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Original Article

Association of Iron Deficiency Anemia and Breastfeeding in Children

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ABSTRACT

Objective: To determine the frequency and association of iron deficiency anemia in breastfed children less than equal to six months of age.

Study Design: Prospective observational study

Place and Duration of Study: Pak Emirate Military Hospital & CMH, Rawalpindi Pakistan from Sep 2020 to Mar 2021

Methodology: All children less than equal to 6 months of age of either sex having birth parameters of term gestation (between 37 and 42 weeks), birth weight 2500 grams or more, uneventful postnatal course were consecutively enrolled. Iron deficiency anemia was defined based on serum ferritin concentration <30 micrograms/L and hemoglobin concentration <11 g/dl. History of breastfeeding status along with the other predictor variables were noted.

Results: Of 315 children 73(23.2%) were exclusively breast fed and 242(76.8%) were non-exclusively breastfed. A significantly higher frequency of iron deficiency anemia was observed in exclusively breast fed as compared to non-exclusively breastfed children, i.e., 26(35.6%) and 36(14.9%) respectively. Moreover, age (*p*-value <0.001), gender (*p*-value <0.001), residence (*p*-value <0.001), mother's educational status (*p*-value <0.001), socioeconomic status (*p*-value <0.001), number of children in family (*p*-value <0.001), mode of delivery (*p*-value <0.001), and smokers in the family (*p*-value 0.037) was found to be significantly associated with iron deficiency anemia.

Conclusion: Iron deficiency anemia was found significantly higher in our cohort with considerably higher prevalence in exclusive breastfed children.

Keywords: Breastfeeding, Hemoglobin, Infants, Iron Deficiency Anemia (IDA)

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INTRODUCTION

Iron deficiency is one of the most common micronutrient deficiencies observed in early childhood.[1] According to a systematic review conducted to assess the global burden of anemia, it was reported that children with 1–4-years of age had higher prevalence of iron deficiency anemia.[2] In another study, the approximate prevalence of iron deficiency anemia in children living in Brazil is reported as 21%, 38% in Nepal, while in Pakistan the reported prevalence was as higher as 70%.[3,4]

It is reported that iron deficiency anemia is associated with various complications as well as it affects the quality of life of the children. Several studies have reported lower cognitive and mental abilities in children with iron deficiency anemia.[5,6]

In last few decades, various studies have been published to investigate the underlying cause of iron deficiency anemia in younger children and a majority of the studies have revealed non-exclusive breastfeeding as one of the strong indicators for the occurrence of iron deficiency anemia in early childhood.[7,8] Studies reported that even though the iron content in breast milk is minimal, however, among infants who breastfed exclusively within the first six months of life, the absorption is relatively higher.9,10 Moreover, studies have also reported that due to its perfect balance of nutrients, human milk is known as the best source of nutrition.[9,10]

Thus, iron deficiency anemia is highly prevalent in Pakistan, other associated complications like impaired mental health, growth retardation, diminish physical activity, and even high mortality is also reported among these children in different studies.[4-8] As during the early childhood period, iron is a fundamental requirement to cater all these issues. Therefore, we have planned a prospective study among children that can assess the frequency of iron deficiency anemia and its association with breastfeeding status in children under six months of age.

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METHODOLOGY

This prospective observation al study was conducted at Pak Emirate Military hospital/ Combined Military Hospital from September 2020 to March 2021. Ethical approval was obtained from the department (letter no EC/278/2021). Moreover, signed informed consent was also obtained from the parents/guardians of the children before inclusion.

Inclusion Criteria: All children less than 6 months of age of either sex with birth parameters of; gestational age (between 37 and 42 weeks), birth weight 2500 grams and uneventful postnatal course were consecutively enrolled from outpatient department.

Exclusion Criteria: While, preterm infants, infant having any infection, having chronic illness like congenital heart disease, congenital chromosomal anomalies, surgical problems, and chronic renal disease were excluded.

Children were divided into two groups i.e exclusively breast fed while the other being non-exclusively breast fed (which further included children who were breast fed and were being supplemented with formula feed/cow milk). The children who were not being breast fed at all were not included in the study. Epi info sample size calculator is used for the estimation of sample size taking confidence interval 95%, margin of error 5%, reported IDA in exclusively breastfed infant 3.4%.[13] The estimated sample size came out to be 315. Iron deficiency anemia was labeled based on presence of ferritin concentration <30 mcg/L and hemoglobin concentration <11 g/dl. A detailed history was obtained from all study participants regarding the demographic characteristics such as age, gender, residence, mother's educational status, mother's occupation, socioeconomic status, and other predicting variables like breastfeeding counseling during antenatal visit, breastfeeding status, mode of delivery, prenatal iron-supplementation, smokers in the family, and number of children in family were noted. Moreover, hemoglobin level, ferritin level, and iron deficiency anemia were also observed.

Statistical analysis was performed using statistical package for social sciences (SPSS) version 24. Mean and standard deviation were computed for quantitative variables like age, weight, hemoglobin level, and ferritin level. Frequency and percentages were calculated for qualitative variables like gender, residence, mother's educational status, mother's occupation, socioeconomic status, and other predicting variables like breastfeeding counseling during antenatal visit, breastfeeding status, mode of delivery, prenatal iron-supplementation, smokers in the family, number of children in family, and iron deficiency anemia. Independent t-test was applied to see the mean difference of breastfeeding status with age, weight, hemoglobin level, and ferritin level. Chis-square test was applied to see the association of iron deficiency anemia with breastfeeding status and other predictor variables. *p*-value ≤0.05 considered as significant. Binary logistic regression analysis was also applied. All those variables found statistically significant in chi-square test were considered for logistic regression.

RESULTS

Of total 315 patients, the mean age of the children was 3.94±1.53 months. There were 169(53.7%) males and 146(46.3%) females. The mean weight of the children was 5.15±1.45 kg. Residence of 169(53.7%) was urban and 146(46.3%) was rural. Most of the mothers had less than equal matric educational status, i.e., 145(46%), followed by illiterate 99(31.4%), and 71(22.5%). There were 171(54.3%) housewives and 144(45.7%) working women. Lower socioeconomic status was observed in 94(29.8%), lower middle in 124(39.4%), and upper middle in 97(30.8%) patients.

Breastfeeding counselling during antenatal visit was reported by 89(28.3%) mothers. Mode of delivery was cesarean in 146(46.3%) while normal in 169(53.7%) children. Prenatal iron supplementation was observed in 110(34.9%) children. Whereas there were 126(40%) smokers in the family. Majority of the children 168(53.3%) had three or more children in family, followed by two children in 77(24.4%), and one in 70(22.2%) children.

There were 73(23.2%) children with exclusive breastfed and 242(76.8%) children with non-exclusive breastfed status. The mean age was significantly higher in children with non-exclusive breastfed than that of exclusive breastfed children (*p*-value 0.008). Similarly, mean hemoglobin level was significantly higher in exclusive breastfed children than that of non-exclusive breastfed children (*p*-value <0.001). However, mean ferritin level was significantly higher in non-exclusive breastfed children than that of exclusive breastfed children (*p*-value <0.001) (Table-I).

The frequency of iron deficiency anemia was observed in 62(19.7%) children. A significantly higher frequency of iron deficiency anemia was observed in exclusively breast fed as compared to non-exclusively

breastfed children, i.e., 26(35.6%) and 36(14.9%) respectively. Moreover, age (*p*-value <0.001), gender (*p*-value <0.001), residence (*p*-value <0.001), mother's educational status (*p*-value <0.001), socioeconomic status (*p*-value <0.001), number of children in family (*p*-value <0.001), mode of delivery (*p*-value <0.001), and smokers in the family (*p*-value 0.037) was found to be significantly associated with iron deficiency anemia (Table-II).

Univariable analysis showed that iron deficiency anemia was significantly higher in; exclusive

Table-I: Mean Difference of Quantitative Variables with Respect to Breastfed Status (N=315)

	Exclusive Breastfed	Non-exclusive Breastfed	*p*-value
Age, months	3.52±1.70	4.06±1.46	0.008
Weight, kg	5.53±1.50	5.04±1.42	0.011
Hb level, g/dl	11.43±1.99	10.01±1.98	<0.001
Ferritin level, mcg/L	29.45±7.23	32.98±4.01	<0.001

Independent t-test applied, p-value <0.05 considered significant

Table-II: Comparison of Iron Deficiency Anemia with Breastfeeding and Other Demographic and Household Characteristics of the Patients (n=315)

Variables		Iron Deficiency Anemia		
		Yes	No	
	Total	n=218	n=97	*p*-value
	n (%)	n (%)	n (%)	
Breastfeeding status				
Exclusive	73	26 (35.6)	47 (64.4)	<0.001
Non-exclusive	242	36 (14.9)	206 (85.1)	
Age, months				
≤4	161	15 (9.3)	146 (90.7)	<0.001
>4	154	47 (30.5)	107 (69.5)	
Gender				
Male	169	17 (10.1)	152 (89.9)	<0.001
Female	146	45 (30.8)	101 (69.2)	
Residence				
Rural	169	13 (7.7)	156 (92.3)	<0.001
Urban	146	49 (33.6)	97 (66.4)	
Mother's Educational Status				
Illiterate	99	38 (38.4)	61 (61.6)	<0.001
Lower and equal to matric	145	20 (13.8)	125 (86.2)	
More than Intermediate	71	4 (5.6)	67 (94.4)	
Mother's Job				
Employed Mother	171	36 (21.1)	135 (78.9)	0.505
Housewife	144	26 (18.1)	118 (81.9)	
Socioeconomic Status				
Poor	94	31 (33.0)	63 (67.0)	<0.001
Lower middle	124	16 (12.9)	108 (87.1)	
Upper middle	97	15 (15.5)	82 (84.5)	
Number of Children in Family				
One	70	20 (28.6)	50 (71.4)	<0.001
Two	77	25 (32.5)	52 (67.5)	
Three or more	168	17 (10.1)	151 (89.9)	
Breastfeeding counselling during antenatal visit				
Yes	89	17 (19.1)	72 (80.9)	0.870
No	226	45 (19.9)	181 (80.1)	
Mode of delivery				
Cesarean	146	51 (34.9)	95 (65.1)	<0.001
Normal	169	11 (6.5)	158 (93.5)	
Prenatal iron supplementation				
Yes	110	24 (21.8)	86 (78.2)	0.485
No	205	38 (18.5)	167 (81.5)	
Smokers in family				
Yes	126	32 (25.4)	94 (74.6)	0.037
No	189	30 (15.9)	159 (84.1)	

Table-III: Regression analysis of factors associated with Iron Deficiency Anemia (n=315)

	OR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Breastfeeding status				
Exclusive	3.16 (1.74-5.74)	<0.001	14.83 (4.93-44.62)	<0.001
Non-exclusive	Ref		Ref	
Age, months				
≤4	0.23 (0.12-0.44)	0.010	0.50 (0.20-1.23)	0.133
>4	Ref		Ref	
Gender				
Male	3.98 (2.16-7.35)	<0.001	1.65 (0.63-4.32)	<0.001
Female	Ref		Ref	
Residence				
Rural	6.06 (3.12-11.75)	<0.001	8.95 (3.13-25.59)	<0.001
Urban	Ref		Ref	
Mother's Educational Status				
Illiterate	10.43 (3.52-30.94)	<0.001	10.54 (2.01-55.34)	0.005
Lower and equal to matric	2.68 (0.88-8.16)	0.083	6.43 (1.36-30.40)	0.019
More than Intermediate	Ref		Ref	
Socioeconomic Status				
Poor	2.69 (1.33-5.40)	0.005	7.64 (2.34-24.91)	0.001
Lower middle	0.81 (0.38-1.73)	0.587	0.98 (0.33-2.88)	0.972
Upper middle	Ref		Ref	
Number of Children in Family				
One	3.55 (1.72-7.30)	0.001	4.47 (1.23-16.22)	0.023
Two	4.27 (2.13-8.53)	0.013	2.75 (0.68-11.17)	0.014
Three or more	Ref		Ref	
Mode of delivery				
Cesarean	7.71 (3.83-15.52)	<0.001	5.13 (1.39-18.82)	0.014
Normal	Ref		Ref	
Smokers in family				
Yes	1.80 (1.03-3.16)	0.039	0.79 (0.25-2.52)	0.703
No	Ref		Ref	

breastfeeding children (OR: 3.16, 95% CI: 1.74-5.74), males (OR: 3.98, 95% CI: 2.16-7.35), rural residence (OR: 6.06, 95% CI: 3.12-11.75), illiterate mother (OR: 10.43, 95% CI: 3.52-30.94) and poor socioeconomic status (OR: 2.69, 95% CI: 1.33-5.40) (Table-III).

The comparison of iron deficiency anemia and baseline characteristics stratified based on breastfeeding status showed that among children with exclusive breastfeeding, iron deficiency anemia was significantly associated with age ≤4 months (*p*-value <0.001), mother's educational status (*p*-value <0.001), socioeconomic status (p-value 0.001), breastfeeding counselling during antenatal visit (p-value 0.007), and mode of delivery (*p*-value 0.006). While, among non-exclusive breastfed children, iron deficiency anemia was significantly associated with age (*p*-value 0.014), gender (*p*-value <0.001), residence (*p*-value <0.001), mother's educational status (*p*-value <0.001), number of children in family (*p*-value <0.001), mode of delivery (*p*-value <0.001), and smokers in family (*p*-value <0.001) (Table-IV).

DISCUSSION

In our study exclusive breastfeeding was observed in one quarter of the children only i.e 23.2% as compare to previously reported frequency from 37% to 54% in Hanif HM *et al.,* and Ali S *et al.,*.,[11,12] Marques RF *et al.,* reported a great difficulty in recruitment of samples containing exclusively breast-fed children and according to the author, majority of the infants had non-exclusive breastfeeding status. Moreover, it was reported that exclusive breastfeeding during the first six months of age is not an easy task and taken as burden.[13] Yaqub A *et al.,* reported that the most the most common reason for non-exclusive breastfed was production of insufficient milk.[14]

According to our study findings, iron deficiency anemia was predominantly higher, 19.7%. The finding was considerably less to what reported in literature. Armitage AE *et al.,* reported that more than 50% of the children in developing regions had iron deficiency anemia.[15] However, the frequency is much lower in developed countries.[16,17] The major reason could be the

Table-IV: Comparison of Iron Deficiency Anemia and Baseline Characteristics Stratified Based on Breastfeeding Status (N=315)

Variables	Exclusive Breastfed (n=73)			Non-Exclusive Breastfed (n=245)		
	IDA			IDA		
	Yes (n=26) n (%)	No (n=47) n (%)	*p*-value	Yes n=192 n (%)	No n=28 n (%)	*p*-value
Age, months						
≤4	5 (10.4)	43 (89.6)	<0.001	10 (8.8)	103 (91.2)	0.014
>4	21 (84.0)	4 (16.0)		26 (20.2)	103 (79.8)	
Gender						
Male	9 (32.1)	19 (67.9)	0.625	8 (5.7)	133 (94.3)	<0.001
Female	17 (37.8)	28 (62.2)		28 (27.7)	73 (72.3)	
Residence						
Rural	8 (22.9)	27 (77.1)	0.029	5 (3.7)	129 (96.3)	<0.001
Urban	18 (47.4)	20 (52.6)		31 (28.7)	77 (71.3)	
Mother's Educational Status						
Illiterate	17 (68.0)	8 (32.0)	<0.001	21 (28.4)	53 (71.6)	<0.001
Lower and equal to matric	9 (29.0)	22 (71.0)		11 (9.6)	103 (90.4)	
More than Intermediate	0 (0)	17 (100)		4 (7.4)	50 (92.6)	
Mother's Job						
Employed Mother	14 (35.9)	25 (64.1)	0.957	22 (16.7)	110 (83.3)	0.391
Housewife	12 (35.3)	22 (64.7)		14 (12.7)	96 (87.3)	
Socioeconomic Status						
Poor	15 (68.2)	7 (31.8)	0.001	16 (22.2)	56 (77.8)	0.084
Lower middle	6 (25.0)	18 (75.0)		10 (10.0)	90 (90.0)	
Upper middle	5 (18.5)	22 (81.5)		10 (14.3)	60 (85.7)	
Number of Children in Family						
One	5 (35.7)	9 (64.3)	0.397	15 (26.8)	41 (73.2)	<0.001
Two	5 (55.6)	4 (44.4)		20 (29.4)	48 (70.6)	
Three or more	16 (32.0)	34 (68.0)		1 (0.8)	117 (99.2)	
Breastfeeding counselling during antenatal visit						
Yes	4 (15.4)	22 (84.6)	0.007	13 (20.6)	50 (79.4)	0.135
No	22 (46.8)	25 (53.2)		23 (12.8)	156 (87.2)	
Mode of delivery						
Cesarean	15 (55.6)	12 (44.4)	0.006	36 (30.3)	83 (69.7)	<0.001
Normal	11 (23.9)	35 (76.1)		0 (0)	123 (100)	
Prenatal iron supplementation						
Yes	12 (33.3)	24 (66.7)	0.688	12 (16.2)	62 (83.8)	0.697
No	14 (37.8)	23 (62.2)		24 (14.3)	144 (85.7)	
Smokers in family						
Yes	6 (31.6)	13 (68.4)	0.669	26 (24.3)	81 (75.7)	<0.001
No	20 (37.0)	34 (63.0)		10 (7.4)	125 (92.6)	

better socioeconomic status, literacy rate, and most importantly adherence of the practice as advised by the world health organization and other recommended bodies in developed countries. In our study, the possible reason for low frequency of iron deficiency anemia may be that non-exclusive breastfed children were considerably higher, and frequency of iron deficiency anemia was significantly lower among non-exclusive breastfed.

In our study, iron deficiency anemia was found to be 14.83 times higher in exclusively breastfed children in contrast to Marques RF *et al.*, who reported that only 3% of exclusively breastfed children had iron deficiency.[13] Moreover, the findings of the current study have revealed that iron deficiency anemia was higher in; males (35% vs 14%), urban residence (33.6% vs 7.7%), illiterate mother (38% vs 13%) and poor socioeconomic status (33% vs 13%). Somewhat similar findings were reported in previous studies as well.[18–20] Higher weight and significantly higher concentration of ferritin level in non-exclusive breastfeeding children was another important finding of the current study

which is supported by several previous studies as well.[21-24] It is reported that for a health growth in the first five years of life, mobility of body iron stores is essential for hemoglobin synthesis and other body tissue iron containing molecules. Tsai *et al.*, was conducted among exclusive breastfed children and reported an improved hemoglobin level and mean corpuscular volume in children who received oral iron supplementation.[25]

In previously published studies it is also reported that iron deficiency anemia increased significantly in breastfed infants.[26,27] Clark *et al.*, reported that though benefits of exclusive breastfed is indisputable, however, exclusive breastfeeding in later infancy is a potential risk factor for iron deficiency anemia.[27] Marol *et al.*, emphasized on the monitoring of iron deficiency in exclusive breastfed infants aged 3-6 months.[26] Several studies have suggested guidelines for preventing iron deficiency anemia in exclusive or predominant breastfed infants.[21-28] Krishnaswamy *et al.*, has suggested iron supplementation for healthy babies from 4 months of age instead of 6 months.[28]

The limitation of our study is that certain important confounding variables like early cord clamping and vitamin D status were not studied. Moreover, the growth pattern of the children was also not observed in the current study. Further large-scale multicenter studies are recommended to preclude the findings of this study.

CONCLUSION

Iron deficiency anemia was found significantly higher in our cohort with considerably higher prevalence in exclusive breastfed children under less than equal to 6 months of age.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SJ & TG: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

QUZK & FI: Data acquisition, data analysis, approval of the final version to be published.

MT & SN: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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