Section: General Medicine

Original Research Article

ASSOCIATION OF DENGUE FEVER AND ABO RH BLOOD GROUP IN A TERTIARY CARE CENTRE IN KERALA

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ABSTRACT

Background: Dengue is an arboviral disease that is a major public health threat globally. Clinical manifestations may range from asymptomatic patients to Dengue Shock Syndrome. It is very important to recognize patients going in for complications and plan management. The ABO blood group system is part of the innate immune system and individuals with different ABO blood groups differ in their susceptibility to infections and diseases. However, not much study has been done worldwide and in India to show the relationship between dengue disease, its severity and ABO blood group. The aim is to determine the association between dengue fever and ABO Rh blood group. **Materials and Methods:** Case Control study. Cases were consecutive dengue fever patients confirmed by Dengue Elisa test admitted in the Medical wards of Govt. Medical College Ernakulam. Two Age and sex matched controls each comprising 150 subjects without dengue fever were selected one from Medical ward and another from community. Odds ratio and its 95% confidence limit were calculated for each ABO blood group. Association between qualitative variables dengue fever and blood groups tested using the Chi-square test. Significance level was fixed at 5 % (p value <0.05). **Result:** The patients with O blood group were more prone for dengue fever and had statistically significant p value(0.004).Patients with blood group O had 1.8 times more risk than other groups for getting dengue fever since the odds ratio was 1.8 (1.2- 2.6). The patients with A group were relatively protected from dengue fever with p value 0.009 and Odds ratio 0.486(0.280-0.843). AB group was also relatively protected from dengue fever since the p value was 0.005 with an odds ratio of 0.206 (0.062- 0.692). No significant association was found between Dengue fever and Rh status and also severity of dengue fever and Rh status. No significant association was found between severity of dengue fever and ABO blood group. No significant sex predominance was found in dengue fever patients in any particular ABO group. **Conclusion:** Patients with blood group O were found to have the highest risk of developing Dengue fever. The patients with A and AB blood group were relatively protected from dengue fever. No significant association was found between Dengue fever and Rh status and also severity of dengue fever and Rh status. No significant sex predominance was found in dengue fever patients in any particular ABO blood group. No significant association was found between severity of dengue fever and ABO blood group.

INTRODUCTION

Dengue is a major public health problem in India and also globally.[1,2] At present, dengue fever causes more illness and death than any other Arbovirus disease affecting humans.[3] Dengue belongs to the family Flaviviridae, genus Flavivirus, species Dengue virus. There are four serologically distinct types of dengue virus (DENV), DENV-1, DENV-2, DENV-3 and DENV-4. These viruses are transmitted to human beings by Aedes mosquitoes such as Aedes aegypti and Aedes albopictus. In the past 50 years, the incidence of Dengue has increased about 30 fold.[4] In India Dengue was first reported in Madras (now Chennai) in 1780, and the first outbreak of Dengue occurred in Calcutta (now Kolkata) in 1963. Thereafter outbreaks occurred in different parts of India. Even though dengue was previously restricted to urban areas, now it has been spread to rural areas as well.[1] Kerala had the maximum number of Dengue patients in India in 2017.[5]

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Objectives

To determine the association between dengue fever and ABO Rh blood group.

REVIEW OF LITERATURE

History: Dengue fever was first referred as "water poison" associated with flying insects in a Chinese medical encyclopedia in 992, however originally published by the Chin Dynasty centuries earlier (265–420 AD). The word "dengue" originated from the Swahili phrase Ka-dinga pepo, meaning "cramp-like seizure". The first case report of dengue was from 1780 epidemic in Philadelphia by Benjamin Rush, who coined the term "break bone fever" due to the symptoms of myalgia and arthralgia. But the term dengue fever came into common use only after 1828.[6,7]

Dengue virus was first isolated in 1943 in Japan by inoculation of serum of patients in suckling mice and at Calcutta in 1944 from serum samples of US soldiers. The earliest virologically confirmed outbreak occurred in 1956 in Vellore, Tamil Nadu. The first large epidemic of dengue began in 1963 in Calcutta, West Bengal.[6,8]

The first case of dengue haemorrhagic fever was reported in Puerto Rico in 1975, and in 1981 there was a dengue epidemic in Cuba with many dengue haemorrhagic fever cases and deaths.[9]

In Kerala Dengue was recorded for the first time, during 1997.Dengue antibodies were detected in human sera from Kerala as early as 1979.[10] Dengue antigen was first detected in Kerala in 2004 from kozhikode.[11]

Dengue Virus: Dengue viruses are single stranded RNA viruses belongs to the family Flaviviridae. Four distinct serotypes, designated DENV-1, DENV-2, DENV-3, and DENV-4, are described. All four serotypes are prevalent in India. Infection with any of the four viruses leads to lifelong immunity to that specific serotype. Like other flaviviruses, they have a single-stranded RNA genome surrounded by an icosahedral scaffold and covered by a lipid envelope.[12]

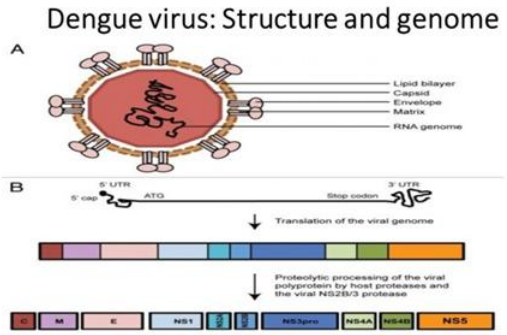

Figure 1: Structure of dengue virus

Epidemiology: According to WHO, around 3.9 billion people, in 128 countries, are at risk of infection with dengue virus.It is also said that almost 75% of the global population exposed to dengue live in Asia-Pacific.[13,14]

In the year 2017, approximately 18,760 cases of Dengue were confirmed from India which was quiet alarming. Kerala was in the top of the list which was having the highest number reported from India. The total number of Dengue patients in Kerala was 9104.[5] All the 14 districts of Kerala were endemic for dengue and it was observed that about 56% of the cases were recorded from the southernmost district, Thiruvananthapuram.[15]

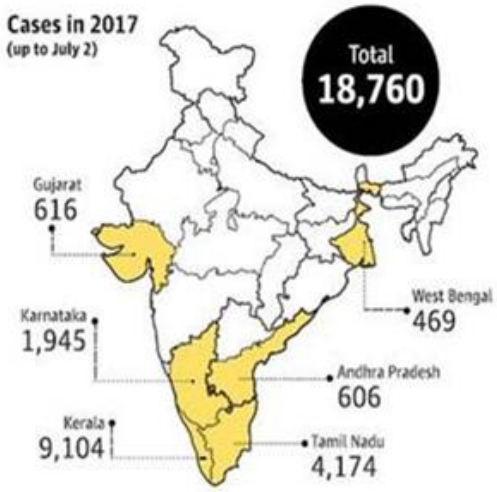

Figure 2: Dengue cases in India during early 2017

Due to low level of reporting, poor disease surveillance, low case fatality rate, difficulties in diagnosis, and inconsistent comparative analyses, the true incidence and impact of dengue is likely to be significantly higher than the currently reported numbers.[14]

Transmission: The dengue viruses are transmitted to humans by the bite of infective female mosquitoes of the genus Aedes (primarily Aedes Aegypti). Aedes albopictus and Aedes polynesiensis are other species which were involved in outbreaks of dengue.[16] Transmission of dengue is now present in every part of the world and now more than 125 countries are known to be dengue endemic.[14]

Figure 3: Aedes Aegypti Mosquito feeding on human host.

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Pathogenesis: Dengue is a syndrome and its pathogenesis remains incompletely understood. Although no correlate of immunity to dengue has been defined, it's hypothesized that the humoral immunity play a vital role for controlling dengue virus infection and for the expression of acquired immunity. Multiple prospective cohort studies have identified secondary infection as an epidemiological risk factor for severe dengue.

Effective CD4+ and CD8+ T-cell responses have been suggested to play an important role in clearance of dengue virus during acute infection. Both serotype- specific and serotype-cross-reactive memory T cells are formed following primary dengue infection.

The leading explanation for increased risk of disease in secondary infection is that non-neutralising, cross-reactive antibodies elicited by a primary infection bind the virus which then has greater potential to infect Fc-receptor bearing cells. This phenomenon, called antibody-dependent enhancement (ADE), which potentially increases the risks of developing severe disease by virtue of accelerating the amount of virus infected cells and thus the viral biomass in vivo.[17,18]

Reduction in the levels of complement components have been described in patients with severe dengue, suggesting that complement activation may have a role in the pathogenesis of severe disease.[17]

Clinical Features: Dengue is a severe, flu-like illness that affects infants, young children and adults, but seldom causes death. Symptoms usually last for 2–7 days, after an incubation period of 4–10 days after the bite from an infected mosquito. The World Health Organization classifies dengue into 2 major categories: dengue (with / without warning signs) and severe dengue. The sub-classification of dengue with or without warning signs is designed to assist the health practitioners triage patients for hospital admission, ensuring close observation, and to attenuate the risk of developing the more severe dengue.[19]

Dengue should be suspected when a high fever (40°C/104°F) is accompanied by 2 of the following symptoms during the febrile phase:

- Severe Headache
- Pain Behind The Eyes
- Muscle And Joint Pains
- Nausea
- Vomiting
- Swollen Glands
- Rash

The clinical manifestations vary between young children and adults. In the children, cough, vomiting and abdominal pain are more common and the mortality rate is higher. The increased severity in the young age group is because of the increased capillary fragility and lower compensatory reserve in this age group. Atypical clinical features include encephalitis, myocarditis, hepatitis, pancreatitis, retinitis and the acute respiratory distress syndrome (ARDS).[17] The laboratory findings associated with dengue fever include a neutropenia followed by a lymphocytosis, often marked by atypical lymphocytes.[3] Thrombocytopenia is an almost universal finding in dengue. This occurs as a result of both reduced production and increased destruction of platelets.[17]

Classification of Dengue: The current World Health Organisation (WHO) case classification into DF/DHF/DSS, formulated by the Technical Advisory Committee at its meeting in Manila, Philippines in 1974 was, to a large extent, based on the pioneering studies at the Children's Hospital, Bangkok, Thailand in 1960s that defined the pattern of disease of that point. Although some minor modifications are suggested, essentially the case definition and case classification of dengue have remained the same.[20]

The group progressing from non-severe to severe disease is difficult to define, but this is often an important concern since appropriate treatment may prevent these patients from developing more severe clinical conditions.

Symptomatic dengue virus infections were grouped by WHO into three categories: undifferentiated fever, dengue fever and dengue haemorrhagic fever.

DHF was further classified into four severity grades. When the haemorrhagic manifestation is provoked (by a tourniquet test), the case is categorised as grade I dengue haemorrhagic fever, but a spontaneous haemorrhage, even if mild, indicates grade II illness. Grades III and IV dengue haemorrhagic fever (incipient and frank circulatory failure, respectively) represent dengue shock syndrome.[9,21]

Table 1: WHO classification of dengue infections and grading of severity of DHF(22)

DF/DHF	Grade	Signs and symptoms	Laboratory
DF		Fever with two of the following • Headache • Retro-orbital pain • Myalgia • Arthralgia/bone pain • Rash • Heamorrhagic manifestations • No evidenc of plasma leakage	• Leucopenia (wbc ≤5000cells/mm3). • Thrombocytopenia(Platelet count <150000 cells/mm3). • Rising haematocrit (5%-10%) • No evidence of plasma loss
DHF	I	Fever and haemorrhagic manifestation(positive tourniquet test) and evidence of plasma leakage	Thrombocytopenia <100000 cells/mm3;HCT rise≥20%.
DHF	II	As in grade I plus spontaneous bleeding	Thrombocytopenia <100000 cells/mm3;HCT rise≥20%.

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DHF	III	As in greade I or II plus circulatory failure. (weak pulse,narrow pulse pressure(≤20 mm Hg),hypotension,restlessness)	Thrombocytopenia <100000 cells/mm3;HCT rise≥20%.
DHF	IV	As in grade III plus profound shock with undetectable BP and pulse	Thrombocytopenia <100000 cells/mm3;HCT rise ≥ 20%.

Risk factors for dengue fever: Viral and host factors play a major role in the development of dengue haemorrhagic fever (DHF) and dengue shock syndrome following a dengue virus (DENV) infection. The pathogenic mechanisms involved in the development of DHF/DSS are not fully understood. Host factors such as ABO blood groups have been shown to be associated with severity of Dengue virus infection.[23-26] Secondary infections, which occur commonly in the areas where dengue disease is endemic, have proven to be one of the main risk factors for severe dengue disease.[27,28] This has led to the development of antibody dependent enhancement theory.[27] Other probable risk factors for dengue disease are the infecting virus serotype, the age of the patient, and the genetic background of the patient.[27] None of these factors alone accounts for the risk of dengue virus infections.

The important role that host genetics plays in determining the susceptibility to infectious pathogens in humans has long been known. Predisposition to dengue disease determined by human leukocyte antigen (HLA) haplotype has been proposed by several researchers, no clear, specific polymorphisms have been unequivocally described for severe forms of dengue disease.[29]

The ABO blood group system is part of the innate immune system. The individuals with different ABO blood groups differ in their susceptibility or resistance to viral and bacterial infections and diseases.[30] A relationship between blood groups and disease was first hypothesized by Kaipainen and Vuorinen,[31] during 1960, and the gene involved in ABO blood groups was discovered in 1990.[32] The ABO blood group also appears to play an important role in making a person susceptible or resistant to diseases like malaria, cholera, Helicobacter pylori and chikungunya infections. A recent study conducted in Wuhan showed females with blood type A were susceptible to COVID-19.[32-40]

In ABO blood-group system, individuals who lack A or B antigen have natural antibodies with the ability to agglutinate cells carrying that antigen.[32] The antigens are carbohydrate in character. The immunodominant sugar in the case of the A antigen is N-Acetyl-D-galactosamine, and in the case of the B antigen is d-galactose. Galactosyltransferases are involved in the synthesis of these carbohydrates.[32] The antibody that recognizes these carbohydrates is primarily of IgM type. Several dengue viral proteins are shown to be glycosylated,[41] and antibodies, particularly IgM, produced in patients with dengue-virus infection have been shown to cross-react with host cells.[42] It has been documented that blood group AB is associated with severity of dengue infection. Since the patients with AB blood group have both the antigens and no antibodies against A and B antigen, antibodies produced by dengue infection may cross react and, hence, AB blood group persons may more susceptible to DHF.[24,43]

Kalayanarooj et al,[24] reported severe forms of secondary Dengue virus infections among 311 serologically confirmed dengue cases in association with blood group AB.

Malavige et al,[26] however, reported an association of blood group O with severe dengue in a different locale of the Colombo District.

Bulugahapitya et al. reported an association with B blood group and complications of dengue infections in a retrospective study conducted in Srilanka.[23]

Ravichandran et al,[43] reported a significant association of AB blood group and dengue fever.

K. Murugananthan et al,[44] reported 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.

Khode et al,[25] reported an association of dengue fever with O blood group in a case control study conducted in Karnataka.

Diagnosis: Diagnosis of Dengue infection is routinely done by demonstration of anti-Dengue IgM antibodies or by NS-1 antigen in patients serum depending upon the day of illness using ELISA kits and commercial kits. Molecular methods (reverse transcriptase PCR) are being increasingly used in diagnosis of Dengue infection.[45]

Treatment: Dengue is a self-limiting viral infection. There is no specific antiviral drug currently available in the market for the treatment of Dengue. Analgesics, fluid replacement with Ringer's lactate, and bed rest are usually satisfactory. Ringer's lactate has been shown to be efficacious in moderately severe DEN, and starch or dextran have been suggested for more severe cases.[46]

Prevention and Control: Prevention is an important aspect in the control of Dengue infection.

Various strategies which should be done are:

- Preventing the mosquitoes from accessing egg-laying habitats by environmental modification.
- Proper disposal of solid waste to remove artificial man-made habitats.
- Covering, cleaning and emptying of domestic water storage containers on a weekly basis.
- Spraying insecticides to water storage outdoor containers.
- Using of personal household protection such as window screens, long-sleeved clothes, insecticide treated materials, coils, vaporizers etc.
- Usage of insecticides as space sprays during outbreaks.

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- Active monitoring and surveillance of vectors to determine the effectiveness of control interventions.[19]

Immunisation: The first dengue vaccine, Dengvaxia® (CYD-TDV) which developed by Sanofi Pasteur was licensed in December 2015.It has now been approved by regulatory authorities in 20 countries for use in endemic areas in persons ranging from 9-45 years of age. The live attenuated dengue vaccine CYD-TDV has been shown in clinical trials to be efficacious and safe in persons who have had a previous dengue virus infection (seropositive individuals), but carries an increased risk of severe dengue in those who had their first natural dengue infection after vaccination (seronegative individuals).[19] This vaccine is given in three dose schedule of 0, 6 and 12 months. In India, Dengvaxia is still not used as it has to undergo Phase III clinical trial.[47]

Future: Many experts hypothesize that dengue infection will increase in the future, including incidence, geographic expansion and reporting to WHO. Increase in global temperature may result in increased survival and or migration of vectors into previously non-endemic geographic areas outside the tropics. A study conducted in the Southwest Pacific suggested that increase in global temperature over the last four decades corresponded with increased risk of dengue outbreaks. Modern contributing factors to the rapid expansion of vector-borne communicable disease include globalization factors, such as travel and trade, associated with vector accommodating trends in modern human settlement and suitable climate conditions. Intercontinental air travel between areas within the tropics has also resulted in transmission of all four dengue virus serotypes in some areas.[14]

The implementation of DengueNet, a global system for standardized epidemiological and virological surveillance, promises to allow a continually updated database to be maintained for timely control measures and epidemiological research. Transgenic technology to interrupt pathogen transmission has been developed for Aedes aegypti, and completion of the genome sequence of Aedes aegypti will facilitate the research process.[12]

MATERIALS AND METHODS

Study Design: Case Control Study

Study Period: January 2019 –December 2019 (12months).

Study Population: Patients admitted in the Medical wards of Govt. Medical College, Ernakulam.

Sample Size

Cases = 150

Control 1=150

Control 2= 150

Inclusion Criteria

Cases are patients with confirmed dengue fever by Dengue Elisa test in the medical wards of Govt Medical College Ernakulam.

Two controls were taken with 150 persons in each group in order to reduce the bias.

Control 1: Age, sex , co morbidity matched controls without fever in the Medical wards of Government Medical College Ernakulam were taken within a period of 10 days of choosing cases.

Control 2: A housing colony in Kalamassery was selected and the ABO Rh blood group of one person above or equal to 18 years was enquired from each family.

Exclusion Criteria

Age less than 18 yrs.

Patients with connective tissue disorder.

Sample Size

$$\frac{(r+1)(P^-)(1-P^-)\left(Z_{beta}+Z_{\frac{alpha}{2}}\right)^2}{r\,(P1-P2)^2}$$

r ratio of control to cases = 1

P1-P2 Difference in proportion

Zbeta represent the desired power 0.84 for 80% power

Z alpha/2 represent the desired level of statistical significance 1.96

$$P^- = \frac{(P1+P2)}{2}$$

According to a study conducted by vithal knode et al (8) proportion of exposed in control group is

P2 = 32% = 0.32 O+ blood group

Proportion of cases exposed P1 =

$$\frac{Odds\ Ratio\ x\ proportion\ of\ control\ exposed}{proportion\ of\ control\ exposed\ (Odds\ ratio-1)+1}$$

To detect on ODDS ratio of 2

$P1 = \frac{2\times.32}{.32(2-1)+1} = 0.48$

$P^- = \frac{P1+P2}{2} = 0.4$

P1-p2 = 0.16

$N = \frac{\frac{1+1}{1}.4\times.6\times(1.96+.84)^2}{(.16)^2}$

Number of cases = 147

Number of controls = 147

Sampling Method: Consecutive dengue fever patients confirmed by Dengue Elisa test admitted in the medical wards of Government Medical College Ernakulam were taken as Cases.

Two controls were taken in order to reduce the bias.

Control 1: Age, sex, co morbidity matched controls without fever in the medical wards of Government Medical College Ernakulam taken within a period of 10 days of choosing cases.

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Control 2: A housing colony in Kalamassery was selected and the ABO Rh blood group of one person above 18 years was enquired from each family serially.

Study Procedure: Patients admitted in the medical wards with suspected dengue fever confirmed by Dengue Elisa test were taken for the study (cases).

Two controls were taken in order to reduce the bias.

Control 1: Age, sex ,co morbidity matched controls without fever in the medical wards of Governmentt Medical College Ernakulam taken within a period of 10 days of choosing cases.

Control 2: A housing colony in Kalamassery was selected and the ABO Rh blood group status of one person above 18 years was enquired from each family.

In both cases and controls groups ABO Rh blood group status was checked by Tube agglutination method. Patients were grouped according to their severity of dengue fever based on WHO classification.

Data Management and Statistical Analysis

Data was properly coded and entered in MS Excel. Data was analyzed using software SPSS version 21. All the continuous data presented as mean ± standard deviation and categorical data as percentage. Odds ratio and its 95% confidence limit were calculated for each ABO blood group. Association between qualitative variables dengue fever and blood groups were tested using the Chi-square test. Significance level was fixed at 5 % (p value <0.05).

Ethical Issues: All dengue fever patients and control group who were willing to give consent were included in the study. All patients and control under study had full freedom to discontinue at any period of time.

Budget: All the expenses for the investigation were met by the investigator.

RESULTS

Out of the 450 subjects, 315 were males and 135 were females. Cases comprising 105 Males and 45 Females. Controls comprising 210 Males and 90 Females. Cases and controls were age and sex matched with a mean age of 38.5and male to female ratio of 2.3:1 respectively.

Table 2: Distribution of ABO Blood Group

	Frequency	Percentage
A	19	12.7
AB	3	2
B	52	34.7
O	76	50.7
Total	150	100

Table 3: Distribution of ABO Rh Blood Group among Dengue Fever Cases.

	Frequency	Percentage
A+	19	12.7
AB+	3	2
B+	52	34.7
O-	12	8
O+	64	42.7
TOTAL	150	100

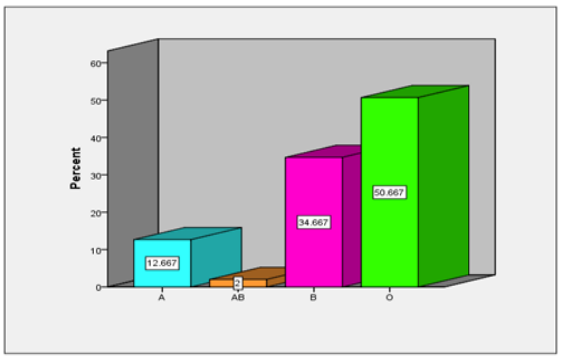

Figure 4: Distribution of ABO Blood Group among Dengue Fever Cases.

Out of 150 dengue cases O group comprises 50.7 %, B group 34.7%, A group 12.7%, AB group 2%. O positive group comprises 42.7%, B positive 34.7%, A positive 12.7%, O negative 8%,AB positive 2%.

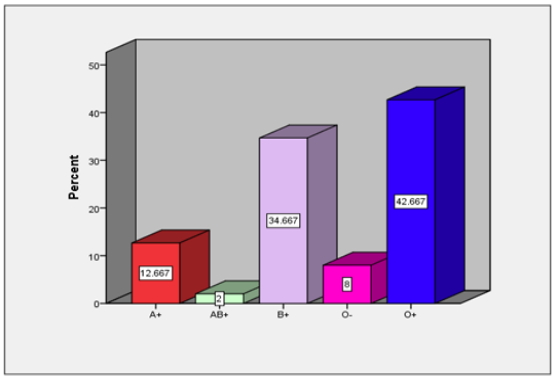

Figure 5: Distribution of ABO Rh Blood Group among Dengue Fever Cases.

Table 4: Distribution of ABO Blood Group among Control Group.

	Frequency	Percentage
A	69	23
AB	27	9

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B	95	31.7
O	109	36.3
Total	300	100

Table 5: Percentage Distribution of ABO Rh Blood Group among Control.

	Frequency	Percentage
A-	4	1.3
A+	65	21.7
AB+	27	9
B-	3	1
B+	92	30.7
O-	8	2.7
O+	101	33.7
Total	300	100

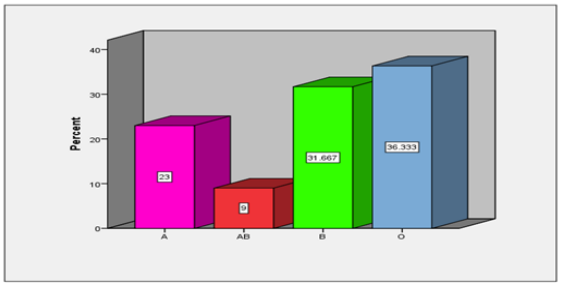

Figure 6: Distribution of ABO Blood Group among Control Group.

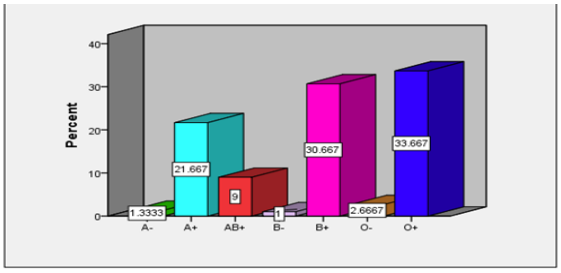

Figure 7: Distribution of ABO Rh Blood Group among Control

Out of 300 control O group constitute 36.3%, B group 31.7, A group 23%, AB 9%. O positive 33.7%, B positive 30.7%, A positive 21.7%, AB positive 9%, O negative 2.7%, A negative 1.3%, B negative 1%.

Out of 150 cases Dengue fever was seen in 113 patients(75.3%). Dengue Hemorrhagic fever was seen in 37 patients (24.7%) comprises DHF1 10(6.7%), DHF2 20 (13.3%), DHF3 7 (4.7%).

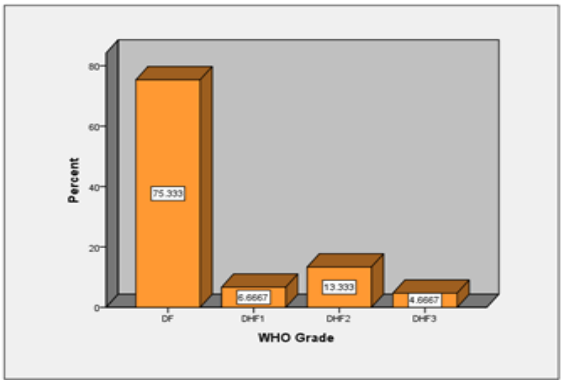

Figure 8: Distribution of Dengue Fever Cases based on WHO Severity Grading.

Association of ABO Blood Group and Dengue Fever

Table 6: Association of Dengue Fever and A Blood Group.

	Case	Control	Total
A group	19(21.6%)	69(78.4%)	88(100%)
Other than A	131(36.2%)	231(63.8%)	362(100%)
Total	150	300	450

Table 7: Association of Dengue Fever and Sex in Patients with A Blood Group.

	Male	Female	Total
A GROUP	13	6	19
OTHER THAN A	92	39	131
Total	45	105	150

The occurrence of Dengue fever in patients with A blood group was significantly different from those with other blood groups since the p value is 0.009. Odds ratio is 0.486(0.280-0.843). The patients with A group were relatively protected from dengue fever. No statistically significant sex predominance was found in dengue fever patients with A blood group (pvalue 0.872).

Table 8: Association of Dengue Fever and B Blood Group.

	Case	Control	Total
B group	52(35.4%)	95(64.6%)	147(100%)
Other than B	98(32.3%)	205(67.7%	303(100%)
Total	150	300	450

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Table 9: Association of Dengue Fever and Sex in Patients with B Blood Group.

	Male	Female	Total
B group	37	15	52
Other than B	68	30	98
Total	105	45	150

The occurrence of dengue fever in B blood group was not statistically different from other blood groups pvalue (0.522). No statistically significant sex predominance was found in dengue fever patients with B blood group (pvalue 0.822).

Table 10: Association of Dengue Fever and O Blood Group.

	Case	Control	Total
O group	76(41.1%)	109(58.9%)	185(100%)
Other than O	74(27.9%)	191(72.1%)	265(100%)
Total	150	300	450

Table 11: Association of Dengue Fever and Sex in Patients with O Blood Group.

	Male	Female	Total
O group	52	24	76
Other than O	53	21	74
Total	45	105	150

The patients with O blood group had more dengue fever cases and with statistically significant pvalue (0.004). Patients with blood group O had 1.8 times more risk than other groups for getting dengue fever since the odds ratio is 1.8 (1.2- 2.6). No statistically significant sex predominance was found in dengue fever patients with O blood group. (p value 0.669).

Table 12: Association of Dengue Fever and AB Blood Group.

	Cases	Control	Total
AB group	3(10%)	27(90%)	30(100%)
Other than AB	147(35%)	273(65%)	420(100%)
Total	150	300	450

Table 13: Association of Dengue Fever and Sex in Patients with AB Blood Group.

	Male	Female	Total
AB group	3	0	3
Other than AB	102	45	147
Total	105	45	150

The occurrence of Dengue fever in patients with AB blood group was significantly different from those with other blood groups since the p value is 0.005. Since the odds ratio was 0.206(0.062- 0.692). AB group is relatively protective from dengue fever. No statistically significant sex predominance was found in dengue fever patients with AB blood group (pvalue 0.252).

Table 14: Association of Dengue Fever and Rh Status.

	Cases	Control	Total
Rh +	138(32.4%)	288(67.6%)	426(100%)
RH-	12(50%)	12(50%)	24(100%)
Total	150	300	450

There was no statistically significant association of dengue fever and Rh group since the p value was 0.075.

Table 15: Association of Severity of Dengue Fever and A Blood Group.

	DHF	DF	Total
A group	3(15.8%)	16(84.2%)	19(100%)
Other than A	34(26%)	97(74%)	131(100%)
Total	37	113	150

No statistically significant association was found between severity of dengue fever and A blood group (p value 0.3).

Table 16: Association of Severity of Dengue Fever and B Blood Group.

	DHF	DF	Total
B group	14(26.9%)	38(73.1%)	52(100%)
Other than B	23(23.5%)	75(76.5%)	98(100%)
Total	37	113	150

No statistically significant association was found between severity of dengue fever and B blood group (p value 0.6).

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Table 17: Association of Severity of Dengue Fever and O Blood Group.

	DHF	DF	Total
O group	20(26.3%)	56(73.7%)	76(100%)
Other than O	17(23%)	57(77%)	74(100%)
Total	37	113	150

No statistically significant association was found between severity of dengue fever and O blood group (p value 0.6).

Table 18: Association of Severity of Dengue Fever and AB Blood Group.

	DHF	DF	Total
AB group	0(0%)	3(100%)	3(100%)
Other than AB	37(25.2%)	110(74.8%)	147(100%)
Total	37	113	150

No statistically significant association was found between severity of dengue fever and AB blood group (p value 0.3).

Table 19: Association of Severity of Dengue Fever and RH STATUS.

	DHF	DF	Total
Rh +	35(25.4%)	103(74.6%)	138(100%)
Rh-	2(16.7%)	10(83.3%)	12(100%)
Total	37	113	150

No statistically significant association was found between severity of dengue fever and Rh status (p value 0.5).

Table 20: Association of Severity of Dengue Fever and Sex.

	DHF	DF	Total
FEMALE	9(20%)	36(80%)	45(100%)
MALE	28(26.7%)	77(73.3%	105(100%)
Total	37	113	150

No statistically significant association was found between severity of dengue fever and sex (p value 0.3).

DISCUSSION

In the present case control study conducted in the medical wards of Government Medical College, Ernakulam during January 2019- December 2019, the total numbers of cases were 150, out of which there were 105 Males (70%) males and 45(30%) females with a male to female ratio of 2.3:1. The mean age of the patients in the study was 38.5. Male preponderance was seen in this study. It was similar to a study conducted by Prasand et al in Karnataka, where 62.8% of the patients were males and 37.2% were females and the male to female ratio was 1.68:1 with a mean age of 24.59.[48]

In our study, 75% were classified as DF patients while 25% were classified as DHF. Dengue fever was seen in 113 patients (75.3%). Dengue Hemorrhagic fever was seen in 37 patients (24.7%) comprises DHF1 10 (6.7%), DHF2 20 (13.3%), DHF3 7 (4.7%). The patients with O blood group had more dengue fever cases and it was statistically significant (p value 0.004). Patients with blood group O had 1.8 times more risk than other groups for getting dengue fever since the odds ratio is 1.8 (1.2- 2.6). No statistically significant association was found between severity of dengue fever and Rh status (p value 0.5). No statistically significant association was found between severity of dengue fever and O blood group (p value 0.6). No statistically significant sex predominance was found in dengue fever patients with O blood group (p value 0.669).

The study conducted by Khode et al showed statistically significant association between O blood group and dengue fever and the severity of disease was not associated with any blood group similar to our study.[25]

In a systematic review and meta analysis on association of dengue disease and severity conducted by Hashan et al found blood group O was found to have the highest risk of developing DF (P-score = 0.01). There was a significant increase (P-value <.001) in the overall odds risk of dengue infection among patients with Rhesus-positive blood groups.[49]

The occurrence of Dengue fever in patients with A blood group was significantly different from those with other blood groups since the p value is 0.009. Odds ratio is 0.486(0.280-0.843). The patients with A group were relatively protected from dengue fever in our study. No statistically significant association was found between severity of dengue fever and A blood group (p value 0.3). No statistically significant sex predominance was found in dengue fever patients with A blood group (pvalue 0.872).

The occurrence of dengue fever in B blood group was not statistically different from other blood groups (p value 0.522). No statistically significant association was found between severity of dengue fever and B blood group (p value 0.6). No statistically significant sex predominance was found in dengue fever patients with B blood group (p value 0.822).

The occurrence of Dengue fever in patients with AB blood group was significantly different from those with other blood groups since the p value is 0.005. Since the odds ratio was 0.206(0.062- 0.692). AB group was relatively protected from dengue fever. No statistically significant association was found

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between severity of dengue fever and AB blood group (p value 0.3). No statistically significant sex predominance was found in dengue fever patients with AB blood group (pvalue 0.252).

But in a study conducted by Ravichandran et al showed individuals with AB blood group were more prone to DF, whereas individuals with blood group O were less prone.[50] In a study conducted by Murugananthan et al reported patients with AB blood group had more than 2.5 times higher risk of developing DHF than those with other blood groups.[44]

Since the various studies showed inconsistent association of dengue fever with any specific blood group, further studies are required to confirm the association.

CONCLUSION

Patients with blood group O were found to have the highest risk of developing Dengue fever.

The patients with A and AB blood group were relatively protected from dengue fever.

No significant association was found between Dengue fever and Rh status and also severity of dengue fever and Rh status.

No significant sex predominance was found in dengue fever patients in any particular ABO blood group.

No significant association was found between severity of dengue fever and ABO blood group.

No significant association was found between severity of dengue fever and sex.

Limitations

The controls were selected from the patients with various other ailments and, therefore, they differ from general population which could have been confounding factor.

Because of the limitations of the sample size in the present study, further studies will be necessary to determine whether dengue severity and ABO are independent variables and whether some blood subgroups are associated with a particularly high risk of dengue-virus infection.

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