The Relation Between Serum Zinc Level and Iron Profile to Community Acquired Pneumonia in Pediatrics

Thesis

Submitted for Partial Fulfillment of M.SC degree in Pediatrics

By

Tasneem Ali Eldosoky Mogahed

M.B.B. CH

Faculty of Medicine – Ain Shams University (2009)

Under Supervision of

Assist. Prof. Asmaa Al Husseiny Ahmed Al Sharkawy

Assistant Professor of Pediatrics

Faculty of Medicine – Ain Shams University

Doctor/ Ahmed Rezk Ahmed

Lecturer of Pediatrics

Faculty of Medicine – Ain Shams University

Doctor / Noha Refaat Mohamed

Lecturer of clinical and Chemical Pathology

Faculty of Medicine-Ain Shams University

Faculty of Medicine

Ain Shams University

2018

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH,** *the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to **Assist. Prof. Asmaa Al Husseiny Ahmed Al Sharkawy,** *Assistant Professor of Pediatrics Faculty of Medicine – Ain Shams University for her keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Doctor/ Ahmed Rezk Ahmed,** *Lecturer of Pediatrics Faculty of Medicine – Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to **Doctor / Noha Refaat Mohamed,** *Lecturer of Clinical and Chemical Pathology Faculty of Medicine- Ain Shams University, for her great help, active participation and guidance.*

Tasneem Ali Eldosoky

To:

My Father, My Mother, My mother in law, My Husband, My Sons and My Sisters, for their moral supports. Without their help I wouldn't be here.

And special thanks to

My Best Friends Drs.:

Dina Ibrhaim, Hoda Reda and Marwa Ghanem

for their help and support

List of Contents

Title	Page No.
List of Tables	6
List of Figures	9
List of Abbreviations	11
Introduction	1
Aim of the Work	16
Review of Literature	
▪ Community Acquired Pneumonia	17
▪ Zinc, iron and their relation to community acquired pneumonia	65
Subjects and Methods	107
Results	115
Discussion	132
Summary	144
Conclusion	148
Recommendations	149
References	150
Arabic Summary	—

List of Tables

Table No.	Title	Page No.

Table (1): Risk factors related to the host and the environment that affect incidence of childhood clinical pneumonia in the community in developing countries 19
Table (2): Definitions of CAP in children. 21
Table (3): Respiratory tract defence mechanisms: 23
Table (4): Community acquired pneumonia syndromes 30
Table (5): Aetiological classification of pneumonia 31
Table (6): The cause of pediatric pneumonia according to age. 33
Table (7): Showing signs of respiratory distress according to WHO 37
Table (8): Showing criteria used in developing and developed countries to define the severity of community acquired pneumonia. 49
Table (9): Recommended Vaccines for Prevention of Childhood CAP. 51
Table (10): Showing empirical therapy for childhood CAP outpatient and inpatient 60
Table (11): Showing adverse reactions of antibiotics used in treatment of childhood CAP. 61
Table (12): Showing definitions of micronutrient deficiencies according to WHO. 65
Table (13): Studies to assess the effect of zinc on acute respiratory infections: 82
Table (14): Factors that could influence iron absorption 96
Table (15): Iron requirements of 97.5% of individuals in terms of absorbed iron*, by age group and sex 97
Table (16): The suggested schemes for intermittent iron supplementation in preschool and school-age children 104

List of Tables Cont...

Table No.	Title	Page No.
Table (17):	Personal data among patient group and control group.	115
Table (18):	Distribution of patient group according to clinical data.	118
Table (19):	Chest x-ray interpretation among patient group.	120
Table (20):	Clinical data of patient group as regard duration of hospital stay, history of previous admission and past history of PICU admission.	121
Table (21):	Distribution of severity, fate and mortality among patient group.	121
Table (22):	CBC values and CRP among patient group.	122
Table (23):	Values of serum iron, TIBC and transferrin saturation among studied groups and distribution of iron and TIBC adequacy among studied patients.	123
Table (24):	Values of serum zinc level among studied groups and distribution of zinc adequacy among studied patient.	124
Table (25):	Comparison between patients subgroups regarding clinical and personal parameters.	125
Table (26):	Comparison between patient subgroups regarding the Chest X ray findings	126
Table (27):	Comparison between patient subgroups regarding HB level, MCV, MCH.	126
Table (28):	Comparison between patient subgroups regarding TLC, Absolute neutrophilic count, Absolute Lymphocytic count and CRP on admission.	127
Table (29):	Comparison between patient subgroups as regards iron profile.	128

List of Tables Cont...

Table No.	Title	Page No.
Table (30):	Comparison between patient subgroups regarding serum zinc level, its adequate and inadequate levels.	129
Table (31):	Outcome of studied patients.	130
Table (32):	Comparison between zinc replete versus zinc deplete regarding hospital stay and complications.	130
Table (33):	Comparison between patients with normal TIBC versus patient with high TIBC regarding hospital stay and complications.	131

List of Figures

Fig. No.	Title	Page No.
Fig. (1):	Pneumonia is the leading killer of children worldwide, as shown by this illustration of global distribution of cause specific mortality among children younger than age 5 yr	20
Fig. (2):	In this figure comparison between normal alveoli and diseased alveoli in pneumonia result in (A) sloughing of alveolar epithelial cells, causing the formation of protein-rich hyaline membranes (B) Neutrophils adhere to the activated capillary endothelium and migrate to the alveolus	24
Fig. (3):	This Figure showing pathogenesis of community acquired pneuomnia	25
Fig. (4):	Shows Lobar bacterial pneumonia which affecting the single lower lobe of the left lung	27
Fig. (5):	Showing types of pneumonia	29
Fig. (6):	Showing the main symptoms of pneumonia	38
Fig. (7):	CXRs of CAP	46
Fig. (8):	Showing Scheme for zinc distribution in the body	68
Fig. (9):	Comparison of the effects of zinc intoxication versus deficiency	72
Fig. (10):	Erythematous dermatitis on the scrotum, penis, and buttocks	73
Fig. (11):	A 5-month-old baby with a 2-month history of a rash a case of acrodermatitis enteropathica	76
Fig. (12):	Iron is bound and transported in the body via transferrin and stored in ferritin molecules	86
Fig. (13):	Showing Schematic representation of iron metabolism	90

List of Figures Cont...

Fig. No.	Title	Page No.
Fig. (14):	Human Iron Homeostasis	92
Fig. (15):	Hepcidin acts by binding to ferroportin, an iron transporter present on cells of the intestinal duodenum, macrophages, and cells of the placenta	93
Fig. (16):	Hepcidin-mediated regulation of iron homeostasis	94
Fig. (17):	Iron Limitation as an Innate Immune Defense	102
Fig. (18):	Comparison between patient group and control group as regard weight revealed that patients were significantly thinner than persons in control group.	116
Fig. (19):	Comparison between patient group and control group as regard height revealed that patients were significantly shorter than persons in control group.	116
Fig. (20):	Socio-economic class among studied groups was significantly different between patient and control group.	117
Fig. (21):	Mother education among studied group, revealed that educated mothers were more in control than patient group.	117
Fig. (22):	Cyanosis frequency among patients.	119
Fig. (23):	Dyspnea frequency among patient group.	119
Fig. (24):	Chest indrawing among patient group.	120
Fig. (25):	Distribution of pneumonia severity among patients.	121
Fig. (26):	Comparison between mean of serum zinc level of studied groups.	124

List of Abbreviations

Abb.	Full term
AAP	*American Academy of Pediatrics*
ALRI	*Acute lower respiratory infection*
APPs	*Acute phase proteins*
AUC	*Area under curve*
BTS	*British Thoracic Society*
CA	*Community-associated*
CAP	*Community acquired pneumonia*
CDC	*Center of disease and control*
CO	*Carbon monoxide*
CPS	*Capsular polysaccharide*
CRP	*C-reactive protein*
CT	*Computerized tomography*
CTMA	*Cetyltrimethyl-ammonium bromide*
CXR	*Chest x-ray*
ESR	*Erythrocyte sedimentation rate*
ESRD	*End-stage renal disease*
FPN	*Ferroportin*
HFE	*Hereditary hemochromatosis*
Hib	*Haemophilus influenzae type b*
HPT	*Haptoglobin*
HPX	*Hemopexin*
IDSA	*Diseases Society of America*
IFA	*Iron and folic acid*
IFN-c	*Interferon-c*
IL-2	*Interleukin-2*
LAIV	*Live attenuated influenza vaccine*
LRTI	*Lower respiratory tract infection*

List of Abbreviations Cont...

Abb.	Full term
MRSA	*Methicillin-resistant Staphylococcus aureus*
NPV	*Negative predictive value*
ORS	*Oral rehydration solutions*
PA	*Postero-anterior*
PCR	*Polymerase chain reaction*
PCT	*Procalcitonin*
PCV13	*Pneumococcal conjugate vaccine*
PPSV	*Pneumococcal polysaccharide vaccine*
PPV	*Positive predictive value*
RBCs	*Red blood cells*
ROC	*Receiver operating characteristic curve*
RSV	*Respiratory syncytial virus*
SPSS	*Statistical Package for Social Science*
TF	*Transferrin*
TfR	*Transferrin receptor*
TIBC	*Total iron binding capacity*
TIV	*Trivalent influenza vaccine*
TNF-a	*Tumor necrosis factor-a*
UIBC	*Unsaturated iron binding capacity*
US	*Ultrasound*
WBC	*White blood count*
WHO	*World health organization*
ZPP/H	*Zinc protoporphyrin/heme*

INTRODUCTION

Community acquired pneumonia (CAP) is an acute infection of the pulmonary parenchyma in a previously healthy patient who hasn't resided in a hospital or health care facility in the preceding 14 days ***(Mandell et al., 2007).***

There are approximately 150 million cases of childhood community acquired pneumonia reported each year ***(Ruuskanen et al., 2011).***

Community-acquired pneumonia (CAP) is the most severe form of an acute respiratory infection, accounting for 80% of all deaths from acute respiratory infection and 20% of all deaths in children ***(Williams et al., 2002).***

Pneumonia accounts for nearly four million deaths in children worldwide each year.

Over 90% of the estimated 1.8 million annual deaths due to acute respiratory infections in children less than 5 years of age occur in developing countries and are mainly due to bacterial infections ***(Bryce et al., 2005).***

Despite progress in life-support measures and antimicrobial therapy, the mortality of severe community acquired pneumonia has not varied since the mid-1990s, suggesting that other factors may affect on the evolution of this infection such as the age of the child, maternal age, the level of

maternal education, acute malnutrition, and lack of breastfeeding ***(Goya and Ferrari, 2005).***

Globally, it is estimated that 11–20 million of the 146 million annual childhood episodes of community-acquired pneumonia (CAP) require hospitalization ***(Rudan et al., 2004).***

Inadequate nutrition and acute lower respiratory infection (ALRI) are overlapping and interrelated health problems affecting children in developing countries ***(Daniel et al., 2008).***

Zinc is an essential micronutrient for human health. It is vital for activating growth, physical and neurological development in infants, children and teenagers. Zinc is found in all parts of the body. It is a component in more than 300 enzymes and influences hormones. Zinc also accelerates cell division, enhances the immune system, and important in wound healing ***(Philip et al., 2012).***

Several studies have suggested that zinc supplementation prevents about one-quarter of episodes of acute lower respiratory tract infection (ALRI), which may translate into a modest reduction in (ALRI) mortality in children ***(Daniel et al., 2008).***

Iron deficiency is the most common single-nutrient deficiency in the world. In developing countries, the prevalence of iron- deficiency anemia among children under 5 years of age is at least 25%, and is often higher ***(Patricio et al., 2010).***

Iron deficiency anemia in children occurs most frequently between the age of 6 months and 3 years, the same period of age when repeated respiratory infections occur ***(Bont et al., 2009).***

Some studies have suggested that improving the nutritional status in children by preventing low hemoglobin might influence the outcome of children with ALRTI ***(Abeer et al., 2013).***