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Research Article

Analysis of mechanism of Genetic polymorphisms which modify the association of blood transfusion in human leukemia disease

Amir Rasool[1], Farhan Aslam[2] and Nuzhat Fatima[3]

[1]Shalimar Medical and Dental college Lahore, Pakistan
[2]Medical Officer at R.H.C 4/14.L Kassowal, Pakistan
[3]Women Medical Officer at THQ Hospital Yazman District Bahawalpur, Pakistan

Corresponding author: Dr Amir Rasool, Shalimar Medical and Dental College, Lahore, Pakistan
Tel: 0092-321-7075202. **E-mail:** amirrasool@hotmail.com
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ABSTRACT

Aims and objectives: The age of genomics has enabled the application of DNA-based molecular methods to clinical laboratory diagnostic testing in the areas of genetics. The main objective of this study is to find the correlation of genetic polymorphisms in which modify the association of blood transfusion in human leukemia.**Material and methods:** We conducted the population based study in which we test the hypothesis that whether genetic polymorphisms in *IL10RA* modify the association of blood transfusion and cause leukemia. For this purpose we collect the data from 2012 to 2013 and analyses it for further study.**Results:** Blood transfusion is not associated with the risk of leukemia. According to data CLL is not related to blood transfusion (OR=0.7 at 95% CIL) and DLBCL (OR=0.9 at 95% CIL).**Conclusion:** Our results suggest that genetic polymorphism in TNF gene modifies the association between blood transfusion and risk of leukemia B-cells.

Key words: Bone marrow, Genotyping, Acute lymphoblastic leukemia, Transplantation

INTRODUCTION

The age of genomics has enabled the application of DNA-based molecular methods to clinical laboratory diagnostic testing in the areas of genetics. Molecular methods are also applicable to blood bank and transfusion service testing[1]. The rapid progress made in determining the genetic basis for blood group and platelet antigen polymorphisms, and the commercial development of polymerase chain reaction (PCR) based technology, makes detection of blood group antigens by probing the gene now possible. Many blood group antigens are the result of single nucleotide gene polymorphisms or SNPs) inherited in a straightforward mendelianmanner.

Before 19th century it was thought that all the blood was same and this misunderstanding was lead to the fetal transfusion of blood. Even human blood is not the same. People belong to the different blood groups depending upon the antigens present in the blood. Almost 25 different types of blood groups were present but most common are ABO and Rh systems[2].Blood transfusion mainly allogeneic blood transfusion can induce immune supression and has been suggested as a risk factor for leukemia[3].Molecular genotyping methods were introduced to the transfusion medicine community over a decade ago. Epidemiological studies linking blood transfusion to the risk of leukemia but they

provided inconsistent results[4]. B-lymphocytes are characterized by the expression of CD19 surface antigen, which is present on the progenitor cells of bone and persists during all stages of B-cell maturation[5].

Objectives of the study

The main objective of this study is to find the correlation ofgenetic polymorphisms which modify the association of blood transfusion in human leukemia.

MATERIAL AND METHODS

Ethical approval

This study was conducted according to the rules and regulations of hospital authority and approved by ethical committee of Shalimar hospital. There was no violence of rules and regulations of authority.

Study population

All histologically confirmed cases of leukemia diagnosed from 2015 to 2013in a Shalimar hospital was selected for study. Enrollment criteria include the age between 20 to 50 years. Pathology slides from all patients were obtained from the original pathology departments and reviewed by two independent pathologists. All cases in this study were classified according to the World Health Organization classification system.

Data collection

The study was approved by the ethical committee and review board of university and department of public health. Participation of all the patients were voluntary and written consent was obtained from all participants. Those who want to participate and signed consent were interviewed by medical staff by using a standardized and structured questionnaire and personal interview (Table 1). Blood transfusion history was also examined by asking subjects whether they transfuse blood first time or this were a long term process.

STATISTICAL ANALYSIS

Unconditional logistic regression was used to find out the odds ratios (ORs) and 95% confidence intervals for relations between blood transfusion, and risk of leukemia. The only potential impenetrable variable included in the final model was age between 25 to 55 years. Other variables, for example smoking, alcohol consumption, time of blood transfusion and family history, did not result in material changes in the observed associations. All *P* values presented in the results are two-sided, and all analyses were performed by using SAS software (version 9.2).

RESULTS

The association between blood transfusion and leukemia B-cells are clearly presented in the table 3. Blood transfusion is not associated with the risk of leukemia (OR=0.9 at 95% CIL) and B-cell lymphoma (OR=0.8 a 95%CIL). According to data CLL is not related to blood transfusion (OR=0.7 at 95% CIL) and DLBCL (OR=0.9 at 95% CIL).

Table1: Selected characteristics of study population

Characteristics	**Cases N=482**	**%**	**p-value**
Age			
<50	146	30.3	0.07
50-70	170	35.7	
≥70	166	34.0	
Family history of blood transfusion			0.02
Yes	76	9.7	
No	406	81.3	
Consumption of alcohol			
Yes	169	35.1	0.19
No	313	64.9	
Smoking			
Yes	211	43.8	0.40
No	271	56.2	

Table 2: Association between blood transfusion and leukemia B-cells

	Overall			**B-cell lymphoma**	
Blood transfusion	**Control**	**Case**	**OR(95%CI)**	**Case**	**OR(95%CI)**
No	124	98	1.0	311	1.0
Yes	417	384	0.9 (0.7–1.2)	75	0.8 (0.6–1.2)
	DLBCL			**CLL**	
Blood transfusion	**Control**	**Case**	**OR(95%CI)**	**Case**	**OR(95%CI)**
No	124	29	1.0	78	1.0
Yes	417	121	0.9 (0.6–1.4)	26	0.7 (0.4–1.2)

We also collected the patient's history and compared this data to those patients who have not the history of blood transfusion. The patients who have the history of blood transfusion are suffering from high risk of leukemia if they carried TNF GG genotype (OR = 1.9, 95% CIL) (Table 3).

Table 3: Associations between *IL10RA* and *TNF* Polymorphisms, Blood Transfusion, and risk of leukemia

	Overall						**B-cell lymphoma**			
	Blood transfusion						**Blood transfusion**			
	No			**Yes**			**No**		**Yes**	
SNPs	**Control**	**Case**	**OR**	**Control**	**Case**	**OR**	**Cases**	**OR**	**Cases**	**OR**
TNF										
GG	289	**277**	**1.0**	**96**	67	0.7	221	1.0	44	0.7
AG/AA	123	**108**	**1.0**	**27**	34	1.6	88	1.0	22	1.5
P-interaction	**0.011**						**0.013**			

Among those patients who carried *TNF* (Table 3) AG/AA genotypes, blood transfusion was associated with an increased risk of leukemia overall (OR = 1.6, 95% CIL) and B-cell lymphoma (OR = 1.5, 95% CIL). Among those patients who carried *TNF* GG genotype, blood transfusion was associated with a decreased risk of leukemia overall (OR = 0.7, 95% CIL) and B-cell lymphoma (OR = 0.7, 95% CIL). A statistically significant interaction between *TNF* and blood transfusion was observed for leukemia overall (*P*-interaction = 0.011), and for B-cell lymphoma (*P* = 0.013).

DISCUSSION

This is the first comprehensive analysis of relation of blood transfusion and risk of leukemia in humans. There is a significant difference were observed in for *IL10RA* and *TNF* for leukemia and the high production of white blood cells. No interactions were observed for blood transfusion and the high production of white blood cells. For the clarification of this statement higher studies will required for further clarification[6].

The IL-10RA receptor chains have an extracellular domain consisting of 200 amino acids, a transmembrane helix consisting of 20 amino acids, and an intracellular domain consisting of 322 amino acids for IL-10RA[7]. IL10 and TNF were considered to be the key genes for lymphomagenesis. Both the genes code the immune regulatory cytokines that are considered to be critical mediators of inflammation and apoptosis and also for lymphoid tumors[7]. Different studies related to TNF and IL10 shows that each cell effects on B-cell lymphomagenesis by direct or indirect way[8].

The long term storage of red blood cells before transfusion has been reported and it can increase the interacellular iron. And they cause the systemic inflammatory response syndrome and it will lead to deleterious consequences[10-15]. Therefore, it may be possible that the genetic variation in TNF and IL10RA genes modify the association between blood transfusion and risk of CLL.

Conclusion: Our results suggest that genetic polymorphism in TNF gene modifies the association between blood transfusion and risk of leukemia B-cells.

Conflict of interest: The authors declare that there is no conflict of interest of financial and fiduciary activities from any author.

Contribution of authors

All the authors contributed equally in this research and for writing this manuscript.

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