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Time to achievement of full enteral feeding and its associated factors In Preterm Infants Admitted at the NICU of University of Gondar comprehensive specialized hospital: A Prospective Cohort Study

Alazar Wogayehu[1]*, Ashenafi Tazebew[1], Biniam Yohannes Wotango[2]

[1]*Department of Pediatrics and Child Health, University of Gondar Comprehensive Specialized Hospital, Gondar, Ethiopia.*

[2]*Clinical Governance and Quality Improvement Directorate, Gandhi Memorial Hospital, Addis Ababa, Ethiopia.*

**Corresponding author: Alazar Wogayehu.*

Abstract

Background: Enteral feeding is important part of the management in preterm newborns, we aimed to study factors associated with achievement of full enteral feeds in these infants and whether there is a difference in time to achievement of full enteral feeds between small for gestational age and appropriate gestational age preterm newborns.

Objectives- To assess factors affecting time to full enteral feeding achievement among preterm infants admitted to University of Gondar pediatrics department Neonatal intensive care unit from November 2020 to September 2021

Methods: Hospital based prospective cohort study to be conducted from November 2020 to September 2021. Spearman's correlation, Mann Whitney u test and multiple regression analysis were used.

Results: Out of the 125 preterm included in the study 81.6% were discharged, while 15(12%) and 3(2.4%) died before and after achieving FEF respectively. Median (interquartile range) gestation, birth weight and time to full feeds were 32(30.5-33) weeks, 1300(1150-1500) grams and 12(8-16) days respectively. Gestational age and birth weight were inversely correlated with time to full feeds while presence of maternal malnutrition, neonatal respiratory distress, neonatal clinically significant anemia, NEC and neonatal use of antibiotics increased the time to full feeds. When evaluated jointly on multivariate analysis, GA ($p<0.001$), occurrence of NEC($P<0.001$), time of initiation of Minimal enteral feeds($p<0.001$) and neonatal clinically significant anemia($p=0.046$) proved to have independent prognostic impact on time to FEF. Finally, there was no statistically significant difference in time to FEF between AGA and SGA preterm neonates ($p=0.11$).

Conclusion- As gestational age increases time to FEF decreases and earlier initiation of MEF decreases time to FEF. Occurrence of NEC and neonatal anemia both prolong the time to FEF.

Keywords: enteral feeding; preterm infant; Gondar; Ethiopia

Introduction: Background

Early provision of optimal enteral nutrition and early achievement of full enteral feeds in preterm infants improves long term outcomes by decreasing the rates of several complications of prematurity such as necrotizing enter colitis and sepsis [1]. On the other hand late introduction and slow advancement of enteral feeding may alter GI motility and disrupt microbial colonization [2], leading to delays in achieving FEF. In our setup there is lack of probiotic supplementation [3], commercially available or locally prepared preterm formulas and parenteral nutrition [4] which has shown to support postnatal growth. So, we rely only on initiation of Minimal enteral feeds[trophic] feeding and progressively advanced feeding until achievement of FEF to support postnatal growth in preterm infants with GA less than or equal to 34 weeks and/or VLBW preterm infants. We use a national protocol which guides us in initiation of MEF and in advancement of enteral feeding [5]. Intitation of MEF and rate of advancement depend on the GA of the infants and associated comorbidities they have. Time to achievement of FEF is generally between 7-10 postnatal days according to different protocols [5].

The time to achievement of FEF, which is one of the measures of assessing postnatal growth in VLBW infants [6], is not studied in our setup, and studying this variable might help us assess the general postnatal growth patterns of VLBW infants in our hospital as compared to others. In addition, there is a general problem of frequent delays in enteral feeding in VLBW preterm infants in our hospital, resulting in delays in achievement of FEF which increases the risk of prolonged hospital stay and associated increased risks of acquiring hospital acquired infections. The magnitude of this problem is not studied as well. The

causes of this frequent delays in feeding have been studied and include some maternal factors like (Preeclampsia and chorioamnionitis's [7, 8], neonatal factor and factors associated with type of milk used in feeding and rates of advancements. But information regarding these factors which might influence achievement of FEF in our setup is not well known and studied. So, the aim of theses Study is to evaluate the time to FEF and associated factors which influence it that will help us improve and optimize our feeding methods and reduce potential for poor outcomes.

Methods

Study setting, Study design and period

Hospital based observational prospective cohort study was done on preterm infants who are VLBW or less than 34 weeks gestation admitted to the NICU of Gondar University comprehensive specialized Hospital [UOGCSH], which is tertiary teaching hospital and one of the oldest universities of Ethiopia. During this period certain neonatal and clinical characteristics of the subjects were followed from time of admission until final outcome through a checklist which includes all the selected variables, maternal clinical and socio demographic characteristics were obtained by interview and revision of maternal charts. The study period was from November 2020 up to September 2021 for 11 months.

Source population

All preterm infants admitted to the NICU at UOGCSH

Study population

Preterm infants who are VLBW or less than 34 weeks gestation admitted to the NICU of UOGCSH during the study period.

Sample size determination and sampling technique

The sample size was calculated with single population proportion approach with 95% confidence interval, 5% margin of error.

The required sample size is calculated using a single population proportion formula:

$$\frac{n = [Z\alpha/2]2\ P\ [1-P]}{d2}$$

$$\frac{n = [1.96]^2 x\ [0.15[1-0.15] = 195.9 = 196}{[0.05]^2}$$

Where n= the minimum sample size

Zα/2= value of standard normal distribution (SND) corresponding to a significance level of alpha at 95% (1.96) P=15%, Taken from a previous study in Jimma university. d = margin of error 5 % (0.05), Non response rate (10%=0.1).

The total sample size with 10% rate of non-response will be =216

Considering the nature of the study and the limited study period all newborns that fulfilled the inclusion criteria and admitted within the study period were included.

Data collecting Instrument

A structured questionnaire was used as the instrument for data collection. The checklist included socio demographic data and data on prenatal neonatal and clinical factors which are listed as variables for the study. The questionnaire was prepared after careful analyzation of all the variables and after reviewing related studies and papers.

Data collecting Tools and Procedures

Selection and training of data collectors was done. Then training was conducted for 6 data collectors (residents, interns and nurses] for 2 days on the objectives of the study and how to collect the data. The questionnaire prepared in English was filled by principal investigator, residents, GPS and trained interns, the chart was revised for each patient including the outcome. The questionnaire was filled starting from the 1st day of admission for each patient until post-conceptional age (PCA] 37 weeks, or less if infants were discharged or died or went against medical advice. And it was attached to corresponding chart of the patient until completion.

Data Analysis

The reliability of data was cross checked by principal investigator among randomly selected patients during data collection. The data was checked for completeness by principal investigator and entered to personal computer; and was compiled and analyzed using SPSS version 25 after the data collected was entered. Descriptive analysis will be done for each variable to summarize base line characteristics of variables. Data will be summarized using frequencies, percentage, means and SDs, medians and interquartile ranges (IQR) as appropriate.

Univarate analysis was conducted individually on the predictor variables and those variables with association p<0.2 with the dependent variable [TFF] were analyzed with multiple regression models to

evaluate for independent association. Tests of linearity, normality, multicollinearity, homoscedasticity as well as effect of outliers were analyzed before conducting multiple regression models. Ninety five percent confidence interval (95% CI) was computed and Variables with p values <0.05 were considered to have significant association with outcome variable [time to FEF]. Non parametric spearman's correlations were done to assess strength and direction of correlation between continuous predictor variables birth weight, gestational age, age at initiation of MEF and outcome variable, age at achievement of FEF. Mann Whitney test was also performed to compare time to full enteral feeding among AGA groups with SGA.

Operational Definitions

- Postnatal Age at achievement of FEF: The postnatal age in days starting from initiation of MEF to achievement of FEF.
- FEF: Provision of the optimal calorie intake for preterm which is 120kcal/kg/day or 150ml/kg/day via NGT either using human milk or formula milk for at least 24 hours
- Maternal Pregnancy Induced Hypertension: Defined as preeclampsia and/ or eclampsia according to ACOG.
- Maternal Malnutrition: Defined as Maternal Mid upper arm circumference <18cm
- Maternal Late Gestation Anemia: Defined as maternal Hemoglobin <11g/dl and/or anemia which required iron therapy or blood transfusion within a month before current delivery
- Chorioamnionitis: Presumed clinical diagnosis made in mothers with high fever >38oc plus one or more of the following [Baseline fetal heart rate >160beats/min, Maternal white cell count >15000, Purulent fluid coming from cervical os via speculum examination or a confirmed diagnosis made by presumed clinical diagnosis plus histopathology or bacteriologic evidence of infection of amniotic fluid]
- Antenatal Steroids: either complete defined as recommended doses given with the last dose administered at least 24hrs before delivery, incomplete or not given at all.
- Mode of delivery: Delivery either through cesarean section or through vaginal delivery (includes either spontaneous, induced or assisted)
- Gestational Age: defined as age in weeks plus days as calculated from the first day of the LNMP or age in weeks calculated by Ballard score. If maternal date unreliable or if there is more than 1 week discrepancy between maternal date and Ballard score the later will be taken as the GA
- Weight for GA: defined as appropriate, small and large for GA (AGA=10-90%, SGA<10%, and LGA>90%, respectively) according to loubchenco curve
- Respiratory Distress: defined as abnormal respiratory rate (either bradypnea or tachypnea) and need for respiratory support [nasal catheter, nasal prongs or CPAP] within the first 24hrs of birth.
- NEC: Defined as probable, definite or advanced using the BELL's criteria.
- Neonatal Anemia: Defined as anemia of any level with cardio respiratory compromise or requiring blood transfusion.
- Polycythemia: Defined as Hematocrit level >65% requiring either hydration or partial exchange transfusion.
- Source of feeding: Defined as either human milk or formula used for enteral feeding, or mixed, both formula and breast milk used.
- MEF: Defined as the amount of first enteral feeding [either human milk or formula] given to the newborn

Results

Time to achievement of FEF is comparable to most protocols including our national guideline.

Recommendation

Based on the outcomes from the study, we recommend all responsible healthcare workers involved in the management of preterm infants to strictly follow the enteral feedings of these newborns with special attention for those with early gestational age, with anemia and NEC as they are at risk of feeding intolerance and will have prolonged time to achieve FEF, which will increase their duration of hospital stay. We also recommend that for a select few preterm neonates who are clinically stable at admission, starting them on earlier MEF would decrease the time to FEF achievement. Finally, we acknowledge that a better powered prospective study is required to support the current study.

Declarations

Ethical Approval and consent to participate

Ethical approval was sought from the Institutional Research Review Boards [IRBs] of University of Gondar Comprehensive Specialized Hospital. Then, permission to carry out the study was sought from the pediatric department and hospitals' administrations. Participation in the study was on voluntary basis. After a detailed explanation of the study purpose, written informed consent was sought from participants. Confidentiality and privacy of the participant was maintained throughout the process of data collection. The data collection teams were trained on how to handle sensitive and emotional issues and on the importance of keeping confidentiality and participants was free to decline or withdraw from participating in the study at any time during the study period.

Consent for publication

Not applicable.

Availability of data and materials

The data underlying this article will be shared on reasonable request to the corresponding author

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

All authors contributed to the conception of the study, design, analysis, interpretation of the data, read and approved the final manuscript.

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