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# **Original Research Article**

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# Association of blood group with severity of dengue in a tertiary care hospital

Chandrakala P., Krithika G. S.\*, Bhavya S.

Department of Pediatrics, Kempegowda, Institute of Medical Sciences, Bengaluru, Karnataka, India

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# \*Correspondence: Dr. Krithika G. S.,

E-mail: kritika.gs@gmail.com

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# **ABSTRACT**

**Background:** The dengue viruses belong to the family of Flaviviridae family and are arboviruses. One of the genetic factors influencing the severity is HLA antigen and ABO blood group.

**Methods:** This was a prospective study conducted during July 2018 to May 2019 in the department of pediatrics of KIMS hospital, Bengaluru. Children between 0-18 years of age were included. The dengue serology, hemogram and blood group of these patients was investigated and compared with the severity of illness.

**Results:** It was found that the distribution of blood groups among cases and controls were similar. However blood group O was slightly more susceptible to dengue infection (54%) than its distribution in general population (41%). In patients with primary infection, blood group O presented with milder forms of dengue (52.43%) as compared to distribution in general population (41.46%). A higher percentage of AB blood group presented as severe forms of dengue (11.63%) as compared with general population (7.32%). In patients with secondary infection, similar findings were observed. Interestingly, no cases of AB blood group presenting with secondary dengue had only mild symptoms and always presented with warning signs (0% incidence) or severe dengue.

**Conclusions:** Dengue infection is prevalent in most parts of India with severe forms having high mortality. This study concludes that although the incidence of dengue fever is higher in children with blood group O, AB blood group is associated with severe forms of dengue, especially in secondary infections.

Keywords: AB blood group, Blood group, Dengue, Severity

# **INTRODUCTION**

The dengue virus is an arbovirus belonging to the family, Flaviviridae. DENV-1, DENV-2, DENV-3, and DENV-4 are the 4 serotypes. It is categorized according to WHO 2009 as non-severe Dengue (with or without warning signs) and Severe Dengue. Dengue fever is endemic in around 100 countries with higher densities in the American, Southeast Asian, and Western Pacific regions. Most states in India show high prevalence of Dengue, resulting in hospitalisation. It has been estimated that 390 million people are annually infected and around 96 million present with the disease. India recorded 188,401 dengue cases and 325 deaths, in 2017. Around the world,

50-100 million people get infected by dengue and around 2-5 lakhs of them present with severe forms.<sup>6</sup>

Predictive factor for severe dengue include age, nutrition, genetics, viral strain, primary/secondary infections and certain laboratory tests. <sup>6,7</sup> Of the genetic factors are HLA and ABO blood group. Human leukocyte antigen (HLA) haplotype has shown to have an association with predisposition to severe dengue, according to several researches, although no specific polymorphisms have been definitively described. <sup>8</sup> The blood group antigen is part of innate immunity. It has been proposed that persons with different ABO blood groups differ in their susceptibility to various infections and diseases. <sup>9,10</sup> In

1960, Kaipainen and Vuorinen first hypothesised the relationship between blood groups and diseases whilst the gene coding for ABO blood groups was finally discovered in 1990. Ph. 1 The blood group antigen plays a significant role in the susceptibility of a person to diseases like malaria, cholera, Helicobacter pylori, and chikungunya infections. Ph. 12-15

Blood group data can be easily tested in hospitals and it would be of great clinical and economic significance if this was found to help predicting the outcome in dengue infections. Thus, this study aims to investigate the association of blood group with severity of dengue infection in patients admitted to a tertiary care hospital in Karnataka, India.

#### **METHODS**

This was a prospective study conducted during July 2018 to May 2019, over 15 months in the department of paediatrics of Kempegowda Institute of Medical Sciences Hospital and Research centre, Bengaluru. Children between 0-18 years of age were included.

All patients with serological confirmation of Dengue (NS1, IgM/IgG positivity) by Rapid Card Method (Standard Diagnostics-BiolineAlera) with hematology data (obtained by hematology automated analyzer Sysmex 1800c) were included. Blood groups (by Forward Blood grouping -Slide method with Anti-A, Anti-B sera from Tulip diagnostics) were also recorded. The severity of dengue was graded according to World Health Organization guidelines.

410 samples of random patients admitted in our hospital were tested for blood group and this was taken as control group for blood group distribution in the particular area.

All details were entered in Microsoft Excel, and the data was analyzed. Patients with concomitant infections like Malaria and Typhoid were excluded from the study.

#### **RESULTS**

Of the 499 cases, 270 were blood group O, 80 were blood group A, 120 were blood group B and 29 were blood group AB (Table 1 and Figure 1).

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

Blood group	Cases	Controls
0	270	170
A	80	80
В	120	120
AB	29	30
Total	499	410

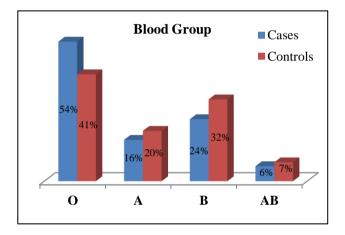


Figure 1: Distribution of ABO blood group among cases and controls.

Table 2: Distribution of blood group among controls.

Blood group	0	A	В	AB	Total
Distribution	136 (41.46%)	64 (19.51%)	104 (31.71%)	24 (7.32%)	410

Table 3: Distribution of blood groups in primary dengue cases.

Dengue severity	0	A	В	AB	Total
Dengue fever without warning signs	137	42	48	9	236
Dengue fever with warning signs	54	14	28	7	103
Severe dengue	15	7	16	5	43
Total	206	63	92	21	382

The control group for blood group distribution was determined by assessment of blood groups of 410 random patient's blood sample (Table 2). In patients with primary

infection, it was observed that the distribution of blood groups between dengue infection cases and general population were statistically significant ( $\varkappa 2=37.33$ , degrees of freedom=6, p=0.0000015). Of the 236 patients who presented with dengue fever without warning signs, 137 (58.05 %), 42 (17.8%), 48 (20.34%) and 9 (3.81%) had blood groups O, A, B, AB respectively (Table 3). When compared with general population, this was statistically significant ( $\varkappa 2=54.45$ , degrees of freedom=3, p=8.98x10<sup>-11</sup>). Blood group O presented with milder forms of dengue as compared to distribution in general population (41.46%).

Of the 103 patients with dengue fever with warning signs, 54 (52.43%), 14 (13.59%), 28 (27.18%) and 7 (6.8%) had

blood groups O, A, B, AB respectively, which was statistically significant ( $\varkappa 2=30.38$ , degrees of freedom=3, p=1.15x10<sup>-6</sup>).

Among the 43 patients with Severe dengue, 15 (34.88%), 7 (16.28%), 16 (37.21%) and 5 (11.63%) had blood groups O, A, B and AB respectively ( $\varkappa 2=27.02$ , degrees of freedom=3, p=5.83x10<sup>-6</sup>). This showed that a higher percentage of AB blood group presented as severe forms of dengue as compared with general population (7.32%).

In our study, it was found that the distribution of blood groups between dengue infection cases and general population was statistically significant ( $\kappa 2=23.70$ , degrees of freedom=6, p=0.00059) even in secondary cases of dengue.

Of the 52 patients who presented with dengue fever without warning signs, 37 (71.15%), 5 (9.62%), 10 (20.34%) and 0 (0%) had blood groups O, A, B, AB respectively (Table 4).

Table 4: Distribution of blood groups in secondary dengue cases.

Dengue severity	0	A	В	AB	Total
Dengue fever without warning signs	37	5	10	0	52
Dengue fever with warning signs	22	8	13	6	49
Severe dengue	5	4	5	2	16
Total	64	17	28	8	117

When compared with general population, this was statistically significant ( $\varkappa 2=28.73$ , degrees of freedom=3, p=2.54 x 10<sup>-6</sup>). It was observed that no cases of AB blood group presenting as with secondary dengue had mild symptoms and always presented with warning signs (0% incidence).

Of the 49 patients with dengue fever with warning signs, 22 (44.9%), 8 (16.33%), 13 (26.53%) and 6 (12.24%) had blood groups O, A, B, AB respectively, which was statistically significant ( $\varkappa 2=11.14$ , degrees of freedom =3, p=0.011).

Among the 16 patients with Severe dengue, 5 (31.25%), 4 (25%), 5 (31.25%) and 2 (12.5%) had blood groups O, A, B and AB respectively ( $\varkappa 2=9.94$ , degrees of freedom =3, p=0.019). 12.5% of this was blood group AB as compared with 7.32% of AB blood group in general population. This also indicated that AB blood group predisposes to severe dengue.

# **DISCUSSION**

In our study, an analysis of blood group patterns, in dengue, has been studied. It was observed that although blood group distribution was in concordance with that of control, blood group O was associated in higher percentages with incidence of dengue disease. This was in agreement with a study by Khode et al, which suggested that blood group O is possibly a risk factor predisposing for dengue disease.<sup>6</sup>

The present study suggests that blood group AB is associated with severe dengue disease when compared to the control group and was statistically significant, which supported the results of the study by Kalayanarooj et al., which stated that AB blood group, was probably a risk factor predisposing to severe dengue disease. <sup>16</sup> Furthermore, this association for noticed more with secondary infections, where majority of patients progressed to severe dengue.

The human innate immune system, consisting of mast cells, NK cells, dendritic cells, macrophages, antibody producing B cells, the complement system, and the host genetic factors-clearly plays a role in the immunity against viral infections.<sup>17</sup>

Among these factors, the genetic factors play a significant role in determining the predisposition of an individual to be susceptible or resistant to certain phenotypes of an infection and also the magnitude of their clinical manifestations. Two genetic factors namely HLA and ABO blood groups have been shown to play a crucial role in resistance to infectious diseases. See the same of the play a crucial role in resistance to infectious diseases.

biochemically blood antigens are group carbohydrates The A blood group has N-acetyl-dgalactosamine as its immunodominant sugar while the B antigen is d-galactose. Galactosyl transferases is the common enzyme involved in the synthesis of both these determinants.9 These antigens stimulate an IgM response. 18 The glycosylated dengue viral protein produces an immune response which also consists of IgM antibodies which probably croos-react with the blood group antigen. Although a correlation between HLA typing and dengue disease has been previously researched, a specific polymorphism which affects the severity has not been identified yet.8

This study does not study the severity amongst the different serotypes of dengue infection (DENV 1, DENV 2, DENV 3, DENV 4) and forms a limitation of the study.

# **CONCLUSION**

The prevalence of dengue infection is high all over India. Most cases are asymptomatic or mild but severe cases have high fatality. Hence an understanding of investigations that help predicting progress to severity is crucial. This study concludes that although the incidence of dengue fever is higher in children with blood group O, AB blood group is associated with severe forms of dengue. Moreover, AB blood groups when associated with secondary infection more commonly progress to severe forms of dengue. Further studies are needed to

determine whether HLA, and ABO are independent variables and whether some blood subgroups are associated with a particularly high risk of DENV infection itself.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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