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Assessment of serum IgE level in patients with transfusion related allergic reaction receiving fresh frozen plasma

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ABSTRACT

Background: Blood transfusion is a routine lifesaving medical intervention which is generally regarded as safe when done properly. However, at the same time it also bears considerable risk. The aim of the study was to assess the serum IgE levels in patients experiencing transfusion-related allergic reactions after receiving fresh frozen plasma.
Methods: This cross-sectional observational study was conducted at the Department of Transfusion Medicine, BSMMU, from March 2019 to August 2021, focusing on patients aged 5 to 60 years receiving fresh frozen plasma. Patients were included after obtaining informed consent from themselves or their legal guardians in the case of minors, according to the eligibility criteria. Data were analyzed using SPSS version 26, with statistical significance set at $p<0.05$, employing Chi-square tests and Pearson's correlation coefficient for variable comparisons.
Results: Raised IgE level was significantly related with transfusion related allergic reaction after receiving fresh frozen plasma ($p<0.05$). The mean IgE was 521.4±434.6 in patients with reaction and 67.8±33.2 in patients without reaction. Significant positive correlation was observed in serum IgE level with age in years.
Conclusions: Patients with transfusion related allergic reaction receiving fresh frozen plasma had higher mean IgE levels as compared to those without reaction.

Keywords: Allergic reaction, Fresh frozen plasma, Pathophysiology, Serum IgE level, Transfusion

INTRODUCTION

Blood transfusion is a routine lifesaving medical intervention which is generally regarded as safe when done properly. However, at the same time it also bears considerable risk. Acute transfusion reaction is more common that includes allergic reaction, febrile reaction, transfusion related acute lung injury (TRALI) and transfusion associated circulatory overload (TACO). Among all the reactions, allergic reactions are more common.[1]

However, newer risks and threats remain. Incidence of adverse reaction to RBC, FFP and PC is 1% to 13.2%.[2] Most reactions are mild and are generally associated with cutaneous manifestations such as urticaria, or hives-erythematous, sharply circumscribed raised lesions, most

often present over the upper trunk and neck usually associated with itching.

Severe allergic reactions, such as anaphylactic shock, are rare, with an estimated incidence of 1 per 20000 to 47000 units of blood and product.[3] Anaphylactic transfusion reactions is the opposite end of hypersensitive reaction. Actually, all of these patients have skin findings-urticaria, angioedema, generalized pruritis.[4] Anaphylactic shock develops very early in the transfusion. Very few milliliters require for developing a severe form of reaction. However mild form of reaction takes longer time to develop. Fever is usually absent in these reactions. Though anaphylactic and anaphylactoid reactions are seen very few but urticarial reaction is more common during transfusion practice.[5] In 1968, the first report of an anaphylactic transfusion reaction related to anti-IgA was published.[6] Pathophysiology of anaphylactic and anaphylactoid reactions are slightly different anaphylactic reaction occurs IgA deficient patient who have associated class specific IgA antibodies. Anaphylactoid reactions happens in patients having normal label of IgA but a limited type specific IgA that react with light chain (kappa or lambda) of the donor's IgA.[4]

Allergic reaction occurs in transfusion of whole blood, red cell concentrates, platelet concentrate and plasma. Plasma proteins are responsible for allergic reaction. Two possible etiologies have been proposed, based on the passive transfer of donor plasma to a patient after transfusion of blood component- presence of soluble substance in donor plasma that binds to preformed IgE antibodies on mast cells, resulting in activation and release of histamine from mast cells. Second one is donor plasma has foreign protein (allergen) with which IgE antibodies in patient plasma react. These antigen antibody complexes attach to the mast cells and cause degranulation of mast cell and release of histamine, serotonin and leukotrienes.[7]

During the last decade, various new discoveries have been made in the field of allergic diseases and transfusion medicine. First, mast cells are not the only cells that play important roles in allergy disorders, especially in the murine immune system. Second, it has been proposed that immunologically active undigested or digested food allergens in a donor's blood could be conveyed to a recipient who is allergic to these antigens, causing anaphylaxis.[5]

IgE has unique properties among immunoglobulin isotypes and plays a key role in the pathophysiology of acute allergic reactions and chronic inflammatory allergic diseases. IgE is very short-lived in plasma (about 1 day), but receptor-bound IgE can remain attached to cells in tissues for weeks or months. In addition, IgE binding to FcεRI increases cell survival and receptor upregulation[8,9] and upon contact with a specific allergen induces the release of pharmacologically active mediators stored in the granules of mast cells (MC) and blood basophils (BS), resulting in clinical manifestations of type 1 hypersensitivity. The allergic reaction includes symptoms like cough, bronchospasm, wheezing, diarrhoea, and urticaria due to this process.[10,11]

Despite prevalent reports of allergic reactions to transfusions, a thorough study on a large series of such incidents is yet to be conducted. The purpose of the study was to evaluate the serum IgE levels in patients experiencing transfusion-related allergic reactions after receiving fresh frozen plasma to improve transfusion safety.

The aim of the study was to assess the serum IgE levels in patients experiencing transfusion-related allergic reactions after receiving fresh frozen plasma.

METHODS

This cross-sectional observational study was conducted at the Department of Transfusion Medicine under Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from March 2019 to August 2021. The study population comprised patients aged 5 to 60 years attending the Day Care Transfusion Unit for receiving fresh frozen plasma. Patients were included after obtaining informed consent from themselves or their legal guardians in the case of minors, according to the eligibility criteria.

Inclusion criteria

Patients aged 5 to 60 years, patients who received fresh frozen plasma transfusion were included.

Exclusion criteria

Patients with a history of atopic conditions such as allergic rhinitis, asthma, and atopic dermatitis, patients with a history of allergies to particular foods, drugs, or other substances, patients taking anti-allergic drugs, patients who received whole blood or blood products other than fresh frozen plasma, patients unwilling to provide informed consent were excluded.

The sample size was estimated at 64, but due to the COVID-19 pandemic, 55 patients were included using convenient sampling. Institutional approval was obtained from the IRB of BSMMU, and ethical considerations followed the Helsinki Declaration. Data collection involved structured interviews and clinical examinations, focusing on demographics, clinical symptoms, vital signs, severity of reactions, units of plasma transfused, and serum IgE levels. Participants were monitored for allergic reactions up to one-hour post-transfusion, with blood samples analyzed using chemiluminescent immunoassay. Data were processed and analyzed using SPSS version 26. Results were expressed as numbers and percentages for qualitative data, and means and standard deviations

for quantitative data. Comparisons were made using Chi-square tests for categorical variables and Pearson's correlation coefficient for quantitative variables. Statistical significance was set at $p<0.05$.

RESULTS

Table 1 shows that among 55 participants the majority (45.5%) belongs to age group 11-20 years which was subsequently followed by 30.9% participants of 21-30 years age group. The mean age of the respondents was 20.7±8.9 (age range: 6-42) years.

Table 1: Age distribution of the study patients (n=55).

Age group (years)	No. of patients	Percentage
<10	5	9.10
11-20	25	45.50
21-30	17	30.90
31-40	7	12.70
41-50	1	1.80
Total	55	100.00

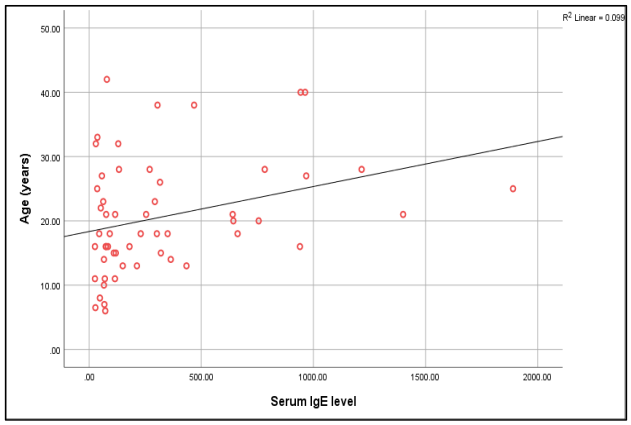

Figure 1: Correlation of serum IgE level with age.

Table 2: Distribution of the study patients by clinical symptoms (n=55).

Clinical symptoms	No. of patients	Percentage
Itching	31	56.4
Urticarial rash	16	29.1
Vomiting	4	7.3
Hypotension	4	7.3
Cough	3	5.5
Tachycardia	2	3.6
Respiratory distress	2	3.6
Angioedema	1	1.8

Table 2 shows the clinical symptoms of the patients, maximum (56.4%) had itching, 29.1% patients had urticarial rash, 7.3% patients had vomiting, 5.5% had hypotension.

Majority of the patients (85.5%) received multiple unit of fresh frozen plasma transfusion, 14.5% patients received single unit (Table 3).

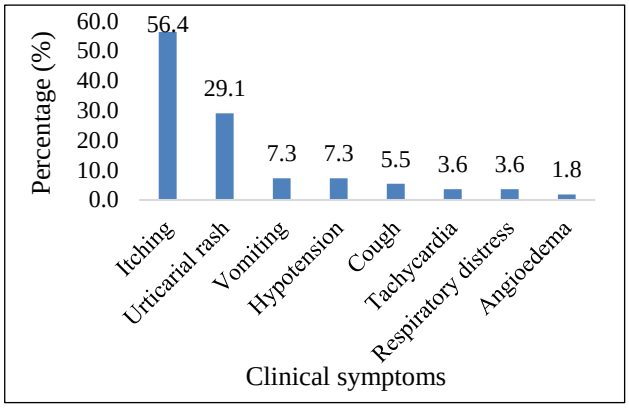

Figure 2: Clinical symptoms of the study patients (n=55).

Table 3: Distribution of the study patients by unit of fresh frozen plasma transfusion (n=55).

Unit of fresh frozen plasma transfusion	No. of patients	Percentage
Single	8	14.5
Multiple	47	85.5
Total	55	100

Table 4: Association of allergic reaction with unit of fresh frozen plasma transfusion (n=55).

Unit of fresh frozen plasma transfusion	Allergic reaction		P-value
	Present (n=32) No. %)	Absent (n=23) No. %)	
Single	1 (3.1)	7 (30.4)	0.005*
Multiple	31 (96.9)	16 (69.6)	
Total	32 (100.0)	23 (100.0)	

*statistically significant.

Transfusion related allergic reaction after receiving fresh frozen plasma was significantly associated with multiple units of fresh frozen plasma transfusion ($p<0.05$) ((Table 4).

Table 5: Distribution of the study patients by reaction type (n=55).

Type of reaction	No. of patients	Percentage
Mild	31	56.4
Severe	1	1.8
Asymptomatic	23	41.8
Total	55	100.0

Regarding reaction of transfusion related allergic after receiving fresh frozen plasma, maximum (56.4%) had

mild reaction, 41.8% patients had asymptomatic and only 1 (1.8%) patient had severe reaction (Table 5).

Transfusion related allergic reaction after receiving fresh frozen plasma was significantly associated with age more than 15 years and 100% male patients had allergic reaction, which statistically significant ($p<0.05$). No significant relationship was found with living area with allergic reaction (Table 6).

Raised IgE level was significantly related with transfusion related allergic reaction after receiving fresh frozen plasma ($p<0.05$). The mean IgE was 521.4±434.6 in patients with reaction and 67.8±33.2 in patients without reaction (Table 7).

Table 6: Association of allergic reaction with demographic variables (n=55).

Variables	Allergic reaction		P value
	Present (n=32) N (%)	Absent (n=23) N (%)	
Age group (years)			
6-9	0 (0.0)	4 (17.4)	
10-15	5 (15.6)	7 (30.4)	0.012*
> 15	27 (84.4)	12 (52.2)	
Sex			
Male	32 (100.0)	20 (87.0)	0.036*
Female	0 (0.0)	3 (13.0)	

*statistically significant.

Table 7: Association of allergic reaction with IgE level (n=55).

IgE level	Allergic reaction		Total (n=55) N (%)	P value
	Present (n=32) N (%)	Absent (n=23) N (%)		
Normal	3 (9.4)	23 (100.0)	67.8±33.2	
Raised	29 (90.6)	0 (0.0)	521.4±434.6	
Total	32 (100.0)	23 (100.0)		<0.001*
Mean ±SD	521.4±434.6	67.8±33.2	331.7±339.8	
Median	335.0	68.0	133.0	
Range	63.0 – 1890	26.0 – 150	26.0 – 1890.0	

*statistically significant.

Boxplots display two common measures of the variability or spread IgE level in patients with reaction and without reaction (Figure 3).

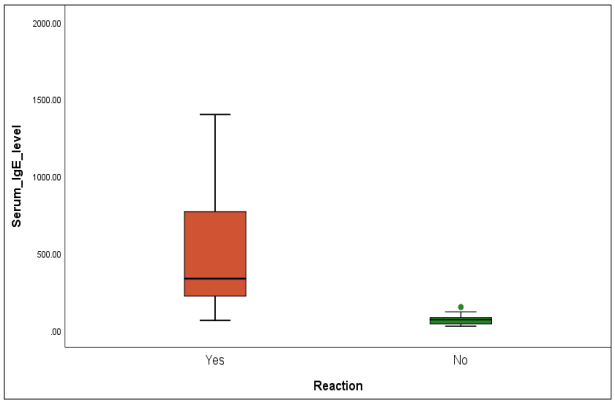

Figure 3: IgE level in patients with or without reaction.

DISCUSSION

This cross-sectional study was conducted with a total of 55 patients aged between 5 to 60 years attending the 'Day Care Transfusion Unit' of the Department of Transfusion Medicine, BSMMU, to receive fresh frozen plasma. The purpose of the study was to assess the serum IgE level in patients with transfusion-related allergic reactions receiving fresh frozen plasma.

The present study showed that transfusion-related allergic reactions after receiving fresh frozen plasma were significantly associated with age over 15 years, and 100% of male patients had allergic reactions, which was statistically significant ($p<0.05$). This finding is consistent with another study, who noted that patients with positive skin tests had higher mean IgE levels compared to those with negative skin tests, although the difference was not significant.[12]

The present study revealed that, after receiving fresh frozen plasma, the majority (56.4%) had mild reactions, 41.8% of patients were asymptomatic, and only 1 (1.8%) patient had a severe reaction. The majority of the patients (85.5%) received multiple units of fresh frozen plasma transfusion, while 14.5% received a single unit.

The present study also showed that the clinical symptoms of the patients varied, with the majority (56.4%) experiencing itching, 29.1% having urticarial rash, 7.3% vomiting, and 5.5% hypotension. In accordance, another study reported adverse reactions due to FFP transfusion among the study population.[13] Predominant adverse reactions were allergic transfusion reactions, with itching being the most common adverse event at 32 (53.33%), followed by urticaria at 22 (36.67%), fever with rigor at 46.67%, and nausea at 2 (3.33%). Another study reported that the five most common predominant symptoms of ATRs were pruritus/itch (27.4%), febrile/increased temperature (19.1%), chills (14.2%), transient urticaria (9.7%), and angioedema (7.7%). In the present study, the values were higher in patients who had reactions than those without.[14]

Immunoglobulin E (IgE) occupies a unique position among immunoglobulins. It is normally present in human serum in extremely small amounts, but its serum concentration may increase several hundredfold in response to specific stimuli. Since its discovery, IgE has been studied in various patient and population studies.[15,16] The immunologic response of individuals exposed to similar environments is not uniform, and a wide range of serum IgE levels has been reported in unselected adults.[17,18] The levels are increased in allergic diseases like allergic rhinitis, allergic bronchial asthma, and atopic dermatitis or urticaria.[19,20] The present study showed that raised IgE levels were significantly related to transfusion-related allergic reactions after receiving fresh frozen plasma ($p<0.05$). The mean IgE level was 521.4±434.6 in patients with reactions and 67.8±33.2 in patients without reactions. Transfusion-related allergic reactions were significantly associated with multiple units of fresh frozen plasma transfusion ($p<0.05$). In agreement with the present study, a study reported that mean IgE levels were significantly higher ($p<0.001$) in allergic rhinitis and urticaria groups of patients than in healthy subjects.[12] Among all age groups, the variance in mean IgE levels between allergic subjects and controls was significant.

A wide variation in serum IgE levels has been documented, and several authors have attempted to define normal levels and ranges in healthy non-allergic adult populations.[12,15] Because of the wide range of serum IgE levels, it has been extremely difficult to establish reliable ranges or 95% confidence limits for this immunoglobulin.[15] The variation in values is probably related to different techniques used for measuring IgE, different populations studied, and possibly the use of different standards.[21] In addition to variations in experimental results, there is also a problem in appropriately expressing mean values for normal subjects or various groups of patients.[12]

The present study showed that the mean IgE level was 521.4±434.6 in patients with reactions and 67.8±33.2 in patients without reactions. The skewed distribution of IgE in all populations that have been studied has necessitated converting from arithmetic to logarithmic values when reporting group means and ranges.[21-23] Another study showed that a normal distribution occurs following logarithmic conversion, with a geometric mean value of 148 IU/ml for healthy subjects. A study by Saeed and Siddiqui et al. from Pakistan reported a normal mean value of 75.3 IU/ml for 200 healthy subjects using the radial immunodiffusion technique.[24] An age and sex relationship also exists with regard to IgE levels in healthy subjects. The peak levels for females are reached during the latter half of the first and beginning of the second decade, then decline thereafter, reaching a low level in subjects over 75 years of age. Males have higher levels than females at any given age.[15] Our data is in agreement with the above-reported findings.

A study found the overall incidence of allergic reactions to be 1.82% of all transfusions and 30.6% of all transfusion reactions, while another study found allergic reactions to be 13.6% of all transfusion reactions.[25] The much higher incidence of 12.6% (fivefold) reported by Ahmed et al. in Northeast Nigeria is most likely due to the pregnant women population in which the study was conducted.[26] In any case, this study shows that the burden of allergic transfusion reactions in relation to the total incidence of adverse reactions was more in adult females (39%) than in adult males (28%), although this was not statistically significant.

This study highlights the relationship between serum IgE concentration and the development of allergic reactions, mainly manifested as itching and rash.

This study had some limitations. The difficulty in maintaining follow-up with patients' post-transfusion hindered comprehensive data collection, and some adverse events occurred after patients had left the hospital. An important limitation of this study was the small sample size, which may limit the generalizability of the findings to a larger population. As it was a single center-based study, more data could not be collected from different centers, potentially affecting the diversity and applicability of the data. The estimated sample size could not be fulfilled during the study period due to the COVID-19 pandemic situation, which may have introduced selection bias.

Limitations

The last but not least limitation was the small budget for conducting the study, which could have restricted the scope of research activities and resources available.

CONCLUSION

Patients with transfusion related allergic reaction receiving fresh frozen plasma had higher mean IgE levels as compared to those without reaction.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Chowdhury FS, Biswas J, Siddiqui MA, Hoque MM, Adnan SK. Transfusion reaction among the blood recipient-A study of 120 cases. J Dhaka Med Coll. 2008;17(2):67-71.
2. Kato H, Uruma M, Okuyama Y, Fujita H, Handa M, Tomiyama Y, et al. Incidence of transfusion-related adverse reactions per patient reflects the potential risk of transfusion therapy in Japan. Am J Clin Pathol. 2013;140(2):219-24.
3. Vamvakas EC, Pineda AA. Allergic and anaphylactic reactions. In: Popovsky MA. Ed. Transfusion Reactions 2nd ed. Bethesdia, Md: AABB press; 2001:83-127.
4. Combs MR, Denomme G. Technical Manual AABB. United States: Elsevier; 2005:633-665.
5. Hirayama F. Current understanding of allergic transfusion reactions: incidence, pathogenesis, laboratory tests, prevention and treatment. Brit J Haematol. 2013;160(4):434-44.
6. Sandler SG, Mallory D, Malamut D, Eckrich R. IgA anaphylactic transfusion reactions. Transf Med Revi. 1995;9(1):1-8.
7. We HW. Implementing inpatient, evidence-based, antihistamine-transfusion premedication guidelines at a single academic US hospital. The Rosetta Cancer Origin Test™ may help. 2014;56.
8. Asai K, Kitaura J, Kawakami Y, Yamagata N, Tsai M, Carbone DP, et al. Regulation of mast cell survival by IgE. Immunity. 2001;14(6):791-800.
9. Kalesnikoff J, Huber M, Lam V, Damen JE, Zhang J, Siraganian RP, et al. Monomeric IgE stimulates signaling pathways in mast cells that lead to cytokine production and cell survival. Immunity. 2001;14(6):801-11.
10. Oettgen HC. Fifty years later: Emerging functions of IgE antibodies in host defense, immune regulation, and allergic diseases. J Alle Clin Immunol. 2016;137(6):1631-45.
11. Ishizaka K. Basic mechanisms of IgE-mediated hypersensitivity. Curr Opin Immunol. 1988;1(4):625-9.
12. Agha F, Sadaruddin A, Abbas S, Ali SM. Serum IgE levels in patients with allergic problems and healthy subjects. JPMA. 1997;47(6):166-9.
13. Haque MR, Biswas DA, Akhter R, Chowdhury FJ, Ahmed ZU. Study of adverse reactions due to fresh frozen plasma transfusion among hemophilia patients. Bangl J Medi Sci. 2020;19(1):148-51.
14. Wang SE, Lara Jr PN, Lee-Ow A, Reed J, Wang LR, Palmer P, et al. Acetaminophen and diphenhydramine as premedication for platelet transfusions: a prospective randomized double-blind placebo-controlled trial. Am J Hematol. 2002;70(3):191-4.
15. Barbee RA, Halonen M, Lebowitz M, Burrows B. Distribution of IgE in a community population sample: correlations with age, sex, and allergen skin test reactivity. J All Clin Immunol. 1981;68(2):106-11.
16. Johansson SG. Raised levels of a new immunoglobulin class (IgND) in asthma. The Lancet. 1967;290(7523):951-3.
17. Loeffler JA, Cawley LP, Moeder M. Serum IgE levels: correlation with skin test sensitivity. Ann Aller. 197331(7):331-6.
18. Johansson SG. Serum IgND levels in healthy children and adults. Int Arch Aller Immunol. 1968;34(1):1-8.
19. Orgel HA, Hamburger RN, Bazaral M, Gorrin H, Groshong T, Lenoir M, et al. Development of IgE and allergy in infancy. J All Clin Immunol. 1975;56(4):296-307.
20. Kumar L, Newcomb RW, Hornbrook M. A year-round study of serum IgE levels in asthmatic children. J AllClin Immunol. 1971;48(5):305-12.
21. Spitz E, Gelfand EW, Sheffer AL, Austen KF. Serum IgE in clinical immunology and allergy. J All Clin Immunol. 1972;49(6):337-47.
22. McGeady SJ, Buckley RH. Depression of cell-mediated immunity in atopic eczema. J All Clin Immunol. 1975;56(5):393-406.
23. Grundbacher FJ, Massie FS. Levels of immunoglobulin G, M, A, and E at various ages in allergic and nonallergic black and white individuals. J All Clin Immunol. 1985;75(6):651-8.
24. Saeed S, Siddiqui S. A comparative study of serum immunoglobulin E levels in patients with allergic disease and healthy subjects. PJMR-Pak J Medi Res. 1994;33(4):255-7.
25. Hoxworth P, Skinner C. Improvement in blood transfusion service: iii. results of 3,077 transfusions of bank blood; a statistical analysis. Arch Surg. 1941;42(3):498-507.
26. Ahmed SG, Kyari O, Ibrahim UA. Preprint version urticarial reactions in obstetric transfusion in maiduguri, north east Nigeria. Nig Postgrad Medi J. 2002;9(3):137-9.

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