Seroprevalence of Human Parvovirus B19 Infection among Thalassemic Children in Babylon Center of Hereditary Blood Disorders

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Abstract

Background: Human Parvovirus B19 is the etiological agent of erythema infectiosum in children, and frequently cause transient red cell aplasia in chidren with chronic hemolytic anemias like thalassemia syndrome.

Objective: To detect the seroprevalence of Human Parvovirus B19 infection in children with thalassemia major in Babylon center of hereditary blood disorders.

Methods: This is a descriptive, comparative hospital based study conducted in Babylon center of hereditary blood disorders in Babylon Gynecology and Children teaching hospital from May of 2012 to August 2012.It include 46 children with thalassemia major age ranging from 2-17 years old and 40 non thalassemic children with matched sex and age attending the same hospital at same time for different reason, as control group.

Anti-HPV B19 IgM and Anti-HPV B19 IgG were done on patient and control sera by ELISA.

Results: Anti-HPV B19 IgM antibodies were detected in 6 of 46 thalassemic patient(13%), and not detected in any children of control group , P value (0.028).

Anti-HPV B19 IgG antibodies were detected in 14 of 46 of thalassemic patient (30.4%)and 2 of 40 in control group(5%), P value(0.004).

Conclusion: Thalassemic children are more prone to get infection with HPV B19 than other nonthalassemic children , so we must consider this possibility specially when thalassemic child develop sudden dropping in hemoglobin and reticulocytopenia.

معدل الانتشارالمصلي للبارفوفايرس ب ١٩ البشري لدى الاطفال المصابين بمرض فقرلدم البحر الابيض المتوسط في مركز بابل لامراض الدم الوراثيه

الخلاصه

الخلفيه:يعد البارفوفايرس ب١٩ البشري هوسببا رئيسيا لمرض الاحمرار الالتهابي لدى الاطفال، واحيانا يسبب مرض التوقف الوقتي لتصنيع كريات الدم الحمر عند الاطفال اللذين يعانون من مرض فقر الدم التحللي ومثال ذالك هو مرضى متلازمة الثالاسيميا.

الهدف: ان الهدف من هذه الدراسه هو تحديد معدل الانتشار المصلي لالتهاب البارفوفايرس البشري ب١٩ لدى الاطفال اللذين يعانون من مرض فقردم البحر الابيض المتوسط العظيم في مركز بابل لامراض الدم الوراثيه.

طريقة العمل: دراسه وصفيه مقارنيه ،مستنده عن طريق المستشفى اجريت لتشمل ٤٦ طفل مريض بمرض فقر الدم البجر الابيض المتوسط (النوع العظيم) اعمارهم تتراوح من ٢-١٧ سنه يراجعون مركز بابل ل امراض الدم الوراثيه في مستشفى بابل التعليمي للنسائيه والاطفال للفتره من شهر اذار الى شهر اب من سنة ٢٠١٢ و٤٠ طفل مطابق جنسا وعمرا غير مصابين بمرض فقر الدم البحر الابيض المتوسط وكذالك يراجعون المستشفى لاسباب اخرى وفي نفس الوقت كمجموعة السيطره.

النتائج: لقد تبين من هذه الدراسه ان ٦ من مرضى المجموعه الاولى(الحاله)وهم الاطفال اللذين يعانون من مرض فقر الدم البحر الابيض المتوسط كانت نتائجهم ايجابيه للاجسام المضاده نوع م لالبارفوفايرس ب١٩ (١٣%)، ولم تسجل اي حاله ايجابيه من اطفال المجموعه الثانيه،وكان هذا الفرق ذو احتلاف اصائي مهم(نسبة الاحتماليه0.028). وكذالك تتين ان ١٦ حاله من المجموعه الاولى

من اصل ٤٦ كانت نتيجتهم ايجابيه لالاجسام المضاده لالبارفوفايرس ب١٩ نوع ج (30.4%) و فقط ٢ من اطفال المجموعه الثانيه كانت نتائجهم ايجابيه لالبارفوفايرس ب١٩ نوع ج (5%) الفارق الاحصائي كان(0.004).

الاستنتاج: مرض فقر الدم البحر الابيض المتوسط العظيم هم اكثر عرضه لالتهاب البارفوفايرس ب١٩ البشري من غيرهم من الاطفال الغير مصابين بمرض فقر دم البحر الابيض المتوسط،لذالك يجب ان نحتمل حصول هذا الالتهاب عندما يصاب طفل فقر الدم البحر الابيض المتوسط بهبوط حاد في نسبة خضاب الدم لديه مع قله في نسبة الخلايا الشبكيه

Introduction

Human Parvovirus B19(HPV B19) is a small, nonenvelopd single stranded DNA belong to the genus Erthrovirus(Paravaviridae) [1] Parvovirus B19 (Latin Parvum means small) is a newly emerging DNA virus discovered by an Austarlain virologist , working in London , when she was testing donor sera for hepatitis B virus , but found the B19 virus in the sera, numbered 19 in row 19 B (donation bank number), she named it B19, later on the B19 virus was plased in the genus Erthrovirus of the family Parvovirhde[2.]

Infection with this virus are very common and can result in a wide range of clinical manifestation depending on patient immunological and hematological status.[3] In immune competent individual, B19 infection can be asymptomatic or benign and may cause Erythema infectiosum(Fifth Disease), and arthropathy[3] However , in patient diminish production or increase loss of erythrocyte , like thalassemia syndrome and other chronic hemolytic anemia, B19 infection result in sever drops of hemoglobin level and anemia which could be life-threatening[4]

Parvovirus B19 is common worldwide , and15% of the children aged 15 years have positive IgG , and common in late winter and early spring[4]The virus is transmitted through exposure to infected droplet or blood which is minimal and vertically from mother to fetus causing congenital anemia and hydrops fetalis.[4,5]Nosocomial transmission also had been documented. The incubation period of the infection is ranged from 4-14 days but can reach 21 days, however marked viremia can last up to a week , subsequently the IgM Abs against the virus raise abruptly and peak at 21 day , the IgG Abs to virus then rises and remain elevated.[4,5]

Clinical condition associated with HPV B19 infection

1- Erythema infectiousum (Fifth disease) common at the age 4-10 year , characterized by facial rash(slapped check) appearance and reticulated or lace-like rash on trunk and extremity .[4]

2-Arthropathy may be as complication of fifth disease or as primary disease .

3- Gloves and Sock syndrome in which the rash may be rublliform or petechial, papulppurpuric involving hand and feet often with fever and enathem[4,6]

4-Transient aplastic crisis(TAC) specially in patient with chronic hemolytic anemia(thalassemia, sickle cell disease, spherocytosis). Patient are highly contagious during aplastic crisis and should be isolated to prevent transmission of virus [7]

5-Chronic red cell aplasia HPVB19 may persist in a immunecomprimized person without Abs, reticulocyte may be absent and transfusion may required , if severe anemia continues ,intravenous Immunoglobulin may be necessary [8]

6- Hydrops fetalis fetal anemia may be severe leading to heart failure and hydrops fetalis [9]

Beta Thalassemia major , owing to chronic hemolytic disorder with shortened half life of RBC, are at

higher risk of acquiring aplastic crisis after exposure to this virus, sudden worsening of anemia, reticulocytopenia, and cessation of erythropiosis of the bone morrow are characteristic feature of transient aplastic crisis [10]

HPV B19 had a strong trophism for hemopoitic stem cell [(11)]. The virus intergrates in a specific site in human genome. The infected cell fail to divide , impairing the production of new RBC , retic count often fall to as low as 0.1 to 0.5% from routine values of 6-20% in patient with hemolytic anemia.[11]

HPV B19 infect mature erythroid progenitor (CFU.E), preventing further replication and maturation, the more primitive precursor (BFU.E) are affected minimally [12]

Aim of Study

To detect the seroprevalence of Human Parvovirus B19 (HPV B19) infection in children with thalassemia major.

Patient and Methods

A descriptive , comparative hospital based study was conducted in Babylon Gynecology and Children Teaching hospital from March 2012 to august 2012 .in this study we have 2 groups: Patient group was include 46 children with thalassemia major aged from 2-17 years attending Babylon center of hereditary blood disorders in the same hospital, all these children were diagnosed as case of thalassemia major by HPLC .Demographical data was obtained from patients group like age, sex, duration of the disease, numbers of blood transfusion units, and serological status of HBsAg, HCV, HIV. Anti-HPV B19 IgM and Anti-HPVB19 IgG also was obtained by using ELISA test kit (uroimmun Medizinsche Labordiagnostika AG /Germany) with order number E1 2580-9601G and oreder number E1 2580-9601 M of .In comparison Control group was include 40 non thalassemic children matched age and sex attending the same hospital for different reason with negative history of blood transfusion . Anti-HPV B19 IgM and Anti-HPVB19 IgG was done for them also. IgM indicate recent infection while IgG indicate past infection.

Statistical analysis

Computerized analysis of the data was carried out using SSPS program version 14.0.

Chi-Square and Fisher Exact test were used to determine the statistical significance of level of differences between patient(case) control group according to Anti- HPVB19 IgM and IgG. P value<0.05 was considered to be significant .

Results

In this study, we found only 6 out of 46 thalassemic patient positive for Anti-HPVB19 IgM (13%), while no any case detected as positive for Anti-HPVB19 IgM in control group with P value(0.028), Also we found 14 patient 0ut of 46 in thalassemic patient positive for Anti-HPVB19 IgG (30.4%) , while only 2 out of 40 child in control group as positive for Anti-HPVB19 IgG(5%) with P value 0.004 as shown in table (1).

Table 1 Distribution of serological markers of Anti-HPVB19 IgM and IgG in thalassemic group and control group

	Anti-HPVB19 IgM +ve	**Anti-HPVB19 IgG +ve**
thalassemic group (no 46)	6 (13%)	14(30.4%)
Control group(no 40)	0	2(5%)
P value	0.028	0.004

Also we found only 2 cases in thalassemic group (33.3%) were positive for Anti-HPVB19 IgM had number of blood transfusion less than 50 units, 3 cases (50%) had number of blood transfusion between 50 to 100 units , and only 1 case (16.7) had number of blood transfusion more than 100 units, with P value 0.499, While we found 7 cases (50%) were positive for Anti-HPVB19 IgG had number of blood transfusion less than 50 units, 5 cases (35.7%) had number between 50 -100 units of blood , and only 2 cases(14.6%) with more than 100 units of blood transfusion with P value 0.905 as shown in table (2)

Table 2 Relation of blood transfusion units and prevalence of Anti-HPVB19 IgM and IgG in thalassemic group

	Anti-HPVB19 IgM +ve	**Anti-HPVB19 IgG +ve**
Blood units <50	2 (33.3%)	7 (50%)
Blood units 50-100	3 (50%	5 (35.7%)
Blood units >100	1 (16.7)	2 (14.6)
P value	0.499	0.905

Also we found 5 cases(83.7%) of positive Anti-HPVB19 IgM were occurred at the age less than 10 years in contrast to 1 case(16.3%) in the age more than 10 years with odd ratio 1.667 and confidence interval (0,1734-16.0235) , While in positive of Anti-HPVB19 IgG , we found 10 cases (71.4%) with age less than 10 years and 4 cases(29.6%) with age more than 10 years with odd ratio 1.429 and confidence interval 0.342-5.970 as shown in table (3)

Table 3 Relation of age and prevalence of Anti-HPVB19 IgM and IgG in thalassemic group

Age limit	**Anti-HPVB19 IgM** +ve	**Anti-HPVB19 IgG +ve**
Age <10 years	5 (83.7%)	10 (71.4%)
Age >10 years	1 (16.3)	4 (28.6%)
P value	1.00	0.72
Odd ratio(OR)	1.667	1.429
Confidence interval(CI)	0.1734-16.0235	0.342-5.970

Regarding the relation of sex, we found female 7.6 times (odd ratio 7.6 with confidence interval 0.723-63.333)more prone to be positive of Anti-HPVB19 IgM than male with P value0.9, While we found male 1.33 times (odd ratio 1.33 and confidence interval(0.3762-4.7248)more at risk to be positive for Anti-HPVB19 IgG than female with P value 0.754 as shown in table (4)

Table 4 Relation of sex and prevalence of Anti-HPVB19 IgM and IgG in thalassemic group

Sex	**Anti-HPVB19 IgM** +ve	**Anti-HPVB19 IgG +ve**
male	1 (16.7%)	8 (57.1%)
female	5 (83.3)	6 (42.9%)
P value	0.9	0.754
Odd ratio(OR)	7.6	1.33
Confidence interval(CI)	0.723-63.333	0.3762-4.7248

Discussion

Parvovirus B19 infection in human is distributed worldwide .Seroepidemiological studies of several countries show that prevalence of HPVB19 infection varied among many countries and population and increase with age[13] , unfortunately we have no data about the exact prevalence of HPVB19 infection in our country.

In this study, a higher prevalence of HPVB19 specific IgM indicative of recent infection (13%) was found in thalassemic group compared to control (zero)with significant statistical difference (P value 0.025). The prevalence of HPVB19 specific IgG (30.4%)in thalassemic group compared to control group(5% with significant statistical difference (P value 0.004), and this is similar to results obtained by Siritant korn et al ;[14]from Thailand , of 60 thalassemic major patient (Anti-B19 IgG is 38% and IgM 4%) . In in Kishore et al . in serological study on 90 indian patient with thalassemia reported much higher rate of Anti-HPVB19 IgM and IgG (41.1% and 81% respectively) [15] .The difference perhaps related to geographical variation in prevalence of HPVB19 infection[(13)] .

The higher prevalence of B19 infection in our thalassemic patient in compare to the control group may be due to risk of multiple blood transfusion[4,5,15]However in our study we found no significant statistical correlation between numbers of units of blood transfusion and higher prevalence of HPVB19 infection in thalassemic group (P value >0.05), and this difference possibly related to small size sample in our study.

Human parvovirus B19 infection is thought to be infection transmitted most frequently by school-aged children , Our data support this observation because (83.7% Anti-B19 IgM +ve and 71.4% Anti-B19 IgG+ve), but no significant statistical difference (P value >0.05) was reported in thalassemic group to age and also for the gender, This is goes with result of Kishore et al[15]

In this study , we found no coinfection in thalassemic group with positive serological marker of HPVB19 with other infection like HCV, HIV, and HBsAg.

Conclusion and Recomindation

The prevalence of HPVB19 infection in patients with thalassemia major is much higher than in non thalassemic patients .Data from this study support need for development of vaccine that primarily protect children with thalassemia major who may be a greater risk of major HPVB19 – related morbidity, when the incidence of HPVB19 is high.

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