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Diversity of Heamatogenetic Markers in Kirkuk Population

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Abstract

Immuno-haematological genetic markers study was carried out to understand the genetic background variations among Kirkuk (Iraq) indigenous population. A cross-sectional study of 179 patients with thalassemia major was conducted in Kirkuk. A detailed review was undertaken to define the relationships between ethnic origins, phenotype and immuno-genetic markers uniformity in relation to genetic isolation and interethnic admixture. A total of 179 thalassemia major patients were subjected to analysis in the hereditary blood diseases centre, including (18(10.05 %)) of intermarriages between different ethnic groups origin, whereas the overall consanguinity marriage rate was estimated at (161 (89.9%)) including (63(35.1%)) for first cousin marriages origin. Out of the 161 cases, 63(39.1%), 52(32.2%) and 46(28.5%) represent Kurdish, Arab and Turkmen ethnic groups, respectively. The distribution of thalassemia major cases within ethnic groups relatively differs (d.f.2, P< 0.2). Arab, (46 (28.5%)) represents the lowest disease (thalassemia) sufferer group because of its relative high rate of outbreeding (14, 77.7%).Blood groups (ABO) and Rhesus (D) genetic marker show no significant differences among the triethnic sample groups (thalassemia patients) of Kirkuk with a preponderance of blood group O. No apparent relationship was found between ABO or Rhesus blood groups and the frequencies of thalassemia major cases.

The study showed a relative genetic heterogeneity and diversity with respect to the immuno-hematological genetic markers. Further, all ethnic populations from Kirkuk were found to harbor thalassemia major genetic marker.

Key Words: Thalassemia, ، genetic isolation ،Inbreeding ، ABO blood groups ، reproductive isolation, gentic variation

Introduction

Thalassemia is the most common, inherited single gene disorder in the world [1] among the several hereditary hemoglobinopathies. Thalassemia major occurs when a person inherits two thalassemia genes, one from each parent. Both parents must have thalassemia minor. When two individuals who have thalassemia minor marry, there is a chance that pregnancy may result in a child with thalassemia Major. As the frequency of thalassemia is increased by the consanguinity mating, it may be assumed that the net effect has been the creation of multiple genetic and reproductive isolates, accentuation of certain recessive alleles. However,

this clinical consequence of this highly complex differentiation, leads to population heterogeneity and genetic diversity [2].Moreover, various evolutionary forces such as waves of people of different ethnic stocks, cultures and languages who either invaded Kirkuk or migrated to Kirkuk from different directions and contributed significantly to the present-day gene pool. These people not only settled in Kirkuk but also gradually merged and mingled with the original local populations [3].

Ethnic origin and migrations are factors that affect population genetics which focus on relative distribution of genes or inherited traits (genetic markers) [4].

Hence this study aims at studying genetic marker polymorphism (hemoglobinopathies and ABO blood groups) to determine the genetic similarity of different ethnic groups of Kirkuk community ,whether these markers are expressed as clinical phenotype or not. [5,6]

Materials and Methods

The study was conducted in the Medical Centre of Hereditary Blood Disorder, main Kirkuk hospital, (All patients were visiting this centre for regular follow-up and blood transfusion at fixed monthly intervals). The study was carried out during a 6-month period between October 2006 and March 2007. The study includes 179 subjects with thalassemia major who attend the Kirkuk hospital from all over Kirkuk for follow up and blood transfusion. Questioner was introduced to each patient to characterize the age, sex, ethnic origins and hematological features of all included blood transfusion dependent thalassemia major patients. Patient data were based on a medical-record review supplemented by patient interview.

Control group

The ABO blood groups distribution of the 1901 blood donors from the Central Blood Bank in Kirkuk was used as a control group for ABO blood groups distribution of the study sample group.

Statistical analysis

Statistical analysis was performed using the SPSS 7.5 statistical software package. Continuous variables were expressed as mean ± SD. Chi square test was used to compare variables between patients and controls or between patient groups, and ($P<0.05$) was considered statistically significant.

Results

One handred seventy nine patients with thalassemia major were eligible for the study. Patient's data were obtained from medical records, and not all the required data were available for some patients.

All patients (179) belonged to three ethnic origins (Turkmen, Arab, and Kurdish) except eighteen patients who had a mixed ethnic background.

Consanguineous marriage has been a historically longstanding practice among the different ethnic classes of Iraq. Hereditary diseases like thalassemia major can prevail in epidemic proportions in areas characterized by high percentage of marriages between relatives [8] that is a common practice in the Kirkuk regions.

The overall consanguinity marriage rate was estimated at (161, 89.9%) including (63, 35.1%) for first cousin marriages origin, While only (18, 10.05 %) have intermarriages origin between different ethnic groups. Arab versus Turkmen, Arab versus Kurdish and Turkmen versus Kurdish, intermarriages were 14(77.7%), 3(16.6%) and 1(5.5%), respectively.

Out of the 161 cases, 63(39.1%), 52(32.2%) and 46(28.5%), represent Kurdish, Arab and Turkmen studied ethnic groups respectively. But the difference out breeding and inbreeding was relatively significant at (d.f.2, P< 0.2). However, this result confirms a fact that high rate out breeding groups display less disease suffer(Arab 46; 28.5%).

Although the disease is prevalent mainly among mediterranean peoples, [9] countries such as Iraq display a large increase of thalassemia patients due to lack of genetic counseling and screening and breeding the people in the local population.

The mean age (mean ± standard deviation [SD]) at diagnosis of all the studied cases (179) was *l.7± 2.2* years (median 1.0). While the mean age (at study time) was 11.6 ± 6.8 years (median 10.0). These results indicate that the mean period of treatment by regular blood transfusion accompanied by good response and survival was 9.7± 6.34 years (median 9.0).However, two patients died at the ages of 3.6 and 13 years, respectively.

Actually, stable populations show more uniform distribution of ages, but in this study, age distribution of thalassemia major patients among different ethnic groups shows that most of the sample group population was youngs; fewer people were beyond the reproductive age (compared to die age distribution of a growing population), and there were no apparent significant differences (d.f.6, PO.05) between different ethnic groups (Table 1).

Any population with many young (pre-reproductive) individuals and few people beyond reproductive age will increase because many people will enter the prime reproductive age group and few will reach the end of their lifespan. [10].

This type of demographic momentum usually serves as an example of how population growth can be predicted from current age structure; but in the present study, the age-related profiles of the sample (thalassemia major patients) have been showed that fewer people are beyond the reproductive age which is most likely due to death before reaching the reproductive ages or due to loss of people or due to high inflow of immigrants.

Eventually, blood indices results of the sample group revealed that the mean values of PCV and hemoglobin levels were 22.52±5.8 and 7.5±6.4, respectively.

Distribution of ABO Blood Groups

The phenotypes and genotypes of ABO blood groups, become more uniform in high degree intermingled population (Nepali GS, 1965).

A part of the raw data and results of this study was performed to "penetrate the essence of the racial traits (ABO & Rh blood groups) speciation of thalassemia major patients of Kirkuk populations based on the potential degree of genetic isolation and intermingling. Phenotype frequency of the four ABO blood groups and the three corresponding allele frequencies of the sample group along with data from control groups are shown in Tables 2 & 3.

In the combined data of thalassemia major patients ,the most frequently occurring blood group is O (40.9%), followed by A (30.4%), B (21.1%) and AB (7.4%). Rhesus blood groupings revealed that the majority of cases (157 (97.5%)) were Rh positive (Rhesus positive), but only 4 cases (2.4%) were represented as Rh negative". Chi square test

(d.f.2,P<0.05) revealed that there were no significant differences between the triethnic groups in A,B & O blood groups.

Comparison of ABO blood groups distribution sequences within the studied tri-ethnic groups of thalassemia major patients with those of the studied control group, revealed that there were significant differences (d.f.l,P<0.05) in AB blood group distribution only. A similar frequency distribution of the ABO blood groups of the control group has been reported in several other scheduled populations of Asian, such as, I long Kong, China, where frequency of blood group O & B showed preponderance over that of the other blood groups. (Table 2).(1)

The most striking feature that emerged from the present study was the relative genetic isolation in almost all the genetic parameters (sero-haematological) which were studied here among Kirkuk ethnicities. This genetic isolation may be due to reproductive isolation which is a category of the mechanisms that prevent two or more populations from exchanging genes. [12]. The separation of the gene pools of populations, under some conditions, can lead to the genesis of distinct diversity [13].

Various factors of population structure - such as population size, density, mating pattern, and micro-evolutionary forces like differential selection, migration, etc., considerably contribute to the diversity within the population. The present analysis indicates that in addition to gene flow and selection, the genetic structure of the ethnic populations of Kirkuk is highly influenced by socio-cultural adaptation and inbreeding. The present analysis strongly suggests that the infrastructure of these ethnic populations is highly influenced by the local inbreeding within each ethnical population.

Thus, the study suggested that the Kirkuk ethnic groups should intermarry more with each other in order to reduce the heterogeneity and the number of recessive genes alleles. However, the study also recommends public education, population screening, genetic counseling and prenatal diagnosis as successful programs for genetic prevention.

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Table (1): Age distribution of thalassemia major patients among the three different ethnic groups

Ethnic group	1-7 years	8- 14 years	15-21 years	22-28 years	Total
Turkmen	16	17	7	6	46
Arab	13 _	24	10	5	52
Kurdish	19	27	11	6	63
Total	48 (29.8%)	68(42.2%)	28(17.3%)	17(10.7%)	161(100%)

Table (2): Distribution of ABO blood groups among ethnic groups

Blood group	Turkmen		Arab		Kurdish		Total	
	No	%	No	%	No	%	No	%
A	15	32.6	18	34.6	16	25.3	49	30.4
B	13	28.2	8	15.3	13	20.6	34	21.1
AB	3	6.5	4	7.6	5	7.9	12	7.4
0	15	32.6	22	42.3	29	46.0	66	40.9
total	46	100	52	100	63	100	161	100

Table (3): Distribution of ABO blood groups among a control group

Blood group	Turkmen No	%	Arab No	%	Kurdish No	%	Total No	%
A	236	23.1	138	21.9	38 15.2		412 21.6	
B	295	28.8	117	18.6	78 31.2		490 25.7	
AB	176	17.2	157	24.9	19 7.6		352 18.5	
O	315	30.8	217	34.4	115	46	647	34
total	1022	100	629	100	250 100		1901	100

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تباين المؤشرات الجينية المناعية الدموية في كركوك

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استلم البحث في: 3 تشرين الاول 2010 قبل البحث في: 18 نيسان 2011

الخلاصة

درست المؤشرات الجينية للعلامات المناعية الدموية لتقدير خلفية بعض التغيرات الجينية في مجتمع محافظة كركوك . اذ أجريت الدراسة على 179 مريضاً بالثلاسميا . وتمت مراجعة تنقيحية للتعرف على العلاقة بين المجاميع الإثنية والنشأة الأنموطية وتوحد المؤشرات المناعية الجينية على خلفية الانعزال الجيني والاختلاف بين المجاميع الإثنية . اخضع المرضى المشمولين بالدراسة (179 مريضا) للفحوصات للدراسة في مركز أمراض الدم الوراثية في كركوك. كان 18 من المرضى(10.05%) كانوا نتاج لتزاوج بين أقليات مختلفة حيث كانت نسبة زواج الأقارب 161 (89.9%) ومن ضمنهم 63 (35.1%) زواج أولاد العم . من الـ 161 مريض كان 63 (39.1%) و 52 (32.2%) و 46 (28.5%) يمثلون أقليات الأكراد والعرب والتركمان على التوالي . وأن توزيع مرضى الثلاسميا المتعاظم في مجموع الأقليات كان نسبياً مختلف ($d.f.2,p<0.05$) اد أظهر العرب أدنى نسبة 46 (28.5%) من المرضى وذلك بسبب النسبة العالية من التزاوج خارج الأقارب . وأظهرت الدراسة عدم وجود فروق ذي دلالة إحصائية في توزيع مجاميع الدم (ABO&Rh) ما بين مختلف الأقليات في كركوك مع زيادة نسبة مجموعة الدم O على بقية المجاميع . وعدم وجود علاقة ما بين مجموعات الدم وتكرار مرض الثلاسميا المتعاظم .خلصت الدراسة إلى وجود نسبة من التغاير والاختلاف في المؤشرات المدروسة . فضلاً عن وجدت الدراسة أن جميع الأقليات يكمن فيهم مرض الثلاسميا المتعاظم .

كلمات المفتاحية : ممجاميع الدم ، التزاوجات الداخلية ، تلاسيميا ، الانعزال الوراثي ، والتغاير

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