Occult Blood in Stool in Exclusively Formula Fed Infants Versus Exclusively Breast Fed Infants in the First 6 months Of Life.

Thesis

Submitted for Partial fulfillment of Master

Degree (M.Sc) In Pediatrics

Ву

HEBA SAMIR YOUNIS

M.B.Bch

Supervised by

PROF. DR. RANIA HOSNI TOMERAK

Professor of Pediatrics

Faculty of Medicine-Cairo University

PROF. DR. MAHAMUHAMEDGAAFAR

Professor of Clinical pathology

Faculty of Medicine-Cairo University

DR. HANAA IBRAHIM RADY

Lecturer of Pediatrics

Faculty of Medicine-Cairo University

Faculty of Medicine

Cairo University

2013

Dedication

To my family who support me to end this work

To my beloved husband for his understanding and support

Heba

بسم الله الرحمن الرحيم يَكَ عَن الرُّوح صَفْل الرُّوح مَن أَمْر مَا أُوتِيذُم مِّنَ الْعِلْم إِلاَّ قَلِيلاً "

صدق الله العظيم

ACKNOWLEDGEMENT

First and foremost, thanks to ALLAH, the most beneficent and most Merciful. Words will never be able to express My deepest gratitude to all those who helped me During preparation of this study. I gratefully acknowledge the sincere advice and guidance of Prof. Dr. Rania Tomerak. Professor of Pediatrics, Faculty of Medicine, Cairo University, For her constructive guidance, Encouragement and valuable help in accomplishing this work. I am really thankful to **Prof. Dr. MahaGaffar**, Professor of Clinical Pathology, Faculty of Medicine, Cairo University, for her great help, Advice, precious time, kindness, and moral support. I am greatly honored to express My deep appreciation to *Dr. HanaaRady*, Lecturer of Pediatrics, Faculty of Medicine, Cairo University for her continuous support, Sincere supervision, direction and meticulous revision of this work. I am realy thankful for Dr. Dina Muhamed, Lecturer of clinical Pathology, Faculty of Medicine, Cairo University for her great help, Precious time and sincere effort in the laboratory work In this study.

CONTENTS

•	Abstact	1
•	Introduction and Aim of Work	2
•	Review of Literature	
	Chapter 1 Breast Feeding	4
	Chapter 2 Formula Feeding	.42
	Chapter 3 Iron Deficiency Anemia	.53
	Chapter 4 Cows' milk Allergy	.69
•	Subjects and Methods	80
•	Results	87
•	Discussion	115
•	Conclusion	125
•	Recommendations	.126
•	Summary	128
•	References	.130
•	Arabic Summary	.158

List of Figures

	page
Review of Literature	
Figure 1: Physiologic model of iron status predictors during infancy	56
Results	
Figure 1: Weight standard deviation frequency among breast fed group	89
Figure2: Weight standard deviation frequency among formula fed group	89
Figure 3: Comparison of levels of Hemoglobinamong the breast fed group and the formula fed group	90
Figure 4: Comparison of levels of Hematocrit among the breastfed group and the formula fed group	91
Figure 5: Comparison of levels of Mean Corpuscular Volume among the breastfed group and the formula fed group	91
Figure 6: Comparison of levels of Serum iron and total iron binding capacity among the breast fedgroup and the formula fed group	93
Figure 7: Comparison of levels of Transferrin Saturation among the breastfed group and the formula fed group	93
Figure 8: Comparison of levels of serum Transferrin among the breastfed group and the formula fed group	94
Figure 9: Comparison between breast fed group and formula fed group as regard frequency of occurrence of occult blood in stool	95
Figure 10: Comparison of levels of serum Hemoglobin among formula fed group as regard occult blood in stool	96

Figure 11: Comparison of levels of serum Hematocrit among formula fed group as regard occult blood in stool	96
Figure 12: Comparison of levels of Mean Corpuscular Volume among formula fed group as regard occult blood in stool	97
Figure 13: Comparison of levels of serum iron and total iron binding capacity among formula fed group as regard occult blood in stool	98
Figure 14: Comparison of levels of Transferrin saturation among formula fed group as regard occult blood in stool	98
Figure 15: Comparison of levels of Serum Transferrin among formula fed group as regard occult blood in stool	99
Figure 16: Comparison between breastfed group and formula fed group as regard frequency of iron deficiency anemia	100
Figure 17: comparison between Anemic infants and non-anemic infants as regard presence of maternal anemia	102
Figure 18: comparison between Anemic and non-anemic infants as regard pregnancy (single or twins)	102
Figure 19: comparison between Anemic and non-anemic infants as regard mode of delivery	103
Figure 20: Comparison between Anemic and non-anemic infants as regard occult blood in stool	103
Figure 21: Comparison between Anemic and non-anemic infants as regard type of infant feeding	104
Figure 22: Comparison between Anemic and non-anemic infants as regard serum levels of iron and total iron binding capacity	106
Figure 23:Comparison between Anemic and non-anemic infants as regard Transferrin Saturation	106

Figure 24: comparison between anemic (IDA) and non-anemic infants as regard levels of serum Transferrin	107
Figure 25:comparison between anemic (IDA) and non-anemic infants as regard serumHemoglobin level	107
Figure 26:comparison between anemic (IDA) and non-anemic infants as regard Mean Corpuscular Volume level	108
Figure 27:comparison between anemic (IDA) and non-anemic infants as regard sex distribution	109
Figure 28: Comparison between the infants with positive history of maternal anemia and those with negative history of maternal anemia as regard serum iron and total iron binding capacity levels	111
Figure 29: Comparison between the infants with positive history of maternal anemia and those with negative history of maternal anemia as regard Transferrin Saturation	112
Figure 30: Comparison between the infants with positive history of maternal anemia and those with negative history of maternal anemia as regard Serum Transferrin	113
Figure 31: Comparison between the infants with positive history of maternal anemia and those with negative history of maternal anemia as regard Hemoglobin level	113
Figure 32: Comparison between the infants with positive history of maternal anemia and those with negative history of maternal anemia as regard Hematocrit level	114
Figure 33: Comparison between the infants with positive history of maternal anemia and those with negative history of maternal anemia as regard Mean Corpuscular Volume	114

Г

List of Tables

Review of literature	Page
Table 1: Composition of prepartum human milk	6
Table 2: Factors influencing human milk fat content and composition	9
Table 3: Nucleotide content of human milk	14
Table 4: Cytokines in Human Milk: Mean Concentrations andFunctions	25
Table 5: Protective functions of human milk lipids	26
Table 6: Non-immunoglobulin anti-pathogens from human milk	28
Table 7: Anti-inflammatory features of human milk	29
Table 8: Anti-parasite factors found in human milk	30
Table 9: Comparison of Breast Milk and Available Infant Formula	45
Table 10: Infant Feeding Intolerance	47
Table 11: Spectrum of Iron Status	64
Table 12: Diferential Diagnosis of Microcytosis	65
Table 13: Factors that condition and favor sensitization	71
Table 14: Adverse reactions to cow's milk proteins.	75

Results	
Table1: Demographic data of the breast fed group and the formula fed group	87
Table 2: Comparison between the breast fed group and theformula fed group as regard weight SD	88
Table 3: comparison of hematological indices between the breastfed infants group and the formula fed group	90
Table 4: Comparison of iron indices values between breast fed group and formula fed group	92
Table 5: Comparison between breast fed group and formula fed group as regard occult blood in stool	94
Table 6: Comparison between positive and negative occult bloodin stool cases among formula fed group as regard hematologicalindices	95
Table7: Comparison between positive and negative occult blood in stool cases among formula fed group as regard iron indices	97
Table 8: Comparison between breast fed group and formula fedgroup as regard frequency of iron deficiency anemia	99
Table 9: comparison between anemic and non-anemic infants asregard possible contributing factors of anemia	101
Table 10: comparison between anemic (IDA) and non-anemicgroups as regard clinical and laboratory parameters	105
Table 11: comparison between anemic (IDA) and non-anemic groups as regard Sex distribution	108
Table 12: Comparison between infants with positive history ofmaternal anemia and those with negative history of maternalanemia as regard iron status	110

ABBREVIATIONS

AA	Arachidonic acid
AAF	Amino acid formula
AAP	American Academy of Pediatrics
AAFP	American Academy of family physician
ADP	Adenosine diphosphate
AGA	Appropriate for gestational age
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
AMP	Adenosine monophosphate
AOM	Acute otitis media
BSSL	Bile salt-stimulated lipase
C3	Complement 3
C4	Complement 4
Ca2+	Calcium
cAMP	Cyclic Adenosine monophosphate
CBC	Compelete Blood Count
CHr	Reticulocyte hemoglobin concentration
CDP	Cytidinediphosphate
cGMP	Cyclic Guanosine monophosphate
CM	Cow milk
CMA	Cow milk allergy
CMI	Cow milk intolerance
CMP	Cytidine monophosphate
CMPA	Cow milk protein allergy
CMPSE	Cow milk protein sensitive enteropathy
CNS	Central nervous system
CRP	C -reactive protein

CVS	Cyclic vomiting syndrome
DBPCFCs	Double blind placebo controlled food
	challenges
DHA	Docosahexaenoic acid
DNA	Deoxyribonucleic acid
E.coli	Escherichiacoli
EGF	Epidermal growth factor
eHFs	Extensively hydrolyzed formula
ELISA	Enzyme-Linked Immunosorbent Assay
EPO	Erythropoietin
FAs	Fatty acids
Fe2+	Iron
FEP	Free erythrocyte protoporohyrin
FFA	Free fatty acid
FMH	Fetal maternal hemorrhage
FOB	Fecal occult blood
FPIES	Food protein induced enterocolitis
	syndrome
GDP	Guanosinediphosphate
GER	Gastroesophageal reflux
GIFN	Gamma interferon
GIT	Gastrointestinal tract
GM1	Ganglioside M1
GMP	Guanosine monophosphate
G6PD	Glucose-6-phosphate dehydrogenase
GRH	Growth hormone releasing hormone
Hb	Hemoglobin
HCT	Hematocrit
Hib	Haemophilusinfluenzae type B
HIV	Human Immunodefeciency virus

HSV-1	Herpes simplex virus type1
ID	Iron Defeciency
IDA	Iron Defeciency Anemia
IgA	Immunoglobulin A
IL	Interleukin
IDDM	Insulin- dependent diabetes mellitus
JRA	Juvenile raumatoid Arthritis
LBW	Low birth weight
LCPUFA	Long-chain polyunsaturated fatty acids
LRIs	Lower respiratory tract illness
MCSF	Macrophage colony-stimulating factor
MCV	Mean Corpuscular Volume
MG	Monoglycerides
MHC	Major histocompatibility complex
Mg2+	Magnesium
NEC	Necrotizing enterocolitis
NPN	Non-protein nitrogen
PAF	Platelet activating factor
PGs	Prostagalndins
PGE	Prostaglandin E
PL	Pyridoxal
PMNs	Polymorphonuclearleukocytes
PN	Pyridoxine
RAST	Radioallergosorbent test
RBCs	Red blood cells
RDW	Red blood cell distribution width
ROM	Recurrent otitis media
RSV	Respiratory syncytial virus
SIDS	Sudden infant death syndrome
SF	Serum ferritin

sIgA	Secretory Immunoglobulin
SPSS	Statistical Package for Studies.
T4	Thyroxine
TfR1	serum transferrin receptor1
TG	Triglycerides
TGF	Transforming growth factor
TIBC	Total iron binding capacity
TNF	Tumor necrosis factor
TRH	thyroid –realeasing hormone
TS	Transferrin saturation
TSH	Thyroid stimulating hormone
TTS	Twin-twin transfusion syndrome
UIBC	Unsaturated iron binding capacity
VLBW	Very low birth weight
WHO	World Health Organization

Abstract

BACKGROUND: Sincemost of infant formulas are based on cow's milk to which allergy can occur, and considering the neurodevelopmental consequences of iron deficiency during infancy; we aimed in this study to verify the occurrence of occult intestinal blood loss in infants during the first 6 months of life in response to being fed Cow's milk based formula versus breast milk and we also studied iron status in those infants in order to assess prevalence of iron deficiency anemia and identify the candidate for Fe supplementation.

METHODS: Healthy full term infants from birth to 6 months who were either exclusively breast fed (n=50) or formula fed (n=50) were considered for enrollment. Hematologic and iron status was evaluated (complete blood count, serum iron, total iron binding capacity and serum transferrin) and occult blood in stool was requested for each infant.

RESULTS: we reported no significant differences in hematologic indices (Hemoglobin, Hematocrit and MCV) between the breast fed group and formula fed group. Formula fed infants had higher levels of total iron binding capacity rather than breast fed infants. We found that 4/50 formula fed infants were positive for occult blood in stool; while only 1/50 breast fed infant was positive occult blood in stool. The prevalence of iron deficiency anemia was higher in formula fed group (14%) rather than in breast fed group (8%).The Prevalence of anemia among infants born to anemic mothers was significantly higher (73%) rather than those born to non-anemic mothers (27%).

CONCLUSION: Breast fed infants attained better iron status rather than formula fed infants. Higher prevalence of anemia among formula fed infants rather than in breast fed infants. Occult blood in stool is considered as an aggravating factor of iron deficiency anemia among formula fed infants. We reported a positive association between maternal anemia during pregnancy and iron deficiency anemia in the first 6 months of life.

Key words:

Breastfeeding - Cow milk based formula - Iron deficiency anemia -Maternal anemia - Occult blood in stool.