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Frequency of Infant Colic: Cohort Study

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ABSTRACT

Background: Infantile colic (IC) is a common Functional Gastrointestinal Disorder (FGID) affecting infants, characterized by excessive crying and discomfort without an identifiable organic cause. It is hypothesized that gut microbiota imbalance (dysbiosis) plays a crucial role in its etiology. Various risk factors such as delivery method, type of feeding, maternal smoking, and antibiotic exposure may contribute to its occurrence.

Objective: our investigation aimed to estimate the frequency of infantile colic and investigate its association with potential risk factors linked to dysbiosis.

Methods: This was a cohort study involving 150 newborns admitted to October 6 University Hospital. Based on how they were delivered, infants were split into two distinct groups.: Group 1 (n=92) born via normal vaginal delivery (NVD) and Group 2 (n=58) born via cesarean section (CS). Data collection included demographic characteristics, maternal and neonatal risk factors, type of feeding, and colic frequency.

Results: Infantile colic was observed in 46.7% and 44.8% in the NVD and CS groups respectively, exhibiting no significant distinctions between the two delivery methods ($p>0.05$). Breastfeeding was negatively associated with increased risk of infantile colic, whereas formula and mixed feeding were linked to a higher prevalence ($p<0.001$). Maternal antibiotic use before delivery and maternal smoking were substantially associated with higher likelihood of colic ($p=0.044$ and $p=0.035$, respectively). Neonatal hospitalization also tended to be higher in colicky infants with no statistical significance.

Conclusion: The study suggests that infantile colic is prevalent among newborns regardless of the mode of delivery. However, factors including antibiotic use by mothers, smoking, and feeding type play a critical role in its development. Promoting exclusive breastfeeding and minimizing perinatal experiencing antibiotic in the perinatal period may help reduce the incidence of infantile colic.

Keywords: *Infantile colic, Dysbiosis, mode of delivery, Antibiotics, Maternal smoking.*

1. BACKGROUND

Infantile Colic (IC) is a frequent condition in early infant period that can have a serious negative impact on both the infants and the entire family (1). All over the globe, infantile colic prevalence ranges from 5 to 25% (2-3).

European surveys have also revealed that the majority of pediatricians rely on their diagnosis only on practical experience (4,5). The modified Wessel's criteria, which was set up for its applicability and viability in medical research, describes IC as crying and/or fussing for at least three hours per day, three days per week, for a duration of one week (6, 7). In medical settings, employing Rome IV criteria will assist to alleviate households enduring by offering quick and prompt assistance, guidance, and convenience to the caregivers of babies with colic (8).

The primary cause of IC is still unexplained despite an extensive amount of research; nevertheless, several conditions in the infant, including inadequate neurodevelopment, Gastrointestinal Tract (GIT) disorders, and the parents' psychological disorders, have been linked to IC (9, 10).

It is also known that systemic inflammation of low degree is linked to infantile colic, which is demonstrated by increased gut and systemic inflammatory indicators as well as aberrant gut flora composition (11,12).

A steadily increasing amount of research indicates that dysbiosis, i.e. an unbalanced gut microbiota, may potentially be a contributing factor. Other potential risk factors include being the first child, advanced maternal age, and having a history of maternal smoking. As other complex diseases that lack a clear etiopathogenesis, there is currently no gold standard treatment approach for IC. (9)

Important and widely recognized mechanical evidence includes the alteration of intestinal permeability caused by gut bacteria (13), gut microorganisms' modification of systemic and local inflammation (e.g., by adjusting T cell and neutrophil responses, as well as by activating Toll-like receptors and corresponding cytokines) (14,15), and alteration of intestinal maturity caused by gut microorganisms and their related byproducts (16,17). The purpose of this study was to estimate the frequency of infantile colic in correlation to risk factors of dysbiosis.

1. Methods

A cohort study was conducted involving 150 newborns presented to October 6 University Hospital, Egypt, from October 2023 to April 2024.

Newborns who are at high risk of dysbiosis including formula feeding, maternal smoking, maternal antibiotics one week before delivery, and neonatal intensive care unit (NICU) admission.

Preterm babies or any neonate with birth anomalies, chronic medical illness and/or surgical diseases were excluded. A consent is essential from the caregiver after thorough explanation of the research.

Data collection included demographic characteristics, maternal and neonatal risk factors, feeding type, medications, and frequency and severity of infantile colic using Wong-Baker face scale (18).

Medical data collected from all patients on three phases, phase I at birth: Personal data and complete history, phase II: at least two or three phone calls during the first two months of birth and phase III: clinic visit to do full examination at the age of 3 months (including anthropometric measurements). Confidentiality of data and the records were maintained.

Statistical analysis was implemented utilizing IBM SPSS version 25.0.

2. Results

There were 150 newborns presented to October 6 University Hospital. Two groups of infants were evolved depending upon their mode of delivery: Group 1 (n=92) born via normal vaginal delivery (NVD) and Group 2 (n=58) born via cesarean section (CS).

Table (1): Demographic data among the two groups studied at phase I.

		Group (1) NVD group (N= 92)		Group (2) CS group (N= 58)		Test value	P-value
		N	%	N	%		
Sex	**Male**	50	54.3%	28	48.3%	X^2= 0.525	0.469
	Female	42	45.7%	30	51.7%		
Residence	**Rural**	35	38.0%	21	36.2%	X^2= 0.051	0.821
	Urban	57	62.0%	37	63.8%		
GA (weeks)	**Mean± SD**	39.57± 0.52		38.24± 0.38		T= 16.05	**<0.001**
	Range	38.8 – 40.7		37.5 – 38.8			
Birth weight (Kg)	**Mean± SD**	3.65± 0.27		2.90± 0.23		T= 17.55	**<0.001**
	Range	3.24 – 4.29		2.53 – 3.22			

P value> 0.05 is not significant (NS), P value< 0.05 is significant (S), P value< 0.01 is highly significant (HS), SD: Standard deviation, GA: gestational age, X2: Chi- Square test, T: Student T test

Demographic data was mentioned in table 1. The NVD group's gestational age and birth weight were significantly higher than those of the CS group (p<0.001), although no statistically significant variance between the two groups in terms of sex or residence (p>0.05) [Table 1].

Table (2): Maternal risk factors among the two groups at phase I.

			Group (1) NVD group (N= 92)		Group (2) CS group (N= 58)		Chi- Square test	
			N	%	N	%	Test value (X^2)	P-value
Maternal Risk Factors	**Maternal antibiotics one week before delivery.**	No	88	95.7%	56	96.6%	0.075	>0.999[FET]
		Yes	4	4.3%	2	3.4%		
	Maternal smoking.	No	88	95.7%	54	93.1%	0.458	0.711[FET]
		Yes	4	4.3%	4	6.9%		
	NICU admission	No	87	94.6%	52	89.7%	1.262	**0.338**
		Yes	5	5.4%	6	10.3%		

NICU: neonatal intensive care unit, P value> 0.05 is not significant (NS), P value< 0.05 is significant (S), P value< 0.01 is highly significant (HS), X2: Chi- Square test, FET: Fischer Exact test

Regarding maternal smoking, NICU admission, and maternal antibiotics taken a week prior to delivery, there was no statistically significant difference between the NVD and CS groups (P > 0.05) [Table 2].

Table (3): Relation between mode of delivery with infantile colic and distension at phase II.

		Group (1) NVD group (N= 92)		Group (2) CS group (N= 58)		Test value	OR	95% CI	P-value
		N	%	N	%				
Infantile colics	Absent	49	53.3%	32	55.2%	X^2= 0.052	0.926	(0.479- 1.791)	0.819
	Present	43	46.7%	26	44.8%				
Distension	Absent	87	94.6%	53	91.4%	X^2= 0.580	1.642	(0.454- 5.938)	0.446
	Present	5	5.4%	5	8.6%				

P value> 0.05 is not significant (NS), P value< 0.05 is significant (S), P value< 0.01 is highly significant (HS),

X2: Chi- Square test, OR: Odds ratio

There was statistically significant distinction between NVD and CS groups regarding infantile colic and abdominal distension (p>0.05) [Table 3].

Table (4): Severity, medications used and age at onset of infantile colic among the two groups with infantile colic at phase II.

		NVD group with infantile colic (N= 43)		CS group with infantile colic (N= 26)		Test value	P-value
		N	%	N	%		
Severity of colic	**Mild**	13	30.2%	8	30.8%	X^2= 2.557	0.325[MC]
	Moderate	27	62.8%	13	50.0%		
	Severe	3	7.0%	5	19.2%		
Medication of colic	**Not received**	33	76.7%	20	76.9%	X^2= 0.001	0.986
	Received	10	23.3%	6	23.1%		
Age at first episode of colic (weeks)	**Mean± SD**	6.31± 1.33		5.99± 1.42		T= 0.946	0.347
	Range	3.7 – 9.1		4.2 – 9.1			

P value> 0.05 is not significant (NS), P value< 0.05 is significant (S), P value< 0.01 is highly significant (HS),

SD: Standard deviation, X^2: Chi- Square test, MC: Monte-Carlo correction

The mean age at first episode of colic was 6.31± 1.33 weeks and 5.99± 1.42 weeks in NVD and CS groups respectively with no statistically significant difference. The NVD and CS groups did not statistically differ in terms of severity of colic and, medications received [Table 4].

Table (5): Anthropometric measurements among the two groups at phase III.

		Group (1) NVD group (N= 92)	Group (2) CS group (N= 58)	Test value	P-value
Weight (Kg)	Mean± SD	5.18± 0.30	4.46± 0.18	T= 18.76	<0.001
	Range	4.7 – 5.9	4.10 – 4.70		
Length (cm)	Mean± SD	53.36± 0.86	51.60± 0.49	T= 16.04	<0.001
	Range	52.0 – 51.6	51.0 – 52.0		
Head circumference (cm)	Mean± SD	37.07± 0.46	37.07± 0.45	Z_{MWU} = 0.043	0.966
	Median (IQR)	37.0 (37- 38)	37.0 (37- 38)		
	Range	36.0 – 38.0	36.0 – 38.0		

P value> 0.05 is not significant (NS), P value< 0.05 is significant (S), P value< 0.01 is highly significant (HS), SD: Standard deviation, IQR: Interquartile range, T: Student T test, ZMWU: Mann Whitney U test

Weight and length were significantly higher in NVD group compared to CS group (p<0.001) while, there was no discernible difference in the two groups' head circumferences (p>0.05) [Table 5].

Table (6): Relation between infantile colic and different categorical parameters in NVD group.

		NVD group (N=92)				Chi- Square test	
		No infantile colics (N= 49)		Infantile colics (N= 43)		Test value	P-value
		N	%	N	%		
Sex	**Male**	26	53.1%	24	55.8%	0.070	0.791
	Female	23	46.9%	19	44.2%		
Residence	**Rural**	19	38.8%	16	37.2%	0.024	0.877
	Urban	30	61.2%	27	62.8%		
Maternal antibiotics before one week of delivery.	**No**	49	100.0%	39	90.7%	4.765	0.044^{FET}
	Yes	0	0.0%	4	9.3%		
Maternal smoking.	**No**	49	100.0%	39	90.7%	4.765	0.044^{FET}
	Yes	0	0.0%	4	9.3%		
NICU admission	**No**	48	98.0%	39	90.7%	2.350	0.181^{FET}
	Yes	1	2.0%	4	9.3%		
Type of feeding	**Breast feeding**	26	53.1%	5	11.6%	17.6	<0.001
	Formula	14	28.6%	23	53.5%		
	Mixed	9	18.4%	15	34.9%		

NICU: neonatal intensive care unit, P value> 0.05 is not significant (NS), P value< 0.05 is significant (S), P value< 0.01 is highly significant (HS),X2: Chi- Square test, FET: Fischer Exact Test

In NVD group, maternal antibiotics one week before delivery and maternal smoking had significantly higher rates in cases with infantile colic than cases without (p=0.044). In addition, infantile colic was significantly higher in infants fed by formula and mixed feeding than breastfed infants (p<0.001). Sex, residence, and neonatal hospitalization did not significantly differ between cases with and without infantile colic in the NVD group. (p>0.05) [Table 6].

Table (7): Relation between infantile colic and different categorical parameters in CS group.

		CS group (N= 58)				Chi- Square test	
		No infantile colic (N= 32)		Infantile colic (N= 26)		Test value	P-value
		N	%	N	%		
Sex	**Male**	15	46.9%	13	50.0%	0.056	0.813
	Female	17	53.1%	13	50.0%		
Residence	**Rural**	14	43.8%	7	26.9%	1.758	0.185
	Urban	18	56.3%	19	73.1%		
Maternal antibiotics before one week of delivery.	**No**	32	100.0%	24	92.3%	2.549	0.197^{FET}
	Yes	0	0.0%	2	7.7%		
Maternal smoking.	**No**	32	100.0%	22	84.6%	5.288	0.035^{FET}
	Yes	0	0.0%	4	15.4%		
NICU admission	**No**	31	96.9%	21	80.8%	4.012	0.080
	Yes	1	3.1%	5	19.2%		
Type of feeding	**Breast feeding**	18	56.3%	7	26.9%	5.473	0.065
	Formula	9	28.1%	10	38.5%		
	Mixed	5	15.6%	9	34.6%		

NICU: neonatal intensive care unit, P value> 0.05 is not significant (NS), P value< 0.05 is significant (S), P value< 0.01 is highly significant (HS), X^2: Chi- Square test, FET: Fischer Exact Test

In CS group, maternal smoking had significantly higher rates in cases with infantile colic than cases without (p=0.035). Neonatal hospitalization and formula feeding tend to be higher in cases with infantile colic than in cases without, but they did not reach the significant level. No statistically significant difference between cases with and without infantile colic in CS group regarding sex, residence, maternal antibiotics before one week of delivery and neonatal hospitalization (p>0.05) [Table 7].

Table (8): Logistic regression analysis for factors predicting infantile colic

Parameters	Univariate				Multivariate			
	P-value	Odds ratio (OR)	95%CI		P-value	Odds ratio (OR)	95%CI	
			Lower limit	Upper limit			Lower limit	Upper limit
Gestational age	0.354	1.211	0.808	1.815				
Sex (male)	0.713	0.886	0.466	1.686				
Birth weight	0.386	1.379	0.667	2.851				
Mode of delivery	0.819	0.926	0.479	1.791				
Maternal antibiotics before one week of delivery	<0.001	4.018	1.879	8.592	0.043	2.287	1.026	5.099
Maternal smoking	0.043	2.287	1.026	5.099	0.305	2.386	0.453	12.560
Neonatal hospitalization	0.026	5.925	1.235	28.437	0.144	3.281	0.667	16.137
Type of feeding (Breast feeding)	<0.001	0.177	0.083	0.379	<0.001	0.199	0.092	0.431
Weight	0.399	1.373	0.658	2.865				
Length	0.375	1.139	0.854	1.518				
Head circumference	0.120	1.784	0.861	3.695				

B: Regression coefficient; S.E.: Standard error,, CI: Confidence interval

Univariate analysis revealed a positive correlation between increased risk of infantile colic and maternal smoking, maternal antibiotics one week before delivery, and neonatal hospitalization while breast feeding was negatively associated with increased risk of infantile colic. In multivariate analysis, it was found that maternal antibiotics one week before delivery and breast feeding were independent predictors for infantile colic [Table 8].

3. DISCUSSION

Our study aimed to estimate the frequency of infant colic in relation to risk factors of dysbiosis.

In this study, we found that 46 % of infants develop IC. This rate is consistent with the majority of reports from both industrialized and developing nations. (2,19-21). Variations in the definition of colic, study design, data collection technique, and population size could all contribute to the disparity in incidence rates (2).

Current study showed no difference in the gender distribution of colic presentation between the NVD and CS groups. This is in accordance with other studies (2, 22-24) who found that males and females have equal incidence of infantile colic presentation.

According to our research, infantile colic is not related to the mode of delivery. This is in line with research done by Savino et al., 2007 (25) and Fazil (26). This may be explained by difference in number of pregnant women exposed to CS from country to another.

There is a strong correlation between age and colic, and it has been proposed that the majority of infants who visited clinics were during the first six weeks of life (9, 21, 27). This supports our findings as most of them were presented in the first 6 weeks of age in both NVD and CS groups.

The number of infants who received medications for IC in both NVD and CS were 10 (23.3%) and 6 (23.1%) respectively. Reduced family life excellence, the extended periods of crying bouts, and parental dissatisfaction were the first three indicators that had the biggest impact on beginning therapy (27). Most physicians prescribed medical therapies, and their preference for a particular treatment was primarily determined by their prior experience with treatment outcomes (5, 28).

Cases with infantile colic were significantly higher in cases fed by formula and mixed feeding. There are numerous studies that support this (29-31). The diversity of infant microbiota is significantly influenced by the feeding method (32-33). The mother's diet has an impact on the infant's fecal microbiota as well and the microorganisms in her milk, though usually to a minor degree (34-36).

On the contrary, various studies revealed that exclusive breastfeeding had no protective effect on the development of colic

(19, 37). This category pertains to the "maternal diet" during breastfeeding, which was examined in two studies (38-39). Protein consumption was found to have a protective effect on infantile colic (40).

In both NVD and CS groups, maternal smoking had significantly higher rates in cases with infantile colic. Among infants of smoking mothers, the prevalence of colic was two-fold higher (37, 41). Recent research has shown that maternal smoking alters the microbiota of the infant (42).

In the NVD group, maternal antibiotics one week before delivery had significantly higher rates in cases with IC which agrees with a report by Azad et al 2016 (43) and Coker et al 2020 (44). The kind and length of antibiotics taken during pregnancy alter the bacterial composition of the amniotic fluid and vagina, which may have an impact on the baby's microbiological makeup at birth (45).

Neonatal hospitalization tends to be higher in cases with infantile colic. Antibiotics administered for a short period of time (≤3 days) decreased the number of bifidobacteria in the newborns' guts from the time of therapy until the third week following delivery (46). The amount of bifidobacteria remained low until the sixth postnatal week after a lengthy therapy (≥5 days). Despite the initial compositional abnormalities, the gut microbiota of children who were given only short-term antibiotics was similar to that of healthy babies which subsequently recovered. In summary, the length of time spent on antibiotics was the primary cause of the microbiota alteration (47-49).

Our study strength is that we investigated our cases in 3 phases. Our study had three limitations, firstly, this was a single-center study, a larger study, include numerous infants from different areas, is recommended for recognition of the prevalence and the risk factors for infantile colic in Egypt. Secondly, the therapeutic and diagnostic methods used by pediatricians in IC, as well as their assessments of treatment response. Future research must concentrate on examining the adequacy of diagnostic criteria for these widely used treatments through head-to-head trials. Thirdly, we did not study the efficacy of mothers' diet on infantile colic. We recommend taking full maternal nutritional history and follow up a nutritional plan and its effect on infantile colic.

4. CONCLUSION

Infantile colic is common among newborns, irrespective of the mode of delivery. Antibiotics for mothers one week prior to delivery and maternal smoking had significantly higher rates in cases with infantile colic. Antibiotics for mothers one week prior to delivery and breast feeding were independent predictors for infantile colic.

5. LIST OF ABBREVIATIONS

CS: cesarean section

FGID: functional gastrointestinal disorders

GIT: gastrointestinal tract

IC: infantile colic

NICU: neonatal intensive care unit

NVD: normal vaginal delivery

6. Acknowledgements

The authors are grateful to the patients and their parents.

7. Authors' contributions:

Eman Sharaf, Manar Aref and Sarah Abdelrashid were involved with study concepts and design. Samir Mohamed was involved with patients' inclusion and data collection. Manar Aref, Samir Mohamed analyzed the data and performed data interpretation and tables' design. Sarah Abdelrashid wrote the manuscript. Eman Sharaf revised the manuscript. All authors reviewed and took full responsibility for the final version of the manuscript.

8. DECLARATIONS

9.

Ethics approval and consent to participate

This study was approved by research ethical committee October 6 University (REC-O6U), Egypt. Prior to enrollment, patients' guardians granted informed consent after being apprised of the study's purpose.

Consent for publication

Not applicable.

Data Availability

The datasets analyzed in this study are available from the corresponding author upon reasonable request.

Competing interests
The authors declare no competing interests.

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