Research Article

CLINICAL INVESTIGATION

Iron deficiency anemia as a risk factor of childhood asthma

Abstract

Background: There are many risk factors for asthma occurrence like gender, atopy, and infection. Trace elements like Fe, Mg and Zn play a role in decreasing airway hyper-responsiveness.

Objectives: To assess Iron Deficiency Anemia (IDA) as a risk factor for childhood asthma and its possible effect on pulmonary functions.

Patients and Methods: Across-sectional comparative study was carried out on 200 children, 6-14 years old who attended the outpatient pediatric clinics and emergency department of Albatool Teaching hospital in Diyala governorate from Oct. 2017 to Oct 2018, they were classified into: group I:100 children with IDA-who was subdivided into group Ia: Asthmatic children and group Ib: Non asthmatic children. Group II: 100 children without IDA, subdivided into group IIa: asthmatic children and group II b: non-asthmatic children.

Results: Children with asthma in group Ia the male to female ratio was 1.75/1.0 and in group II b the ratio was 1.4/1.0. The anemic group with asthma constitutes 66% of group I, while in group II the asthmatic children constituted 24% of included children. Anemic asthmatic children had significant difference regarding Pulmonary Function Tests (PFT) (FEV1, FVC, FVC/FEV1) in comparison to non-anemic asthmatics.

Conclusion: Asthma was more common in males, anemic asthmatics group constituted 66%, and anemia had significant detrimental effects on PFT in comparison to non-anemic asthmatics.

Keywords: children asthma • Fe deficiency • Anemia

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Introduction

The known risk factors for asthma are gender, airway hyper-reactivity, atopy, allergens, infections, tobacco smoke, obesity, and perinatal factors [1-4]. Iron status is recognized to affect the capacity to oxygenate tissues and produce energy, but how iron influences immune and non-immune-triggered inflammatory processes are indistinct. Iron and Zinc displayed a significant decrease in Delayed type hypersensitivity and possess significant anti-asthmatic effect which may be ascribed to its immunomodulatory and anti-inflammatory features [4,5-8]. Higher iron stores were inversely associated with asthma and lower body iron and higher tissue iron need were associated with lower lung function [5,7,9-12]. Pathophysiologic events producing asthma, including inflammation, increases in Th2 cells, and muscle contraction, can correlate with iron availability [2,3,8]. Preservation of iron homeostasis is of extreme importance for the respiratory physiology and pathophysiology as well as local iron deficit or accumulation may result in certain respiratory function impairment FEV1, FVC, FEV1/FCV, and PEF [12,13-17]. It had been shown that iron-supplemented diet had markedly decreased allergen-induced airway hyperreactivity, by decreasing mast cell activation [3,4,17-19]. Identification of further treatments that could preclude or decline the severity of asthma would offer major progress in the clinical care of patients with allergen-triggered asthma [20,21]. The aim of this study was to investigate iron anemia deficiency as a risk factor for childhood asthma and its possible effect on pulmonary functions.

Subjects and Methods

This cross-sectional comparative study was carried out on 200 children in the age group of 6-14 years who attended the outpatient pediatric clinic and emergency department of Albatool Teaching hospital with upper or lower respiratory tract infection, 100 patients with IDA and 100 children without IDA and they were examined and investigated for diagnosis of bronchial asthma during the period from Oct 2017 to Oct 2018.

The patients were classified into:

Group I: 100 children with IDA that was subdivided into:

Group Ia: asthmatic children

Group Ib: non-asthmatic children

Group II: 100 children without IDA that was subdivided into:

Group IIa: asthmatic children

Group IIb: non-asthmatic children

Inclusion criteria

A. The diagnosis of bronchial asthma in children was based on the criteria mentioned in previous studies [17-19]:

1. A history of intermittent or chronic symptoms typical of asthma
2. The findings on physical examination of characteristic musical wheezing (present in association with symptoms and absent when symptoms resolve)
3. A post-bronchodilator increase in FEV1 of >12%

B. Criteria for diagnosis of anemic children:

The child is considered to be anemic if Hb level<11gm/dL. Blood film showed hypochromic microcytic RBCs and MCV <72fLRed cell distribution width>15%. The serum Fe<30 µg/dLand serum ferritin level<12 µg/dl [5,10].

Exclusion criteria

- Anemia other than IDA
- Chronic chest disease other than bronchial asthma
- Heart disease
- Liver disease
- Kidney disease

All patients were subjected to

I. Full history taking and physical examination: With special attention to intermittent attacks, Cough and shortness of breath, wheezy dyspnea and Chest tightness, Tachypnea, Signs of hyperinflation, prolonged expiratory phase, Expiratory Rhonchi, and pallor. Body mass index (BMI) was calculated using the following formula: BMI=Weight/Height^2 in meter square.

II. Laboratory investigations:

- Complete blood count
- Serum ferritin level
- Kidney function tests
- Liver function tests

III. Plain Chest X-ray PA view: The chest radiograph was done to exclude other causes of wheezing other than asthma.

Spirometer was used to measure the Forced Expiratory Volume in one second (FEV 1) and Forced Vital Capacity (FVC) using principles laid by Miller [15]. Calculation of Peak Expiratory Flow (PEF) done by the following equation. The equation for the calculation of predicted normal values for PEF for males and females are as follows [12]:

Males: PEF (L•s-1) = (6.14 × height) – (0.043 × age) + 0.15

Females: PEF (L•s-1) = (5.50 × height) – (0.030 × age) – 1.11

Ethical consent: The study protocol and the methods were carried out according to principles of the Declaration of Helsinki, as well as reviewed and approved by the College of medicine, university of Diyala Ethics Research Committee. Verbal consents were also taken from the parents and caregivers of children involved in the study.

Statistical analysis: Data were analyzed using Statistical Package for Social Sciences version 23 (SPSS Inc., Chicago, IL, USA). Qualitative data were presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data were presented as mean ± SD. Student's t-test was used to compare between two groups. Pearson's correlation coefficient was used to test the correlation between variables. $p<0.05$ was considered to be statistically significant.

Results

Table 1 showed the characteristics variables of two hundred studied children, where children with asthma in group Ia the male to female ratio was 1.75/1.0 and in group IIb the ratio was 1.4/1.0. The anemic group with asthma constitutes 66% of group I, while in group II the asthmatic children constituted 24%. **Table 2** showed the relationship between hemoglobin and

Table 1. Characteristics variables of 200 children in the present study

Variable	Groups	Age	Male	Female	Asthma		BMI		p-value
					Yes	No	>25	<25	-
Anemic	Group Ia	6-14	42 (63.6%)	24 (36.3%)	66% a	-	26 (39.3%)	40 (60.6%)	-
	Group Ib	6-14	26 (76.4%)	8 (23.5%)	-	34%	10 (29.4%)	24 (70.5%)	-
Total	100	-	68%	32%	100%	-	-	-	-
None anemic	Group IIa	6-14	14 (58.3%)	10 (41.6%)	24%	-	8 (33.3%)	16 (66.6%)	-
	Group IIb	6-14	36 (47.3%)	40 (52.6%)	-	76% b	12 (15.7%)	64 (84.2%)	-
Total	100	-	50%	50%	100%	-	-	-	-

[a]p value=0.001
[b]p value=0.000

Table 2. Relationship between hemoglobin and serum ferritin level with pulmonary function parameters among100anemic group I (Ia and Ib)

Lab. test	Group I	Pulmonary functions	No. of children	Measurement	p- value
Low Hb level low serum ferritin	Ia	FVC	12	Normal values for age	0
			54	Below normal values for age	
		FEV1	8	Normal values for age	0
			58	Below normal values for age	
		FEV1/FVC	10	Normal values for age	0
			56	Below normal values for age	
		PEF	8	Normal values for age	0
			58	Below normal values for age	
Low Hb level Low serum ferritin	Ib	FVC	32	Normal values for age	0
			2	Below normal values for age	
		FEV1	30	Normal values for age	
			4	Below normal values for age	
		FEV1/FVC	31	Normal values for age	
			3	Below normal values for age	
		PEF	32	Normal values for age	
			2	Below normal values for age	

Table 3. Comparison between groups (Ia) and (IIa) regarding pulmonary functions

Group		FVC	FEV1	FEV1/FVC
GROUP (Ia) No=66 Anemic asthmatic	Range	(53-72)	(53-76)	(54-65)
	Mean+SD	61.2 ± 9.5	57.5 ± 8.3	52.3 ± 10.0
GROUP (IIa) No=24 Non anemic asthmatic	Range	(64-76)	(58-78)	(51-64)
	Mean+SD	71.0 ± 8.4	63.0 ± 6.4	61.4 ± 8.0
p-value		<0.05	<0.05	<0.05

serum ferritin level with pulmonary function parameters among 100 anemic groups I (Ia and Ib, where children with low Hb and low serum ferritin and asthma had more pronounced deterioration of pulmonary function on spirometry study p-value<0.05. **Table 3** showed a comparison between groups (Ia) and (IIa) regarding pulmonary functions, where those with asthma with anemia had more pronounced deterioration of pulmonary function on spirometry study than asthma alone p-value<0.05.

There is a statistically significant difference between group Ia and group IIa regarding pulmonary function parameters (FVC, EEV1, FEV1/FVC) (p<0.05) as it was better in-group IIa.

Discussion

Asthma affects >300 million individuals worldwide. Anemia and respiratory tract infections are common problems among primary school children and a complex relationship exists between iron status and infection. In the current study, the ages of group I ranged from 6 to 14 years and mean was 10.2 ± 3.1 and in group II their ages ranged from 6 to 14 years and mean was 10.9 ± 3.2. The study showed no significant statistical difference between groups I and group II regarding age (p>0.05). This study showed more boys affected with asthma than girls which is statistically significant (p<0.05) as it was noted by many studies [2,7,17]. Although BMI is an important risk factor of asthma [2,5,20] in this study we did not find any significant statistical difference between studied groups p- value>0.05. This may be due to different sampling technique and probably related to decreased obesity and overweight in the studied sample. Iron and anemia are associated with impaired immunocompetence which results in increased morbidity [8]. The Hb facilitates oxygen (O_2) and CO_2 transport. It carries and inactivates Nitric Oxide (NO) and plays the role of the buffer as well as responsible for stabilizing the oxygen pressure in the tissues [10,11]. We noticed that asthma was significantly higher in group Ia than in group IIa which is in accordance with other studies as Fe deficiency is a risk factor for asthma [1,3,4,8,9]. Pulmonary function tests provide valuable information about the status of an individual's respiratory system and work capacity [1,3,9,14,]. In the present study, there was a significant correlation between Hb level and pulmonary function tests in anemic asthmatic group Ia, in comparison to non-anemics, as low Hb level plays a significant role in cardiopulmonary function Similarly in this study there was a significant correlation between serum ferritin level and FVC, FEV, FEV1/EVC and PEF. In this study, there was a statistically significant difference between group Ia and group IIa regarding pulmonary function parameters (p<0.05), this is explained on the basis of physiologic effects of low Hb on cardiopulmonary dynamics. Anemia affects the immune system of the body and reduces immunity, so increases the risk of infection especially viruses, which in turn increase the risk of asthma. A decrease in strength of respiratory muscles including diaphragm reduces the pulmonary functions as well as peak expiratory flow rate, FEV1 [15]. Maximum voluntary ventilation is markedly reduced due to the decreased depth of respiration as well.

Conclusion

- Iron deficiency anemia may be considered as an indirect risk factor for the development of asthmatic attacks in children
- Iron deficiency anemia may have a negative effect on spirometry results in asthmatic children that may lead to increased severity of asthmatic attacks

Recommendations

Based on this study we can recommend the following:

- Hb level should be checked for every asthmatic child and if it is low, proper investigations for the type of anemia should be initiated to exclude IDA

- Prevention of IDA is important since it is common in our community, to improve immunity and decrease the risk of asthma and its severity

Limitations of the Study

- The sample was small since larger sample needed to generalize the recommendations
- Absence of PFT lab in our hospital and the patients need to be sent to another hospital to do the test

Executive summary

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