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Incidence of Amebiasis Among Bloody Diarrhea And Malnutrition Patients With Relation To Gamma Interferon Bellow Five Years of Age in Babylon Province In Iraq

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Abstract :-
Malnutrition is an underlying factor in many diseases in both children and adults, it increases the incidence of infection including bloody diarrhea (parasite infection mostly Entamoeba histolytica) and potentiates the severity of the disease. Increased levels of gamma interferon from stimulated peripheral blood mononuclear cells and a mucosal IgA antilectin antibody response have been associated with protection from Entamoeba histolytica infection.

Aim of study
To study the incidence of amebiasis among patients with bloody diarrhea and malnutrition below 5 years of age and its correlation to serum level of gamma interferon.

**Key word : malnutrition , bloody diarrhea , amebiasis ,gamma interferon, Babylon governorate*

Introduction

Malnutrition is an underlying factor in many diseases in both children and adults [(1)] . Amebiasis and bacterial infection are important causes of bloody diarrhea worldwide, the prevalence is disproportionately increased in developing countries because of poor socioeconomic conditions and sanitation levels.[(2)].

The Factors that influence whether infection of Entamoeba histolytica leads to asymptomatic or invasive disease include the Entamoeba histolytica strain and host factors such as genetic susceptibility, age and immune status [3,4] .

The risk factors for severe disease and increased mortality include young age, , corticosteroid treatment, malignancy, and malnutrition ([3,4]). Several lines of evidence suggest an important role for cell-mediated immunity via cytokine activation of macrophages and neutrophils to kill ameoba[5]. Leptin is a product of the LEPgene on chromosome 7 that functions to signal satiety and is implicated in regulation of the immune system and the gastrointestinal tract [6]. Circulating leptin concentrations are low in malnourished patients and are associated with a suppression of proinflammatory cytokine production [7].

The association of antibody responses and IFNγ (gamma interferon) to innate and acquired immunity to amebiasis indicates a role for CD4+ T cells in protection [8] (There is substantial evidence from *in vitro* and animal model studies of an important role for interferon-gamma(IFNγ) including IFNγ activation of macrophages to kill the parasite) [9]

There was a positive correlation of peripheral blood mononuclear cell (PBMC) production of IFNγ with height for age Z score (HAZ)and weight for age Z score (WAZ)for stimulation with soluble ameobic antigen (malnourished or stunted children had significantly lower IFNγ[9]

Aim of study

To study the incidence of amebiasis among malnutrition and bloody diarrhea for the patients of less than 5 years of age and its relation with gamma interferon and socioeconomic factors .

Patients and Methods

A case-controlled study was conducted on 150 patients(81 males and 69 females) with bloody diarrhea and malnutrition ,who were attending the Babylon maternity and children hospital in the period from April 2012 to the end of June 2013. Their age ranged from 1 month to 5 years with mean age 30 ± 1 months,

They were studied for incidence of amebiasis ,in comparison to 100 patients with bloody diarrhea and well nourished ,attending the hospital as control group (47 males and 53 females) ,with no past history of recurrent diarrhea and no history of chronic disease.

Detailed history and clinical examination were obtained for every patient and control group which including:

[A] exclusion criteria in the history (to exclude other causes of bloody diarrhea like history of bleeding tendency, receiving plasma or other blood products, history of inflammatory bowel disease) and examination to exclude surgical causes of bloody diarrhea.

[B]anthropometric measurements:

Weight, height or length, weight-for-age (W/A), height-for-age (H/A), weight-for-height (W/H) and mid upper arm circumference .

These variables are useful in assessment of nutritional state for each patient and control group.

i. Weight and height were measured using age appropriate scale (all measurements were obtained in Kilograms or centimeter and transformed into growth chart[10] .

ii. Mid arm circumference(independent of age and sex between 9 months to 5 years of age) was measured in cm using tape measure[11].

>13.5 cm ⟶ good nutrition

≤13.5 - ≥12.5 cm ⟶ mild malnutrition

<12.5 - ≥11 cm ⟶ moderate malnutrition

<11 cm ⟶ severe malnutrition

state of nutrition for each patient and control group were classified into normal state ,mild, moderate and severe malnutrition according to the weight/age centile and Z-score as follow [10] :-

Normal state ⟶ > 10^{th} percentile or Z-score zero or more.

Mild malnutrition ⟶ 5^{th} – 10^{th} percentile or Z-score -1SD.

Moderate malnutrition ⟶ 3^{th} – 5^{th} percentile or Z-score -2 or -3 SD.

Severe malnutrition ⟶ < 3^{th} percentile or Z-score < -3 SD.

Fresh stool sample was obtained for each patient and control group ,sent for general stool examination (GSE) and should be repeated for 3 times if it was negative for amebiasis (Stool which collected , should be fresh, blood contained, not taken from napkins or toilet, not mixed with urine or disinfectants, not leaving exposed to air or room temperature for long time).

Blood samples were aspirated for each patient and control group , it sent for gamma interferon (normal value between 25-1000pg/ml)(gamma interferon was measured by ELISA technique according to the instruction of manufacturer manual (Cusabio-china and Abcam-USA) respectively .

This study was approved by our hospital ethics committee(Babylon maternal and pediatric hospital) and all patients or parents provided oral informed consent before being allowed to include in the study .

Statistical analysis

The statistical analysis utilized chi-square test, using SPSS version 18. Categorical variables were presented as frequency and percentages.

P-value of less than 0.05 is consider to be significant and of less than 0.001 is consider to be highly significant.

Results

The incidence of amebiasis was increased among malnourished patients(58%) ,in comparison to control group (30%) and is statistically significant with p-value 0.0011 and the gamma interferon is very low in malnutrition and amebiasis patients 8.5ρg/ml, while its level in control group is 250 pg/ml .

Amebiasis was increased with decreased nutritional state from mild and moderate to severe malnutrition , associated with reduction of gamma interferon from 75 pg/ml in mild malnutrition to 0.5 pg/ml in severe malnutrition .also its incidence is increased with decreasing level of education, but there was no relation regarding the sex, residence and age of patients.

Table one: Incidence of Amebiasis among malnourished patients &control group with their relation to gamma interferon .

	Malnourished group			Control group			p-value
	+ve	Total no. Of patients	%	+ve	Total no. Of patients	%	
amebiasis	87	150	58	30	100	30	0.001
Gamma interferon level	8.5 pg/ml			250pg/ml			0.001

*+ cases : diagnosed amebiasis .

no. : number

There was decreasing production of gamma interferon in patients with malnutrition associated with increased incidence of amebiasis in comparison to control group . p value 0.001

Table two : The incidence of amebiasis and gamma interferon in malnourished patients with the severity of malnutrition

	mild			moderal			severe		
	+ ve	Total no.	%	+ ve	Total no.	%	+ ve	Total no.	%
Amebiasis	12	40	30	35	60	58.3	40	50	80
Gamma Interferon	75 pg/ml			15 pg/ml			0.5 pg/ml		

Decreased production of gamma interferon with increased severity of malnutrition . p-value 0.05

Table three : Distribution of amebiasis in malnourished patients according to age , sex and address

factors	+ve cases	%	Total no.	p.value
< 3 years Age ≥3years	60	58.8	102	0.5
	27	56.26	48	
males sex	48	59.2	81	0.44
females	39	56.5	69	
urban Address	35	53.8	65	0.54
rural	52	61.1	85	

No statistical significant of amebiasis regarding age , sex and address .

Table four : Distribution of amebiasis according to level of education in malnourished patients .

Level of education	+ve	Total no. of patients	%
Higher	8	32	25
moderate	44	69	60.3
Low	35	49	70.5
Total no.	87	150	58

Increased incidence of amebiasis with decreased education level of their families .

Discussion

The results of our study showed that 58% of malnourished patients developed amebiasis ,in comparison to 30% in control group which statistically highly significant with p-value 0.001. This indicates that malnutrition is important risk factor for Entamoeba histolytica(EAH) infection as result from decreased gamma interferon , showed 1.5 ρg /ml in malnourished patients , in comparison to 250 ρg /ml in control group .

Gamma interferon is producing from peripheral mononuclear cell , it is important to activate macrophage to kill EAH [12] or stimulate cell mediated immunity against amoeba [13] and decreased circulating leptin concentration (leptin promotes differentiation , proliferation , survival and function of both innate and adaptive immune cell , modulate intestinal barrier function as well as stimulating mucin secretion and maintaining intestinal morphology [14].

This result is similar approximately to the results done in Bangladesh 47% [15] and in India 58% [14].

There was significant statistically of increased incidence of amebiasis with increased severity of malnutrition from 30% in mild and 58.5% in moderate to 80% in severe state as result from decreased concentration of gamma interferon in mild to severe (75 pg/ml, 15pg/ml and 0.5pg/ml respectively) .

Amebiasis was increased with reduced level of education from 25% in higher education to 70.5% in lower education and statistically is highly significant with p-value 0.001 as may related to increasing factors associated with increased transmission of micro-organism in lower education like ignoring , untreated water , night soil and food or water contamination with cyst [16].

There was no statistical significant difference regarding the age ,sex and address of patient because of both genders lived in the same community and generally engaged in similar activities and hence exposed to the same hazards continually[17], also the rate is equal in urban and rural areas which may be explained by the greater number of villagers resides in urban area [18].

Conclusion

1. Entamoeba Histolytica infection is the leading cause of bloody diarrhea in malnourished**.**

2. Malnourished children is important risk factor because it is associated with decreasing concentration of gamma interferon and the incidence of infection is effected by the level of education and nutritional state while sex, age and residence show no effect.

Recommendation

1-It is important to prevent or correct of malnutrition and increased the education level of their families.

2-Encourage research for vaccine to Entamoeba histolytica to be used in future especially in malnourished and immune compromised children.

Competing interest : The author declares that he has no competing interests .

Author contribution : Hattim conceived and designed the study .

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