbes to newborns is an important aspect in the development of a core gut microbiota. In our study the majority of children (58.3%) were delivered by normal vaginal delivery in comparison to (41.7%) by cesarean section. Although the rate of good response to treatment among children who have been delivered vaginally was(81.4%) but it was significantly ($p = 0.017$) lower than those delivered by Cesarean section (96%). On contrary a study conducted in Japan, revealed that the prevalence of constipation was higher among toddlers who were born by cesarean section (13.1%) compared to those byvaginal delivery (12.1%).[29]

In young infants, functional constipation often develops at the time of dietary transition (example, from breast milk to formula, the addition of solid foods into the diet, from formula to whole milk). In this study more than two thirds of children on mixed feeding showed good response for conservative treatment on the second visit compared to only one third of those onbreast feeding and more than half of those on bottle feeding. In Moore et al.'s study mentioned that infants who were exclusively breastfed had a significantly higher frequency of daily stoolcompared to infants who were exclusively bottle-fed.[30]

In the current study, duration of constipation is significantly associated with the response to treatment in the second and third visits. Duration of 30-35 months was associated with lower rate of response to treatment. Tabbers et al.'s study shows that

children with chronic constipation will require treatment for at least six months.[31] They also reported that 80% of children who are treated early will restore their normal bowel function without the use of laxatives at six months follow up compared to 32% of children with delayed treatment.[31] Theaim for all children should be: Prevention, Early identification, Effective treatment.

If information about the signs and symptoms of constipation were included in all parent-held child health records and discussed at all routine contacts by health visitors and school nurses, there would be less stigma and embarrassment, and families would recognize the problem earlier and know how and when to seek help. Crucially, prompt proactive treatment with laxatives would reduce the incidence of the condition becoming chronic.[32]

Another significant finding in our study was that the percentage of children whose age of onsetof constipation was less than 6 months and diagnosed to have HD was higher than later ages of onset (two children out of three diagnosed as HD their onset of constipation was less than 6months). In Khan et al.'s study the majority of cases who were diagnosed with HD were less than 1 month old.[33]

No significant association was detected between the prevalence of Hirschsprung disease and family history of constipation in this study ($p > 0.999$). In a study conducted over 34-year period by Moore et al. showed that 28 patients among 370 patients who were being treated forHD had a family member with histologically proven HD. Neuronal intestinal dysplasia found in one of the parents was associated to total colonic ganglionosis in two siblings of those parents. This suggests that there is a genetic component of HD.[30]

Rectal biopsy is recommended for children with constipation and probable Hirschsprung illness. A suitable indication should be considered because this is an invasive treatment to reduce the number of needless biopsies.[34] in our study, 120 children with chronic constipation were identified using Rome IV criteria and treated conservatively for about four months.
The majority of these children were responded to this treatment, and only 15 (12.5%) required additional intervention, including contrast enema and rectal biopsy. Although contrast enema results of all of them were suggestive for HD, yet only 3 (20%) children tested positivefor HD by rectal biopsy. This finding is consistent with a comprehensive assessment study byFriedmacher F. and Puri P. that examined 14,053 rectal suction biopsies from 58 studies and showed that HD incidence was 19%.[18] Another study conducted from 2013 to 2018, included225 children with constipation, aged 1 day–17 years, had a rectal biopsy at the Oslo University Hospital, 49/225 (22%) of these children, were diagnosed with HD.[34]

LIMITATION OF THE STUDY

A longer period of follow up may be warranted to ensure that even if there is a good response to conservative treatment, children should further be assessed for recurrence once the treatments are tapered or interrupted, and how to deal with it. This study was retrospective, andthe duration of follow up for every participant was restricted to about four months only becauseof the management protocol already applied and the availability of data.

CONCLUSIONS

- Infants and toddlers with chronic constipation who have good response to conservative treatment were 64.2% on the second visit and reach to 87.5% on the third visit.
- The lowest rates of good response to conservative treatment both on the 2nd and 3rd visit wereamong infants and toddlers of families of low economic status, history of delayed passage of meconium, age of onset of constipation of less than six months and those on breast feeding.
- Only 15 (12.5%) of the study group did not response to conservative treatment and need contrast enema and rectal biopsy.
- Infants and toddlers with chronic constipation who diagnosed to have Hirschsprung disease in this study were only3 (2.5%).
- Delayed passage of meconium and age of onset of constipation less than six months were the risk factors that significantly associated with Hirschsprung diseases.

RECOMMENDATIONS

- Further studies could be conducted with a larger sample size and a broader age range in orderto come up with a standard guideline for management of pediatric constipation that suits the lifestyle of our community.
- Encourage pediatricians and family doctors to manage children with constipation using a systematic, evidence-based approach which involves conservative treatment before sending them to a pediatric surgeon.

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