Association of ABO blood groups with dengue fever and its complications in a tertiary care hospital

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Abstract:

CONTEXT: Dengue fever (DF) has been steadily increasing in India with outbreaks in certain areas taking the proportion of epidemics. Along with secondary dengue, several risk factors predispose to dengue hemorrhagic fever and dengue shock syndrome. Very few studies associating the relationship between dengue and its severity with ABO blood group have been documented.

AIMS: The aim of this study was to determine the association between distribution of ABO Rh blood groups and DF and DF with thrombocytopenia.

SETTINGS AND DESIGN: This was a retrospective descriptive study conducted at the clinical laboratory of the department of microbiology.

MATERIALS AND METHODS: Dengue patients whose case record contained information on blood group were screened for details of blood group and confirmed dengue diagnosis. Randomly 384 case records were selected. These were divided into two groups; Group 1 included DF cases (platelet count >20,000) and Group 2 included DF cases with thrombocytopenia (platelet count <20,000). Control group consisted of patients other than dengue, whose blood grouping had been done; randomly 390 were selected and analyzed.

STATISTICAL ANALYSIS USED: P value was calculated using the Chi-square test. Odds ratio were calculated using the Fisher's exact test.

RESULTS: DF was higher in 23% of individuals with AB blood group as compared to 8.5% of controls ($P = 0.0004$), whereas patients with blood group O were significantly less affected with DF ($P = 0.0048$). Disease severity was not associated with any of the blood groups.

CONCLUSIONS: Individuals with AB blood group are more prone to DF, whereas individuals with blood group O are less prone.

Key words:

ABO blood group, dengue fever, platelet count

Introduction

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Dengue fever (DF) is endemic in more than 100 countries, with most cases reported from the American, Southeast Asian, and Western Pacific regions of WHO. Dengue is endemic in almost all states in India and is the leading cause of hospitalization.[1] It has been estimated that there would be 390 million dengue

infections per year (95% credible interval: 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease).[2] In 2017, India has recorded 188,401 dengue cases and 325 deaths. There is a sudden upsurge of dengue cases in the Union territory of Puducherry, from 490 (2016) to 4568 and seven deaths in 2017.[3] DF may result in complications such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[4] Coinfection with more than one serotype of dengue

virus (DENV) is attributed to increased incidence of complications.[5]

The predisposition to DHF or DSS is determined by human leukocyte antigen (HLA) haplotype which has been proposed by several researchers; no clear, specific polymorphisms have been unequivocally described.[6] The ABO blood group is part of innate immunity, and it has been described that individuals with different ABO blood groups differ in their susceptibility or resistance to viral and bacterial infections and diseases.[7,8] A relationship between blood groups and disease was first hypothesized by Kaipainen and Vuorinen during 1960,[9] and the gene involved in ABO blood groups was discovered in 1990.[7] The ABO blood group plays a considerable role in making a person susceptible or resistant to diseases such as malaria,[10] cholera,[11] *Helicobacter pylori*,[12] and chikungunya[13] infections.

A study conducted by Kalayanarooj *et al*. found that blood group AB was associated with more severe dengue disease with dengue serotypes 2, 3, and 4 than with dengue serotype 1.[14] A study conducted in Karnataka observed that dengue infections were higher in individuals with O-positive blood group (42.8%) when compared with controls (32%).[15]

However, there are few studies globally including India regarding the association of ABO blood group, dengue disease, and its severity, predicting the outcome of DENV infection. Using the ABO blood group, data may have a clinical and financial implication for management of patients. The present study was designed to determine the association between distribution of ABO Rh blood groups and DF and DF with thrombocytopenia.

Materials and Methods

This was a retrospective descriptive study conducted during May–June 2018 in the department of microbiology. The study was reviewed and approved by the institute research and ethics committees. A waiver of consent was sought and granted.

Case records of patients who tested positive for dengue NS1 antigen/dengue immunoglobulin M (IgM) antibodies/both with information on blood group were included in the study. A calculated sample size of 384 was included in the study based on prevalence rate of 47.7% (2017 outbreak), 5% precision, and 95% confidence interval. The study population was divided into two groups. Group 1 included DF cases (platelet count >20,000), whereas Group 2 included DF cases with thrombocytopenia (platelet count <20,000). Control group consisted of patients in whom dengue had been excluded from January 2017 to December 2017 and whose blood grouping was done. Of these, 390 were randomly selected by simple random sampling.

After screening the case records for inclusion criteria, 384 records were randomly selected by simple random sampling (Research Randomizer [https://www.randomizer.org/]). A detailed pro forma including the demographic details; clinical features including duration of fever and presence of rash; comorbidities such as diabetes, hypertension, bleeding manifestation, if any; and presence of acute respiratory distress syndrome (ARDS) was used. Vitals such as blood pressure and pulse rate and laboratory parameters such as serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), hemoglobin, mean corpuscular volume (MCV), total leukocyte count, and platelet count were noted. Patient outcome was also recorded. All details were entered in Microsoft Excel, and the data was analyzed.

Statistical analysis
All continuous data are presented as mean ± standard deviation and categorical data as percentiles. Data were analyzed using IBM SPSS Statistics for Windows, version 22.0. IBM Corp., Armonk, NY, USA. DF and DF with thrombocytopenia were compared using the Chi-square test. Odds ratio were calculated using the Fisher's exact test to test for the strength of association between risk factors. $P < 0.05$ was considered as significant.

Results

Out of the 384 cases, 118 were blood group B, 90 were blood group AB and 88 were each of blood group A and O [Figure 1]. The frequency of blood group among the control group is represented in Figure 1.

It was observed that dengue infections were higher in individuals with AB blood group (23%) when compared with controls (8.5%), $P = 0.0004$. Blood group O considerably less affected with DF had $P = 0.0048$ [Table 1].

Dengue cases were more in males compared to females. It was more among the age group of 21–30 years. Dengue NS1 antigen was positive in 248 cases, IgM positive in 27 cases, and both positive in 109 cases [Table 2]. Laboratory parameters are represented in Table 3. There was no significant difference in these parameters among different blood groups.

Bleeding manifestations were seen in 14 cases (blood group: A positive – 2 cases, B positive – 7, AB positive – 2, and O positive – 3). ARDS was seen in 3 cases (blood group A – 2 cases and B – 1 case). Five of the patients
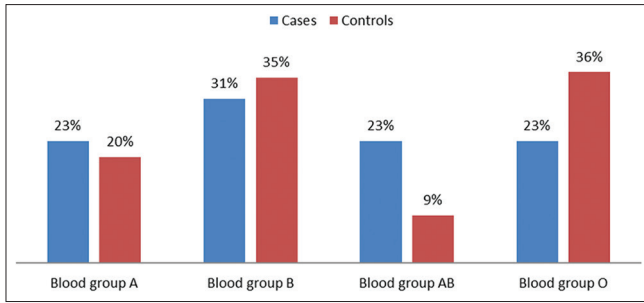
Figure 1: Distribution of ABO blood group among dengue cases and controls

Table 1: Frequency of ABO blood group among dengue cases and controls

Blood group	Cases	Controls	*P*	OR	95% CI
A	88	79			
B	118	137	0.197	1.2933	0.8748-1.9121
AB	90	33	0.0004	0.4084	0.2474-0.6743
O	88	141	0.0048	1.7848	1.1917-2.6732

Chi-square test was used to compare the cases and controls. *P*<0.05 considered as significant. OR=Odds ratio, CI=Confidence interval

Table 2: Demographic details, serology, and comorbidities of dengue cases

Blood group	A	B	AB	O	Total
Gender					
Male	48	73	51	53	225
Female	40	45	39	35	159
Age group (years)					
<10	11	6	13	8	38
11-20	23	23	21	19	86
21-30	19	39	23	21	102
31-40	21	28	11	16	76
41-50	7	10	12	13	42
51-60	3	7	7	8	25
>61	4	5	3	3	15
Serology - ELISA					
NS1 Ag positive	56	74	63	55	248
IgM positive	7	7	6	7	27
Both NS1 and IgM positive	25	37	21	26	109
Comorbidities					
DM	8	7	5	8	28
HTN	4	3	2	4	13

HTN=Hypertension, DM=Diabetes mellitus, NS1=Non structural protein 1

went against medical advice, and 379 patients improved and were discharged.

The distribution of each blood group among patients with DF was similar to that among patients with DF with thrombocytopenia (platelet count <20,000). In dengue virus infections, all four blood groups and Rh had similar susceptibility to severe disease, that is, no association between blood group and disease severity was seen [Table 4].

Discussion

Dengue is an endemic disease which is associated with morbidity and mortality. DHF and DSS are the complications in secondary DF. There are many predisposing factors which are allied with dengue, one of which could be blood group. Blood group antigens help in determining the susceptibility to infections.[6,8]

The present study suggests that blood group AB is associated with dengue disease when compared to the control group and was statistically significant, which was in concordance with the results of the study by Kalayanarooj *et al*., wherein blood group AB was a risk factor predisposing for severe dengue disease.[14] Blood group distribution in controls was consistent with those in the general South Indian population.[15] The distribution of each blood group among patients with DF was similar to that among patients with DF with thrombocytopenia (platelet count <20,000). In dengue virus infections, all four blood groups and Rh had similar susceptibility to severe disease, that is, no association between blood group and disease severity was seen.

On the other hand, in the current study, patients with blood group O were considerably less affected with DF (statistically significant); in contrast, a study by Khode *et al*. suggested that blood group O is possibly a risk factor predisposing for dengue disease.[16]

In the current study, there was an association between AB blood group and DF but no association between

Table 3: Laboratory parameters of dengue cases

Blood group	SGOT	SGPT	Hemoglobin (g/mL)	MCV	Total leukocyte count ×1000 cubic mm	Platelet count ×1000
A						
Mean±SD	138.51±165.905	78.27±83.770	12.955±2.0452	81.90±7.738	5.473±2.7252	72.20±53.595
B						
Mean±SD	157.27±156.052	86.86±80.632	13.286±1.9528	82.88±7.631	5.140±2.8552	60.58±56.659
AB						
Mean±SD	102.97±122.362	67.43±121.777	13.189±2.1427	83.61±6.980	5.166±2.8050	85.07±68.543
O						
Mean±SD	147.66±222.219	86.72±120.517	13.024±2.0986	83.42±8.222	4.929±2.3860	70.41±77.552

MCV=Mean corpuscular volume, SD=Standard deviation, SGOT=Serum glutamic-oxaloacetic transaminase, SGPT=Serum glutamic-pyruvic transaminase

Table 4: Distribution of ABO and Rh blood groups in dengue fever without and with thrombocytopenia

Blood group	Group 1: Platelet count > 20,000	Group 2: Platelet count < 20,000	P	OR	95% CI
A positive	70	16			
A negative	2	0	0.9203	0.8545	0.0391-18.6563
B positive	81	33			
B negative	4	0	0.3527	0.2703	0.0142-5.1613
AB positive	78	11			
AB negative	1	0	0.6117	2.2754	0.0874-59.269
O positive	67	17			
O negative	2	2	0.1575	3.9412	0.5171-30.038

Chi-square test was used to compare the two groups: Dengue fever with platelet count >20,000 and Dengue fever with platelet count <20,000. *P*<0.05 considered as significant. OR=Odds ratio, CI=Confidence interval

AB blood group and DHF. A short communication by Murugananthan *et al*. reported that a significantly higher proportion of patients with AB blood group had DF and DHF when compared to the general population.[17]

Majority of dengue-positive cases in the present study were blood group B individuals which is in agreement with the observations made by Bulugahapitiya and Satarasinghe.[18] but not statistically significant when compared to the control group.

The innate immune system consisting of natural killer cells, dendritic and mast cells, macrophages, natural antibody-producing B-cells, the complement system, and host genetic factors plays a role in elimination of viral infections.[19] Among these innate factors, a predilection for an individual to be susceptible or resistant to phenotypes of infectious diseases and their clinical manifestations resides in host genetic factors. Two genetic factors (HLA and ABO blood groups) have, to some extent, been demonstrated to play an imperative role in resistance or susceptibility to infectious diseases.[7]

The blood group antigens are carbohydrate in nature; the immunodominant sugar in case of A determinant is N-acetyl-d-galactosamine, and for B determinant, it is d-galactose. Galactosyltransferases are involved in the synthesis of these carbohydrates.[7] The antibody that recognizes these carbohydrates is mainly natural IgM.[20] IgM antibodies produced against glycosylated dengue viral proteins, in patients with DENV infection, have been shown to cross-react with host cells. Consequently, whether the combination of ABO blood group and the level of natural IgM antibody circulating in individuals has an effect on dengue disease needs to be explored. The study was limited by its retrospective case record-based design where several parameters could not be explored.

A correlation between HLA and dengue disease has been reported, but no specific polymorphisms have been found to be unambiguously associated with disease severity.[6] It, therefore, is of interest to see whether there is any correlation between a polymorphism in the galactosyltransferase gene and dengue disease severity. Stephens *et al*. studied the association of HLA and dengue-virus infection and found that the infecting viral serotype influenced the strength of the association between specific HLA alleles and dengue disease severity.[21]

Conclusions

This study concludes that AB blood group is associated with a higher risk of developing DF than those with other blood groups. While patients with blood group O were significantly at a lower risk of developing DF compared to the general population. There is no association between blood group and disease severity as patients of all four blood groups and Rh had similar susceptibility to severity of the disease. Further studies are needed to determine whether dengue serotype, HLA, and ABO are independent variables and whether some blood subgroups are associated with a particularly high risk of DENV infection.

Conflicts of interest
There are no conflicts of interest.

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