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ORIGINAL ARTICLE

ABO discrepancy in pediatric lymphomas and solid organ tumors.

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ABSTRACT… Objective: To determine the frequency of ABO discrepancies in pediatric patients of lymphoma and solid organ tumors and to categorize these discrepancies and their resolution. **Study Design:** Cross-sectional study. **Setting:** Department of Hematology & Transfusion Medicine, The University of Child Health Sciences & The Children's Hospital, Lahore. **Period:** November 2020 to September 2021. **Material & Methods:** ABO blood group discrepancies were assessed by tube method of blood grouping, using antisera A, B, AB & D for forward grouping and A, B, and O cells for reverse grouping. Auto control was also run. The resolution techniques were used accordingly. The collected data was checked for its completeness, consistency and accuracy before analysis which was done on SPSS version 26. **Results:** In this study, a total of 105 subjects were included with mean age of 5.64 ±2.1 years. Among them 72(68.6%) were male and 33(31.4%) were female. Out of total samples processed, three (2.9%) discrepancies found, 1 in female and 2 in male patients. There were two cases of Group I ABO discrepancies, one of which was resolved by elution, antibody screening and identification and other by incubation at 37°C and correlation with previous transfusion history. One case of Group II ABO discrepancy which was resolved by incubation at 4°C for 30 minutes. **Conclusion:** This shows that ABO discrepancies occur in pediatric patients of lymphoma and solid organ tumors. So, the interpretation of forward and reverse ABO blood grouping, identification and resolution of ABO discrepancies in these patients should be done very carefully to avoid any transfusion related adverse reactions.

Key words: ABO Blood Groups, ABO Discrepancies, Lymphoma, Malignancy.

INTRODUCTION

The discovery of ABO blood group system by Landsteiner has revolutionized transfusion medicine since 1900s. The clinical importance of ABO blood group antigens and antibodies depends on immunogenic properties. For the provision of safe blood units, pre-transfusion testing, starting from simplest procedures of blood grouping and cross-match to the complicated serological investigations is vital. The validity of testing of ABO blood group antigens is established by reverse grouping to find out corresponding antibodies.[1]

A blood group discrepancy exists when the red cell or forward grouping results do not match with those of serum or reverse grouping.[2] The discrepancy may arise because of technical errors or clinical conditions of the patients. They are categorized into four groups. Group I discrepancies occur due to missing or weakly reacting antibodies. While Group II discrepancies are associated with unpredicted reaction in forward grouping because of weak or missing antigens. In Group III protein and plasma aberrations result in rouleaux formation and pseudo-agglutination leading to spurious blood grouping results. Lastly, Group IV Discrepancies are due to varied problems such as autoantibodies and Polyagglutination.[3]

Blood group discrepancies in various diseases have been documented. They may occur in both hematopoietic and non-hematopoietic malignancies. Unwarranted blood group substances formed by the cancerous cells or alteration of red cells antigens can result in

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spurious blood group results.[4] In hematological malignancies, genetics and epigenetic variations in genes of A and B transferases can lead to the loss or fading of red cell antigen expression.[5] Other important factors can be the counteraction of tying antisera by the serum soluble blood group substances secreted by tumor cells or loss of ABH antigens as seen in some lymphoid malignancies. Group II discrepancy has been seen more in patients of solid organ malignancies and group III discrepancies have been reported in patients with Hodgkin lymphoma.[6] Itzkowitz SH et al observed certain alteration of Blood Group Substance expression in gastrointestinal cancer tissue and found absence of A, B, H or Le antigen in 25% of cases.[7]

Our study was focused to determine ABO discrepancies in pediatric hematological and non-hematological cancers excluding leukemias, and to find their resolution so that the most suitable and safest blood units can be selected. Since such patients require frequent transfusion support and dealing with pediatric population, the utilization of such serological transfusion techniques becomes inevitable. This study will be one of its kind since pediatric oncological patients are not studied in our region in this regard.

To determine the frequency of ABO discrepancies in pediatric patients of lymphoma and solid organ tumors and to categorize these discrepancies and their resolution.

MATERIAL & METHODS

It was a cross-sectional study, conducted at The Hematology & Transfusion Medicine Department of The University of Child Health Sciences & The Children's Hospital, Lahore from November 2020 to September 2021 after Institutional Ethical committee approval IRB No. 1326/SAHS. After taking informed consent from parents/ guardians, history proforma was filled including demographic details, diagnosis, stage of disease and chemotherapy status.

Participants samples (3ml) were collected in vacutainers containing EDTA for forward blood grouping and in serum gel vial for reverse blood grouping. The unlabeled or mislabeled, hemolyzed and lipemic samples were excluded. ABO blood group discrepancies were assessed by tube method of blood grouping, using antisera A, B, AB & D for forward grouping and A cells, B cells, and O cells for reverse grouping according to hospital blood bank lab protocols. Auto control was also run. The samples which showed discrepancies were run in duplicate and blood grouping repeated after 12 hours on fresh samples from the same patients. The resolution techniques were applied accordingly. The collected data was checked for its completeness, consistency and accuracy before analysis which was done on SPSS version 26.

RESULTS

A total of 105 blood and serum samples were collected from pediatric patients with diagnosis of lymphoma and solid organ tumor. Among them 72 (68.6%) were male and 33 (31.5%) were female with male to female ratio of 2.1:1. The mean age was 5.64 ±2.1 years.

Among the cases 92 (87.6%) patients had the history of recent transfusion (<1 month) and there were 88.6% of patients on chemotherapy. According to the disease stage, 44.8% had stage III and 36.2% patients had stage II disease.

Forward and Reverse blood grouping showed that 97.1% samples had no blood group discrepancy but 2.9% demonstrated ABO discrepancies. Among the positive cases, one blood group discrepancy was found in female patient and two in male patients.

There were 2 cases of Group I (unexpected reaction in reverse grouping) ABO discrepancy. One patient had T-cell Lymphoblastic lymphoma and presented with mediastinal mass. Further testing showed positive Direct Anti-globulin test (DAT). The heat elution was performed and antibody screening and identification panel revealed Anti-C. So, donor phenotyping was done for the offending antigen and antigen negative blood was arranged. The other case was of Ewing sarcoma with B positive blood group and had unexpected agglutination of B cells. On further

history it was found that he had a recent O Rh positive whole blood transfusion from his native village. The antibodies transfused in O plasma were responsible for giving spurious result. Both IgG and IgM Anti-B antibodies detected.

One case of Group II ABO discrepancy was found in Stage IV Hodgkin Lymphoma patient. The patient's previous record showed AB Rh positive blood group but there was weak (+1) reaction with anti-sera A and A1 lectin. The sample was incubated at 4^0C for 30 minutes and test was repeated which showed +3 reaction.

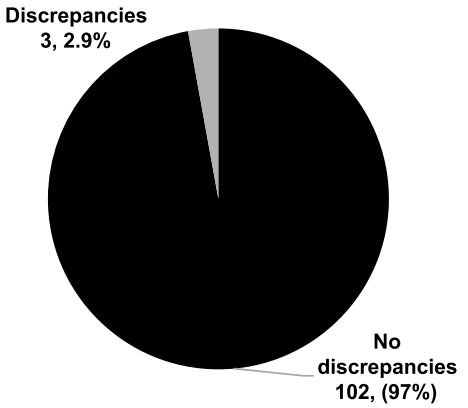

Figure-1. Graphical representation of frequency blood group discrepancies among pediatric lymphoma and solid organ tumors

Stage of Disease	Frequency (N) (%)	Discrepancy
Stage I	7 (6.7%)	00
Stage II	38 (36.2%)	01
Stage III	47 (44.8%)	01
Stage IV	13 (12.4%)	01
Total	105 (100%)	03

Table-I. Frequency distribution of disease according to stage and ABO discrepancies

History Questions	Frequency (N) (%)
Recent Transfusion (<1 month)	92 (87.6%)
Lymphoma	56 (53.3%)
Other tumors	49 (46.6%)
Chemotherapy started	93 (88.6%)
Transfusion of components only	83 (79.0%)
History of frequent Transfusions (≥1/week for last two months)	72 (68.5%)

Table-II. Frequency of relevant history questions

DISCUSSION

ABO discrepancies arise when the results of forward grouping are incongruent with the result of reverse grouping. In lymphoma and solid organ tumors, there is a risk of developing such discrepancies because these patients receive frequent blood transfusions and chemotherapy for their survival. The present study was performed in pediatric oncology patients with an attempt to determine whether multiple transfusions, chemotherapy or the disease itself can result in ABO discrepancies or not. Our study also focused on the resolution of such difficult pre-transfusion situations which need to be dealt immediately and cautiously to avoid transfusion related complications.

Our study has revealed ABO discrepancy incidence of 03/105 in oncology patients of pediatric age group. This frequency is higher as compared to the studies done on healthy donors or patients with other diagnosis. A French study conducted in multiple hospitals showed the incidence of one per 3400 regarding ABO discrepancies.[8] The most frequent underlying causes were phlebotomy and clerical errors. Similar study from Saudi Arabia reported 261 discrepancies in 549229 samples.[9]

Case	Discrepancy Group	Probable Blood Group	Diagnosis	Resolution
1	Group I	B Rh positive	T-cell Lymphoblastic lymphoma	Elution, Antibody screening and Identification and Donors Red cells phenotyping done
2	Group I	B Rh Positive	Ewing sarcoma	Detailed transfusion history, incubation at 37^0C to determine IgG antibodies
3	Group II	A Rh Positive	Hodgkin Lymphoma	For weak reaction enhancement, sample incubation done at 40^0C for 30 minutes

Table-III. Blood group discrepancies in relation to blood groups and their resolution

Nepal B et al. has reported incidence of one per 384 discrepancies among adult patients. Among the discrepancy cases 23% had diagnosis of carcinoma.[10]

Among different types of discrepancies, we found two cases of Group I and one case of Group II. Arumugam P et al. analyzed and resolved 21 samples of ABO discrepancy out of which majority were of type IV followed by type II discrepancies. They recognized technical errors in two cases.[11] Subramanian R. et al, concluded that rarely patient with carcinoma and lymphoma can develop excess serum blood group substances that can deactivate the typing antisera.[12] Joshi et al, reported a case of ovarian mucinous cystadenoma who presented with blood group discrepancy due to surplus secretion of A blood group substance. The disappearance of the discrepancy after the tumor resection proved their findings.[13] ABH changes found in solid tumors are shown to affect prognosis and metastatic ability.[14] Children with different diagnosis are found to have blood group discrepancies including case reports among oncology patients.[15] ABO discrepancies among adult Pakistani population have been studied previously.[16]

Previous studies revealed that the most common responsible factor for ABO discrepancies was clerical errors including mixing-up of samples, identification and phlebotomy errors.[9,10] In present study we have omitted such cases. In our study, we found that frequent transfusions in cancer patients was a leading cause of ABO discrepancy followed by weakened expression of red cells antigens which were enhanced by lowering of temperature.

The strength of the study was that it included pediatric patients with lymphomas and solid tumors to find ABO discrepancies and their resolution. Previously, no such study has been done on patients with such disorders. The limitation of the study was lack of history details in some patients and inclusion of smaller number of cases due to limited time period.

So, whenever samples for blood grouping are received from pediatric oncology patients, a detailed history regarding diagnosis, stage of disease, previous transfusions and chemotherapy becomes vital. For blood grouping in all such cases, the method used in the first place should have included forward and reverse blood grouping to find any ABO discrepancies since they won't be detected by tile method. When ABO discrepancy is detected, it should be immediately notified and resolved appropriately to provide most compatible and safest blood unit to the patient.

CONCLUSION

In conclusion, we found ABO discrepancy ratio of 03/105 among pediatric patients diagnosed with lymphomas or solid tumors. We found that multiple transfusions and weak antigen expressions in malignancy resulted in ABO discrepancies that were resolved by detailed history and proper serological workup to avoid any transfusion related adverse reaction.

REFERENCES

1. Reid M.E, Mohandas N. **Red blood cell blood group antigens: Structure and function.** Seminhematol.2004; 41(2): 93-117. https://doi.org/10.1053/j.seminhematol.2004.01.001.

2. Shanthi B, Ravibabu K. **Analysis of ABO group discrepancies in a tertiary care centre South India.** Journal of Evolution of medical and Dental Sciences. 2017; 6:5615-5618. DOI: 10.14260/JEMDS/2017/1218 Corpus ID: 80430583.

3. Meny GM. **Recognizing and resolving ABO discrepancies.** Immunohematology. 2017 Jun; 33(2):76-81. PMID: 28657767.

4. Ting, S. C. **Discrepancy of ABO typing in acute leukemia patients.** Kaohsiung Journal of Medical Sciences.2016; 32(11), pp. 595–596. https://doi.org/10.1016/j.kjms.2016.06.004.

5. Bianco T., Farmer B.J., Sage R.E., Dobrovic A. **Loss of red cell A, B, and H antigens is frequent in myeloid malignancies.** Blood. 2001; 97(11):3633–3639. DOI: 10.1182/blood. v97.11.3633

6. Vadivelu M.K, Damodaran S, Solomon J, Rajaseharan A. **Distribution of ABO blood groups in acute leukaemias and lymphomas.** Ann Hematol. 2004 Sep; 83(9):584-7. doi: 10.1007/s00277-004-0888-1.

7. Itzkowitz S.H, Yuan M, Ferrell L.D, Ratcliffe R.M, Chung Y.S, Satake K, et al. **Cancer-associated alterations of blood group antigen expression in the human pancreas.** J Natl Cancer Inst. 1987 Sep; 79(3):425-34.

8. Chiaroni J, Legrand D, Dettori I, Ferrera V. **Analysis of ABO discrepancies occurring in 35 French hospitals.** Transfusion. 2004; 44(6):860-4. DOI: 10.1111/j.1537 2995. 2004. 03337. x.

9. Qutub H, ABIM A. **Analysis of ABO Discrepancies Occurring at a University Hospital, Al-khobar, Saudi Arabia.** Bahrain Med Bull. 2009; 31(4).

10. Nepal B, Shrestha B, Maharjan S, Bhasima S, Shrestha SK. **ABO blood group discrepancies: Study of prevalence and related factors.** Grande Medical Journal (GMJ) 2019; 1(2): 88-91.

11. Arumugam P, Hamsavardhini S, Ravishankar J, Bharath RR. **Resolving ABO discrepancies by serological workup-an analysis of few cases.** Int J Res Med Sci. 2017; 5(3):893-900.

12. Subramaniyan, R. and Gaspar, B. L. **A closer look into blood group discrepancy arising due to an underlying malignancy.** Rev Bras Hematol Hemoter. 2016 Oct-Dec; 38(4): 361–363. doi: 10.1016/j.bjhh.2016.04.007.

13. Joshi J.R., Parekh H.T., Joshi P.J., Roy P.B. **An unusual difficulty in blood grouping due to soluble group substance in a patient's serum.** Indian J Pathol Microbiol. 1979; 22(3):255–258.

14. Le Pendu J, Marionneau S, Cailleau-Thomas S, Rocher J, Le Moullac-Vaidye B, Clément M. **ABH and Lewis histo-blood group antigens in cancer.** APMIS. 2001; 109: 9-26. https://doi.org/10.1111/j.1600-0463.2001. tb00011.x

15. Hermelin, D, Zhang, D, Blackall, D. **Resolution of an unexpected ABO typing discrepancy in a 9-month-old patient with juvenile myelomonocytic leukemia.** Clin Case Rep. 2020; 8: 2358– 2360. https://doi. org/10.1002/ccr3.3101.

16. Khan MN, Khan TA, Ahmed Z. **Discrepancy in ABO Blood grouping.** J Coll Physicians Surg Pak. 2013; 23:590-592.

AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Naghmana Mazher	Data analysis and proof reading.	
3	Tooba Fateen	Results compilation and statistical analysis.	
4	Anum Parveen	Data collection and methodology.	
5	Sundas Arshad	Literature review and references check.	
6	Maryiam Rana	Data collection.	