



UNLOCKING THE LINK: DENGUE SEROLOGICAL MARKER AND PLATELET DYNAMICS

General Medicine

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ABSTRACT

Background: Dengue a vector borne disease considered hazard to public health. Diagnosis is by dengue specific antigen and antibody detection. Decrease in platelet count consider as warning sign in dengue positive cases. Hence this study was done to correlate various dengue parameter and platelet count. **Material and Methods:** A Retrospective analytical study conducted from period of September 2022- September 2023. A total of 1670 serum samples tested for dengue using ICT kit, 82 samples were tested positive. Platelet count recorded for all the cases. **Results:** 1670 serum sample tested for dengue, 82 sample tested positive for dengue antigen or antibody by ICT based test. Thrombocytopenia (platelet count < 100,000/ml) observed in 20 cases. Association of thrombocytopenia in dengue positive cases was more significant as compared to dengue negative cases. **Conclusion:** A necessary to provide association of thrombocytopenia and various dengue markers to physician in management of dengue infection, which further help in reducing complications as thrombocytopenia association in dengue case was significant as compared to other dengue negative cases.

KEYWORDS

Thrombocytopenia, Dengue, ICT

INTRODUCTION

Dengue is considered one of the hazards to public health. The infection generally affects urban dwellings and cases usually peak in the rainy season. Dengue fever (DF) caused by virus which belongs to family Flaviviridae there are four serotypes of dengue virus (DV)-1,2,3,4 (Dengue Knowledge and Preventive Practices) and spread by mosquito Aedes aegypti and Aedes albopictus (Gomard et al., 2020).

Primary infection with one serotype results in lifelong immunity to that serotype and results in cross reactivity to other serotype. Severity are usually related to this cross-reactivity (Martina et al., 2009).

The diagnosis is clinical and laboratory based virus isolation, nucleic acid amplification technology, IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA) and the rapid dengue immunochromatography test (ICT) (Shu & Huang, 2004). Patient usually presents with symptoms of fever, joint pain, body ache, retro orbital pain, generalised weakness and sometime nausea and vomiting (World Health Organization. Dengue: Guidelines 2009.) Virological diagnosis is primarily by serological by detection of both NS1 antigen and IgM/IgG antibody (Chen et al., 2018). Detection of NS1 is highly sensitive and specific that appears 1-4 days of fever (Libraty et al., 2002). Haematological parameter correlating with severity of disease are leukopenia and thrombocytopenia (Quirino-Teixeira et al., 2022).

Hence this study was conducted in our hospitals to compare immunochromatography (ICT) based dengue serology tests (NS, IgM, IgG) and to correlate with platelet count of probable dengue cases and disease severity.

MATERIAL AND METHODS

Study Design: A record based retrospective analytical study

Place of Study: Department of laboratory science in Military hospital, Jabalpur

Duration of Study: 12 months from September 2022 to September 2023

Sample Size: 82 serum samples that are positive for dengue serology during the period

Dengue ICT Testing: NS1, IgM and IgG by using Recombigen Dengue rapid test kit

Platelet Count: Automated haematology analyser Beckman coulter LH750, Platelet count further compared by peripheral blood smear (PBS)

Data was analysed using Microsoft excel and SPSS version 21. Discrete and nominal data was represented as percentage and continuous data as mean (SD). Chi-square and ANOVA tests were used to find the association between age, sex and dengue serology with platelet count. P value ≤ 0.05 was considered as significant.

RESULTS

During the study period, a total of 1670 serum sample were recorded for dengue serology and 82 samples were found positive for dengue specific parameters as shown in table 1 & 2. Age of the patients ranges from 14-84 years with mean (SD) was 31.9 (17.9) years and median age of 28.5 years. Male to female ratio was 3.8:1 and further association of platelet count with dengue parameter analysed as shown in table 3.

Out of 82 positive cases thrombocytopenia was seen in 20 cases (24%). From 44 NS1 positive cases, thrombocytopenia was seen in 12 cases (27%). Where as in case of antibodies alone thrombocytopenia was seen in 8 out of 39 cases (21%). There was no significant difference was seen in above parameter of antigen and antibody in relation to thrombocytopenia ($p=0.503$).

Table 1: Distribution Of Viral Markers Among Dengue Cases

Parameter	Total	Percentage (%)
NS1 only	43	52.4
IgM only	09	11.0
IgG only	23	28.0
NS1 and IgM	01	1.2
IgM and IgG	06	7.3

Table 2: Distribution Of Thrombocytopenia With Various Permutations And Combinations Of Dengue Parameter

Parameter	Total	Platelet count less than 1,00,000/ml	Percentage (%)
NS1 only	43	12	28
IgM only	09	03	33
IgG only	23	03	13
NS1 and IgM	01	00	0
IgM and IgG	06	02	33
Total	82	20	100

Table 3: Association Between Age, Gender And Dengue Parameters With Platelet Count

Variables		Platelet count		Chi Square	p value
		>1 lakh	< 1 lakh		
Age	0-14 years	-	-	6.116	0.410
	14-19 years	14 (87.5)	1 (12.5)		
	20-29 years	18 (66.7)	9 (33.3)		
	30-39 years	11 (78.6)	3 (21.4)		
	40-49 years	10 (66.7)	5 (33.3)		
	50-59 years	5 (71.4)	2 (28.6)		
	60 years & above	4 (100.0)	0		
Gender	Female	14 (82.4)	3 (17.6)	0.529	0.545
	Male	48 (73.8)	17 (26.2)		
Dengue (RDT)	NS1 Ag	31 (72.1)	12 (27.9)	2.351	0.503
	IgM	6 (66.7)	3 (33.3)		

	IgG	20 (87.0)	3 (13.0)		
	Combination	5 (71.4)	2 (28.6)		

DISCUSSION

The burden of dengue has increased significantly in tropical and subtropical regions worldwide in recent decades. For this reason, it is crucial to diagnose dengue as soon as possible using clinical parameters like platelet counts and serological markers in order to prevent dengue outbreaks and to lower the disease's morbidity and mortality.

Gold standard for diagnosis of dengue is virus isolation which is expensive and time consuming and RT-PCR is often not available in most of hospital and laboratories settings. (Anand, 2016), the primary method for diagnosing dengue infection has been the detection of dengue-specific IgM/IgG and NS1 antigens. (Datta & Wattal, 2010)

Our study shown that most of the cases occurred in the age group of 14-40 years with mean age of 31.9 years which was similar to a study by Krupal D. Mehta et al., that shown similar age group of 11-30 years and a study by Vikas Ingale S. et al., also shown the similarly. A study conducted by Cheah et al has shown mean age of dengue affected case as 32.2 years. (Liew et al., 2016) Most of the dengue cases occurs in working age group attributed to as they are the age group with regular involvement in outdoor activities and travel to endemic areas as compared to other age groups.

Most of the cases reported in our study were males (79.3%) which was similar to others studies (69.9% & 56%) in India. The highest number of males in our study as compared to other studies might reflects the clientele of our health facility those are mostly the serving armed force personnel.

In our study out of 82 dengue cases positive for NS1 were 44 (53%) indicated acute dengue infection and 43 cases were exclusively positive for NS1 (52%) may reflects the early testing within two to three days. Hence it indicate that large number of cases 52% would have missed if NS1 antigen was not included along with antibodies. A study conducted by Shrivastava A et al (2011) has shown 140 out of 600 samples positive for NS1 antigen (Shrivastava et al., 2011) another study by RD Kulkarni et al (2011) shown 320 cases, 95 (30%) were positive for only NS1 antigen which were comparatively less than our study (Kulkarni et al., 2011).

Out of 82 positive cases thrombocytopenia was seen in 20 cases (24%). From 44 NS1 positive cases, thrombocytopenia was seen in 12 cases (27%). Where as in case of antibodies alone thrombocytopenia was seen in 8 out of 39 cases (21%). Whereas, a cross sectional study among 563 cases of dengue, 391 (69.4%) showed thrombocytopenia. In 363 cases that were positive for NS1, thrombocytopenia was evident in 235 (64.7%) cases and in cases with IgM positive, thrombocytopenia was noted in 148 of 200 (74%) cases. Association of thrombocytopenia with IgM was found to be higher. It is also statistically significant ($p=0.03$) which was completely contrast to our study which may reflects the low sample size in our study. There was no significance found between dengue parameters and thrombocytopenia in our study that was similar to a study conducted by Jyothi et al., (Jyothi & Metri, 2015).

CONCLUSION

Most of the laboratories lack viral culture which is consider as gold standard for dengue diagnosis. In our institute enzyme linked immunosorbent assay (ELISA) and polymerase chain reaction was not available which is consider higher sensitivity as compared to ICT. (Hang TV, et al.) But in most of the resource limited settings ICT is available for diagnosis. Hence it is necessary to provide association of thrombocytopenia and various dengue markers to physician in management of dengue infection, which further help in reducing complications.

REFERENCES

- Anand, A. M. (2016). Evaluation of NS1 Antigen Detection for Early Diagnosis of Dengue in a Tertiary Hospital in Southern India. JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH. <https://doi.org/10.7860/JCDR/2016/15758.756>
- Chen, H.-R., Lai, Y.-C., & Yeh, T.-M. (2018). Dengue virus non-structural protein 1: A pathogenic factor, therapeutic target, and vaccine candidate. Journal of Biomedical Science, 25(1), 58. <https://doi.org/10.1186/s12929-018-0462-0>
- Datta, S., & Wattal, C. (2010). Dengue NS1 antigen detection: A useful tool in early diagnosis of dengue virus infection. Indian Journal of Medical Microbiology, 28(2), 107–110. <https://doi.org/10.4103/0255-0857.62484>
- Gomard, Y., Lebon, C., Mavingui, P., & Atyame, C. M. (2020). Contrasted transmission efficiency of Zika virus strains by mosquito species *Aedes aegypti*, *Aedes albopictus* and

- Culex quinquefasciatus* from Reunion Island. Parasites & Vectors, 13(1), 398. <https://doi.org/10.1186/s13071-020-04267-z>
- Hang TV, Nguyet MN, Trung TD, Tricou V, Yoksan S, Minh ND, et al. Diagnostic Accuracy of NS1 ELISA and Lateral Flow Rapid Tests for Dengue sensitivity, Specificity and Relationship to Viraemia and Antibody Responses. (n.d.).
- Jyothi, P., & Metri, B. C. (2015). Correlation of serological markers and platelet count in the diagnosis of Dengue virus infection. Advanced Biomedical Research, 4, 26. <https://doi.org/10.4103/2277-9175.150396>
- Kulkarni, R., Patil, S., Ajantha, G., Upadhyay, A., Kalabhavi, A., Shubhada, R., Shetty, P., & Jain, P. (2011). Association of platelet count and serological markers of dengue infection-importance of NS1 antigen. Indian Journal of Medical Microbiology, 29(4), 359–362. <https://doi.org/10.4103/0255-0857.90159>
- Libraty, D. H., Young, P. R., Pickering, D., Endy, T. P., Kalayanarooj, S., Green, S., Vaughn, D. W., Nisalak, A., Ennis, F. A., & Rothman, A. L. (2002). High Circulating Levels of the Dengue Virus Nonstructural Protein NS1 Early in Dengue Illness Correlate with the Development of Dengue Hemorrhagic Fever. The Journal of Infectious Diseases, 186(8), 1165–1168. <https://doi.org/10.1086/343813>
- Liew, S. M., Khoo, E. M., Ho, B. K., Lee, Y. K., Omar, M., Ayadurai, V., Mohamed Yusoff, F., Sulis, Z., Mudin, R. N., Goh, P. P., & Chinna, K. (2016). Dengue in Malaysia: Factors Associated with Dengue Mortality from a National Registry. PLOS ONE, 11(6), e0157631. <https://doi.org/10.1371/journal.pone.0157631>
- Martina, B. E. E., Koraka, P., & Osterhaus, A. D. M. E. (2009). Dengue Virus Pathogenesis: An Integrated View. Clinical Microbiology Reviews, 22(4), 564–581. <https://doi.org/10.1128/CMR.00035-09>
- [PDF] Dengue Knowledge and Preventive Practices among Rural Residents in Samar Province, Philippines | Semantic Scholar. (n.d.).
- Quirino-Teixeira, A. C., Andrade, F. B., Pinheiro, M. B. M., Rozini, S. V., & Hottz, E. D. (2022). Platelets in dengue infection: More than a numbers game. Platelets, 33(2), 176–183. <https://doi.org/10.1080/09537104.2021.1921722>
- Shrivastava, A., Dash, P. K., Dash, P. K., Tripathi, N. K., Sahni, A. K., Gopalan, N., & Lakshmana Rao, P. V. (2011). Evaluation of a commercial Dengue NS1 enzyme-linked immunosorbent assay for early diagnosis of dengue infection. Indian Journal of Medical Microbiology, 29(1), 51–55. <https://doi.org/10.4103/0255-0857.76525>
- Shu, P.-Y., & Huang, J.-H. (2004). Current Advances in Dengue Diagnosis. Clinical and Vaccine Immunology, 11(4), 642–650. <https://doi.org/10.1128/CDLI.11.4.642-650.2004>
- World Health Organization. Dengue: Guidelines for diagnosis, treatment, prevention and control: New edi. Geneva: World Health Organization;2009. Available at <https://www.ncbi.nlm.nih.gov/books/NBK132015/>. (n.d.).