SHORT COMMUNICATION

Blood group AB is associated with severe forms of dengue virus infection

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Abstract Several viral and host factors are believed to contribute to the development of severe forms of dengue such as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) following a dengue virus (DENV) infection. The pathogenesis of DHF/DSS is not fully understood, however, host factors like ABO blood groups have been shown to contribute to the severity of DENV infection. The present study investigated the association of blood groups with severity of DENV infection in the northern region of Sri Lanka. The blood-groups of 405 patients positive for DENV NS1 antigen and anti-DENV IgM/IgG were determined using the standard haemagglutination assay recommended by the national blood bank/s. The occurrence of severe dengue in patients with certain blood groups was significantly different ($p < 0.001$) to those with other blood groups. Patients with AB blood group had more than 2.5 times higher risk of developing DHF than those with other blood groups. On the other hand, patients with blood group O were significantly under represented for DHF relative to the proportion of this blood

group in the general population. Thus dengue patients with blood group O appear to have a low risk of developing DHF than those with other blood groups.

Keywords Dengue fever · Dengue haemorrhagic fever · ABO blood groups

Several factors such as viral and host factors are believed to contribute to the development of dengue haemorrhagic fever (DHF) and dengue shock syndrome following a dengue virus (DENV) infection. Although the pathogenic mechanisms involved in the development of DHF/DSS are not fully understood, host factors including ABO blood groups have been shown to be associated with severity of DENV infection [3, 7, 9, 11]. There seems to be some protection against infectious diseases from inheritance of polymorphisms in genes encoding and regulating the expression of ABH and Lewis antigens in the body secretions. The ABO blood group also appears to play an important role in making a person susceptible or resistant to diseases [1, 5] like malaria [4, 12], cholera [6], *Helicobacter pylori* [2, 8] and chikungunya [10] infections.

As ABO blood group data can be easily tested in hospitals and clinics and predicting the outcome of DENV infection using the ABO blood group data has clinical and economic significance for the patient management. Thus, the objective of this study was to investigate the association of blood groups with the severity of clinically apparent DENV infection in laboratory-confirmed DENV patients admitted to the Teaching Hospital, Jaffna, in the northern Sri Lanka.

The study was conducted using protocols approved by the Ethical Review Committee of the Faculty of Medicine, University of Peradeniya, Sri Lanka. Blood samples were

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taken from a total of 405 DENV NS1 and anti-DENV IgM/IgG positive patients managed at the medical and paediatric wards of the Teaching Hospital, Jaffna from 2010 to 2012 after obtaining the informed consent. Blood samples were tested using a standard hemagglutination assay recommended by the National Blood Bank, Sri Lanka for ABO blood group typing. The clinical and demographic data were also obtained using a pre-tested performa. To determine the ABO blood group distribution in the region, the blood groups of 5348 consecutive donors were obtained from the donor database from the Hospital Blood Bank. Then the distribution of blood groups of patients affected with dengue fever (DF) and DHF was tested against the distribution of blood groups from donors within the general donor population using a Chi square test. The expected frequencies of the normal population for the Chi square test were calculated based on the proportions of blood groups in the normal, reference population (Table 1) [13]. The differences between the frequencies were considered as significant at $p < 0.05$.

Of the 405 patients admitted to the Teaching Hospital, Jaffna, 229 (56.5%) had DF and 176 (43.5%) had DHF based on clinical assessment of the patients. Of the 229 patients with DF, 59 (25.76%), 61 (26.64%), 38 (16.59%) and 71 (31%) had blood group A, B, AB and O, respectively (Table 1). Of the 176 patients with DHF, 43 (24.43%), 57 (32.95%), 29 (16.48%) and 46 (26.14%) had blood group A, B, AB and O, respectively (Table 1). The blood groups of patients with DF and DHF were significantly different [$\chi^2 = 48.2$; degrees of freedom (df) = 3; $p < 0.001$] when compared to the donor population of the area (Fig. 1). Patients with AB blood group had 2.55 times higher risk of having dengue compared to patients with blood group O who had significantly lower risk of having dengue ($\chi^2 = 12.4$; $df = 2$; $p < 0.005$). The trend in patients with blood groups exhibiting DHF was very similar ($\chi^2 = 39.86$; $df = 3$; $p < 0.001$) to that of DF. Patients with blood group AB were 2.53 times more likely to have DHF than others. Similarly, blood group O had less number

Fig. 1 Distribution of ABO blood group among DF and DHF patients when compared to that in the normal blood donating population in the Jaffna District, northern region of Sri Lanka

of DHF cases ($\chi^2 = 12.97$; $df = 2$; $p < 0.005$). The patients with blood groups A and B with DENV infection or DHF showed no significant deviation from their representation in the blood donor population in the study area.

We have identified differences in the susceptibility to DENV infection in patients with different blood groups. AB positive patients are 2.5 times more susceptible to develop DF and DHF than others ($p < 0.001$). In agreement with our findings, Kalayanarooj et al. [7] reported severe forms of secondary DENV infections among 311 serologically confirmed dengue cases in association with blood group AB. On the other hand, in the current study, patients with blood group O were significantly less affected by clinically apparent DENV infections (Table 1). In contrast to our findings, Malavige et al. [11], however, reported an association of blood group O with severe dengue in a different locale of the Colombo District. Moreover, according to a more recent study, clinically apparent DENV infection is more common in blood group O, however, DHF is not associated with any blood groups in their study sample [9]. Majority of our patients had blood group B and this finding is in agreement with the observations made in the Colombo District, the Western

Table 1 Distribution of ABO blood group in patients with DF and DHF in the study sample, from the Jaffna District, northern region of Sri Lanka

Blood group	Patients (n = 405)		% Blood group distribution in the population (n = 5348)
	% DF (n = 229)	% DHF (n = 176)	
A	25.76 (59)	24.43 (43)	19.95 (1067)
B	26.60 (61)	32.95 (58)	31.11 (1664)
AB*	16.59 (38)	16.47 (29)	6.51 (348)
O [^]	31 (71)	26.13 (46)	42.43 (2269)

*Significantly higher proportion of patients with AB blood group had DF and DHF when compared to the general population

[^]Significantly lower proportion of patients with blood group O had DF and DHF when compared to the general population

Province of Sri Lanka [3] although that study did not report have any association of blood group B with DHF.

There is paucity of research on the reasons for why individuals with some blood groups are more susceptible to DF and DHF. Similarly why patients with blood group O are less prone to develop DHF is also not known. When conducting such studies it is important to consider the blood group distribution of the local population where the study sample is recruited. Previous studies from Sri Lanka [3, 11], Thailand [7] and India [9] have not taken this into account. If the blood group distribution of the local population from which the study samples were recruited is not taken into account, the findings of those studies cannot be compared with the current study findings. Moreover, the present study sample size is higher than that in the previous studies and therefore the present findings are powered for a strong interpretation.

In conclusion, the results of the present study suggest a strong association of blood group AB with the development of DF and DHF among patients in the Jaffna District, northern region of Sri Lanka. Patients with blood group O were less likely to have clinically apparent DENV infections in the present study sample.

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