Original paper

Functional gastrointestinal disorders in Jordanian infants: a pilot study

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Abstract

Introduction: Functional gastrointestinal disorders (FGIDs) encompass a wide spectrum of disorders that may be diagnosed using the Rome criteria.

Aim: To identify the prevalence and risk factors for the development of FGIDs in Jordanian infants.

Material and methods: We conducted a cross-sectional study to investigate the prevalence of FGIDs among infants and characterise any possible risk factors. Between 1 January 2020, and 30 December 2020, patients who presented to the paediatric follow-up clinic at King Abdullah University Hospital were recruited. Parents were interviewed and asked to complete an Arabic version of the Rome IV diagnostic questionnaire for pediatric gastrointestinal disorders for neonates and toddlers. Data regarding the parents' gastrointestinal symptoms and children's medical history were collected. Children's electronic medical files were also reviewed.

Results: The study included 127 children, 78 (61%) were males. The median age was 40 days. According to the Rome IV criteria eighty-two (64%) of the infants fit the diagnosis for at least one disorder. The most prevalent disorder was functional constipation (n = 78, 95%) followed by infant dyschezia (n = 11, 13%). Compared to infants who did not meet the diagnostic criteria, herb intake and circumcision rates were significantly higher among those who did. Univariate analyses revealed that Infants with FGIDs were more likely to ingest herbs.

Conclusions: FGIDs were common among young infants. Functional constipation was the most commonly diagnosed FGID. Infants with with FGIDs were more likely to intake herbs to ease the symtpoms.

Introduction

Infant and toddler functional gastrointestinal disorders (FGIDs) comprise an array of age-dependent disorders that are characterized by the chronicity of symptoms and the lack of organic pathology. Due to children's inability to effectively communicate their symptoms, physicians must rely primarily on reports from parents as well as their own diagnostic experience. Although FGIDs do not impose any dangerous consequences, the lack of effective treatment can impose a burden on parents; therefore, any management should address both the child's symptoms and parental concerns [1]. Currently, the Rome IV criteria represents the cornerstone of diagnosis; modified in 2016, it includes 7 distinct disorders [1, 2]. However, the initial Rome criteria for FGIDs was created only for adults [3]. Rome II included the first description of childhood disorders; however, it was not until Rome III that childhood disorders were subdivided into infant and toddler vs. child and adolescent disorders, respectively [4–6].

In a systematic review of the available literature, the prevalence of FGIDs ranged from 27.1% to 38%, of which 20.8% had 2 concurrent disorders [7]. This demonstrates both the high occurrence of these illnesses and their effects on patients and healthcare services. It is clear that these illnesses can arise in a variety of combinations, notwithstanding their distinctions. They negatively affect an infant's quality of life, breastfeeding period, and drug prescriptions, particularly when the number of accompanying disorders increases [8]. Overall, they pose a serious challenge to gastrointestinal clinics because most of these illnesses are not effectively treated, leading to increased wasteful resource

use [9]. In addition to the burden that FGIDs inflict on families due to the unexplained symptoms experienced by children, they also cause maternal depression, infantile abuse, poor maternal bonding, and physical growth [10, 11]. Moreover, symptoms experienced by school-aged children result in poor social and physical functioning, school absence, psychological distress, and low quality of life [12].

Although many theories have been proposed to identify the underlying pathophysiological mechanisms involved in the emergence of functional disorders, some illnesses do not yet have a theoretical foundation [1]. Generally, FGIDs are characterized by multi-layered dysfunction in the gut–brain axis [13]. Pain is a complicated multifactorial symptom associated with functional diseases, in which impaired pain regulatory systems, sensory inputs into the central nervous system, and environmental and genetic predispositions result in increased vulnerability, with several pathological mechanisms involved [14]. In contrast to older children who can use pain scales as a quick and reliable way to express the severity of their discomfort, chronic pain in FGIDs in infants is particularly troublesome because there are no readily available equipment or practical methods to determine its presence [1].

Finally, prevalence studies for infant and toddler FGIDs are lacking, especially in Middle Eastern nations. This cross-sectional, non-interventional study aimed to estimate the prevalence of FGIDs in Jordanian infants using the Rome IV criteria. In addition, multiple associations were identified as potential predictors using regression that may play a role in the development and progression of FGIDs.

Aim

To identify the prevelance of FGIDs among Jordnian infants, and characterise any associated risk factors.

Material and methods

This was a cross-sectional study that included patients seeking medical attention at the neonatal follow-up clinic at King Abdullah University Hospital, a tertiary care facility in northern Jordan, between 1 January 2020, and 30 December 2020. Ethical approval was granted by the institutional review board and research committee of our institution, and written informed consent was obtained from the parents before data collection. Data were collected using the available medical records and the Rome IV diagnostic questionnaire for paediatric gastrointestinal disorders for neonates and toddlers aged < 3 years. The Rome foundation was contacted by E. A., and permission was obtained for the use of their questionnaire for research purposes. A research assistant then interviewed the patients' parents to obtain data about the gestational age, age, sex, antenatal history, and any parental gastrointestinal symptoms using an Arabic version of the parent report on GI symptoms, in which they were asked to choose specific symptoms from a predefined list. The Rome IV questionnaire was completed by the parents, and a trained research assistant was present to provide any required clarification. Corresponding data were retrieved from the medical records, including the patient's birth weight, pregnancy complications, pregnancy medications, mode of delivery, postpartum complications, neonatal jaundice, time of food introduction, neonatal intensive care unit (NICU) admission, NICU length of stay (LOS), cause of admission, treatment if any, and type of feed.

Patients who presented to the clinic with a diagnosis that could explain their complaint were excluded from the study along with any patient in whom physical examination, laboratory tests, or imaging modalities confirmed physical evidence of the symptoms. Prematurity was defined as a gestational age of fewer than 37 weeks.

Ethical approval and consent to participate

This cross-sectional study was conducted considering the regulations governing human research at the King Abdullah University Hospital. The institutional review board, as the responsible organizational party, issued ethical approval (number 20200102 [67/128/2019]).

Statistical analysis

Data were entered into an Excel spreadsheet, in which they were transformed into a format ready for analysis. Statistical analysis was performed using IBM SPSS Statistics for Windows version 26 (Armonk, NY, USA). Data are presented as frequency (percentage) for categorical variables and median (interquartile range) for continuous variables. Normality was assessed using the Shapiro-Wilk test. Categorical variables were compared using χ^2 or Fisher's exact test. Numerical variables were compared using Mann-Whitney *U* test, expect for the father's age which was the only normally distributed numerical variable hence independent *t*-test was used. Univariate logistic regression models were created to identify any risk factors that might play a role in the development of FGIDs. The presence of at least one FGID was given the value 1 for "having the disease", and 0 for "not having the disease". Furthermore, all FGIDs subtypes were considered as "having the disease", regardless.

Results

All 127 patients included in the study, were aged below 1 year, with a male predominance (61%). The median age was 40 days, and 88 children were aged below 3 months. Nearly one-half of the pregnancies were complicated and medications were administered during the pregnancy period. Caesarean section was dominant (69%) compared to normal vaginal delivery. Additionally, only 37.8% of the children were breastfed. The cohort of patients included was prominently premature, and of them, ICU-admitted children prevailed (63.8%), with a median NICU LOS of 7 days. Only 29 male patients underwent circumcision (Tables I and II).

Of the 127 infants, 82 (64.6%) met the Rome IV criteria for the diagnosis of FGIDs. Functional constipation (n = 78) was the most prevalent, followed by infant dyschezia (n = 11), and infant regurgitation (n = 3). Ten out of the 11 patients diagnosed with infant dyschezia had concomitant disorders. Rumination syndrome, cyclic vomiting, infant colic, and functional diarrhoea were not identified in any of the patients (Table III). The patients were divided into 2 groups: FGIDs (n = 82) and non-FGIDs (n = 45). Both groups were similar in terms of baseline characteristics and demographics, except for the NICU LOS (p = 0.024); patients in the FGIDs group had a longer LOS. Table I shows the baseline characteristics and patient demographics. No statistical difference was observed between gestational age, birth weight, breastfeeding, chronological age, duration of neonatal jaundice, or NICU admissions.

Parents' gastrointestinal complaints among the 2 groups were similar, with unremarkable differences (p = 0.360) when compared to total complaints. Despite the insignificance, parents of paediatric patients with FGIDs had a higher number of complaints (n = 46). Table IV illustrates the total number of complaints and subcategories of complaints in the 2 study groups. Table II demonstrates that herb intake was significantly higher in the FGIDs group (p = 0.007), which may be in response to the symptoms of FGIDs; hence, parents tried to resolve the symptoms using the administration of herbs. In addition, male patients who underwent circumcision had a higher prevalence of FGIDs (p = 0.016).

Table I. Demographics and baseline characteristics

Variable	Total (n = 127)	FGID (n = 82)	Non-FGID (n = 45)	P-value
Mother's age [years]	30.0 (8.0)	29.0 (9.0)	30.0 (7.0)	0.088
Father's age [years]	35.5 ± 5.7	35.3 ± 5.9	35.8 ± 5.4	0.468
Gestational age [weeks]	36.0 (4.0)	36.0 (5.0)	37.0 (4.0)	0.406
Chronological age [days]	40.0 (60.0)	45.0 (67.0)	37.0 (60.0)	0.422
Birth weight [kg]	2.7 (1.5)	2.8 (1.6)	2.7 (13.5)	0.815
Pregnancy complications	47 (37.0)	31 (37.8)	16 (35.6)	0.802
Pregnancy medications	54 (42.5)	31 (37.8)	23 (51.1)	0.147
Mode of delivery:				0.942
Caesarean section	88 (69.3)	57 (69.5)	31 (68.9)	
Normal vaginal	39 (30.7)	25 (30.5)	14 (31.1)	
Postpartum complications	12 (9.5)	8 (9.8)	4 (8.9)	0.572
Sex:				0.890
Male	78 (61.4)	50 (61.0)	28 (62.2)	
Female	49 (38.6)	32 (39.0)	17 (37.8)	
Breastfeeding	48 (37.8)	29 (35.4)	19 (42.2)	0.446
Feeding started [days of life]	2.0 (5.0)	3.0 (5.0)	2.0 (2.0)	0.125
Age at neonatal jaundice [days]	4.0 (3.0)	4.0 (4.0)	4.0 (3.0)	0.522
Duration of neonatal jaundice [days]	7.0 (8.0)	7.0 (11.0)	5.0 (5.0)	0.082
Time of food introduction [months]	5.0 (2.0)	5.0 (2.0)	5.0 (–)	0.450
NICU admission	81 (63.8)	54 (65.9)	27 (60.0)	0.512
NICU LOS [days]	7.0 (16.0)	7.5 (22.0)	5.0 (13.0)	0.024

Data presented as median (interquartile range), mean ± standard deviation, frequency (percentage), NICU – neonatal intensive care unit, LOS – length of stay.

Table II. Patient's parameters of the neonatal period

Variable	Total (*n* = 127)	FGID (*n* = 82)	Non-FGID (*n* = 45)	*P*-value
Antibiotics administration	72 (56.7)	47 (57.3)	25 (55.6)	0.743
Sepsis	2 (1.6)	1 (1.2)	1 (2.2)	0.547
Circumcision	29 (22.8)	24 (29.3)	5 (11.1)	0.016
Gastroenteritis	8 (6.3)	5 (6.1)	3 (6.7)	1.000
Pacifier use	70 (55.1)	40 (48.8)	30 (66.7)	0.053
Neonatal jaundice	74 (58.3)	43 (52.4)	31 (68.9)	0.072
Food intake	17 (13.4)	12 (14.6)	5 (11.1)	0.786
Drugs or vitamins intake	60 (47.2)	36 (43.9)	24 (53.3)	0.309
Herbs intake	63 (49.6)	48 (58.5)	15 (33.3)	0.007

Data presented as frequency (percentage).

Univariate analysis did not return NICU admission, LOS, pregnancy complications, antibiotics use, the timing of first feed, gastrointestinal parental complaints, breast feeding, and mode of delivery to be significantly associated with the development of FGIDs.

Nevertheless, univariate analysis showed that children with FGIDs were more likely (OR = 2.824; 95% CI: 1.321, 6.036, p = 0.001) to receive herbal medications compared to healthy children (Table V).

Discussion

To the best of our knowledge, this study is the first to estimate the prevalence of FGIDs in Jordan and one of the few in the Middle East. Of the children included in the study, at least 64% had one FGID and almost 12% had a concomitant FGID. The most commonly diagnosed disorder was functional constipation, followed by infant dyschezia in 11 patients, 10 of whom were diagnosed with functional constipation. Furthermore, it was apparent that children with FGIDs were more likely to consume herbs, which can be explained by the prevalent social beliefs encouraging the use of herbal remedies and traditional treatments before seeking medical attention. This practice is partially explained by the socioeconomic status of patients; according to a previous report, 40% of parents utilize complementary and alternative therapies to manage FGID symptoms [15]. However, there is not enough evidence to evaluate the effectiveness or efficacy of herbs and spices for the treatment of FGIDs, and despite their widespread use, only some evidence suggests the benefits of STW 5 and peppermint oil use [15].

Table III. Frequency of functional gastrointestinal disorders (FGIDs)

FGID	Frequency
Infant regurgitation (G1)	3
Rumination syndrome (G2)	0
Cyclic vomiting (G3)	0
Infant colic (G4)	0
Functional diarrhoea (G5)	0
Infant dyschezia (G6)[1]	11
Functional constipation (G7)	78

[1]*Ten patients had concomitant functional constipation (G7).*

According to the Rome criteria for diagnosis, FGIDs are a group of symptoms that have been recognized and categorized into respective disorders. These symptoms signify dysfunction at the level of the gut or central processing of incoming gut information [16]. FGIDs in infants and toddlers have been categorized into 7 major disorders: infant regurgitation, infant rumination syndrome, cyclic vomiting syndrome, infant colic, functional diarrhoea, infant dyschezia, and functional constipation [1]. Ferreira-Maia *et al.* systematically reviewed the literature and showed that the prevalence of FGIDs ranged from 27.1% to 38%, as opposed to the currently estimated prevalence of 64% in Jordanian infants. Only 12% of patients in our cohort had 2 concurrent illnesses, compared to the 20.8% reported in the literature [7].

In contrast to the results from a study by Ferreira-Maia *et al.*, who found functional constipation to be one of the most common FGIDs (ranging from less than 1% to 31%) along with infant regurgitation (ranging from less than 1% to 25.9%), we found functional constipation to be the most prevalent (95.1%), followed by infant dyschezia (13.4%) [7]. In contrast to our cohort, which only included infants up to 1 year of age and mostly under 3 months of age, the age categories included in the studies evaluated (up to 4 years) differed from those of our cohort. It is noteworthy that research using Rome II and III criteria were used in this systematic review. According to Huang *et al.*, the prevalence of FGIDs in Chinese children below the age of 4 years is 27.3%. The most prevalent FGID in children aged 0–6 months was infant

regurgitation, while in children aged 1–4 years the most prevalent FGID was functional constipation [17]. Similar results have been reported across a variety of geographic and ethnic groups [18–21]. It is well established that FGIDs can result from typical developmental processes such as infant regurgitation or from a maladaptive reaction to an internal or external stimulus [1]. This may account for the low frequency of infant regurgitation diagnoses in our study, because parents appeared to be more reticent in seeking medical attention.

Numerous risk factors for FGIDs have been identified, ranging from parental causes to neonatal, peri-

Table IV. Maternal and paternal gastrointestinal complaints

Variable	Total (*n* = 127)	FGID (*n* = 82)	Non-FGID (*n* = 45)	*P*-value
Combined GI parents' complaint	75 (59.1)	46 (56.1)	29 (64.4)	0.360
Chronic constipation:				–
Father	4 (3.1)	1 (1.2)	3 (6.7)	
Mother	10 (7.9)	8 (9.8)	2 (4.4)	
Heartburn:				–
Father	15 (11.8)	9 (11.0)	6 (13.3)	
Mother	15 (11.8)	10 (12.2)	5 (11.1)	
Both	9 (7.1)	3 (3.7)	6 (13.3)	
Epigastric pain:				–
Father	9 (7.1)	2 (2.4)	7 (15.6)	
Mother	9 (7.1)	5 (6.1)	4 (8.9)	
Abdominal distention:				–
Father	10 (7.9)	4 (4.9)	6 (13.3)	
Mother	12 (9.4)	8 (9.8)	4 (8.9)	
Both	1 (0.8)	1 (1.2)	–	
Vomiting:				–
Father	1 (0.8)	1 (1.2)	–	
Mother	2 (1.6)	–	2 (4.4)	
Migraine:				–
Father	3 (2.4)	3 (3.7)	–	
Mother	10 (7.9)	4 (4.9)	6 (13.3)	
Both	3 (2.4)	3 (3.7)	–	
Chronic diarrhoea:				–
Father	–	–	–	
Mother	1 (0.8)	1 (1.2)	–	
Recurrent abdominal pain:				–
Father	1 (0.8)	–	1 (2.2)	
Mother	4 (3.1)	1 (1.2)	3 (6.7)	
Food allergy:				–
Father	2 (1.6)	–	2 (4.4)	
Mother	1 (0.8)	1 (1.2)	–	
Both	1 (0.8)	1 (1.2)	–	
IBS:				–
Father	12 (9.4)	6 (7.3)	6 (13.3)	
Mother	18 (14.2)	15 (18.3)	3 (6.7)	

Data presented as frequency (percentage), IBS – irritable bowel syndrome, GI – gastrointestinal.

Table V. Univariate analysis as predictability model for FGIDs

Variable	OR (95% CI)	
	Univariate analysis	*P*-value
Prematurity	1.289 (0.619–2.666)	0.502
NICU length of stay	1.027 (0.995–1.059)	0.094
Pregnancy complications	1.102 (0.517–2.347)	0.802
Antibiotics	0.705 (0.172–2.896)	0.628
First feed time	1.027 (0.978–1.078)	0.281
GI parents' complaint	0.705 (0.333–1.493)	0.361
Herbs	2.824 (1.321–6.036)	0.007
Any breastfeeding	0.749 (0.355–1.577)	0.446
Mode of delivery	0.971 (0.442–2.133)	0.942
NICU admission	1.286 (0.607–2.725)	0.512

NICU – neonatal intensive care unit, GI – gastrointestinal, NA – not applicable.

natal, and environmental factors. In addition to the full spectrum of FGIDs, several other associations have been identified for given diseases. For example, neonatal antibiotics and immaturity have been linked to an increased incidence of FGIDs, notably infant colic and regurgitation. Moreover, according to Salvatore *et al.*, caesarean delivery and feeding practices increase the risk of infant dyschezia and functional diarrhoea [22]. According to the risk factor analysis by Huang *et al.*, children of educated mothers and those born underweight had a higher prevalence of infantile colic. In contrast, males who were exclusively breastfed for at least 4 months, resided in a rural region, and started formula feeding during the first month experienced infantile regurgitation more frequently. Nonetheless, vaginal delivery has been found to play a protective role against functional constipation [17]. Hvelplund *et al.* found that congenital abnormalities, female sex, prematurity, immigration status, maternal smoking during pregnancy, and being the firstborn child increased the risk of FGIDs [23]. Similarly, Turco *et al.* found that female sex and acetaminophen use increased the risk of functional constipation [24]. The 2 characteristics most frequently associated with the onset of gastrointestinal symptoms were low gestational age and birth weight [25]. Breastfed infants had a lower chance of regurgitation, with other factors including sex, ethnicity, prematurity, and birth weight insignificantly contributing to FGIDs [21]. Contrary to our findings that indicated that parental complaints had no discernible impact on the child's disease, the risk that the child would have hard stools was enhanced if the parent also experienced this symptom [26]. Despite the tremendous amount of work in this area, the literature remains scarce and contains abundant risk factors without any well-established associations.

As well as existing singularly, FGIDs also exist in combinations; Bellaiche *et al.* reported that 63% of infants with FGIDs had 2 disorders and 15% had 3 or more disorders [8]. In our study, infant dyschezia was associated with functional constipation in almost all cases. Gut dysbiosis has been linked to infantile colic, bloating, and delayed gut maturation, thus providing evidence of these symptoms' interconnection [27, 28]. However, to the best of our knowledge, no solid explanation for the pathophysiology of these combinations has been put forth. Noviello *et al.* reviewed their cohort with infantile dyschezia who underwent barium enema and found redundancy of the colon, which later resulted in constipation [29].

Our study has certain limitations. The sample size considered was small. The cohort of infants was collected from a single tertiary centre in northern Jordan; however, such chronic symptoms with no acute and emergent onset are more likely to cause patients' parents to approach primary health care physicians without the need of a specialty gastrointestinal clinic. Furthermore, the cohort of patients included those with previous medical issues and NICU admissions, and their visit represented a follow-up visit. The nature of the questionnaire renders it liable to the influence of recall bias.

Conclusions

Functional constipation was the most prevalent FGID in Jordan observed in this study; however, its prevalence in infants was different from that observed in the literature. Additionally, Jordanian infants with gastrointestinal symptoms were more likely to receive herbs before being seen by a gastroenterologist.

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Conflict of interest

The authors declare no conflict of interest.

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