Evaluation of Iron Profileasan Assistant Diagnostic Tests for Children with Pneumonia

تقويم مستويات الحديد كفحوصات مختبرية مساعدة في تشخيص الأطفال المصابين بذت الرئة

Dr. Ammar Lateef Hussein*

Dr. Hani Lateef Hussein**

الخلاصة:

خلفية البحث: يعد الحديد من العناصر المطلوبة لمعظم الكائنات الحية كعامل مساعد أساسي في معظم الفعاليات الحيوية المهمة. حيث أن هناك العديد من الخلافات العلمية في ما يخص دور العناصر الغذائية وخصوصا عنصر الحديد في الإصابة بالتهابات القناة التنفسية. علاوة على ذلك، فان نقص عنصر الحديد مرتبط بفشل كفاءة المناعة والذي ربما يؤدي الى زيادة حالات الوفاة.

الهدف: تهدف هذه الدراسة الى إختبار إمكانية إستخدام مستويات الحديد كفحوصات مختبرية تشخيصية لمرضى ذات الرئة لدى الاطفال.

المنهجية:صممت هذه الدراسة كدراسة مقارنة بين مجموعتي المرضى و السيطرةحيث انها أجريت على ١٥٠ طفل تراوحت أعمارهم بين (٦ – ٧٢) شهر، ١٠٠ طفل مصاب بذات الرئة (٥٧% ذكور) و(٤٣% اناث) وكذلك ٥٠ من الأطفال الأصحاء كمجموعة سيطرة (٥٤% ذكور) و (٤٦% اناث) في قسم الأطفال التابع لمستشفى سامراء العام للفترة من أيلول ٢٠١٥ الى أذار ٢٠١٧. تم تحليل النتائج بيانيا بإستخدام البرنامج الإحصائي SPSS) (V.20حيث تم إستعمال الإحصاء الوصفي والذي تضمن التكرارات، النسب المئوية، الوسط الحسابي إضافة الى إختبار (T-test لمقارنة النتائج.

النتائج:بينت النتائج أن هناك نقصا معنويا في كل من مستوى الحديد، الفرتين و الهيموغلوبين للأطفال المصابين بمرض ذات الرئة مقارنة بمجموعة السيطرة(12.23±1.07 and 5.79±1.66, 75.86±1.87 vs 9.4±1.10 and 3.99±2.06, 66.48±15.9) بالتتالي، بينما لم يكن هناك أي فرق معنوي في مستوى السعة الكلية لإرتباط الحديد بين الأطفال المصابين بذات الرئة ومجموعة السيطرة (390.93±47.78 vs 393.74±34.64, respectively).

الاستنتاج: خلصت نتائج هذه الدراسةإن مرض ذات الرئة عند الاطفال يؤدي إلى نقص مستوى الحديد، الهيموغلوبين والفرتين بينما لا يؤثر على السعة الكلية لإرتباط الحديد.

التوصيات:توصي الدراسة بإستخدام القياسات المبكرة والدقيقة لمستويات الحديد والتي تشمل كل من الحديد، والفرتين وبعض المركبات التي يدخل فيها الحديد بشكل مباشر مثل الهيموغلوبينكفحوصات مختبرية تضاف الى عوامل التشخيص لمرض ذات الرئة عند الأطفال.

ABSTRACT:-

Back ground: Iron is required by most organisms as an essential cofactor in many important biological processes. There are controversies regarding the role of nutrients especially iron in respiratory tract infections in childhood. Furthermore, iron deficiency is also associated with impaired immunocompetence and therefore can lead to increased morbidity.

Objective: the aim of this study was to testthe possibility of using the iron profile as a laboratory and diagnostic tests for pneumonia in children.

Methodology: Case-control study was designed to hypothesize that lower iron, ferritin, and TIBC would be associated with a greater risk of pneumonia in children. The study was performed on 150 children with ages between (6 – 72) months, 100 children with pneumonia (57% male) and (43% female,) and 50 control (54% female) and (46% female) in pediatric department of Samarra general hospital from September 2015 till March 2017. The data were analyzed through the SPSS V.20 application, descriptive data analysis was done through frequency, percentage, mean, standard deviation in addition to T-test to compare results.

***Lecturer, PhD in Clinical Biochemistry, Biochemistry Department-**
Collage of Medicine/Tikrit University.
****Pediatrician, High Diploma in pediatric Medicine, Pediatric Department/Samarra General Hospital.**
E-mail: am_tucom@yahoo.com

Results: The results showed there was a significant decreased in the levels of Iron, ferritin, and hemoglobin when compared to control group(66.48±15.9, 3.99±2.06 and 9.4±1.10 vs 75.86±1.87, 5.79±1.66 and 12.23±1.07 respectively), while there was no significant difference of TIBC in study group when compared to control group(390.93±47.78 vs 393.74±34.64, respectively).

Conclusion: The results of this study were concluded that the pneumonia in children lead to significant decrease on iron levels, hemoglobin and ferritin while don't effect on TIBC.

Recommendations: The use early and accurate measurements of iron profile that which includes iron, ferritin and certain compound which contain iron such as hemoglobin as a laboratory diagnostic tests add to the diagnostic tool for pneumonia in children.

Key words: Iron, Ferritin, hemoglobin, TIBC, Pneumonia.

Introduction

Pneumonia has a high morbidity and mortality rate all around the world today[1]. Physicians are becoming more and more interested in the use of biomarkers since there is no "gold standard" which is both sensitive and specific enough to help them reach the "correct" diagnosis.

Some of the biomarkers which are at the offing as an adjunct in the diagnosis of pneumonia include C-reactive protein, leukocyte count, immunoglobulins, and proinflammatory cytokines. There are other biomarkers whose importance is growing in the medical field. They are procalcitonin (PCT) and Triggering receptor expressed on myeloid cells-1 (TREM-1)[1].

Iron is required by most organisms as an essential cofactor in many important biological processes[2].A child would be anemic if its hemoglobin concentration was below 11 g/dL regardless of age, based on recommendations of the World Health Organization[3]. Anemic children are at a greater risk of developing various consequences of anemia including infections[4]. Recent studies have shown that nutritional factors such as zinc, iron and others are closely related to the body's resistance to infection. Decrease in such nutrients may be a risk factor for development of infection. However, there are controversies regarding the role of nutrients especially iron in respiratory tract infections in childhood[5].

The interaction between iron and infection has been the subject of debate in nutritional immunology, primarily because iron deficiency impairs components of cell mediated immunity[6]. Subsequently, iron does appear to participate directly to immunity and lung injury which suggest several different approaches to prevention and treatment of lung disease[5]. The host's iron status can have a significant impact on susceptibility to and the course of infectious disease, and conversely, that infection and inflammation can alter iron homeostasis[7].

WHO reported that, in 2005, 60.3% of the Egyptian children from 6 months to 8.2 years of age had hemoglobin levels less than 11 g/dl[3].Low hemoglobin level is a risk factor for acute lower respiratory infections as it was detected in 62.5% of pneumonic patients, 56.25% of bronchiolitis cases, and 42.71% of the control group, with a *P*-value of 0.044[8]. Moreover, among Indian children, Hussain *et al.*[9]reported that 64.5% of their hospitalized patients and 28.2% of the healthy controls were anemic and that the anemic children were 4.6 times more susceptible to lower respiratory tract

infection.Approximately two million children under five die frompneumonia each year, accounting for nearly one in five childdeaths globally[10]. A study done by Luis Huicho et alidentified that pneumonia caused about 20% of allunder-five deaths in Peru[11]. Several studies done indifferent parts of Ethiopia showed that pneumonia is majorcause of mortality and morbidity among under-five children[11].

Objective

The objective of this study is to evaluate the importance of the Iron profile as early diagnostic test for pneumonia in children.

Methodology

This case–control studywas achieved in pediatric department, of Samarra general hospital from September 2015 till May 2017. It included 100 children aged from 24 months to 6 years. They were divided into two groups. Group 1 included 100 patients hospitalized for pneumonia (range 24 –72 months): 32 male and 18 female patients. Group 2 included 50 clinically healthy controls (range 9–72 months) attending the outpatient clinic of the same hospital: 31 male and 19 female.

Data analysis was performed using statistical package of social science (SPSS) version 20.0 of windows. Numerical variables were reported in terms of mean and (T-Test) for comparison between categorical variables. The ($p < 0.05$) was considered statistically significant for interpretation of result.

Blood Samples:-

Blood samples (3 ml) were drawn from each child by means of vein puncture and divided in to two parts: one part was put in an EDTA tube for PCV and hemoglobin, the other part was transferred to a plain vacutainer tubes for serum iron, TIBC, and serum ferritin[12].

Inclusion Criteria:-

All hospitalized children between 24 months and 6 years with a diagnosis of pneumonia according to the WHO[13]criteria — namely, cough and/or difficult breathing, with or without fever, fast breathing, or lower chest wall in drawing where their chest moves in or retracts during inhalation (in a healthy person, the chest expands during inhalation).

Excluded Criteria:-

Excluded criteria included children with other systemic illnesses like congenital chest anomalies, intake of iron supplements, tuberculosis, protein energy malnutrition and children who had already received antibiotics from outside were excluded from the study.

Results:

Table (1): Gender frequency and percentage of patients group.

	Frequency	Percent	Valid Percent	Cumulative Percent
Male	57	57.0	57.0	57.0
Female	43	43.0	43.0	100.0
Total	**100**	**100.0**	**100.0**	

Table 1 shows that150 children aged between (2-6) years were enrolled in the study. One hundred patients were admitted to the pediatric department in Samarra general hospital with pneumonia according to the inclusion criteria, (male, 57%) and (female, 43%).

Table (2): Gender and percentage of control group.

	Frequency	Percent	Cumulative Percent
Male	27	54.0	54.0
Female	23	46.0	100.0
Total	**50**	**100.0**	

Another 50 healthy controls were studied in the outpatient department, 54% were males and 46% females as in (Table 2). Both groups age ranged from (2-6) years.

Table (3): The age frequency of study group

Age in months	Frequency	Percent	Cumulative Percent
24.00	3	3.0	3.0
28.00	2	2.0	5.0
30.00	5	5.0	10.0
36.00	20	20.0	30.0
38.00	9	9.0	39.0
39.00	1	1.0	40.0
40.00	4	4.0	44.0
42.00	10	10.0	54.0
46.00	4	4.0	58.0
48.00	10	10.0	68.0
50.00	3	3.0	71.0
52.00	3	3.0	74.0
54.00	5	5.0	79.0
56.00	1	1.0	80.0
60.00	6	6.0	86.0
62.00	3	3.0	89.0
65.00	1	1.0	90.0
66.00	4	4.0	94.0
68.00	1	1.0	95.0
70.00	1	1.0	96.0
72.00	4	4.0	100.0
Total	100	100.0	

Table 3 shows that 100 children investigated in the study, pneumonia was more prevalence in age 36 months (20 children, 20%).

Table (4): the mean iron profile for study group compared with control group.

Iron profile	Patients group	control group	P value
Iron	Mean = 66.48 SD±15.88	Mean = 75.86 SD±1.64	p< 0.05
Ferritin	Mean = 3.99 SD±2.06	Mean = 5.79 SD±1.66	p<0.05
Hemoglobin	Mean = 9.35 SD±1.11	Mean = 12.23 SD±1.07	p<0.001

Table 4 revealed a significant decrease of Iron, ferritin and Hemoglobin in study group when compared to control group (66.48±15.9, 3.99±2.06 and 9.4±1.10 vs 75.86±1.87, 5.79±1.66 and 12.23±1.07 respectively).

Table (5):the mean TIBC for study group compared with control group.

	Study group		Control group		
	mean	SD	Mean	SD	P value
TIBC	390.93	±47.78	393.74	±34.64	p>0.05

On the other hand, there was no significant difference of TIBC in study group when compared to control group (390.93±47.78 vs 393.74±34.64, respectively) p>0.05.

Table (6): Distribution of study group according toresidence .

	Frequency	Percent	Cumulative Percent
rural	63	63.0	63.0
urban	37	37.0	100.0
Total	100	100.0	

Table 6 show that the prevalence of pneumonia in children was more in rural (63%) than urban (37%).

Discussion

Pneumonia has a high morbidity and mortality rate all around the world today[1]. Physicians are becoming more and more interested in the use of biomarkers since there is no "gold standard" which is both sensitive and specific enough to help them reach the "correct" diagnosis.

Some of the biomarkers which are at the offing as an adjunct in the diagnosis of pneumonia include C-reactive protein, leukocyte count, immunoglobulins, and proinflammatory cytokines. There are other biomarkers whose importance is growing in the medical field. They are procalcitonin (PCT) and Triggering receptor expressed on myeloid cells-1 (TREM-1)[1].

The result of our study revealed that both genders of children are susceptible to iron deficiency (ID) as shown in table (1).Since anemia is the most important indicator of iron deficiency, the terms ID and IDA (iron deficiency anemia) are often used

interchangeably. Also our study showed that the prevalence of pneumonia were more prevalence in children with age between (36 – 42) months table (3), most of them where iron deficient.

The results of the present study also showed that serum iron, ferritin, and hemoglobin was significantly lower in cases of pneumonia when compared to control group(Table 4). Johnson and Wessling-Resnick, 2012 reported that, iron is essential for the function of iron proteins that play a role in the innate immune response, such as hepcidin, lactoferrin, siderocalin, haptoglobin, hemopexin, Nramp1, ferroportin and the transferrin receptor[14].For this reason iron deficiency leads to reduced immunity and increases the incidence of infection. Collectively, these data suggest that iron deficiency in children may contribute to the development of pneumonia by increasing the chance of infection[5].

The present results agreed with Hussein M. Abdel-Maksoud et al[14]who stated that was a significant decrease of RBCs, Hemoglobin, iron, ferritin in study group of children with pneumonia when compared to control group.

Ramakrishnan and Harish , found, in a study of 200 infants and children between 9 months to 16 years, that 74% of cases and 33% of controls were anemic (with 80 and 82% IDA, respectively)[16]. Moreover, anemia was found to be a risk factor for chest infections in general (OR 15.55; CI 4.88–49.53;and $P < 0.001$) and pneumonia in particular (OR 4.03;CI 1.71–9.49; and $P = 0.001$). Thus, anemic children were about four times more susceptible to develop pneumonia compared with nonanemic children[17].

Our results also showed there was no significant deference in TIBC between study group and control group (390.93±47.78 vs 393.74±34.64, respectively) as shown in table (5). This can be explained by thefact that infection can affect iron panel studies by decreasing the iron level and TIBC[18].

Results of our study also revealed that the prevalence of pneumonia was more in rural (63 %) than urban (37 %) table (6), and this is due to low socio and economic status. Univariate analysis of IDAprevalence in adults (≥19 yr, n=5,906) relative to socioeconomic and nutritional factors showed that IDA was associated with low income, underweight, insufficient dietary iron or vitamin C intake (according to the recommended nutritional intake)[19]. From the other hand Children from severely crowded houses were four timesmore likely to develop pneumonia compared to childrenfrom under-crowded houses. Crowding at home increasesrisk of transmission of illness[20].

In developing countries, low socio-economic status,malnutrition, low birth weight, non-exclusive breastfeeding,indoor air pollution, crowding, parental smoking, zincdeficiency, mother's experience as a caregiver, mother's age,lack of education in the mother, humid conditions, highaltitude, vitamin A deficiency, birth order and outdoor airpollution were found as possible risk factors associated withpneumonia among children[21].

Conclusion

Low level of iron, Hemoglobin and ferritin was found in children with pneumonia. Thus there was a significant correlation between Iron, ferritin, and hemoglobin and prevalence of pneumonia in children, and there was no significant correlation between TIBC and pneumonia in children.

Recommendation

Early and accurate measurement of iron profile such as serum iron, serum ferritin, and certain biochemical parameter that which contain iron such as hemoglobinis important test in diagnosis and treatment of pneumonia in children.

References:

1. S. Sharma, B. Maycher, and G. Eschun, "Radiological imaging in pneumonia: recent innovations," *Current Opinion in Pulmonary Medicine*. 2007; 3: 159–169.
2. Beard JL. Iron biology in immune function, muscle metabolism and neuronal functioning. *J Nutr*. 2001;131:68–80.
3. World Health Organization Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia. Geneva, Switzerland: WHO; 2008. 48 p.
4. Pasricha, S.R., J. Black, S. Muthayya, A. Shet and V. Bhat. Determinants of anemia among young children in rural India. *Paediatrics*.2010;126: 140-149.
5. Zuo, X.F., J.X. Li and W.D. Zhou. The nutrient status of Chineseinfants with pneumonia. *Biomed. Res*. 2014;25: 317-320.
6. Roth, D.E., L. E. Caulfield, M. Ezzati and R.E. Black. Acutelower respiratory infections in childhood: opportunities for reducing theglobal burden through nutritional interventions. *Bull*. World HealthOragan. 2008; 86: 321- 416.
7. Bobby J. Cherayil. The role of iron in the immune response to bacterial infection. *Immunol Research.*2011; 50(1): 1-9.
8. El-Sakka AS, Imam SS, Amer HA, Moustafa SA. Vitamin Ddeficiency and low hemoglobin level as risk factors for severity ofcute lower respiratory tract infections in Egyptian children. *Egyptian Pediatric Association Gazette*. 2014;62(1): 1-7.
9. Hussain SQ, Ashraf M, Wani JG, Ahmed J. Low hemoglobin level a risk factor for acute lower respiratory tract infections (ALRTI) inchildren. *J Clin Diagn Res*. 2014; 8 :1-3.
10. Deribew A, Tessema F, Girma B. Determinants of under-five mortality in Gilgel Gibe Field Research Center, Southwest Ethiopia*. Ethiopian Journal of Health Development.* 2007;21(2):117-124.
11. Huicho L, Trelles M, Fernando Gonzales F. National and sub-national under-five mortality profiles in Peru: a basis for informed policy decisions. *BMC Public Health*. 2006; 6(173).
12. Forman, D. and Parker, S*. Ann. Clin. Lab. Sci*.10:345; 1980.
13. WHO. 2014. Pneumonia; fact sheet no. 331. [Last accessed on 2015 Apr 10].
14. Johnson, E.E. and M. Wessling-Resnick. Iron metabolism and the innate immune response to infection. *Microbes Infect*. 2012; 14: 207-216.

15. Hussein M. Abdel-Maksoud, Kamel Abdelghafar Hasan, Mohamed Ahmed Helwa. Evaluation of Iron Deficiency Anemia asa Predisposing Factor in the Occurrence of Pneumonia in Children. *Trends Med. Res.,*2016; 11(2):69-75.

16. Ramakrishnan, K. and P.S. Harish. Hemoglobin level as a riskfactor for lower respiratory tract infections. *Indian J. Pediatr*, 2006; 73:881-883.

17. Rashad Mohamed M.a, Fayed Sahar M.b, El-Hag Aly Mona K.c.Iron-deficiency anemia as a risk factor for pneumonia in children.*Benha Medical Journal*. 2015; 32:96–100.

18. Sipahi T, Köksal T, Tavil B, Akar N. The effects of acute infection on hematological parameters. *Pediatr Hematol Oncol* 2004; 21:513–520.

19. Jeong-Ok Lee et al. Prevalence and Risk Factors for Iron DeficiencyAnemia in the Korean Population: Results of the Fifth Korea National Health and Nutrition Examination Survey. *J Korean Med Sci*. 2014; 29(2): 224–229.

20. Tessema T, Hailu S, Anbebir S and Mitikie G. Household illness prevalence and its determinants in the under five children, North Western Ethiopia. *Ethiopian Journal of Health Development.* 2000; 15 (3):173-178.

21. Emmelin A and Wall S. Indoor Air Pollution: A poverty-related cause of mortality among children of the world. *Chest disease Journal*, 2007; 132(5):1615-1623.