



COLLEGE OF HEALTH SCIENCES SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

THE PRACTICE OF IRON SUPPLEMENTATION AND ANEMIA FOR PRE-TERMS AND LOW BIRTH WEIGHT INFANTS AT HIGH-RISK INFANT CLINIC, TIKUR ANBESSA SPECIALIZED HOSPITAL AND GMH, ADDIS ABABA, ETHIOPIA

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DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

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AbbreviationsAcronyms:

AAU	Addis Ababa University
AOP	Anemia of prematurity
CI	Confidence Interval
GA	Gestational age
ELBW	Extremely low birth weight
LBW	Low birth weight
VLBW	Very low birth weight
NICU	Neonatal Intensive care unit
ID	Iron deficiency
IDA	iron deficiency anemia
MD	Medical doctor
MRN	Medical record number
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
TASH	Tikur Anbessa Specialized Hospital
WHO	World Health Organization
FMOH	Federal minister of health

Abstract

Background: Iron supplementation is providing of prophylaxis's iron for pre-terms and low birth weight infants to supply sufficient iron for growth and development without increasing the risk of iron overload. Preterm infants are deprived of the significant iron accretion that occurs in the third trimester of pregnancy and have reduced iron stores at birth compared with term infants. Iron deficiency in infancy is associated with a range of clinical and developmentally important issues including neurodevelopmental deficits, delayed maturation of the auditory brainstem response, risk for poor cognitive, motor, social-emotional and neurophysiological development.

Objective: The primary objective of this study is to evaluate the current iron supplementation practice and anemia for pre-terms and low birth weight infants at Tikur Anbessa specialized hospital and Gandhi memorial hospital from January 1, 2019 to December 31, 2020.

Method: A cross-sectional study was done by using patient charts review that were evaluated at newborn intensive care unit, wards and high-risk infant clinic of Tikur Anbessa specialized hospital and Gandhi memorial hospital. Data was collected through retrospective chart review which meet the inclusion criteria by using structured check list which is prepared from previous literature with few amendments. The data was coded, cleaned and entered into Epi data version 4.6 and then transferred to SPSS version 26 software program for further analysis. Descriptive summary measures were presented using Tables and Figures. The data was categorized and summarized with descriptive statistics.

Result: There were 245 pre-terms and low birth weight infants included in this study. Iron prophylaxis supplementation practice was 53.1%, where 54.6% of supplemented infant was females. Mean iron prophylaxis starting time was 7.4 weeks and average dose of supplementation was 1.94 mg/kg/day. Mean duration of iron supplementation was 5.4 months. One hundred thirteen (86.9%) of supplemented infants were below 34 weeks GA. Ninety-four (72.3%) of iron supplemented infants birth weight were below 1500 grams. Around 65.4% of infants were started iron prophylaxis in the range of (3-8) weeks of post-natal age and 65.4% of infants supplemented 2 to 4 mg/kg/day of elementary iron. According to this study prevalence of anemia was 39.6% and 4.1% severe anemia, 20.6% moderate and 75.3% had mild anemia where all of severe anemia was non-supplemented infants.

Conclusion: Iron prophylaxis practice was low in TASH and GMH and a great variability in the timing of beginning, dose, and ending of iron prophylaxis which needs standardization. Iron prophylaxis supplementation practice is imperative to protect anemia in preterm and low birth weight infants. Anemia was high for those non-supplemented infants whereas preventive iron prophylaxis prevents severe anemia significantly.

1. INTRODUCTION

1.1. BACKGROUND

Infantes with anemia of prematurity (AOP) increased now a day because of increment the frequency of prematurity and low birth weight (LBW) in both the developed and developing world due to increasing indicated preterm birth and preterm delivery of artificially conceived multiple gestation(1).

World health organization defined prematurity one that occurs at less than 37 weeks and more than 20 weeks of gestational age (GA) and LBW birth weight less than 2500g (2,3). World Health Organization defines anemia as a decrease in the concentration of circulating red blood cells or a hemoglobin (Hb) concentration 2 standard deviation(SDs) below the mean Hb concentration for a normal population of the same gender and age range (1).

The transition from a relatively hypoxic state in utero to a relatively hyperoxia state with increased tissue oxygenation after birth leads to a decline in erythropoietin (EPO) concentration. Anemia of prematurity (AOP) is an exaggerated, pathologic response of the preterm infant to this transition (1). Iron deficiency in infancy is associated with a range of clinical and developmentally important issues including neurodevelopmental deficits, delayed maturation of the auditory brainstem response, and abnormalities of memory and behavior (1)

Preterm babies comprise the largest group of children atrisk of iron deficiency and iron deficiency anemia becauseof both their low iron stores (due to the reduced thirdtrimester iron transfer) and their increased demand (due tothe proportionally more rapid postnatal growth than that ofthe term infant (1). Increased hemolysis, reduced red blood cell life span, low circulating erythropoietin levels, blood sampling, and loss of blood due to surgery. Pregnancy complications, including gestational diabetes mellitus and fetal growth restriction, as well as maternal lifestyle factors such as smoking and obesity, also compromise infant iron stores (4).

Iron deficiency was defined by ferritin levels $<10 \mu\text{g/l}$, transferrin saturation $<10\%$ and mean corpuscular volume $<80 \text{ fl}$. Anemia diagnosis was based hemoglobin a hemoglobin (Hb) concentration 2 SDs below the mean or $<11 \text{ g/dl}$ at 12mont post-natal age (5). As iron is essential for brain development, iron deficiency is demonstrated not to be only a hematologic disease, but a developmental disrupter with long-term poorneurocognitive outcome. The effects of iron deficiency on the developing brain are permanent and life-altering (6).

Apart from the considerable impact of preterm birth itself, infants delivered preterm are at a high risk of iron deficiency owing to the increased postnatal iron required to facilitate rapid growth and an earlier onset of erythropoiesis, which occurs 1–3 months earlier than in term infants. Most infants are asymptomatic even if HbG is less than 7g/dl

Iron supplementation is recommended for all breast-feeding preterm infants, although extreme caution is warranted, as the potential risk of iron overload is high (6). High iron doses from supplementation or blood transfusions can result in excess iron, which contribute to the production of reactive oxygen species that can affect sensitive organ systems, such as the heart, liver, pancreas, and developing brain (6). So, the complication can be prevented by supplementation of for all preterm infant (<37 weeks' gestation) with appropriate dose, duration. Infants who are on human milk feeding should receive a supplement of elemental iron at 2 mg/kg per day starting by 2 weeks of age and extending through 12 months of age (6,7).

Preterm infants fed a standard preterm infant formula (14.6 mg of iron per L) or a standard term infant formula (12.0 mg of iron per L) will receive approximately 1.8 to 2.2 mg/kg per day of iron, assuming a formula intake of 150 mL/kg per day (6). Despite the use of iron-containing formulas, 14% of preterm infants develop ID between 4 and 8 months of age (6).

The prevalence of anemia among under five children was 47.5% of which 18.3% were mildly anemic, 25% were moderately anemic, and 4.1% were severely anemic (8). But in Ethiopia the iron supplementation practice for LBW and premature infants is not known. Therefore, this research was conducted to identify the gaps and help to prepare to fill those gaps.

1.2. Statement of the problem

Although AOP is a widespread public health problem associated with increased risk of morbidity and mortality and a lot is known and documented about anemia on a global perspective, very little is known about its supplementation and management practice for premature and LBW infants in most developing countries. Furthermore, although there are good databases in developed countries concerning iron supplementation surveillance system, Iron deficiency is estimated to range between 25 to 80% in pre-terms during infancy (7). There are no formal current iron supplementation practices report in most of the low-income countries. Hence, information on this public health issue remains insufficient

The World Health Organization (WHO) has estimated that the global prevalence of anemia to be ~24.8% including (47%) children younger than 5 years among this pre-terms account 26.2% (9). Although the prevalence of anemia is estimated 9% in countries with high development, in countries with low development the prevalence is 43% (9).

Africa and Asia accounting for more than 85% of the absolute anemia burden and about 67.6% of under-five children in Africa are suffering from anemia indicating anemia as a severe health problem (9). Several factors contribute to the occurrence of anemia and nearly half of (43%) the anemia cases in childhood are due to iron deficiency (9). It is the commonest cause of anemia and is also a common deficiency among nonanemic children, especially among children of resource limited countries (9,10).

In infants and under five children Iron deficiency is the commonest nutrient deficiency in the world and a major public health risk in both the developing and industrialized countries (9,10) Iron deficiency and iron deficiency anemia is common and distinct feature for premature and low birth weight infants and have highest incidence at 4 to 12 weeks of age (9).

The incidence of iron deficiency and AOP in the general newborn population increased due to increment of LBW and prematurity (11,6). In developed countries ID and AOP decreased due to Proper supplementation and presence of fortified formula feeding. 4% of pre-terms will have AOP at 8 weeks of post-natal age and 12% at age of 12 months (6). In VLBW infant average HBG concentration fell from 18.2mg/dl at birth to 9.5g/dl at 6 weeks of age. Values b/n 7 to 8g/dl common in 24% of less than 1000g and 21% weight b/n 1000 to 1500g. many infants are asymptomatic even HBG less than 7g/dl (6).

According to 2016 DHS in Ethiopia, the prevalence of anemia among under-five children was 57%, of which 72% are infants (12). Even though the national prevalence of anemia in under five children and infants are high in Ethiopia data on iron supplementation practices for premature and LBW is not Studying. Studies with regard to iron supplementation practice in a particular region would help to identify the gap and allow early diagnosis and supplement of such cases, which in turn should reduce morbidity. Identifying supplementation practices and gaps in a given setting and population group is very important to prevent or treat anemia.

1.3. Significance of the study

Since there were no study done on iron supplementation practice for pre-terms and LBW infants in this country, and no study done at both HRIC and NICU of TASH and GMH, it is believed that valuable information was gained from the study.

Despite WHO recommends iron supplementation for all preterm and low birth weight infants (7), from my observational view proper iron supplementation was not routinely done indicating a suboptimal proactive follow up of these premature neonates, so this study assessed the gap and potential intervention areas of iron supplementation practices

This research identified the iron supplementation gaps which was then help to organize trainings for those who work at HRC to improve iron supplementation practice. At the end it will decrease IDA related burdens for pre-terms and LBW infants.so, assessment of iron supplementation practice for premature and LBW is important. Furthermore, it would serve as a baseline for further study in the area

2.LITRATURE REVIEW

2.1. worldwide

After clinical report covers diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants (both breastfed and formula fed) AAP recommended all LBW and pre-terms infant who fed human milk should receive a supplement of elemental iron at 2 to 4mg/kg per day starting by 1 month of age and extending through 12 months of age (6). Preterm infants fed a standard preterm infant formula need 1.8 to 2.2 mg/kg per day of iron. Despite the use of iron-containing formulas, 14% of preterm infants develop ID between 4 and 8 months of age [6].

After 684 records identified, 27 articles systematic review done aimed to investigate the effects of enteral iron supplementation on iron status, growth and neurological development on 12, December 2019 WHO recommends iron supplementation for all pre-terms and LBW infants, with elementary iron dose of 2 to 4mg/kg/d(7)

Iron group receiving 2 to 4mg /kg/day of iron supplements from about 2 weeks and a late iron group that did not receive iron supplements until 2 months of age. Late iron group had required blood transfusions. WHO recommends to start at post-natal age of 2 weeks (7). Iron supplementation should be delayed in infants who have received multiple blood transfusions and have high serum ferritin concentration. Iron supplementation should be continued after discharge, at least until 6 to 12 months of age depending on diet(7).

At 6 to 8 weeks: hemoglobin with or without MCV at approximately 6 to 8 weeks postnatal found a lower hemoglobin in the non-iron supplementation group which was maximal at six weeks (6 g/L in 1000 g to 1500 g birth weight; 7 g/L in 1501 g to 2000 g birth weight (7). Statistically significant difference in hemoglobin concentration at 6 to 8 weeks remained in subgroup trials of formula-fed infants (n = 389) 0.7 g/L; 95% CI -1.1 to 2.6). In trials of partially or fully breast-fed babies (n = 137) a statistically significant difference in favor of iron supplementation was noted: (4.1 g/L; 95% CI 0.6 to 7.7) (7).

At 3-to-6-month Meta-analysis found a borderline statistically significant difference in hemoglobin concentration(7)

At 6-to-9-month the research showed a statistically significantly higher hemoglobin concentration in the iron supplemented group (WMD 6.6 g/L; 95% CI 3.1 to 10.1) (Outcome 1.6.1)(7). Hemoglobin when compared to placebo for both 2 mg/kg/day of elemental iron (MD 8.0 g/L; 95% CI 5.2 to 10.8) (Outcome 1.6.2) and 1 mg/kg/day of elemental iron (MD 3.8 g/L;

95% CI 1.2 to 6.4) (Outcome 1.6.3) reported as statistically significant difference in hemoglobin concentration (WMD 16.0 g/L; 95% CI 10.7 to 21.3) (Outcome 1.7)(7).

Type of feeding and hemoglobin at 6 to 8 weeks: 'early commencement' (WMD 1.55 g/L; 95% CI -0.12 to 3.2), 'late commencement' (WMD -1.1 g/L; 95% CI -8.8 to 6.6) (Outcome 1.16.4); and hemoglobin at 3 to 4 months: 'early' (WMD 0.75 g/L; 95% CI -2.4 to 3.9) (Outcome 1.17.3), 'late' (WMD 5.6 g/L; 95% CI 1.4 to 9.8) (Outcome 1.17.4)(7)

Daily dose of supplemental iron administered: 'low dose' (2 mg/kg/day or less) and 'high dose' (more than 2 mg/kg/day). The studies using a low dose of iron (including doses of both 2 mg/kg/day and 1 mg/kg/day) of iron, hemoglobin at 6 to 8 weeks: 'low dose' (WMD 3.9 g/L; 95% CI 1.5 to 6.3) (Outcome 1.16.5), 'high dose' (WMD -0.76 g/L; 95% CI -3.0 to 1.5) (Outcome 1.16.6); and hemoglobin at 3 to 4 months: 'low dose' (WMD 4.0 g/L; 95% CI 0.85 to 7.2) (Outcome 1.17.5), 'high dose' (WMD -0.15 g/L; 95% CI -4.2 to 3.9) (Outcome 1.17.6)(7).

Gestational age or birth weight of participants, or both: less than or equal to 33 completed weeks 'or less than 1500 g and more than 33 completed weeks' or 1500 g or more. Only two studies dealt specifically with low-birth-weight infant on quantitative meta-analysis for hemoglobin at six to eight weeks, 'under 1500 g' (WMD -0.42 g/L; 95% CI -4.3 to 3.4) (Outcome 1.16.7); '1500 g or over' (WMD 0.77 g/L; 95% CI -1.2 to 2.7) (Outcome 1.16.8). Early versus late supplementation
Six to eight weeks: Hemoglobin concentration was higher in the early iron group: (WMD 1.7 g/L; 95% CI 1.4 to 1.8) (7).

A retrospective project involving neonates cared for in the 10-year period between January 2006 and December 2015 to know iron supplementation time and supplementation practice in the perinatal intensive care units of Intermountain Healthcare (18 hospital units at units in Utah and Idaho). Patients admitted to a NICU with a diagnosis of preterm, IDM, SGA, or VLBW were studied, only 11.8% received any supplemental iron in the hospital. Of 1403 SGA neonates, 9.8% received iron, and of 1813 VLBW preterm neonates, 27.1% received iron. For all groups, less than 20% of those who received supplemental iron had it started by day 14 (thus <20% were compliant with the 55% to 60% had the iron started by day 30 and 82% to 88% had it started by 8 weeks (56 days) ($p=0.038$)(14).

Study done at three regions of Italy Neonatal Units on the current practices of iron prophylaxis in preterm and lowbirth weight newborns Units Birth weight is considered an indicative parameter in 64% of LNUs and 71% of NICUs, supplementation practice in the three regions (86%, 20% and 62%, respectively; $p < 0.001$). Iron supplemented to infants with a birth weight between 2000 and 2500 g is only 25% of LNUs and 21% of NICUs, and to late-preterm (gestational age between 34 and 37 weeks) in a minority of Units (26% of LNUs, 7% of NICUs)(15).

A study done in Brazil with birth weight <1500 g and gestational age <34 weeks on iron prophylaxis were followed up to 12 months. Anemia diagnosis was based on hemoglobin <11 g/dl. Neonatal data and feeding at 6- and 12-months' (breastfeeding and/or cow's milk or infant formula); Prevalence of anemia in 310 participants was 26.5% [95% confidence interval (CI) 21.8–31.6% and of iron deficiency was 48% (95% CI 39.0–56.9%). Increased consumption of cow's milk at 6 months [relative risk (RR) 1.687; 95% CI 1.146–2.483], lower maternal age (RR 0.953; 95% CI 0.923–0.983), high number of pregnancies (RR 1.256; 95% CI 1.122–1.406) and being born small for gestational age (RR 1.578; 95% CI 1.068–2.331) were independently associated with anemia after adjustments(16).

2.2. Africa

In Africa there was no research done about iron supplementation practice other than countries like Nigeria, Kenya, Ruanda using AAP iron supplementation for pre-term infants guideline.

2.3. Ethiopia

No research done in Ethiopia about iron supplementation practice but Ethiopian Neonatal intensive care unit training participants manual recommends all pre-terms less than 1500g and GA of less than 34 weeks must supplement iron 2 to 4mg /kg/d for 12 months (17).

Prospective, observational study was done to all preterm babies who delivered at five Ethiopian hospitals to determine Hematologic Profiles of Ethiopian Preterm Infants with Clinical Diagnoses of Early-Onset Sepsis, Perinatal Asphyxia, and respiratory distress syndrome and others who were referred to hospitals before 7 days of life from July 2016 to May 2018. A total of 3852 were admitted to one of the studies NICUs. Of the total admissions, 2633 (68.35%) had a CBC determined and were included. The mean values for HGB, and platelets were 17.9mg/dL. HGB value was less than 7mg/dL in 8 (0.6%) of the preterm infants admitted with a clinical diagnosis of EONS, 3 (1.7%) of preterm infants admitted with a clinical diagnosis of PNA and 5 (0.4%) of preterm infants admitted with a clinical diagnosis of RDS. Two hundred thirty-seven (19.1%) preterm infants with EONS were found to be anemic (18).

3. STUDY OBJECTIVE

3.1. General objective

- To assess iron supplementation practice for pre-terms and/or low birth weight infants at HRIC of TASH and GMH, Addis Ababa, Ethiopia from January 1, 2019 to December 31, 2020

3.2. Specific objectives

- To determine the iron supplementation practice for pre-terms and low birth weight infants at HRIC of TASH and GMH
- To determine the effect of iron supplementation to degree of anemia.

4.METHETDS

4.1. Study area

The study was conducted in TASH and GMH at HRIC Addis Ababa. Addis Ababa is the capital city of Ethiopia and the seat of Africa union. According to 2007 census, it has population of 2,739,551 (19). It has an altitude of 2355m above sea level and its land area is 527 square km. It coordinates at 9°1'48''N 38°44'4''E (20). TASH was opened in 1972 and it has become the university teaching hospital under AAU since 1998. It is the largest tertiary hospital in the nation and the hospital has many clinical departments including pediatrics, emergency medicine, internal medicine, gynecology /obstetrics, general surgery, family medicine, psychiatry, ophthalmology, ENT, dentistry, neurology and other specialty and subspecialty departments. It has a total of 21 specialty departments. TASH has 2000 doctors, 379 nurses and 115 other health professionals dedicated to providing health care services. The various departments, faculties and residents under specialty training in the School of Medicine provide patient care in the hospital (21).

The High-Risk Infant Follow-up Clinic provides evaluation of the growth and development of infants and young children who are at risk for neurologic problems or developmental delays because of premature birth, low birth weight or other problems at birth (22). The HRIC supplement iron and other vitamins for low birth weight and premature infants. The clinic gives service five days in a week and run by nurses, year II residents, neonatology fellow and neonatologist.

4.2. Study design

An institutional based cross-sectional study was conducted on pre-terms and LBW infants who had follow-up at HRIC of TASH and GMH.

4.3. Study period.

This study was conducted from January 1, 2019 to December 31, 2020 and Data collection was carried out from June 20, 2021 to August 20, 2021

4.4. Population

4.4.1. Source population

All pre-terms and LBW infants who had follow-up at HRIC during the study period

4.4.2. Study population

Pre-terms and LBW infants who had follow-up at HRIC during the study period which full fill inclusion criteria

4.5. Inclusion and Exclusion criteria

4.5.1. Inclusion criteria

All pre-terms (<37 weeks) and/or LBW (<2500g) infants who had follow-up during the study period was included to the research

4.5.2. Exclusion criteria

- Post-natal age less than 2 week.
- Infants whose GA greater than 37 weeks
- Birth weight above 2500grams.

4.6. Sample size determination

The sample size was calculated by using the formula for single population proportion for cross sectional survey considering the following assumption: 95% level of confidence with 0.05 α value (which yields $Z_{\alpha/2} = 1.96$ on the standard normal distribution curve), 5% margin of error.

Where, n = is sample size

z = The value of the standard normal curve score corresponding to the given

Confidence interval = 1.96

p == Estimated proportion preterm infants not supplemented iron is 50%

d = The permissible margin of error (the required precision) = 5%

$$n = \frac{(1.96)^2 (0.50)(1-0.50)}{(0.05)^2} = 384$$

Since the population is less than 10,000 a correction formula will be used. Therefore, using the correction formula:

$n = \frac{n_0}{1 + n_0/N}$ Where n_0 is the initial sample size and N is the total population

$$n = \frac{384}{1 + (384/\text{source population}(530))}$$

$$n = 223$$

After adding 10% non-response rate = 245

4.7. Sampling method

All pre-terms and LBW infants who fulfill the inclusion criteria and follow-up between the study period was included. From these pre-terms two hundred forty-five was selected by systematic random sampling with a sampling interval of 2 which was calculated as $K=N/n=530/245=2.16$ from a total of 530 coded cards.

4.8. Data collection

After preparing a structured check list developed which was adapted using prior literatures-based study objectives, Total of 530 cards were collected and coded from Tikur Anbessa HRIC and GMH HRIC from the card office by patient record storage and retrieval office workers in the office. For this purpose, the card number in the registration book was used. After selecting the 245 cards (123) of the structured format was filled by principal investigator and half (122) of the check list was by trained data collectors and reviewed by the principal investigator (PI). During data collection 145 cards was from TASH and 100 was from GMH. The data collectors are two nurse who are currently working at HRIC and trained by the principal investigator. They had one day training on how to trace information on the charts of the patients and fill the questioner. The necessary modifications were made on the data collection tool based on the findings.

4.9. Data quality assurance

The primary investigator was examining the appropriateness of the methodologies followed. At time of data collection filled questionnaires was checked for completeness and consistency of information by PI in daily based. Any ambiguity and other problems of data collectors were addressed. The template was having internal consistency checks. The study was done as per the ethical code of conduct.

4.10. Data analysis

Data extracted from patient's medical charts was coded, cleaned and the registry was entered into computer using Epi data version 4.6 and then transferred to SPSS version 26 software program for further analysis. Simple descriptive statistics such as frequencies, percentages, mean, and Standard deviation was used to characterize the variables. The analyzed data was described using tables, graphs and figures accordingly

4.11. Variables

4.11.1. Independent variable

- Birth weight
- Gestational age
- Starting time
- Dose
- Duration
- Maternal complication

4.11.2. Dependent variable

- Iron supplementation practice

4.12. Operational definitions

Anemia: Defines a hemoglobin concentration 2 SDs below the mean hemoglobin concentration for a normal population of the same gender and age range or <11 g/dl at 12 months post-natal age (6).

Degree of anemia:

- Mild (HbG=8.9 to 10.9g/dl)
- Moderate (7 to 8.9g/dl)
- Severe (≤ 7 g/dl)

Short duration supplementation: iron given <6 months

Long duration supplementation: iron given ≥ 6 months

Low dose of elementary iron: elementary iron <2mg/kg/day

Delayed starting time :> 4 weeks

4.13. Ethical considerations

The study was conducted after an ethical approval obtained from DPACH research and publication committee. The objective of the study was briefed to the staff of the documentation department. Documents and Information obtained at each course of study were kept confidential.

4.14. Dissemination of result

The findings of the study will be presented to department of PACH /AAU. Depending on the findings from the data, conclusion and recommendations were made. Then, copies of the research paper were submitted to AAU College of health science and department of PACH. If possible, it will be published on journals as well

5. RESULT

There were 245 preterm and low birth weight infants selected at Tikur Anbessa specialized hospital and Gandhi memorial hospital high-risk infant clinic in the study period. The iron supplementation practice was 53.1%.

Socio-Demographic Characteristics of infants and mother

The number of male and female infants were 120(49%) and 125(51%) respectively. Mean maternal age was 28.4 years whereas; 92% of them were below 35 years. One hundred seventy-one (69.8%) were from AA and 74(30.1%) outside Addis Ababa (Table 1).

TABLE 1. SOCIO-DEMOGRAPHIC CHARACTERISTICS PERCENTAGE DISTRIBUTION TABLE OF INFANTS AT TASH AND GMH HRIC, ADDIS ABABA, ETHIOPIA FROM JANUARY 1, 2019 TO DECEMBER 31, 2020

variables		Frequency (%)
Sex	Males	120(49%)
	Females	125(51%)
Maternal age	15-20	16(6.5%)
	21-35	209(85.3%)
	36-50	20(8.2%)
	2001-2500gram	27(11%)
Place of residence	Urban	171(69.8)
	Rural	72(30.2%)

Maternal condition

Ninety-five (38.8%) and 150(61.2%) were primipara and multipara respectively. Around 213(86.9%) of mother took iron during pregnancy. The commonest complication during pregnancy was preeclampsia 68(27.8%) (table 2).

TABLE 2. MATERNAL CONDITIONS PERCENTAGE DISTRIBUTION AT TASH AND GMH HRIC ADDIS ABABA, ETHIOPIA FROM JANUARY 1, 2019 TO DECEMBER 30, 2020 G.C.

Variables		Frequency (%)
Parity	Primipara	95(38.8%)
	Multipara	150(61.2%)
Supplemented status	Supplemented	213(86.9%)
	Not supplemented	32(13.1%)
Maternal complication	APH	26(20.8%)
	GDM	8(6.4%)
	Preeclampsia	68(54.4%)
	PPH	11(8.8%)
	Other	12(9.6%)

Neonatal condition

Mean gestational age of the infants were 33.7(\pm 2.02) weeks whereas,186(75.9%) of infants were below thirty-four weeks. Median 1500(IQR 1220 -1900) g and 56.3% of the infants were below 1500gram.In this study 186(75.9%) of infants were \leq 34 weeks of gestation and 138(56.3%) of infants were less than 1500gram table (3)

TABLE 3. PERCENTAGE OF DISTRIBUTION OF GA AND BW

Variables	Frequency (%)	
Gestational age	\leq 31 weeks	53(21.6%)
	32-34 weeks	133(54.3%)
	35-37 weeks	59(21.4%)
Birth weight	\leq 1000gram	11(4.5%)
	1001-1500gram	127(51.8%)
	1501-2000gram	80(32.7%)
	2001-2500gram	27(11%)
Types of feeding	Breast	102(78.5%)
	Formula	8(6.2%)
	Cow	4(3.1%)
	Mixed	15(11.5%)

Iron supplementation based on GA and birth weight

Among 245 participants 130(53.1%) were iron supplemented and 30 % of them took iron after they develop anemia. High number of supplemented infants were females which account 54.6%. Among 130 supplemented infants 82 were from TASH which showed iron supplementation practice of 56.6% and 48 participants were from GMH HRIC where the iron supplementation practice was 48%.

The mean iron prophylaxis starting time was 7.35(\pm 2.86) weeks and the average iron dose was 1.94(\pm 0.55) mg/kg/day. The median duration of iron prophylaxis was 4(IQR 2 to 7) months.

One hundred thirteen (86.9%) of supplemented infants were below 34 weeks of GA and ninety-four (72.3%) of iron supplemented infants birth weight were below 1500 grams. Only 26(20% of infants were started iron prophylaxes in the range of (2-4) weeks of post-natal age and 65.4 percent of infants supplemented 2 to 4mg/kg/day of elementary iron. The highest number of infants were breast milk feeders 102(78.5%) (Table 4)

TABLE 4. PERCENTAGE DISTRIBUTION OF IRON SUPPLEMENTATION BASED ON GA, BW, STARTING TIME, IRON DOSE AND DURATION OF SUPPLEMENTATION

Variables		Iron supplantation frequency (%)
Gestational age (In weeks)	≤31	38(71.7%)
	32-34	75(56.4%)
	35-37	17(28.8%)
Birth weight in (Grams)	≤1000	9(81.8%)
	1001-1500	85(66.9)
	1501-2000	30(37.5%)
	2001-2500	6(22%)
Iron started time (In weeks)	2-4	26(20%)
	5-8	60(46.2%)
	9-12	36(27.7%)
	≥12	8(6.2%)
Dose of iron supplementation In mg/kg	<2	41(31.2%)
	2-4	86(66.2%)
	5-6	3(2.3%)
Duration of iron supplementation in month	≤2	16(12.3%)
	3-8	50(38.5%)
	9-12	19(14.6%)
	≥13	9(6.9%)

Level of anemia

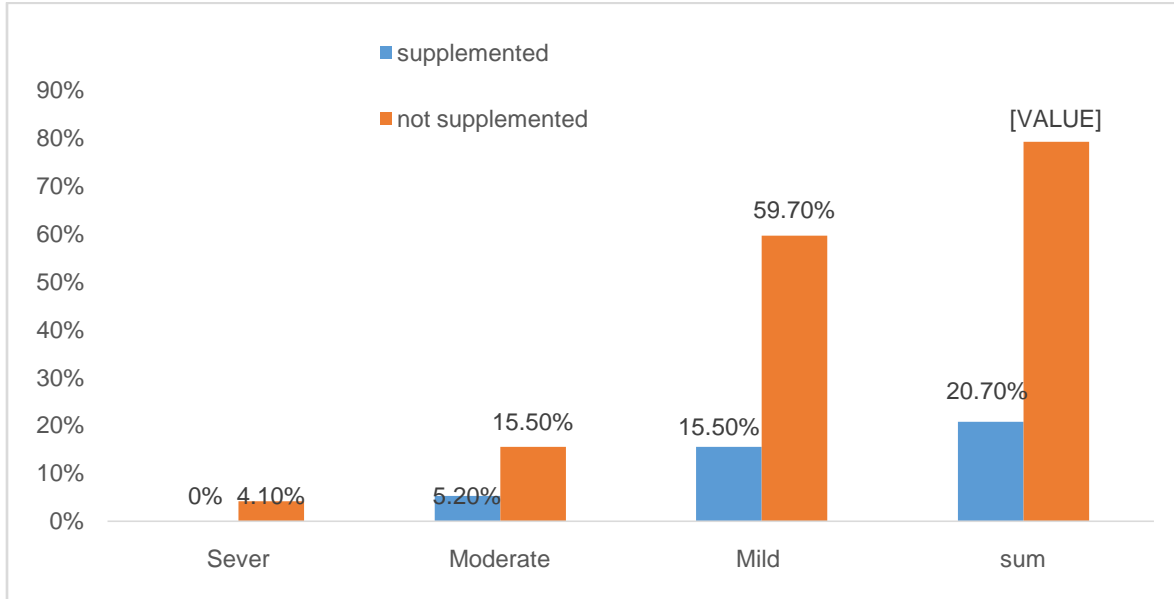
Over all anemia level in this study was 97(39.6%) where 20(20.6%) and 77(79.4%) of anemic infants were iron supplemented and none supplemented respectively. All the severely anemic infants were non-supplemented group. Among infants who took iron and developed anemia 80% of them were took iron less than 2mg/kg/day. Around 31(12.7%) of infants required blood transfusion where 19 infants required once 12 infants required transfusion twice. Around 50% of anemic infants had maternal complication (table 5)

TABLE 5. PERCENTAGE DISTRIBUTION OF LEVEL OF ANEMIA BASED ON GA, BW, STARTING TIME, IRON DOSE AND DURATION OF SUPPLEMENTATION

Variables		Percentage of anemia
Gestational age	≤31 weeks	25/53(47.2%)
	32-34 weeks	49/133(36.8%)
	35-37 weeks	23/59(38.9%)
Birth weight in (Grams)	≤1000	7/11(63.6%)
	1001-1500	44/127(34.6%)
	1501-2000	40/80(50%)
	2001-2500	6/27(22.2)
Dose of iron supplementation (In mg/kg)	<2	16/41(39%)
	2-4	4/86(4.7%)
	5-6	0/3(0%)
Type of feeding	Breast	80/201(39.8%)
	Formula	4/16(25%)
	Cow	6/6(100%)
	Mixed	7/22(31.8%)
Maternal iron supplementation	supplemented	81/213(38%)
	Not supplemented	16/32(50%)
Maternal complication	APH	12/26(46.2%)
	GDM	1/8(12.5%)
	Preeclampsia	24/68(35.3%)
	PPH	4/8(50%)
	Other	4/15(26.6%)

According to this study prevalence of anemia was 39.6%. where 4.1 % was severe,20.6% moderate and 75.3% was mild anemia .all of severe anemia was non-supplemented infants.

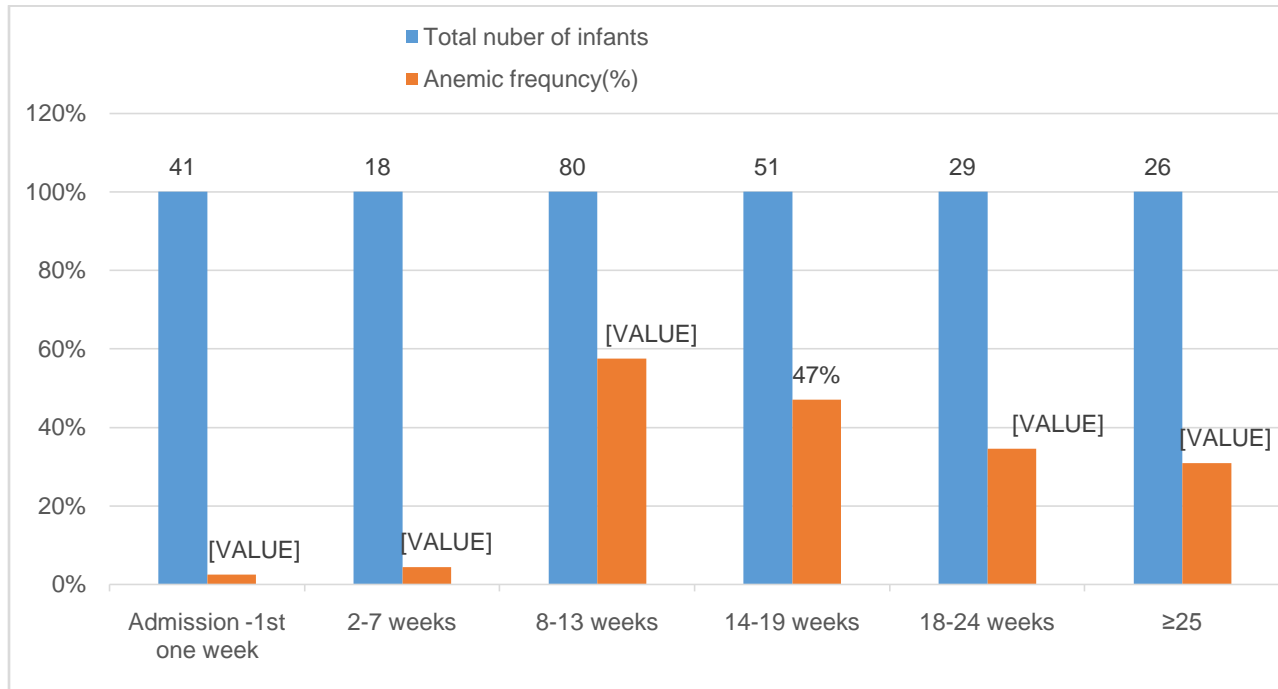
Figure 1.percentage distribution of degree of anemia



Laboratory results

Anemia was Peake during 8 to 13 weeks of post-natal age. Ninety-seven (39.6%) of infants RDW >3SD for age and 43.7% of infants MCV is below 2SD for their age (%figur2)

FIGURE 2. PERCENTAGE DISTRIBUTION OF ANEMIA AND THE TIME WHEN CBC DONE



6. DISCUSSION

As mentioned in the literature review preterm and low birth weight babies comprise the largest group of children at risk of iron deficiency and iron deficiency anemia because of low iron stores and they are at risk for developmental problems (1). The problem can be prevented by giving prophylaxis iron for all preterm and low birth weight infants (1).

Based on this study, the prophylaxis iron supplementation practice for preterm and low birth infants was 53.1%. The practice in TASH was 56.3% and 48% in GAMH. These are substantially lower than WHO, AAP recommendation which recommended as all pre-terms and low birth weight infants need iron prophylaxis (6,7). A possible explanation for this might be due to my data includes all preterm and low birth weight infants which was recommended by WHO, but our supplementation practice includes only pre-terms ≤ 34 weeks gestational age and birth weight < 1500 grams. The result is low compared to study done in three hospitals of Italy which was 74.7% (1), the reason for this difference could be data includes all preterm and low birth weight infants which was recommended by WHO.

In this study iron supplementation practice in GA of (35 -37) weeks was 28.8% and birth weight 2000 -2500g was 22% which was lower than study done in Italy, which was 37,% 48% respectively (15).

In this study mean iron prophylaxis starting time was 7.4 weeks which is delayed comparing to WHO and AAP recommendation which recommended starting time of 2 to 4 weeks (7,6), the possible explanation might be our local guide line not mentioned about the exact iron supplementation time. (21)

In this study average dose of supplementation was $1.94(\pm 0.55)$ mg/kg/day. Nearly 31.2% of infants started elemental iron dose of < 2 mg/kg/d which was lower than WHO recommendation (2 to 4 mg/kg/day).

In this study, the median duration of iron prophylaxis was 4 (IQR 2-7) month and only 14.6% of infants supplemented for 12 months which was lower than WHO, recommendation (6 to 12 month), AAP, recommend (12 month)

It was also lower than study done in Italy, mean duration of supplementation was 8.2 month and 50% of infants supplemented for 12 months. The possible explanation may be no clear guide line at national level as well as at intuitional level regarding to the duration of iron prophylaxis (15)

In this study the anemia out come to preterm and low birth weight was 39.6% which may be more than this because there were infants whose CBC was done at the time of admission and in the first few weeks which might not had anemia at this time. Anemia was higher than study done in Brazil which was 25.5% (16). This might be due to our poor iron supplementation practice and poor protocol based follow up. But it was lower than 2016 EDHS report anemia in infancy which was 72% (12). The possible explanation might be high significant number of infant's CBC was done at admission and in the first one week of post-natal age which may not show anemia at this time.

Based on this study 4.1 % of infants has severe anemia 20.6% and 75.3% of infants had moderate and mild anemia respectively. The level of severe anemia was higher in this study compare to study done in Brazil and in Ethiopia research done on sick pre-terms and age less than one week which was 0.6% for pre-terms and EONS, 1.7% preterm and PNA this might be due to age of infants where less than one week where prematurity related anemia is common at this age (18).

7.LIMITATION

Anemia diagnosis relied entirely on CBC and we were unable to apply more detailed diagnostic techniques such as serum erythropoietin, iron, transferrin level, therefore this limited diagnosis and some of the CBC was done early neonatal age which may not have anemia at this time. There were not enough studies on this topic which could be important to peak limitation.

8. CONCLUSION AND RECOMMENDATION

8.1 Conclusion

The prophylaxis iron supplementation practice is imperative to protect anemia in preterm and low birth weight infants. Iron prophylaxis practice was poor in our set up and this survey documents a great variability in the timing of beginning, dose, and ending of iron prophylaxis of preterm and low birth weight infants, and underlines the urgent need for standardization. The prevalence of anemia was high to the level of universal supplementation.

8.2. Recommendation

Since iron supplementation is low and anemia was common in GA(35-37) and LBW (1500-200)g, it is better to supplement this age group of infants. For health care workers who is working at HRIC, should start prophylaxis iron on appropriate time, dose, duration. Further study is recommended to determine the cause of poor practice and other outcome of preterm babies.

9. ANNEX

Annex I. References

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Annex II. Data collection format

Title: The iron supplementation practice for pre-terms and low birth weight infants at HRIC of TASH and GMH from January 1,2019 to December 31,2020

- I. Sociodemographic data
 - a. Maternal age_____
- II. Place of residence
 - a. Urban
 - b. Rural
- III. Parity
 - a. Primipara
 - b. Multipara
- IV. Iron supplementation status__?
 - i. Yes
 - ii. no
- V. Maternal complication
 - a. APH
 - b. GDM
 - c. Preeclampsia
 - d. PPH
 - e. Other specific__
- VI. characteristic of neonate
 - a. Age at the last follow-up_____
 - b. Sex:
 - i. Male
 - ii. Female
 - c. Birth Weight in grams
 - d. Gestational age in weeks
- VII. Type of feeding
 - a. breast
 - b. formula feeding
 - c. Cowmilk
 - d. mixed feeding
- VIII. Iron supplementation status
 - a. Supplemented_____

- b. If yes when he/she started____
 - i. After anemia diagnosed
 - ii. Before anemia diagnosis
 - c. if not reason____
- IX. If question VII yes post-natal age at iron supplementation started in week_____
- X. Supplemented elementary iron dose in mg/kg_____
- XI. Duration of iron supplementation in months_____
- XII. Blood transfusion history
 - a. no
 - b. if yes
 - i. once
 - ii. twice
 - iii. three times
- XIII. Age at CBC done in weeks_____
- XIV. CBC profile
 - a. HGB g/dl_____
 - b. MCV_____
 - c. RDW_____
- XV. Outcome
 - a. Supplemented
 - i. Anemic
 - ii. Not anemic
 - b. Not supplemented
 - i. Anemic
 - ii. Not anemic

