Section: Microbiology

Original Research Article

A SEROLOGICAL STUDY ON COINFECTION OF LEPTOSPIROSIS AND DENGUE FEVER IN PATIENTS ADMITTED WITH ACUTE FEBRILE ILLNESS IN A TERTIARY CARE HOSPITAL

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Received : 29/04/2024
Received in revised form : 06/07/2024
Accepted : 19/07/2024

Keywords:
Dengue, Leptospirosis, Acute Febrile illness, Coinfection

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DOI: 10.47009/jamp.2024.6.4.69

Source of Support: Partially by TNSRC,Chennai
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (4); 343-346

Abstract

Background: Dengue and Leptospirosis are the two important causes of acute febrile illnesses in tropical and subtropical areas. We conducted this study to know the serological coinfection of leptospirosis and dengue fever in patients admitted with acute febrile illness in a tertiary care hospital and analyze various factors associated with coinfection of dengue and leptospirosis and its outcome. **Materials and Methods:** This cross sectional study was conducted in the Department of Microbiology , Government Medical College Hospital, Thiruvallur, over a period of 6 months from April 2023 to September 2023.The blood sample were collected from the in-patients admitted with acute febrile illness and screened for Dengue IgM antibody by ELISA Method. All the Dengue IgM positive samples were screened for leptospirosis IgM antibody. Samples positive for Both Dengue IgM antibody and Lepto IgM antibody were defined Coinfection. Demographic, clinical data and other lab parameters were collected and analyzed **Result:** A total of 508 patients with acute febrile illnesses were evaluated, Out of this 508 patients, Dengue and Leptospirosis Coinfection found in 9 patient (8.4%)and 106 patients with were confirmed as Dengue Mono infection. **Conclusion:** Current knowledge and increased alertness about the coinfection and high index of suspicion will be helpful to reduce the mortality and more benefit to the patients as well as the treating physicians.

INTRODUCTION

In tropical countries including India, patients with diseases like malaria, dengue typhoid and leptospirosis, present with acute febrile illness with nonspecific symptoms and signs. Dengue and Leptospirosis are the two important causes of acute febrile illnesses in tropical and subtropical areas. Dengue fever is one of the most prevalent arboviral disease in the world and can be caused by any of the four serotypes of the virus. Every year more than 100,000 people are infected by dengue in India[1]. Leptospirosis is a zoonosis caused by pathogenic Leptospira species. The annual incidence of leptospirosis ranges from 0.1-1.0 per 100,000 in temperate regions to 10-100/100,000 in humid regions[6] (WHO, Human leptospirosis, 2003). Early clinical signs of both the diseases are nonspecific and similar.

Similarity of clinical presentation makes diagnostic challenge for Physicians and management in confusion particularly when co- infection is present [7&10&5&4]. It is important to ascertain and differentiate these two diseases because specific antibiotic therapy is necessary in leptospirosis[10], whereas Dengue is treated by symptomatic supportive management . The diagnosis of one pathogen does not exclude the other, since coinfection between both diseases have been described with a prevalence of 3.4% and 4.1%[4.&9]. Increased awareness about the presence of co-

ISSN (O): 2687-5365; ISSN (P): 2753-6556

infection is necessary, so that a high index of suspicion is needed for early diagnosis and successful management of the patients . Only limited study data are available regarding the dengue and leptospirosis coinfection in Tamil Nadu .

The main objective of this study was to determine the seropositivity of Leptospirosis in Dengue IgM antibody positive patients, presenting with acute febrile illness and also to analyze the demographic, clinical data and other lab parameters in those patients with serological coinfection of Dengue and Leptospirosis.

MATERIALS AND METHODS

Study Design: This hospital-based cross-sectional study conducted in the Government Medical College Hospital, Thiruvallur, over a period of 6 months from from April 2023 to September 2023.

Study place : Department of Microbiology, Department of General Medicine and Department of Pediatrics, Government Medical College Hospital , Thiruvallur

Ethical Approval: Institutional Ethics Committee approval was obtained prior to the commencement of the study.

Inclusion criteria: All patients admitted with acute febrile illness with clinical diagnosis of suspected dengue and leptospirosis were included in this study.

Exclusion criteria: Patients admitted with definitive alternate diagnosis were excluded from this study .

Methodology

Sample collection: The blood sample (5ml of blood) was collected under aseptic precaution after obtaining written informed consent from the patients. Upon receipt of sample in the Microbiology Department Lab , serum separated through centrifugation. All the samples were screened for Dengue IgM antibody by ELISA Method and all the Dengue IgM positive Samples were then screened for Leptospirosis IgM antibody .

Dengue IgM antibody detection was done by using Panbio Dengue IgM capture ELISA Kit for Qualitative detection of IgM antibody against dengue virus antigen in the serum. Cut off value calculated and Index value of sample was calculated by dividing the sample absorbance by cutoff value . Panbio Units calculated by multiplying the index value by 10. Panbio units more than 11 was interpreted as Positive for Dengue IgM antibody. Serological sensitivity of the test kit is 94.7% and specificity of the test is 100%. The cross reactivity analysis Panbio Dengue IgM capture ELISA shows the cross reactivity was observed for Malaria and Rheumatoid factor and West Nile fever but not against Leptospirosis.

Lepto IgM Microlisa Kit was used to detect Leptospirosis IgM antibody in the patient serum sample based on Indirect ELISA. Sample OD ratio was calculated by dividing the sample sample OD value by cutoff value and Lepto IgM Units were calculated by multiplying the sample OD Ratio by 10. If the Lepto IgM unit is more than 11 , then the sample is interpreted as Positive for Lepto IgM antibody. The sensitivity of the Kit is 99.62%.specificity is 99.92%and false positive occurs in less than 1% of sample testes due to cross reaction with Influenza A &B , Brucella , Dengue Virus and EBV as per kit Manufacturer.

Coinfection in this study was defined as samples positive for Both Dengue IgM antibody and Lepto IgM antibody .

Demographic ,Clinical details and laboratory parameters like Total WBC count Platelet count Hemoglobin level , Renal function test , Liver function test and Blood grouping &Typing of all the patients were collected and documented using a specific proforma and collected data were analyzed. The outcome of present illness of patients were followed up till their discharge from Hospital.

RESULTS

Statistical analysis :

Statistical analysis was performed by Statistical Product and Service solution software version 24.0 (SPSS Inc., Chicago ,IL, USA). For continuous variables ,the significance was determined using Independent t-test .The categorical variables were analyzed by Fisher's exact test.

Table 1: Demographic features of the study participants positive for Dengue Mono infection & Leptospirosis + Dengue coinfection.

Demographic Characteristics	Dengue Mono Infection (n= 106)	Dengue &Leptospirosis coinfection (n=9)	P value
Age :			
0-19	68	7	0.409
20-44	30	2	0.696
45-59	6	0	0.999#
>60	2	0	0.849#
Gender			
Male	69	7	0.440
Female	37	2	

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 2: Laboratory values at the time of admission to the hospital for Dengue Mono infection & Leptospirosis + Dengue coinfection

Clinical condition /Lab parameters	Dengue alone Mono Infection (n= 106)	Leptospirosis + Dengue coinfection, (n = 9)	P value
Thrombocytopenia [Platelet <100000]	47	6	0.188
Leukocytosis [TWBC>11000]	2	0	0.999#
Leukopenia [TWBC <4000]	26	2	0.999#
Aneamia [Hb <8gm%]	5	1	0.402
Hyper bilirubineamia [Sr.Bilurubin >1.5mg/dl]	2	0	0.999#
Elevated SGOT [>47Units/L]	11	5	0.001
Elevated SGPT [>55Units /L]	11	5	0.001
Elevate Blood Urea Nitrogen [>25mg/dl]	2	1	0.434#
Elevated Sr. creatinine [>1.3mg/dl]	0	1	0.155#

Table 3: Clinical presentation at the time of admission to the hospital

Clinical presentation	Dengue Mono Infection (n= 106)	Leptospirosis + Dengue coinfection (n = 9)	P value
Fever	106	9	-
Vomiting	58	8	0.044
Abdominal pain	40	9	0.001#
Myalgia/arthralgia	24	7	0.001
Rashes	25	4	0.161
Bleeding manifestation (skin, GIT, Gum and nasal bleeding)	28	5	0.060
Free fluid accumulation in 3rd space	24	3	0.457
Decreased urine output	18	1	0.657

Summary of Leptospirosis and Dengue coinfections (n = 9)

S.no	Age	Sex	Blood group& type	Dengue IgM titre Units	Lepto IgM titre Units	Inpatient days	LFT	RFT	Outcome
1	22	F	O positive	13.09	16.67	5	Abnormal	Normal	Improved and discharged
2	7	M	B positive	35.22	22.98	6	Abnormal	Normal	Improved and discharged
3	8	M	B positive	24.32	28.56	6	Normal	Normal	Improved and discharged
4	12	M	B positive	12.71	13.42	6	Normal	Normal	Improved and discharged
5	41	M	B positive	11.40	11.23	4	Abnormal	Normal	Improved and discharged
6	10	M	B positive	25.76	14.24	4	Normal	Normal	Improved and discharged
7	11	F	O positive	30.92	24.04	5	Normal	Normal	Improved and discharged
8	11	M	O positive	44.62	11.11	9	Abnormal	Abnormal	Improved and discharged
9	9	M	A positive	21.52	16.77	6	Abnormal	Normal	Improved and discharged

Total number patients samples received as per the inclusion criteria	508
Total number of patients serologically Positive for Dengue IgM antibody	115
Total number of patients with Dengue Mono Infection (Dengue IgM antibody Positive alone)	106
Total number of patients with Coinfection (Both Lepto IgM antibody and Dengue IgM antibody Positive patients)	9

DISCUSSION

Dengue and leptospirosis are the most common causes of acute febrile illness in tropical countries particularly in India . Both infections present with clinical symptoms and signs which are mostly similar. Several studies done on the Dengue and Leptospirosis coinfection revealed that the coinfection is more than what actually reported in the past .

We performed this cross sectional study in a tertiary care Hospital ,Thiruvallur District from the period of April 2023 to September 2023.

We evaluated 508 patients admitted with acute febrile illness with clinical suspicion of Dengue during that period. 115 patients with AFI were confirmed as serologically Dengue IgM positive (20.8%) which is comparable to previous study done by Anitha Madhavan et al (29%).

Leptospirosis IgM antibody were positive in 9 samples (8.4%) in those samples positive for Dengue IgM antibody .

The coinfection [8.4%] in our study is higher than previous studies done by Anita Ravinder et al [4%] and Anitha Madavan et al [3.4%] , both were conducted in southern India . Oilveria et al in Brazil(2014) reported coinfection of Dengue and Leptospirosis in his study as 14% .

Of the 9 patients with coinfection, abdominal pain [100%]and vomiting [80%] are the most common

ISSN (O): 2687-5365; ISSN (P): 2753-6556

symptoms reported in our study followed by myalgia[77%].(Pvalue<0.05). Bleeding manifestations is reported 26% in Dengue mono infection patients but 55% in patients with coinfection.

Thrombocytopenia [Platelet count <100000] is reported 37% in patients with Dengue mono infection but 66% in coinfection which is comparable to the study reported by Kumar et al[3] [64%].

Leukocytosis is not reported among the coinfection cases in our study which is discordant with study by Kumar et al[7&8] (35%) in coinfection patients. Leukopenia is reported 24 % in Dengue mono infection patients and 22% in coinfection patients. Anemia [Hb < 8gms%] were reported in 4.7 % cases of Dengue mono infection but 11% in coinfection patients.

The LFT markers (SGOT &SGPT)in our study were abnormal in 10% of Dengue mono infection patients but 55% in coinfection patients with significant P value 0.001%.

Male predominance has been reported 77% in our study which concordant with findings of Subbiah et al but discordant with findings of Anita Madhavan et al[5]

Among the out come related variables, the mean duration of hospital days is 5.8 days which is almost equal to the mean duration of mono infection cases [5.2days] .

All the patients with coinfection were survived after the management at hospital and Nil mortality in our study, the data which is concordant a study conducted in Chennai by Ananthi et al [11] but Sharma et al[6] reported 12.69% mortality in coinfected patients in his study.

In general deranged hepatorenal function is very common in coinfection[8] but in our study only one case is reported with both hepatorenal dysfunction which is comparable with the study reported by Ananthi et al [11].

Limitation

This study only done with IgM antibody detection by ELISA method for detection of Dengue and Leptospirosis but not done the specific confirmation test for leptospirosis by Polymerase Chain Reaction or Microscopic Agglutination test [MAT]. Moreover we not done the dengue serotype to know which serotype is more associated with Leptospirosis and dengue coinfection.

CONCLUSION

Dengue and leptospirosis coinfection may be underrecognized combination of concurrent infection in the tropical country , particularly India. Identifying and treating the coinfection is essential for rapid recovery because definitive antibiotic therapy is essential for leptospirosis infection treatment. Current knowledge and increased alertness about the coinfection and high index of suspicion will be helpful to reduce the mortality and more benefit to the patients as well as the treating physicians.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556