

Symptom Co-Occurrence Patterns in Healthy Infants: Assessing the Interplay Between Feeding Modalities and CoMiSS™ Profiles

Irfiani Nurrachmawati*, Rachel Gracia**, Badriul Hegar***, Yvan Vandenplas****

*Faculty of Medicine, Syarif Hidayatullah Jakarta Islamic State University, Banten, Indonesia

**Faculty of Medicine, Christian University of Indonesia, Jakarta, Indonesia

***Department of Health, Faculty of Medicine, Universitas Indonesia

****KidZ Health Castle, UZ Brussel, Vrije Universiteit Brussel, Brussels, Belgium

Corresponding Author:

Irfiani Nurrachmawati. Syarif Hidayatullah Jakarta Islamic State University, Jl. Ir. H. Juanda No. 95, Ciputat, Banten, Indonesia. Phone: +62-21-7401925. Email: irfiani18@gmail.com

ABSTRACT

Background: Breast milk is the optimal source of infant nutrition, with formula feeding serving as an alternative when exclusive breastfeeding is not feasible. Feeding modalities may influence behavioral (crying), gastrointestinal (stool consistency), and dermatological manifestations. However, population-based comparative data in Indonesia remain scarce. Therefore, this study aimed to evaluate and compare the prevalence and patterns of symptoms between exclusively and non-exclusively breastfed infants.

Methods: An analytical cross-sectional study was conducted at an outpatient clinic in Tangerang, Indonesia, utilizing structured parental interviews and clinical evaluations. A total of 290 healthy participants aged 0–12 months were enrolled, including 260 exclusively and 30 non-exclusively breastfed infants. Symptom severity over the preceding week was assessed using the standardized Cow's Milk-related Symptom Score (CoMiSS™) framework, while chi-square and Fisher's Exact Tests were used to analyze symptom prevalence and co-occurrence patterns.

Results: No significant differences were observed between the exclusively and non-exclusively breastfed groups in terms of abnormal stool consistency (8.5% vs. 10.0%), increased crying duration (5.4% vs. 3.3%), or skin rashes (41.2% vs. 40.0%). There was no co-occurring symptom between stool consistency and crying in either group. No infant showed concurrent gastrointestinal and behavioral symptoms, with or without dermatological symptoms. Skin rashes were highly prevalent across the sample (~41%), but had no statistical association with gastrointestinal or behavioral manifestations.

Conclusion: Feeding methods do not influence the clinical patterns of common infantile symptoms. Furthermore, stool abnormalities and excessive crying present as distinct entities rather than a unified cluster, offering reassurance to clinicians and parents managing these benign variations.

Keywords: Crying, Exclusively breastfed, Feeding methods, Infant, Exanthem, Feces

ABSTRAK

Latar Belakang: ASI merupakan sumber nutrisi optimal bagi bayi; namun, ketika menyusui eksklusif tidak memungkinkan, susu formula menjadi alternatif yang diperlukan. Pola pemberian makan dapat memengaruhi manifestasi perilaku (menangis), saluran cerna (konsistensi feses), dan dermatologi, tetapi data perbandingan berbasis populasi di Indonesia masih terbatas. Penelitian ini bertujuan mengevaluasi dan membandingkan prevalensi serta pola gejala tersebut antara bayi yang mendapat menyusui eksklusif dan tidak eksklusif.

Metode: Penelitian potong lintang analitik dilakukan di klinik rawat jalan di Tangerang, Indonesia, menggunakan wawancara terstruktur dengan orang tua dan evaluasi klinis. Sebanyak 290 bayi sehat usia 0–12 bulan (260 menyusui eksklusif; 30 tidak eksklusif) dilibatkan. Keparahan gejala selama satu minggu terakhir dinilai menggunakan panduan skor standar Cow's Milk-related Symptom Score (CoMiSS™). Uji Chi-square dan Fisher's Exact digunakan untuk menganalisis prevalensi dan pola kemunculan bersamaan gejala.

Hasil: Tidak ditemukan perbedaan bermakna antara kedua kelompok pada konsistensi tinja abnormal (8,5% vs 10,0%, $p = 0,732$), peningkatan frekuensi menangis (5,4% vs 3,3%, $p = 1,000$), maupun ruam kulit (41,2% vs 40,0%, $p = 1,000$). Tidak terdapat kemunculan yang bersamaan antara konsistensi tinja dan frekuensi menangis pada kedua kelompok, serta tidak ada bayi yang menunjukkan kombinasi keduanya, baik dengan maupun tanpa ruam kulit. Ruam kulit cukup sering ditemukan (~41%), namun tidak berhubungan dengan gejala saluran cerna maupun perilaku.

Kesimpulan: Metode pemberian makan tidak berpengaruh signifikan terhadap pola gejala. Abnormalitas tinja dan tangisan berlebihan tampak sebagai entitas yang berbeda, bukan bagian dari satu kelompok gejala yang sama, sehingga dapat memberikan rasa tenang bagi klinisi dan orangtua.

Kata kunci: ASI eksklusif, Bayi, Konsistensi tinja, Metode pemberian makan, Ruam kulit, Tangisan

INTRODUCTION

Infant feeding practices, particularly exclusively and non-exclusively breastfeeding, are a subject of extensive study due to the significant implications for early development. Breast milk is widely recognized as the optimal source of nutrition for infants, containing a complex matrix of bioactive compounds. These include immunoglobulins and prebiotics that modulate immune system development and gastrointestinal maturation.^{1,2} However, various factors can necessitate non-exclusive breastfeeding, namely maternal medical contraindications, perceived insufficient milk supply, early return to work, anatomical challenges (infant conditions such as cleft palate), and sociocultural preferences.³ Despite the well-established benefits of exclusively breastfeeding for promoting long-term health and reducing infectious morbidity, its relationship with common, non-severe functional symptoms, such as variation in stool consistency, daily crying duration, and skin rashes remains incompletely understood.

Gastrointestinal symptoms, particularly variations in stool consistency, represent a primary source of parental concerns during early infancy. Exclusively breastfed infants typically show distinct patterns characterized by softer, more frequent, and looser stools compared to their non-exclusively breastfed counterparts.⁴ In Indonesia, infantile gastrointestinal symptoms are highly prevalent. For instance,

regurgitation has been documented in up to 77% of infants under three months of age, emphasizing the burden of these conditions in the local population.⁵ Concurrently, excessive crying affects approximately one in five infants during the first three months of life, serving as a major driver of parental anxiety and healthcare utilization.⁶ The etiology of excessive crying is multifactorial, comprising gastrointestinal disturbances (e.g., gastroesophageal reflux, cow's milk protein allergy, or immature gut motility), neurological factors related to temperament, and psychosocial dynamics.^{7,8} Feeding modalities are hypothesized to influence crying patterns through mechanisms such as differential gastrointestinal transit time, variations in gut microbiota composition affecting the gut-brain axis, and early exposure to potentially allergenic dietary proteins.

Dermatological manifestations, particularly atopic dermatitis, affect approximately 15-30% of children, with onset frequently occurring during the first six months of life.^{9,10} The concurrent presentation of gastrointestinal, behavioral, and dermatological symptoms during early infancy has received limited systematic attention. This persists despite evidence that these symptoms frequently co-occur and may be driven by common underlying mechanisms, including immature barrier function, altered microbiota colonization, and early allergic sensitization.

Given the increasing recognition of the gut-skin

axis and the role of the gut microbiota in modulating systemic health, exploring symptom co-occurrence patterns may help generate hypotheses regarding shared pathophysiological mechanisms. Therefore, this study aimed to evaluate the prevalence and pattern of stool consistency, total crying duration, and skin rashes among exclusively versus non-exclusively breastfed infants. The relationship among these symptoms within each feeding group was also investigated. The results are expected to give valuable insights into underlying etiologies, thereby establishing evidence-based clinical guidance to assist healthcare providers in counseling anxious parents and distinguishing benign functional variations from pathological presentations.

METHODS

Study Design and Setting

An analytical cross-sectional study was conducted at the outpatient clinic of Premier Bintaro, a secondary referral hospital in Indonesia, from September 2022 to September 2023.

Participants and Sampling Strategy

The population comprised parents of infants aged 0–12 months visiting the outpatient clinic during the study period. A convenience sampling strategy with consecutive enrollment was adopted. All eligible infants were recruited sequentially until the final sample size (n=290) was reached.

1. **Inclusion Criteria:** Infants aged 0–12 months, either exclusively or non-exclusively breastfed, written informed consent from parents, and full completion of the study questionnaire.
2. **Exclusion Criteria:** Infants with congenital abnormalities, which include major structural abnormalities identified at birth or prenatally, and suspected or confirmed chromosomal abnormalities or genetic disorders. The criteria also included visible chronic diseases that could affect growth, dietary habits, or overall health, acute illness at the time of examination, or current treatment with medication for an existing medical condition. Before enrollment, all parents received a detailed explanation regarding the study objectives, procedures, and the rights to voluntary participation and withdrawal.

Data Collection

Clinical data and symptoms were documented through physician-led evaluations and structured parental interviews, utilizing the validated Cow's Milk-related Symptom Score (CoMiSS) framework to ensure objectivity and uniformity. In addition to infant demographics, the collected data comprised feeding methods, complementary feeding practices, and specific clinical symptoms, including daily crying duration, stool consistency, and skin rash over the preceding week.

To reflect clinically and developmentally distinct periods during the first year of life, infants were categorized into three age groups:

- 0–4 months: The period captures the peak period for infantile colic presentation, aligning with the Rome IV criteria (birth to 4–5 months).
- 4–8 months: The period corresponds to the introductory phase of complementary foods, which typically influences gastrointestinal function, stool patterns, crying behavior, and skin symptoms.
- 8–12 months: The period represents an established phase of complementary feeding and developmental maturation.

This age categorization is in line with observed age-related shifts in CoMiSS™. For the primary analysis, infants were also stratified by feeding type into two groups, such as exclusively and non-exclusively breastfed.

Application of The CoMiSS™ Tool and Symptom Classification

Symptoms were evaluated using selected domains of the Cow's Milk-related Symptom Score (CoMiSS™) questionnaire. This is a validated clinical tool designed to raise awareness of cow's milk protein allergy (CMPA). Since the study aimed to compare the prevalence of individual symptoms rather than to predict the overall likelihood of CMPA, only the domains corresponding to the primary outcomes of interest were utilized, and the total cumulative CoMiSS™ score was not calculated.

Crying Classification

Average daily crying duration over the preceding week was reported by parents and scored based on standard CoMiSS™ criteria of ≤ 1.5 , 1.5–2, and >2 hours/day. For analytical purposes, "increased crying" was defined dichotomously as a duration of more than 2 hours per day, which corresponds with the highest severity score within this domain.

Stool Consistency Classification

Stool consistency over the preceding week was classified into five standard CoMiSS™ types such as formed, soft, watery, hard, or mucous. For the final analysis, stool patterns were dichotomized into normal (formed and soft) and abnormal (watery and hard) categories, in line with standard pediatric practice.

Skin Rash Classification

Skin rash severity was assessed using the CoMiSS™ skin symptoms domain. Parents evaluated the presence and severity of atopic eczema across two distinct body regions, such as (1) head, neck, and trunk, as well as (2) extremities. Each region was scored on a scale from 0 to 3, where 0, 1, 2, and 3 signified absent, mild, moderate, and severe, respectively. A total symptom score was calculated by summing the scores of both regions (range 0–6), with higher values reflecting greater clinical severity.

Complementary Feeding Data

Data on complementary feeding practices were collected and utilized strictly for descriptive purposes. Due to the limited sample size within certain strata, complementary feeding was not adjusted for as a confounding variable in the primary comparative analyses.

Data Management

To protect participant confidentiality, all collected data were completely anonymized upon entry. The data were then stored securely in a password-protected electronic database accessible only to the study team.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (Version 29.0.2.0). Descriptive statistics

were used to summarize frequency distributions and cross-tabulations. To evaluate the relationship among the clinical symptoms of abnormal stool consistency, increased crying duration, and skin rash, the data were stratified according to feeding group. Within each stratum, associations between categorical variables were analyzed using the Chi-square test. Fisher's Exact Test was applied when expected cell counts fell below 5. Finally, statistical significance was defined as a p-value less than 0.05.

Ethical Considerations

This study analyzed a specific geographic subset of data comprising Indonesian infants, derived from a larger, international multicenter project titled *'Difference in Cow Milk-Related Symptoms Score'*, in which co-authors (BH) and (YV) participated. The dataset analyzed in the current study was strictly distinct from the data reported in the primary multicenter investigation, representing an independent secondary analysis. Ethical approval for the overarching multicenter investigation was officially granted by the Ethics Committee of UZ Brussel (Approval No. EC: 2017/012).

RESULTS

Participant Characteristics and Demographic Profile

A total of 290 infants aged 0 to 12 months were enrolled in this study, consisting of 260 exclusively (89.7%) and 30 non-exclusively breastfed infants (10.3%) (**Table 1**). Among infants aged 0–4 months, which was the youngest cohort, 152 (97.4%) and 4 (2.6%) were exclusively and non-exclusively breastfed, respectively. Similarly, in the 4–8 months age group, exclusive breastfeeding remained the predominant feeding method, practiced by 71 infants (91.0%) compared to 7 (9.0%).

Table 1. Characteristic of Study Population

Characteristic	Exclusively Breastfed n=260	Non-Exclusively Breastfed n=30	Total, n=290
Age Group (months)			
0-4	152 (97.4%)	4 (2.6%)	156 (100.0%)
4-8	71 (91.0%)	7 (9.0%)	78 (100.0%)
8-12	37 (66.1%)	19 (33.9%)	56 (100.0%)
Sex			
Male	133 (90.5%)	14 (9.5%)	147 (100.0%)
Female	127 (88.8%)	16 (11.2%)	143 (100.0%)
Complimentary Feeding			
Yes	65 (75.6%)	21 (24.4%)	86 (100.0%)
No	195 (95.6%)	9 (4.4%)	204 (100.0%)

The overall study population showed a balanced sex distribution (50.7% male and 49.3% female), with comparable proportions observed across both feeding categories. Complementary feeding had been introduced to 86 infants (29.7%) at the time of the study. Within the subset, the distribution of complementary feeding expectedly increased in line with the advancement of the infants' age group. This corresponded with the operational distribution of feeding practices across the categories.

Symptom Pattern Among Exclusively and Non-Exclusively Breastfed Infants

The distribution and clinical patterns of individual symptoms, comprising stool consistency, crying duration, and skin rash among exclusively and non-exclusively breastfed infants are presented in Figures 1 and 2, respectively. Both feeding groups featured broadly similar symptom trends, with minor variations observed across the different age categories.

As shown in **Figure 1**, formed stools represented the predominant stool consistency across all age categories, accounting for 91.0% of exclusively breastfed infants. Hard stools (7.0%) were primarily observed within the 4–8 months age group, while watery stools (1.0%) were reported in the youngest age group of 0–4 months.

In terms of crying behavior, the vast majority of exclusively breastfed infants showed standard patterns. Duration of less than 1.5 hours per day was the most prevalent classification at 51.0%. Across the entire feeding group, a small subset showed higher tiers. Specifically, 20 infants had a crying duration exceeding 1.5 hours per day, within which 14 met the strict CoMiSS™ threshold for "increased crying".

Dermatological evaluations showed that most exclusively breastfed infants presented with normal skin conditions (58.0%). Rashes were most frequently documented in the younger 0–4 months age group and showed a clear age-dependent decline, occurring less frequently as the infants aged.

As presented in **Figure 2**, non-exclusively breastfed infants showed a clinical symptom pattern broadly comparable to the exclusively breastfed group. Formed stools remained the predominant classification across all age categories. It accounted for 90.0% of the infants in the group, with no documented cases of watery stools. Based on observation, hard stools were reported in 10.0% of the sample.

In terms of crying profiles, the vast majority of non-exclusively breastfed infants showed standard durations, with 96.0% crying for less than 1.5 hours per day. Only a small subset (3.0%) met the criteria for increased daily crying, presenting with frequent durations of 2–3 hours per day. Dermatological evaluations showed that a normal skin condition predominated across every age category (60.0%). However, contrary to the exclusively breastfed group, skin rashes were most frequently observed within the older 8–12 months age group.

Infants in both feeding groups predominantly presented with normal stool consistency, standard crying durations, and an absence of skin rashes. However, subtle variations were observed between the two categories. Non-exclusively breastfed infants showed a slightly higher proportion of hard stools, while exclusively breastfed infants presented with occasional watery stools that were strictly limited to the youngest age group (0–4 months). Additionally, the chronological distribution of skin rashes differed between the groups. Dermatological manifestations occurred earlier among exclusively breastfed infants, while a later onset was observed within the non-exclusively breastfed group.

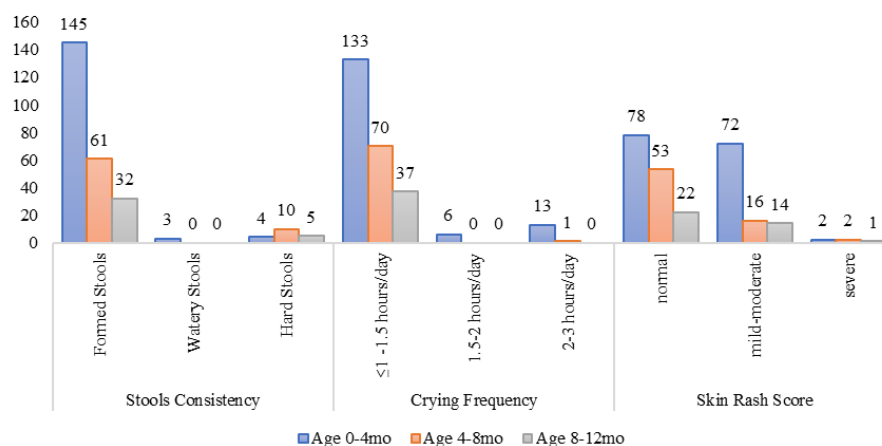


Figure 1. Symptom Pattern in Exclusively Breastfed Infant

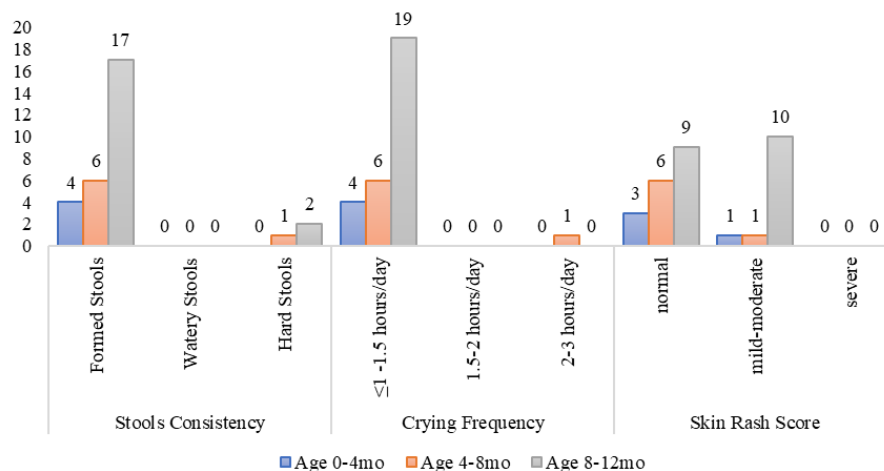


Figure 2. Symptom Pattern in Non-Exclusively Breastfed Infant

Table 2. Age-Stratified Symptom Comparison

Age Group	Symptoms	Exclusively Breastfed n=260	Non-Exclusively Breastfed n=30	P-value
0-4 months n=156	Abnormal Stool Consistency	7 (4.6%)	0 (0.0%)	1.000
	Increased Total crying duration	13 (8.5%)	0 (0.0%)	1.000
	Skin Rash	74 (48.6%)	1 (25.0%)	0.621
4-8 months n=78	Abnormal Stool Consistency	1 (1.4%)	1 (14.2%)	1.000
	Increased Total crying duration	1 (5.4%)	1 (14.2%)	0.172
	Skin Rash	18 (25.3%)	1 (14.2%)	1.000
8-12 months n=56	Abnormal Stool Consistency	5 (8.5%)	2 (10.0%)	1.000
	Increased Total crying duration	0 (0.0%)	0 (0.0%)	1.000
	Skin Rash	15 (40.5%)	10 (52.6%)	0.411

Note: p-value from Fisher's Exact Test (two-sided). Some cells had expected counts less than 5; results should be interpreted with caution.

Table 3. Prevalence of Symptoms by Feeding Methods

Symptoms	Exclusively Breastfed n=260	Non-Exclusively Breastfed n=30	95% CI	P-value
Abnormal Stool Consistency	22 (8.5%)	3 (10.0%)	(-10.2% to 7.2%)	0.732
Increased Total crying duration	14 (5.4%)	1 (3.3%)	(-4.5% to 8.7%)	1.000
Skin Rash	107 (41.2%)	12 (40.0%)	(-16.3% to 18.7%)	1.000

*Note: Fisher's Exact Test (two-sided).

An age-stratified analysis of symptom prevalence across the feeding groups is presented in **Table 2**. Within the youngest age range of 0–4 months, no statistically significant differences were observed between the exclusively and non-exclusively breastfed infants for any evaluated symptom such as abnormal stool consistency (4.6% vs. 0.0%, $p=1.000$), increased crying duration (8.5% vs. 0.0%, $p=1.000$), and skin rash (48.6% vs. 25.0%, $p=0.621$). Similarly, no significant disparities were detected for any of the clinical symptoms within the 4–8 months age category.

In the oldest age group of 8–12 months, non-exclusively breastfed infants presented with a higher descriptive prevalence of both skin rashes (52.6% vs. 40.5%) and abnormal stool consistency (10.0% vs. 8.5%) compared to exclusively breastfed infants.

These differences did not reach statistical significance at $p=0.411$ and $p=1.000$, respectively.

Comparison of Symptom Prevalence Between Exclusively and Non-Exclusively Breastfed Infants

The prevalence of gastrointestinal, behavioral, and dermatological symptoms between the two feeding methods was compared by analyzing 260 exclusively breastfed and 30 non-exclusively breastfed infants. No significant differences were observed between the feeding groups for any of the three evaluated symptoms, as detailed in **Table 3**.

An age-stratified analysis of symptom prevalence across the feeding groups is presented in **Table 2**. Within the youngest age range of 0–4 months, no statistically significant differences were observed

between the exclusively and non-exclusively breastfed infants for any evaluated symptom such as abnormal stool consistency (4.6% vs. 0.0%, $p = 1.000$), increased crying duration (8.5% vs. 0.0%, $p = 1.000$), and skin rash (48.6% vs. 25.0%, $p = 0.621$). Similarly, no significant differences were detected for any of the clinical symptoms within the 4-8 months age category. In the 8-12 months age category, non-exclusively breastfed infants presented with higher descriptive prevalence of both skin rash (52.6% vs. 40.5%) and abnormal stool consistency (10.0% vs. 8.5%). However, the differences did not reach statistical significance at $p = 0.411$ and $p = 1.000$, respectively.

Co-Occurrence of Symptoms Among Exclusively and Non-Exclusively Breastfed Infants

To examine the co-occurrence of gastrointestinal (abnormal stool consistency), behavioral (increased total crying duration), and dermatological (skin rash) symptoms, analyses were stratified by exclusively breastfed ($n = 260$) and non-exclusively breastfed ($n = 30$). Utilizing Chi-square and Fisher's Exact, no significant association in symptom co-occurrence was observed between any symptom pair within either group (all $p > 0.05$; **Table 4**). There was no infant in

either feeding category that concurrently presented with both abnormal stool consistency and increased total crying duration. Given the nature of this analysis, the results remain descriptive and exploratory and should not be interpreted as causal associations.

Symptom clustering was further explored by descriptively examining the frequency of combined symptoms, as detailed in **Table 5**. Among exclusively breastfed infants, the most prevalent presentation was abnormal stool consistency co-occurring with a skin rash, which was observed in 13 infants (5.0%). This was followed by the combination of a skin rash and increased crying duration, observed in seven infants (2.7%).

Among non-exclusively breastfed infants, the concurrent presentation of abnormal stool consistency and a skin rash was reported in two infants (6.7%). None in either feeding category presented with the combination of abnormal stool consistency and increased crying duration, regardless of the presence or absence of an accompanying skin rash. Due to the limited sample size within the non-exclusively breastfed group ($n=30$), statistical comparisons between the two feeding categories were not performed for the descriptive combinations.

Table 4. Co-Occurrence Pattern of Symptoms by Feeding Methods (Exploratory Analysis)

Group	Co-Occurrence Symptom		Normal	Abnormal	Total	P-value
Exclusively Breastfed $n=260$	Stool Consistency	Normal Stool	224 (94.1%)	14 (5.9%)	238	0.616
	x Frequent Crying	Abnormal Stool	22 (100%)	0 (0.0%)	22	
	Stool Consistency	Normal Stool	144 (60.5%)	94 (39.5%)	238	0.111
	x Skin Rash	Abnormal Stool	9 (40.9%)	13 (59.1%)	22	
	Frequent Crying x Skin Rash	Normal Crying	146 (59.3%)	100 (40.7%)	246	0.580
Non-Exclusively Breastfed $n=30$	Stool Consistency	Abnormal Crying	7 (50.0%)	7 (50.0%)	14	1.000
	x Frequent Crying	Abnormal Stool	26 (96.3%)	1 (3.7%)	27	
	Stool Consistency	Normal Stool	3 (100.0%)	0 (0.0%)	3	0.548
	x Skin Rash	Abnormal Stool	17 (63.0%)	10 (37.0%)	27	
	Frequent Crying x Skin Rash	Normal Crying	1 (33.3%)	2 (66.7%)	3	1.000
	Stool Consistency	Abnormal Crying	17 (58.6%)	12 (41.4%)	29	
	x Frequent Crying	Abnormal Stool	1 (100.0%)	0 (0.0%)	1	

*Note: Fisher's Exact Test (two-sided). The analysis is descriptive and exploratory because it describes the co-occurrence of symptoms within each feeding group and should not be interpreted as evidence of causal association. For the non-exclusively breastfed group, some cells had expected counts less than 5; hence, results should be interpreted with caution.

Table 5. Frequency of Symptom Combination by Feeding Group

Symptoms	Exclusively Breastfed $n=260$	Non-Exclusively Breastfed $n=30$
Abnormal Stool Consistency x Skin Rash	13 (5.0%)	2 (6.7%)
Abnormal Stool Consistency x Increased Total crying duration	0 (0.0%)	0 (0.0%)
Skin Rash x Increased Total crying duration	7 (2.7%)	0 (0.0%)
Abnormal Stool Consistency x Skin Rash x Increased Total crying duration	0 (0.0%)	0 (0.0%)

* Note: These data describe the co-occurrence of symptoms within each feeding group and are presented for descriptive purposes only. No statistical comparison was performed due to the limited sample size in the non-exclusively breastfed group ($n=30$).

DISCUSSION

The present study investigated the prevalence and patterns of gastrointestinal (abnormal stool consistency), behavioral (increased total crying duration), and dermatological (skin rash) symptoms among exclusively breastfed against non-exclusively breastfed infants within an Indonesian outpatient setting. The results showed that symptom prevalence did not differ significantly between feeding groups. Within each group, no significant associations were observed among the three evaluation symptoms. There is no infant in either category that reflects the concurrent presentation of abnormal stool consistency and increased total crying duration.

A prior cross-sectional study on functional gastrointestinal disorders (FGIDs) in Indonesian infants reported crying-related symptoms in 16.8% of 433 infants aged 6 weeks to 4 months and constipation in 5.5%. No significant association was observed between formula feeding and either symptom.¹¹ The results correspond with the observation that feeding type does not significantly influence gastrointestinal or crying-related symptoms in Indonesian infants. This lack of disparity may be explained by biological mechanisms engaging the gut microbiota and the gut-brain axis. Breast milk contains human milk oligosaccharides (HMOs) that selectively promote beneficial bacteria, while formula without HMOs may alter stooling patterns. These compositional differences do not necessarily result in clinically significant differences among healthy infants.¹²⁻¹³

The results contrast with a large Italian cross-sectional study of 508 infants, which identified formula feeding as a significant risk factor for FGID recurrence (adjusted OR = 1.8, 95% CI: 1.2–2.7), though individual symptoms remained distinct.¹⁴ This geographical discrepancy may originate from variations in sample sizes, distinct assessment methodologies (Rome IV criteria versus specific CoMiSS™ domains used in our study), cultural differences in symptom reporting, and different adjustments for confounding factors. However, the results are in line with official statements from the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), which showed no significant differences in general symptom prevalence between exclusively and non-exclusively breastfed infants.¹⁵ This supports the observation that stool abnormalities and excessive crying function as distinct clinical manifestations rather than interconnected components of a single symptom complex.

The absence of a significant association between abnormal stool consistency and increased total crying duration in this study is further supported by Vandenplas et al. In the extensive multinational review of functional gastrointestinal symptoms in infants, analysis showed that infantile colic and constipation frequently co-occur epidemiologically, as well as represent distinct functional entities rather than a unified syndrome.¹³ The authors observed that these symptoms often resolve spontaneously without clinical intervention. From a clinical standpoint, the co-occurrence of gastrointestinal and crying symptoms, particularly when accompanied by dermatological manifestations, should properly raise clinical suspicion for underlying conditions such as CMPA.¹⁶

Regarding stool patterns specifically, a large prospective cohort study of 1,052 healthy term infants reported softer and more frequent stools in the exclusive breastfed group,¹⁷ consistent with physiological variation within the normal clinical range. A study of 808 Egyptian infants established that the prevalence of individual symptoms was not dependent on the feeding method ($p=0.603$).¹⁸ This reinforces the current results where feeding type does not independently influence the prevalence of individual symptoms when assessed specifically through the CoMiSS™ domains.

A high prevalence of skin rash was observed in both feeding groups at approximately 41%. This is consistent with a multinational study reporting variations in median CoMiSS™ scores between Jakarta (1.5) and Sergipe, Brazil (4.0), emphasizing that parental perceptions of "normal" symptoms vary extensively across distinct populations.¹⁹ A prospective cohort study also showed that CoMiSS™ scores naturally decrease with age and do not differ between exclusively and non-exclusively breastfed infants under six months.²⁰

Within the emerging framework of the gut-skin axis, a network meta-analysis of 23 randomized controlled trials showed that breastfeeding improved overall infant growth compared with certain formulas. However, its relationship with dermatological symptoms remained complex.²¹ The absence of a significant difference in rash prevalence between the present study groups suggests that skin manifestations in healthy infants may be more strongly influenced by genetic predisposition, environmental exposures, and skin care practices than by feeding methods alone.

The present study features an unbalanced design between the exclusively and non-exclusively breastfed groups. However, the disparities are inherently common

in observational cross-sectional studies, where group allocations cannot be artificially controlled. To address this limitation, the statistical analyses were tailored using Fisher's Exact Test to minimize potential bias and provide reliable comparative insights despite the sample size discrepancy.

CONCLUSION

In conclusion, no significant differences were observed in the prevalence of abnormal stool consistency, increased daily crying duration, or skin rashes between exclusively and non-exclusively breastfed infants included in this study. The absence of concurrent stool and crying abnormalities suggested that the manifestations may represent distinct clinical entities rather than a unified symptom cluster.

The substantial sample imbalance (exclusively vs. non-exclusively breastfed infants) necessitated a cautious interpretation regarding feeding equivalence. However, these preliminary data offered valuable clinical reassurance that neither feeding method inherently elevated the risk of the common infant symptoms. The results established a meaningful descriptive baseline for local outpatient settings, underscoring the need for larger, adequately powered prospective trials to definitively confirm the clinical relationships.

STRENGTHS AND LIMITATIONS

The study features a relatively large infant sample size (n=290), which provides a comprehensive overview of feeding practices, daily crying duration, stool consistency, and skin rash prevalence among infants presenting to the outpatient clinic.

This study has several limitations that need to be addressed. First, participants were recruited using a consecutive convenience sampling strategy, resulting in an unbalanced study design because the numbers of exclusively and non-exclusively breastfed infants could not be predetermined. However, this sampling method reflects the natural distribution of feeding practices within the study population. To address potential bias associated with unequal group sizes, appropriate statistical methods were applied. In particular, Fisher's exact test was used for contingency tables with low expected cell frequencies, providing robust statistical comparisons despite the group imbalance.

Data were collected over one year from September 2022 – September 2023, which is a common practice in cross-sectional studies. This timeframe places the data collection approximately two to three years prior to the current submission. However, the results remain relevant, as the clinical presentation of common infant symptoms is not subject to rapid temporal changes. Consistent with the nature of any cross-sectional study, the simultaneous assessment of feeding modalities and infant symptoms precludes the establishment of a definitive temporal relationship or causal inference regarding whether specific feeding methods directly drive symptom development.

CONFLICT OF INTEREST

None Declared.

FUNDING

No funding was received from any public, commercial, or not-for-profit funding agency for this study.

AUTHOR CONTRIBUTIONS

- Data gathering: BH, IN
- Conceived the study, conducted the study, and drafted the manuscript: IN, BH.
- Statistical analysis: IN, RG
- Supervised the conduct of the study: BH, YV
- All authors reviewed, revised, and approved the final version.

ACKNOWLEDGEMENT

The principal author is grateful to the co-authors for their support in this study. The author is also thankful to Badriul Hegar and Yvan Vandenplas for their guidance and consultation on data analysis and manuscript preparation.

DATA AVAILABILITY

The data supporting the results of this study are available from the corresponding author upon reasonable request.

REFERENCES

1. Rollins NC, Bhandari N, Hajeebhoy N, et al. Why invest, and what it will take to improve breastfeeding practices? *Lancet*. 2016;387(10017):491-504. doi: 10.1016/S0140-6736(15)01044-2.
2. Hegar B, Vandenplas Y. Breastfeeding for gut infant health. *Indones J Gastroenterol Hepatol Dig Endosc*. 2018;19(1):1-6.
3. Victora CG, Bahl R, Barros AJ, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet*. 2016;387(10017):475-490. doi:10.1016/S0140-6736(15)01024-7.
4. Tunc VT, Camurdan AD, Ilhan MN, Sahin F, Beyazova U. Factors associated with defecation patterns in 0-24 month old children. *Eur J Pediatr*. 2018;177(5):735-742.
5. Hegar B, Dewanti NR, Kadim M, et al. Natural evolution of regurgitation in healthy infants. *Acta Paediatr*. 2009;98(7):1189-1193. doi:10.1111/j.1651-2227.2009.01343.x.
6. Wolke D, Bilgin A, Samara M. Systematic review and meta-analysis: fussing and crying durations and prevalence of colic in infants. *J Pediatr*. 2017;185:55-61.e4.
7. Vandenplas Y, Hauser B, Salvatore S. Functional gastrointestinal disorders in infancy: impact on the health of the infant and family. *Pediatr Gastroenterol Hepatol Nutr*. 2019;22(3):207-216.
8. Wang Z, Cai Y, Wang X, et al. The significance of an infant's cry: a narrative review of physiological, pathological, and analytical perspectives. *Front Pediatr*. 2025;13:1558951.
9. Silverberg JI, Barbarot S, Gadkari A, et al. Atopic dermatitis in the pediatric population: a cross sectional, international epidemiologic study. *Ann Allergy Asthma Immunol*. 2021;126(4):417-428.e2.
10. Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI. Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three. *J Allergy Clin Immunol*. 2009;124(6):1251-1258.e23. doi: 10.1016/j.jaci.2009.10.009.
11. Lestari LA, Wibowo Y, Mulyani C, et al. Prevalence and risk factors of functional gastrointestinal disorders in infants in Indonesia. *Pediatr Gastroenterol Hepatol Nutr*. 2023;26(1):58-69. doi:10.5223/pghn.2023.26.1.58
12. Inchingolo F, et al. Differences in the intestinal microbiota between breastfed infants and infants fed with artificial milk: a systematic review. *Pathogens*. 2024;13(7):533. doi:10.3390/pathogens13070533.
13. Vandenplas Y, Abkari A, Bellaiche M, et al. Prevalence and health outcomes of functional gastrointestinal symptoms in infants from birth to 12 months of age. *J Pediatr Gastroenterol Nutr*. 2015;61(5):531-537.
14. Scarpato E, Salvatore S, Romano C, et al. Prevalence and risk factors of functional gastrointestinal disorders: a cross-sectional study in Italian infants and young children. *J Pediatr Gastroenterol Nutr*. 2023;76(2):e27-e35. doi:10.1097/MPG.0000000000003653.
15. Vaz SR, Tofoli MH, Avelino MAG, da Costa PSS. Probiotics for infantile colic: is there evidence beyond doubt? A meta-analysis and systematic review. *Acta Paediatr*. 2024;113(4):672-681. doi: 10.1111/apa.17045.
16. Vandenplas Y, Salvatore S, Vieira MC, Savino F, Heine RG, Huysentruyt K, et al. Infantile colic: when to suspect cow's milk allergy. *Nutrients*. 2025;17(22):3600. doi: 10.3390/nu17223600.
17. Solasaari T, Korpela K, Kolho KL, et al. Bowel function in a prospective cohort of 1052 healthy term infants up to 4 months of age. *Eur J Pediatr*. 2024;183(8):3557-3565. doi:10.1007/s00431-024-05625-0.
18. El Farargy MS, El Naga AA, Abo El Fotoh WMM, et al. The cow's milk-related symptom score (CoMiSS™) in presumed healthy Egyptian infants. *Nutrients*. 2024;16(16):2666. doi:10.3390/nu16162666.
19. Knockaert N, Huysentruyt K, Hegar B, et al. Difference in cow's milk-related symptom score (CoMiSS™) among presumed healthy infants in Indonesia and Brazil. *Pediatr Gastroenterol Hepatol Nutr*. 2025;28(2):124-134.
20. Bajero K, Salvatore S, Dupont C, et al. The evolution of cow's milk-related symptom score (CoMiSS™) in presumed healthy infants. *Eur J Pediatr*. 2024;183(10):4329-4335. doi:10.1007/s00431-024-05693-2.
21. Li T, Zheng Q, Xu J, et al. Comparison of 11 formulas and breastfeeding for atopic dermatitis and growth in pediatric cow's milk protein allergy: a systematic review and network meta-analysis of 23 randomized controlled trials. *J Evid Based Med*. 2025;18(2):e70026.