ORIGINAL ARTICLE

Quarterly Patterns and Delivery-Type Differences in Infant Diarrheal Disease: A Survival Analysis in India

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ABSTRACT

Background: Diarrheal diseases remain a leading cause of morbidity and mortality in children under five, with infants particularly vulnerable during their first year of life. Age-related variations and biological factors such as delivery type may influence diarrheal risk. **Aim & Objective:** To examine quarterly patterns of diarrheal morbidity in infancy and assess whether delivery mode modifies the risk during infancy. **Methodology:** A prospective community-based cohort study was conducted in rural Varanasi, India, from November 2022 to February 2024. A total of 150 infants were enrolled at birth and followed for one year through structured quarterly assessments. Generalized Estimating Equations (GEE) with Poisson regression were applied to evaluate associations between delivery type, infant age, and diarrhea incidence. **Results:** The cohort experienced an average of 2.92 diarrheal episodes per child-year. GEE analysis revealed a significant age-dependent increase in diarrheal risk: OR = 1.58 (95% CI: 1.12-2.23) for 4-6 months, OR = 3.13 (95% CI: 2.23-4.40) for 7-9 months, and OR = 2.67 (95% CI: 1.85-3.87) for 10-12 months, compared with 0-3 months. **Conclusion:** Diarrheal morbidity in infancy is strongly age-dependent. Strengthening exclusive breastfeeding promotion, safe complementary feeding practices, and WASH interventions is essential to reduce the diarrheal burden in early childhood.

KEYWORDS

Diarrhea, Infants, Survival Analysis, Delivery Mode, Complementary Feeding, Rural India

INTRODUCTION

Diarrheal illnesses remain a significant contributor to morbidity and mortality in children under five, especially in low- and middle-income nations. In 2021, diarrhea was responsible for an estimated 1.17 million deaths and 30.9 million disability-adjusted life years (DALYs) globally in this age group. (1) Although these figures demonstrate a marked decline compared with the early 1990s, the disease burden remains substantial. Among the identified etiological agents, rotavirus accounted for 35.2% of fatal cases in this age group, followed by *Shigella* (24.0%) and adenovirus (23.8%). (1)
In 2017, an estimated 1.7 billion diarrheal episodes occurred worldwide among children, resulting in more than half a million deaths. Diarrhea remains the second leading cause of under-five mortality globally. (2) According to the United Nations International Children's Emergency Fund (UNICEF), malnutrition contributes to nearly 45% of all deaths among children under five years of age. The leading direct causes of mortality in this age group include pneumonia (15%), diarrhea (8%), and malaria (5%).(3,4) In developing countries, diarrheal disease is a leading contributor to malnutrition and continues to rank among the top three causes of under-five mortality. (2,3) Moreover, diarrheal illnesses lead to repeated outpatient visits and hospitalizations. On average, children living in

developing countries experience approximately three episodes of diarrhea each year. (5-7)

In recent years, India has implemented several interventions to reduce the burden of diarrheal diseases. These include the Integrated Child Development Scheme; Water, Sanitation and Hygiene (WASH) initiatives and trials (8); the National Diarrhoeal Disease Control Programme (9,10); and nutrition-focused policies for childhood development. (11) However, despite these initiatives, diarrheal diseases remain a major public health challenge, highlighting the need for context-specific evidence to guide more effective preventive strategies.

In India, the impact of diarrheal diseases is particularly pronounced. Evidence suggests that South Asia accounts for more than half of diarrhea-related episodes and deaths in children under five, with India contributing a substantial share. (12)

Emerging evidence also highlights the role of biological factors, particularly mode of delivery, in shaping infant susceptibility to infections. Longitudinal studies confirm that caesarean delivery significantly alters the establishment of the infant gut microbiota, with delayed and reduced colonization by key beneficial taxa such as *Bacteroides*, sometimes persisting up to 6-18 months postnatally. (13, 14) These microbial alterations are linked to changes in immune profiles, including epithelial cell activation, lymphocyte subpopulations, regulatory T cells, and cytokine responses; which may predispose infants to a higher risk of infections, including diarrheal diseases. (15)

Aim & objective

- To examine the quarterly distribution and timing of diarrheal episodes during the first year of life.
- To compare the risk of diarrheal disease between infants born by vaginal delivery and caesarean section using survival analysis.

MATERIAL & METHODS

Study Design: This prospective cohort study was conducted over a one-year follow up period, from November 2022 to February 2024, to assess the incidence of diarrhea among infants based on delivery type and first four age quarter of life.

Study Setting: The study was undertaken in the rural region of Varanasi, India, with a focus on infants born through either caesarean section or vaginal delivery. Data collection was conducted within the community development block, where newborns were identified using monthly delivery records procured from the community health centre.

Study Population and Sample Size Determination: The study included newborns delivered to mothers who were permanent residents of the study area and had provided written informed consent to participate. The sample size was estimated using assumptions derived from previous literature (Tefera M. et al., 2020) (16), considering differences in morbidity risk between infants born by vaginal and caesarean delivery. The 4:1 ratio of unexposed to exposed groups was determined using the reported prevalence of caesarean deliveries in rural India (17.6% as per NFHS-5). After incorporating a 10% allowance for non-response and applying a continuity correction, the final estimated sample size was 150, which included 30 infants delivered by caesarean section and 120 born through vaginal delivery.

Eligibility Criteria: Infants were eligible for inclusion if their mothers were permanent residents of the study area and had given written informed consent. Newborns were excluded if they were stillborn, part of a multiple pregnancy, born to mothers temporarily residing outside the study location, or if parental consent was not obtained.

Study Instrument: Data were gathered using a pre-designed, validated, semi-structured questionnaire. Alongside the interview schedule, anthropometric measurements such as weight, length/height, head circumference, chest circumference, and mid-upper arm circumference were obtained for all newborns.

Strategy for Data Collection - Baseline & Follow-up

Data collection commenced after obtaining institutional ethical clearance. Eligible newborns were randomly selected from the monthly delivery lists of the community health centre. Each infant was followed for one year, with a baseline assessment shortly after birth and four subsequent follow-up visits at 3, 6, 9, and 12 months, making a total of five visits per child.

After the baseline, morbidity surveillance specifically targeted diarrheal illness. At each follow-up, caregivers were interviewed using a standardized questionnaire to document the occurrence of diarrheal episodes. For every episode, information on onset, duration, and severity was collected, with severity classified according to Integrated Management of Neonatal and Childhood Illness (IMNCI) guidelines.

At the 3-month visit, data captured the total number of diarrheal episodes occurring from birth up to that point, along with their duration and treatment received. By 6 months, reassessment focused on cumulative diarrheal burden since birth, differentiating between first episodes and recurrent ones, and recording severity,

hospitalizations, and medical interventions. At 9 months, tracking continued for new episodes arising since the previous visit, with detailed information on frequency, severity, and treatment-seeking behavior, including outpatient and hospital care. Finally, at 12 months, a comprehensive summary of diarrheal morbidity across the first year of life was compiled, capturing the total number of episodes, their timing, recurrence, and severity, thereby outlining age-specific patterns of diarrheal risk.

Statistical analysis: Data were first entered into Microsoft Excel and subsequently analyzed using SPSS trial version 25 for Windows, with additional verification performed in R and Python to enhance analytical rigor. Descriptive statistics were applied to summarize the incidence of diarrheal episodes across delivery types. Furthermore, crude odds ratios (COR) comparing diarrhea occurrence in infants born by caesarean section versus vaginal delivery were computed for each quarterly age interval to present unadjusted estimates.

Kaplan-Meier survival analysis was then applied to estimate the time to first diarrhea episode, thereby assessing differences in survival probabilities between infants delivered by caesarean section and vaginal delivery. The Log-Rank (Mantel-Cox) test was employed to determine the statistical significance of differences observed between the survival curves. The curves were plotted with 95% confidence intervals, shaded around the survival lines, to indicate the degree of uncertainty in the estimates.

Further, Generalized Estimating Equations (GEE) with a Poisson regression model were used to examine the incidence of diarrhea episodes, considering delivery mode and infant age (grouped into quarterly intervals: 0-3 months [reference], 4-6 months, 7-9 months, and 10-12 months) as predictors. An exchangeable working correlation structure was assumed to account for within-subject correlation arising from repeated measurements. Regression coefficients, standard errors, and p-values were computed, and odds ratios (OR) with 95% confidence intervals (CI) were derived to quantify the relative risk of diarrhea episodes across predictor variables A p-value of <0.05 was considered statistically significant, and all estimates were presented along with their 95% confidence intervals.

RESULTS

A total of 150 mother-infant pairs were included in the study. The mothers had a mean age of 25.27 ± 2.81 years, indicating that the study cohort predominantly comprised young women. Regarding educational attainment, 52.7% of mothers had completed high school or intermediate education, 35.3% were graduates or held higher degrees, and only 0.7% were illiterate, indicating a generally literate cohort. The majority of mothers (86.7%) were homemakers, while 3.3% were employed in government service, 6.0% in the private sector, 2.7% in business, and 1.3% in skilled labor. Multiparity was observed in 54.0% of mothers, whereas 46.0% were primiparous (Table 1).

Birth spacing analysis revealed that 62.0% had an interpregnancy interval of 1-2 years, 17.3% had less than 1 year, and 20.7% had more than 2 years between pregnancies. Birth order distribution showed that first-order births constituted 46.0% of deliveries, second-order births 42.7%, and third-order or higher births 11.3%. The majority of infants (86.7%) were born at term (37-40 weeks), with 10.7% born preterm (<37 weeks) and 2.7% post-term (>40 weeks). Caesarean section accounted for 20.0% of deliveries, while 80.0% were vaginal births. In terms of religion, 84.0% of participants were Hindu and 16.0% were Muslim. According to the Modified BG Prasad socioeconomic classification, nearly half of the mothers (48.7%) were categorized in Class IV, followed by 23.3% in Class III, 20.7% in Class V, 6.0% in Class II, and 1.3% in Class I, reflecting that the study population predominantly belonged to lower socioeconomic strata. (Table 1).

Table 1: Socio-Demographic Characteristics of Study Subjects (N=150)

Socio-Demographic Characteristics		Number (N=150)	Percentage (100%)
Mother's Age (in years)	Mean age:- 25.27 ± 2.81		
Mother's Education	Illiterate	1	0.7
	Primary & Middle	17	11.3
	High School & Intermediate	79	52.7
	Graduation & above	53	35.3
Mother's Occupation	Government Service	5	3.3
	Private	9	6.0
	Business	4	2.7
	Skilled Labour	2	1.3

	Housemaker	130	86.7
Parity	Nulliparous	69	46.0
	Multiparous	81	54.0
Birth interval	< 1 year	26	17.3
	1-2 years	93	62.0
	> 2 years	31	20.7
Birth order	1st order	69	46.0
	2nd order	64	42.7
	3rd & above	17	11.3
Gestation period	Pre-Term (< 37 weeks)	16	10.7
	Term (37-40 weeks)	130	86.7
	Post Term (>40 weeks)	4	2.7
Whether the delivery was CS/Vaginal	Caesarean section	30	20.0
	Vaginal delivery	120	80.0
Religion	Hindu	126	84.0
	Muslim	24	16.0
Socio-Economic Status	Class I	2	1.3
	Class II	9	6.0
	Class III	35	23.3
	Class IV	73	48.7
	Class V	31	20.7

During the first year of life, the incidence of diarrheal disease varied substantially across months (Table 2). The lowest incidence was observed during the 4th month (0.09 episodes per child-month), followed closely by the 1st month (0.10) and 3rd month (0.12). Incidence began to rise from the 5th month (0.15) and increased sharply from the 6th month onward, peaking in the 8th month at 0.43 episodes per child-month, when 43.3% of infants experienced at least one episode. Elevated incidence persisted through the 9th (0.39) and 10th (0.36) months, followed by a gradual decline in the 11th (0.29) and 12th (0.28) months. Overall, the mean annual diarrhea incidence was 2.92 episodes per child, indicating a substantial burden during infancy, with a pronounced clustering of cases in the latter half of the first year.

Table 2: Distribution of Diarrhea Episodes & Incidence During the First Year (N = 150)

Month	**Diarrhea Episodes**		
	%	Episodes	Incidence
1st month	10.0%	15	0.10
2nd month	12.7%	19	0.13
3rd month	10.7%	18	0.12
4th month	9.3%	14	0.09
5th month	14.7%	22	0.15
6th month	30.7%	46	0.31
7th month	26.7%	40	0.27
8th month	43.3%	65	0.43
9th month	38.67%	58	0.39
10th month	36.0%	54	0.36
11th month	28.7%	43	0.29
12th month	28.0%	42	0.28
Annual Diarrhea Episodes per child		2.92	

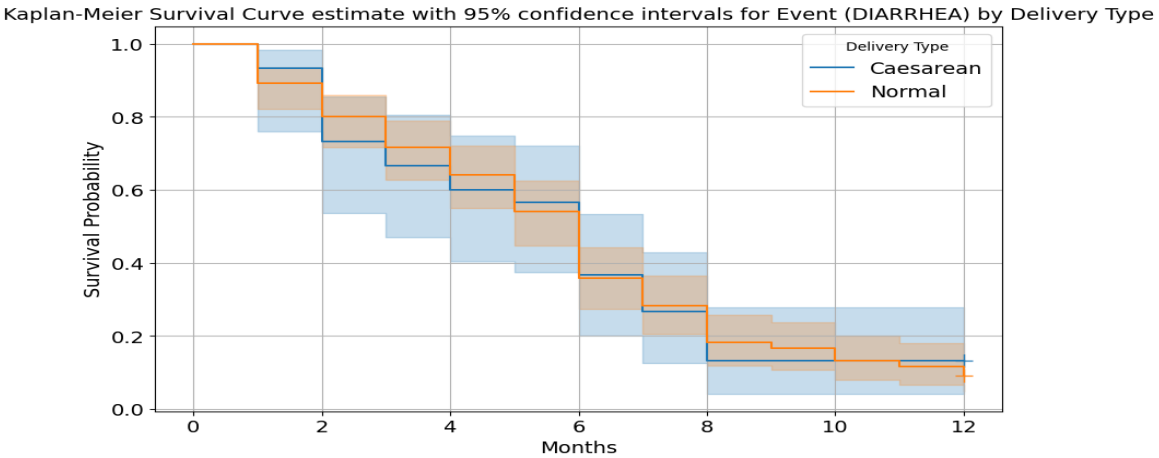
The association between delivery mode and diarrheal disease incidence varied across the four age quarters of infancy. In the first quarter, infants born by CS had 1.26 times the odds of experiencing diarrhea compared to those born VD (95% CI: 0.54-2.98, p = 0.655). In the second quarter, the odds ratio decreased to 0.87 (95% CI: 0.39-1.96, p = 0.839), suggesting slightly lower odds of diarrhea among CS-born infants, but again without statistical significance. During the third quarter, the odds ratio rose to 1.30 (95% CI: 0.55-3.10, p = 0.669), indicating higher odds in the CS group, whereas in the fourth quarter the odds ratio declined to 0.65 (95% CI: 0.29-1.45, p = 0.313). Across all quarters, no statistically significant association was observed between mode of delivery and diarrhea incidence (Table 3).

Table 3: Odds Ratios for Diarrheal Disease by Delivery Mode and Age Quarter

Quarter	COR (CS vs VD)	95% CI	P-value
1-3 months	1.26	0.54-2.98	0.655
4-6 months	0.87	0.39-1.96	0.839
7-9 months	1.30	0.55-3.10	0.669
10-12 months	0.65	0.29-1.45	0.313

Among Caesarean-born infants, 26 (86.7%) experienced diarrhea, with 4 (13.3%) censored, compared to 109 (90.8%) events and 11 (9.2%) censored among vaginal deliveries. Overall, 135 infants (90%) experienced diarrhea, while 15 (10%) were censored. The Kaplan-Meier survival curve showed a progressive decline in diarrhea-free probability across both groups, indicating increased risk over the first year. Infants delivered by Caesarean initially had higher survival probability but exhibited a steeper decline in the early months, converging with vaginal deliveries around 5-6 months. Thereafter, vaginally delivered infants maintained relatively better survival, while the Caesarean group demonstrated continued decline, creating a late divergence between the two curves (Figure 1).

Figure 1: Kaplan-Meier Survival Curves for Time to First Diarrhea event



Infants delivered by Caesarean had a mean survival time of 5.67 months (95% CI: 4.48-6.86) and a median of 6 months (95% CI: 5.14-6.86), while vaginally delivered infants showed a mean of 5.83 months (95% CI: 5.24-6.43) and the same median of 6 months (95% CI: 5.39-6.61). Overall, the cohort had a mean survival time of 5.8 months (95% CI: 5.27-6.34) and a median of 6 months (95% CI: 5.44-6.56). The log-rank test (p = 0.877) indicated no significant difference in diarrhea-free survival between delivery modes (Table 4).

Table 4: Comparison of Means and Medians for Survival Time (Diarrhea)

Modes of delivery	Mean[a]				Median				Log Rank (Mantel-Cox) P value
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval		
			Lower Bound	Upper Bound			Lower Bound	Upper Bound	
CS	5.667	0.608	4.475	6.858	6.000	0.440	5.138	6.862	0.877
Normal	5.833	0.305	5.235	6.431	6.000	0.309	5.394	6.606	
Overall	5.800	0.273	5.265	6.335	6.000	0.287	5.438	6.562	

a. Estimation is limited to the largest survival time if it is censored.

The GEE Poisson regression analysis demonstrated that diarrhea incidence varied significantly across age quarters within the same birth cohort, while mode of delivery showed no effect (Table 5). For the reference category (Caesarean section, 0-3 months), the expected episode count was low (intercept OR = 0.35, 95% CI: 0.24-0.51, p < 0.001). No significant difference was observed between vaginal and Caesarean deliveries (OR = 0.98, 95% CI: 0.72-1.34, p = 0.896), indicating that delivery mode

did not influence incidence rates. In contrast, as the cohort aged, a progressive increase in diarrhea episodes was observed. Compared to the 0-3 month period, the risk rose by 58% during 4-6 months (OR = 1.58, 95% CI: 1.12-2.23, p = 0.010), tripled during 7-9 months (OR = 3.13, 95% CI: 2.23-4.40, p < 0.001), and remained elevated at 10-12 months (OR = 2.67, 95% CI: 1.85-3.87, p < 0.001). These findings highlight that the same group of infants experienced progressively higher incidence of diarrhea as they advanced in age through the first year, independent of delivery mode.

Table 5: GEE Poisson Regression Analysis for Diarrhea Episodes by Delivery Mode and Age Quarter

Variable	Coefficient	Standard Error	p-value	Odds Ratio	CI Lower	CI Upper
Intercept	-1.0429	0.1911	0.0000*	0.3524	0.2423	0.5126
VD	-0.0207	0.1586	0.8964	0.9796	0.7179	1.3367
4 -6 months	0.4555	0.176	0.0096*	1.5769	1.1169	2.2263
7-9 months	1.1425	0.1733	0.0000*	3.1346	2.2317	4.4027
10-12 months	0.9832	0.189	0.0000*	2.6731	1.8454	3.8719

*p<0.05

DISCUSSION

The present findings are consistent with previous research demonstrating that diarrheal morbidity is strongly age-dependent, with the burden increasing as infants transition from exclusive breastfeeding to complementary feeding and greater environmental exposure. Studies from India and other low- and middle-income countries have similarly reported peaks in diarrheal incidence during the latter half of infancy, particularly between 6-11 months of age, coinciding with the introduction of complementary foods and increased mobility of children. (17,18) Our observed mean of 2.9 episodes per child-year aligns with earlier community-based studies in rural India, which have documented between 2-3 episodes annually in infants. (19,20)

The GEE Poisson model in the present study demonstrated a stepwise increase in diarrheal risk with age: OR = 1.58 (95% CI: 1.12-2.23) for 4-6 months, OR = 3.13 (95% CI: 2.23-4.40) for 7-9 months, and OR = 2.67 (95% CI: 1.85-3.87) for 10-12 months (reference 0-3 months). These effect sizes are compatible with the well-documented concentration of diarrhoeal burden in late infancy. Global analyses estimate that diarrhoea incidence is highest in infants aged 6-11 months, with modelled rates of approximately 4.5 episodes per child-year in 2010 for this age group (down from ~5.3 in 1990), reflecting markedly elevated exposure during this period.(21) Similarly, reviews of LMICs report average diarrhoea incidence close to 2.9-3.0 episodes per child-year across early childhood, a magnitude that closely mirrors the annual incidence of 2.92 episodes per child observed in our cohort.(22)

With respect to mode of delivery, our adjusted GEE estimate for vaginal versus caesarean birth (OR = 0.98, 95% CI: 0.72-1.34) indicates no association with diarrhoeal incidence. This contrasts with pooled estimates from high-income country meta-analyses reporting a modestly increased risk of gastrointestinal infection requiring hospital admission after caesarean delivery (pooled hazard ratios ≈ 1.19-1.20 for emergency and elective caesarean, respectively).(23) The divergence likely reflects contextual differences: while caesarean delivery has been linked to altered neonatal gut colonization and small but measurable increases in infection risk in well-resourced settings, the effect may be attenuated or masked in high-exposure rural LMIC environments where environmental determinants (unsafe water, sanitation, complementary feeding practices) are the primary drivers of diarrhoeal morbidity.(24,25)

Several factors may explain the observed age-related increase in diarrheal risk. In the first three to four months of life, most infants in the study were likely protected by exclusive breastfeeding, maternal antibodies, and relatively limited exposure to contaminated food or water, resulting in a lower incidence of diarrhea. However, after six months, the introduction of complementary feeding increases the likelihood of exposure to unsafe water, improperly stored food, and inadequate feeding practices, which are well-documented risk factors for diarrheal illness. (26,27) Greater mobility and hand-to-mouth behaviours during this stage may further amplify vulnerability to infection. The pronounced peak around eight months coincides with the period when breastfeeding alone is no longer sufficient for nutritional needs, yet hygienic standards of complementary feeding are often suboptimal in rural settings.

The lack of association between delivery type and diarrhea incidence in this cohort can be attributed to contextual influences. While caesarean delivery is known to alter gut microbial colonization and immune development, these biological effects may be overshadowed in environments with high

pathogen load, where both caesarean- and vaginally-born infants are exposed to similar risks. In such settings, environmental determinants including sanitation, hygiene practices, and access to safe drinking water likely play a much greater role in shaping diarrheal outcomes than early-life microbiota differences. These findings are supported by other studies from low-resource contexts, which similarly found that delivery mode was not a major predictor of infant diarrheal morbidity. (28)

Conclusion

This community-based cohort study demonstrated that diarrheal morbidity during infancy is strongly age-dependent, with risk rising markedly after six months of age and peaking in the latter half of the first year. In contrast, mode of delivery did not significantly influence diarrheal incidence, suggesting that environmental and behavioral determinants outweigh delivery-related biological factors in this rural Indian setting. These results highlight the need to encourage exclusive breastfeeding practices, promote safe and adequate complementary feeding, and reinforce WASH-related measures to mitigate the risk of diarrheal illnesses in early childhood.

Recommendation

Interventions should focus on the post-six-month period by strengthening exclusive breastfeeding promotion, ensuring safe complementary feeding practices, and reinforcing WASH measures. Larger multicentric studies with pathogen-specific analysis are recommended for future research.

Limitation of the Study

The study was conducted in a single rural area with a modest sample size, which may limit generalizability. Diarrheal episodes were based on caregiver recall, introducing possible recall bias. Microbiological confirmation was not performed, and some environmental confounders may not have been fully captured.

Relevance of the Study

This study provides longitudinal community-based evidence on age-specific patterns of diarrheal disease in infancy. It highlights that the risk increases markedly after six months of age and demonstrates that delivery mode does not significantly influence diarrheal incidence in a high-exposure rural setting. The findings help identify critical windows for targeted preventive interventions.

Authors Contribution

AK: Concept design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, manuscript review. HS: Concept design, definition of intellectual content, literature search, manuscript preparation, manuscript editing, manuscript review. DKS: Concept design, definition of intellectual content, manuscript preparation, manuscript editing, manuscript review.

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Nil

Conflict of Interest

There are no conflicts of interest.

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Declaration of Generative AI and AI Assisted Technologies in the Writing Process

The authors haven't used any generative AI/AI assisted technologies in the writing process.

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