

Incidence, Clinical Signs and Co-morbidities of Feeding Intolerance among Preterm Infants Aged 28-34 Weeks of Gestation in a Tertiary Care Hospital of Western Nepal- A Prospective Observational Study

BINOD KUMAR GUPTA¹, RANJANA BISTA², SANDEEP SHRESTHA³, DEEPAK RAJ BHANDARI⁴, RAJU KAPHLE⁵, DINESH CHAUDHARY⁶, NAGENDRA CHAUDHARY⁷



ABSTRACT

Introduction: Feeding intolerance is common among the preterm neonates and is associated with different co-morbidities like respiratory depression, respiratory distress syndrome, apnea, hyperbilirubinaemia, and hypoxic ischaemic encephalopathy.

Aim: To find the incidence of feeding intolerance in preterm neonates from 28-34 weeks of gestation along with the clinical signs and co-morbidities associated with feeding intolerance.

Materials and Methods: A prospective observational hospital based study was conducted in Neonatal Intensive Care Unit (NICU) and postnatal ward of Universal College of Medical Sciences, a tertiary care hospital situated in western Nepal for 12 months (June 2018 to May 2019). All admitted preterm neonates between 28-34 weeks of gestation were included in the study and were followed-up for any neonatal morbidities along with feeding intolerance. Feeding intolerance was defined when the newborn had vomiting and/or abdominal distension and/or increased gastric residual volume with normal disruption of feeding process. Babies with feeding intolerance were subjected to final analysis for clinical signs and co-morbidities.

Results: Out of 490 admitted preterm babies (28-34 weeks), 54 (11.02%) had feeding intolerance with 33 (61.1%) babies in the very low birth weight group. The mean birth weights of the total enrolled babies (n=490) and feed intolerant (n=54) babies were 1550 gm and 1418 gm, respectively. Different co-morbidities associated with feeding intolerance were respiratory distress (25.9%), respiratory distress syndrome (22.2%), jaundice (16.7%), apnea (5.6%) and necrotising enterocolitis (3.7%). Among the total 37 preterm deaths, four babies were in the feeding intolerance group. Majority of all feed intolerant babies had vomiting 49 (90.7%) followed by gastric residue (57.4%), abdominal distension (55.6%), and reduced or absent bowel sounds (7.4%), respectively. The incidence of feeding intolerance was increased in babies fed with formula feed (p=0.46) and when feeding was started <24 hours (p=0.22) but the results were statistically insignificant.

Conclusion: The incidence of feeding intolerance was 11.02% in the preterm neonates (28-34 weeks) with high proportion in very low birth weight babies. Vomiting, gastric residue and abdominal distension were three important signs of feeding intolerance in newborns.

Keywords: Abdominal distension, Necrotising enterocolitis, Vomiting

INTRODUCTION

Preterm birth complicates about one-eighth of all deliveries and is the leading cause of perinatal morbidity and mortality. About two-third proportion of perinatal mortality in developed countries are due to prematurity [1]. Mothers with various illnesses and co-morbidities are more likely to deliver preterm babies in comparison to mothers without co-morbidities (10.9% vs 4.7%) [2]. Preterm infants have higher rate of temperature instability, respiratory distress, infections, apnea, hypoglycaemia, seizures, jaundice, kernicterus, feeding difficulties, necrotising enterocolitis, periventricular leukomalacia, and rehospitalisations [3].

There is no universal definition for feeding intolerance and therefore, various indicators comprising of symptoms (vomiting, lethargy and apnea) and signs (abdominal distension with or without visible bowel loops, increased gastric residuals, abdominal tenderness, reduced or absent bowel sounds) are used as important indicators for feeding intolerance. Among these features, vomiting, abdominal distension and increased gastric residuals are considered as the triad to define feeding intolerance. Feeding intolerance is commonly seen in preterm infants and

providing adequate enteric nutrition in such infants is one of the major clinical challenges to the neonatologists throughout the world [4]. The incidence of feeding intolerance observed is nearly 29% in preterm neonates [5]. Poor co-ordination during sucking and swallowing in preterm newborns, incompetent lower oesophageal sphincter, reduced gastric capacity along with delayed gastric emptying time and intestinal hypomotility are important factors leading to feeding intolerance [6-8]. Therefore, gut immaturity in preterm babies leads to abnormal intestinal colonisation, poor balance between microbiota and immune response [9,10]. Underlying medical conditions such as neonatal sepsis, inappropriate feed volume, hyperosmolar medications/feeds and necrotising enterocolitis are also important factors which may lead to feeding intolerance [11].

Feeding intolerance could also be an early indicator of necrotising enterocolitis which is the most dangerous gastrointestinal complication of prematurity leading to withhold enteral feeds with prolongation of use of intravenous fluids and total parenteral nutrition which increases the risk of sepsis and liver cholestasis in such babies [12].

The co-ordination between sucking, swallowing and breathing in babies is usually achieved at 34-36 weeks of gestation. Poor sucking along with sucking swallowing incoordination are the major causes of feeding intolerance in those newborns which may finally lead to breastfeeding failure increasing the risk of hypoglycaemia, excessive weight loss, hyperbilirubinaemia, and dehydration [13].

Studies on incidence along with clinical presentations and associated co-morbidities of feeding intolerance, in preterm between 28-34 weeks, are sparse in developing nations like Nepal. Therefore, this study was conducted to estimate the incidence of feeding intolerance and find the associated clinical signs and co-morbidities.

MATERIALS AND METHODS

A prospective hospital based observational study was conducted in Universal College of Medical Sciences, Bhairahawa, Nepal, for a duration of 12 months (June 2018 to May 2019). Informed verbal and written consent was obtained from the parents of the babies enrolled in the study. The study was approved by the Institute Review Committee (ref no- UCMS/IRC/060/18).

Inclusion criteria: All babies with 28-34 weeks gestation admitted in NICU and postnatal wards (both in-born and out-born) were included in the study and followed-up till discharge, after obtaining informed and written consent from the parents.

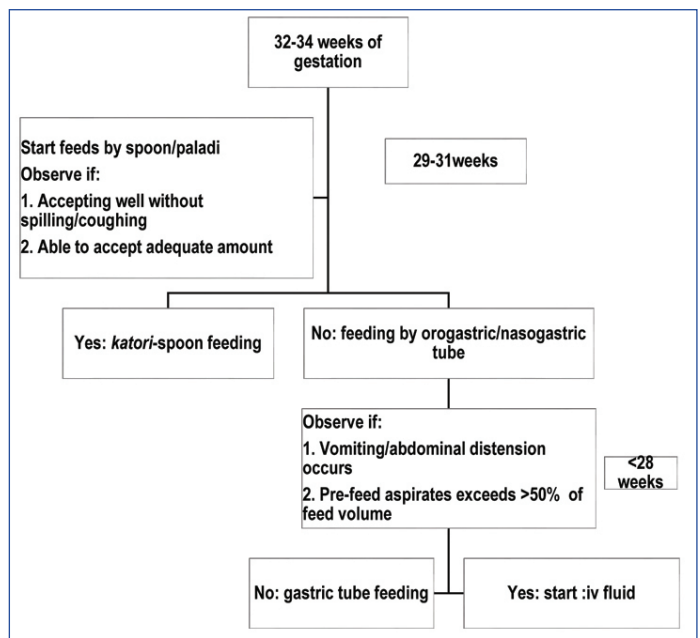
Exclusion criteria: Babies with any congenital intestinal anomalies and parents not giving the consent were excluded from the study.

Study Procedure

Detailed history and examination of the preterm babies were done. The period of gestation was confirmed according to last menstrual period or first trimester ultrasound or Ballard scoring as required. The babies were followed-up till discharge, mortality or Leave Against Medical Advice (LAMA)/referral and managed according to the hospital protocol.

All haemodynamically stable preterm babies were started on trophic feeds (10 mL/kg) as per the hospital protocol. Haemodynamically unstable babies were given fluid resuscitation along with inotropes and feed was started once inotropes were stopped. Feeding was started with either orogastric tube or katori spoon depending on the age of gestation of the babies as shown in [Table/Fig-1]. Feeding was increased by 10-15 mL/kg/day till full feeds were reached. The feeding method used was calculated bolus feeds every two hourly. Human breast milk was used and if not available, preterm formula feed was used. Human milk fortifier was added to expressed breast milk once the feed volume reached 100 mL/kg/day, till the baby's weight reached 2000 gm.

Gavage feeding was done by selecting soft orogastric tube (size- 5F external and approximately 0.05 cm internal diameter) with a rounded atraumatic tip and two holes on alternate sides. The length of tube was measured from bridge of nose to earlobe, then to the point halfway between the end of the sternum and the navel. The tube was inserted through nose/mouth by lubricating it with 2% xylocaine. The placement of the tube was confirmed by aspirating gastric content or injecting air bolus from free end and auscultating gushing sounds in epigastrium and tube was secured with tape. The free end of the tube has an adapter into which the tip of a syringe is fitted and a measured amount of feed was given by gravity. The feeding tube was not removed in between the feeds and was replaced by a new tube daily.



[Table/Fig-1]: Flow diagram showing feeding methods based on gestation in 28-34 weeks babies.

Study definitions:

- Respiratory distress syndrome and other causes of respiratory distress were diagnosed based on gestational age, proper history and examination, history of administration of antenatal steroids and X-ray findings. The severity of respiratory distress was assessed using Silverman Score and score more than six was kept in Continuous Positive Airway Pressure (CPAP), Early rescue surfactant was administered in neonate on CPAP and need of more than 40% Fraction of inspired Oxygen (FiO₂) and on mechanical ventilation with FiO₂ more than 35% [14].
- Apnea was diagnosed by cessation of breathing for longer than 20 seconds or for shorter duration in presence of bradycardia and/or change in skin colour (pallor or cyanosis). Apnea of prematurity was diagnosed after exclusion of secondary cause and was treated with methylxanthine [15].
- Diagnosis of feeding intolerance: Presence of one or more signs leading to interruption of enteral feeding regime- more than 2 mL/kg gastric residue or more than 50% gastric residue of the previous feeding, greenish or haemorrhagic residue, vomiting (altered milk, bile or blood stained), abdominal distention (increase in abdominal girth by 2 cm or more in between feedings with or without visible bowel loops), bloody stools, visible bowel loops, reduced or absent bowel sounds, abdominal tenderness with systemic signs (cyanosis, bradycardia, apnea, etc.) [11].

STATISTICAL ANALYSIS

Data was collected in predesigned performa and entered in Microsoft excel chart and analysis was done by using Statistical Package for the Social Sciences (SPSS) software, version 16.0 (SPSS Inc., Chicago, IL). The analysed data were expressed as frequencies, percentage, mean, percentile and Standard Deviation (SD). Chi-square test was applied for categorical variables. The p-value <0.05 was considered statistically significant.

RESULTS

Out of total 7054 admitted newborns during the study period, 1024 (14.5%) were preterm. Among the preterm babies, 490 (47.9%) were between the age-group 28-34 weeks gestation and were included in the study.

The mean gestation of the enrolled babies (n=490) was 32 weeks±2 days and 322 (65.7%) were delivered by normal vaginal delivery. The birth weight of babies ranged from 935 to 2550 gm with a mean of 1550 gm. Among the 490 preterm babies, 296 (60.4%) received feeding within 24 hours of delivery, whereas rest 194 (39.6%) received it after 24 hours of life [Table/Fig-2]. Among the population, 334 were induced with mothers' breast milk and 156 were induced with formula milk. Total 308 (62.8%) babies had one or more neonatal morbidities and 37 (7.6%) babies died during the follow-up in the hospital.

Parameters	Enrolled babies (n, %)	Feed intolerant babies (n, %)
Birth weight		
ELBW	6 (1.22)	2 (3.7)
VLBW	207 (42.25)	33 (61.1)
LBW	270 (55.1)	19 (35.2)
NBW	7 (1.43)	0 (0)
Mean gestation (weeks±days)	32±2	31.54±4
Mean birth weight (gm)	1550	1418
Delivery		
NVD	322 (65.7)	36 (66.7)
LSCS	168 (34.3)	18 (33.3)
Time of feeding		
<24 hours	296 (60.4)	31 (57.4)
≥24 Hours	194 (39.6)	23 (42.6)
Mortality	37 (7.6)	4 (7.4)

[Table/Fig-2]: Baseline characteristics of enrolled preterm (n=490) and feed intolerant (n=54) babies. ELBW (<1000 gm); extremely low birth weight; VLBW (<1500 gm), very low birth weight; LBW (<2500 gm); low birth weight; NBW: normal birth weight; NVD: Normal vaginal delivery; LSCS: Lower segment caesarean section

Among the enrolled 490 babies, there were 544 different morbidities in 308 babies. Among them, the most common morbidity was respiratory distress syndrome which was present in 116 (23.7%) neonates [Table/Fig-3].

Neonatal morbidities	Enrolled preterm babies (n, %)	Feed intolerant babies (n, %)
Respiratory distress	73 (14.9)	14 (25.9)
RDS	116 (23.7)	12 (22.2)
HIE	11 (2.24)	4 (7.4)
Apnea	38 (7.8)	3 (5.6)
NEC	9 (1.83)	2 (3.7)
Shock	50 (10.2)	5 (9.3)
IVH	14 (2.9)	3 (5.5)
Jaundice	68 (13.9)	9 (16.7)
Seizure	4 (0.8)	1 (1.85)
Sepsis	92 (18.8)	15 (27.8)
Hypothermia	46 (9.4)	4 (7.4)
Hypoglycaemia	23 (4.7)	8 (14.8)
Maternal co-morbidities		
Oligohydramnios	75 (15.3)	11 (20.4)
Per vaginal leaking	112 (22.9)	19 (35.2)
PIH	117 (23.9)	9 (16.7)
Chronic medical illness	12 (2.4)	2 (3.7)
None	174 (35.5)	13 (24.1)

[Table/Fig-3]: Maternal and neonatal co-morbidities in enrolled preterm babies (n=490) and feed intolerant babies (n=54). RDS, respiratory distress syndrome; HIE, hypoxic ischaemic encephalopathy; NEC, necrotising enterocolitis; IVH, intra ventricular haemorrhage; PIH, pregnancy induced hypertension

Out of 490 babies with 28-34 weeks of gestation that were followed up, 54 had feeding intolerance with incidence rate of 11.02%. The mean period of gestation of these 54 babies was 31.54 weeks and ±4 days. Their birth weight ranged from 935 gm to 2550 gm, with mean of 1418 gm±207 gm. The maximum numbers of babies having feeding intolerance were very low birth weight babies 33 (61.1%) followed by low birth weight 19 (35.2%) and extremely low birth weight babies 2 (3.7%). A 44 (81.5%) babies with feeding intolerance were initiated with formula feeds whereas rest with mother's milk [Table/Fig-2].

Maternal and foetal co-morbidities in feeding intolerant babies:

Total 41 (75.9%) of mothers who delivered babies with feed intolerance had one or more co-morbidities. Among them, PV leaking of >18 hours (35.2%), oligohydramnios (20.4%) and PIH (16.7%) were most common co-morbidities [Table/Fig-3].

Out of 54 feed intolerant babies, respiratory distress was present in 14 (25.9%) cases, respiratory distress syndrome in 12 (22.2%) patients and neonatal jaundice in 9 (16.7%) patients. Two babies developed NEC (Bell's stage I). Ten of them required invasive mechanical ventilation and four babies died.

Signs of feed intolerance: There were 117 one or more signs of feed intolerance in the 54 babies. A 49 (90.7%) of all feed intolerant babies had vomiting followed by gastric residue (n=31), abdominal distension (n=30), reduced or absent bowel sounds (n=4) and apnea (n=3), respectively [Table/Fig-4].

Signs of feeding intolerance	Number of babies (n)	Percentage (%)
Vomiting	14	25.9
Vomiting and abdominal distension	9	16.7
Vomiting and gastric residue	10	18.5
Vomiting, abdominal distension and gastric residue	9	16.7
Gastric residue and abdominal distension	5	9.3
Vomiting, abdominal distension, gastric residue, apnea	3	5.6
Vomiting, abdominal distension, gastric aspirate, reduced/absent bowel sound	4	7.4
Total	54	100

[Table/Fig-4]: Characteristics in feed intolerant babies (n=54).

The incidence of feeding intolerance was increased in primiparous mothers, babies fed with formula feed and when feeding was started <24 hours but the results were statistically insignificant (p-values 0.96, 0.46 and 0.22, respectively) [Table/Fig-5].

Parameters	Feed intolerance (n, %)	Total enrolled babies	p-value
Parity of mother before birth			
Primiparous	35 (64.8)	319	0.96
Multiparous	19 (35.2)	171	
Type of feeding			
Breast milk	10 (18.5)	334	0.46
Formula feed	44 (81.5)	156	
Feeding start			
<24 hrs	31 (57.4)	296	0.228
>24 hrs	23 (42.6)	194	

[Table/Fig-5]: Comparison of various parameters with feed intolerance babies.

DISCUSSION

Prematurity is an important factor for the development of various complications leading to increase in neonatal death worldwide. Feeding intolerance is one of the important complications in

preterm babies. The incidence of feeding intolerance in the present study was 11%. The study population included preterm between 28-34 weeks of gestation (who were fed by gavage, katori spoon or were on intravenous fluids initially) in this study and found the incidence of feeding intolerance to be 11%. Preterm babies more than 34 weeks were not included in the study as they were directly subjected to mother's breast whereas babies less than 28 weeks were excluded due to their less number in our setting.

The overall incidence of feeding intolerance in a Chinese study (2007-2009) was 27.5% with about 76.4% in very low birth weight babies [16]. Another study conducted by Ahammad F et al., from Bangladesh found the overall incidence of feeding intolerance of 36.7% in 28-36 weeks babies which was three fold more than the present study [17]. The incidence of feeding intolerance was even more (40%) in 28-32 weeks babies in their study. This shows that there is large variation on the incidence of feeding intolerance from one study to another. The low incidence of feeding intolerance in the present study could have been due to the protocol based feeding practices in the setting. Inclusion of specific gestational age babies between 28-34 weeks and not including newborns less than 28 weeks or greater than 34 weeks could also have been another important factor affecting the incidence. The mechanism behind feeding intolerance in preterm could be the immaturity of mechanical and hormonal control of the gastrointestinal system in preterm babies which result in poor co-ordination of sucking and swallowing, incompetent lower oesophageal sphincter, small gastric capacity, delayed gastric emptying time and intestinal hypomotility [18,19].

Although, feeding intolerance was noted to be more in primiparous (64.8%), neonates being fed on formula feeds (81.5%) and feeding when initiated after 24 hours (57.4%); there was no statistical significance (p-values 0.96, 0.46 and 0.22, respectively). Contrarily, the study done by Tang Z et al., (China) showed higher incidence of feeding intolerance in babies with delayed initiation of feeds (p<0.05) and concluded that low gestational age, low birth weight, birth asphyxia and respiratory distress being important factors contributing feeding intolerance [16]. A randomised controlled trial by Dunn L et al., found that introduction of early enteral feeds was significantly beneficial without an increased incidence of complications [20].

Feeding intolerance usually refers to a combination of clinical signs and symptoms suggesting an inability by the newborn to tolerate enteral nutrition. Although, the definition of feeding intolerance varies from author to author, the most comprehensive definition defines feeding intolerance as the inability to digest enteral feedings presented as gastric residual volume of more than 50%, abdominal distension or emesis or both, and the disruption of the patient's feeding plan [7]. Out of 54 babies with feeding intolerance in the present study, 25.9% babies had vomiting, 18.5% had vomiting and gastric residue and 16.7% had vomiting and abdominal distension suggesting that vomiting, gastric residue, and abdominal distension to be the three major signs associated with feeding intolerance. Considering only abdominal distension in babies with CPAP has a poor predictive value for feeding outcome in preterm infants [21].

Feeding intolerance is associated with several neonatal co-morbidities. Ahammad F et al., analysed co-morbidities (respiratory distress syndrome, suspected sepsis, phototherapy, and infant

of diabetic mothers), and found a significant association of feed intolerance with suspected sepsis (p=0.0003) [17]. The common co-morbidities associated with feeding intolerance in the present study were respiratory distress, respiratory distress syndrome, sepsis and neonatal jaundice.

Limitation(s)

This study also had few limitations. This was a single centred study and the findings may not represent the entire population. This emphasises the requirement of further multicentric studies. Secondly, many other factors may be associated with feeding intolerance which were not included in the study.

CONCLUSION(S)

Feeding intolerance is common in preterm very low birth weight babies with vomiting, gastric residue and abdominal distension being three important cardinal signs in those newborns. Formula feeding and initiation of feed before 24 hours are related to increased incidence of feeding intolerance in preterm newborns.

Acknowledgement

The authors acknowledge the NICU staffs of UCMS-TH for their co-operation during the study.

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PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal.
2. Junior Resident, Department of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal.
3. Assistant Professor, Department of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal.
4. Consultant Pediatrician, Department of Paediatrics, Kirtipur Hospital, Kathmandu, Bagmati, Nepal.
5. Associate Professor, Department of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal.
6. Assistant Professor, Department of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal.
7. Associate Professor, Department of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Nagendra Chaudhary,
Associate Professor, Department of Paediatrics, Universal College of Medical Sciences,
Bhairahawa, Nepal.
E-mail: enagendra@hotmail.com

PLAGIARISM CHECKING METHODS: [\[Jan H et al.\]](#)

- Plagiarism X-checker: Feb 27, 2021
- Manual Googling: Jun 08, 2021
- iThenticate Software: Jul 08, 2021 (15%)

ETYMOLOGY: Author Origin**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes (Parental consent was taken)
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 26, 2021**Date of Peer Review: **May 20, 2021**Date of Acceptance: **Jun 16, 2021**Date of Publishing: **Aug 01, 2021**