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Original Research Article

Relative bradycardia- indicator of severe dengue fever: a comparative study between PICU and ward patients

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ABSTRACT

Background: Mortality due to dengue fever during epidemics is very high with all the four serotypes actively found in India. It is very difficult to distinguish and manage illness of viral aetiologies based on initial clinical features. Bradycardia can be seen as notable clinical finding in severe dengue fever. Clinical features that can be used in the initial assessment of febrile patients are essential tools for physicians in limited resource settings. Awareness of bradycardia as an early indicator of severe dengue fever could help in the early recognition and potentially reduce morbidity and mortality.
Methods: This is an observational comparative study of 40 dengue fever positive paediatric patients admitted in PICU and general ward. The study was conducted at Atal Bihar Vajpayee Govt Medical College, Vidisha from 20 August to 20 November 2020 (3 months).
Results: Bradycardia, as a significant clinical feature was present in almost all PICU patients as compared to ward patients. It can be taken as a clinical marker of severity to prevent life threatening complications of dengue like shock and haemorrhage.
Conclusions: With specific WHO guidelines to classify and treat dengue fever, we try to prevent its deadly consequences but in resource limited settings like ours, initial clinical judgement can prevent much causality and prepare us to foresee and timely manage the complications.

Keywords: Relative bradycardia, Dengue fever, PICU

INTRODUCTION

The dengue virus is a mosquito borne virus Arbovirus, belonging to the family Flaviviridae and genus Flavivirus, transmitted, primarily by Aedesaegypti and Aedesalbopictus. Dengue is caused by four distinct serotypes of viruses; DEN-1, DEN-2, DEN-3 and DEN-4, causing a spectrum of illness ranging from self-limiting classical dengue fever (DF) to life threatening dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[1,2] Disease is predominant in urban and suburban areas, has emerged as important disease in tropical and subtropical countries. Dengue fever and dengue hemorrhagic fever is endemic in certain areas of South East Asia like Bangladesh, India, Indonesia, Myanmar, Sri Lanka and Thailand and is a major cause of hospitalization and death among children in these regions. Case fatality rates in endemic countries are 2.5%. During epidemics of dengue, attack rates among susceptible are 40-90%.[3] The first major epidemic illness compatible clinically with dengue occurred in Madras (Chennai) in 1780 and now India comes under category B of the classification meant for SEAR. Relative bradycardia apart from dengue fever has been reported in many infectious diseases, including typhoid fever, legionnaires disease, psittacosis, typhus, leptospirosis, malaria. It was first reported from Singapore in 2005. Prior to that, the association of this sign with Dengue fever was not known. No specific clinical features

distinguish dengue from other febrile illnesses; thus, diagnosis relies heavily on results of laboratory investigations, i.e. virus-specific immunoglobulin M (IgM) antibodies which become detectable after 5-7 days, and false-positive results can confound the diagnosis. Dengue fever may adversely affect cardiac function like depressed myocardial contractility and suboptimal heart rate and in some cases acute reversible hypokinesia and reduced left ventricular ejection fraction.[4,5] The underlying mechanisms were postulated to be immune in origin, although myocarditis may be a contributory factor. Concentrations of cytokines, including tumour necrosis factor, interferon-γ, IL8, IL-10, and IL-12, are substantially increased during dengue infection and their levels may correlate with specific clinical manifestations and illness severity. The relationship of cytokines to relative bradycardia is unknown[6].Awareness of bradycardia as aclinical finding, could help in the early recognition of Dengue and potentially reduce complications and death associated with it.[7] The initial temperature may rise to 102 to 105°F, and fever may last for 2 to 7 days. The fever may drop after a few days, only to rebound 12 to 24 h later (saddleback). A relative bradycardia is noted despite the fever.[8]

Studies relating bradycardia with dengue fever in our country are scarce. Hence, this study was taken up to observe the pattern of heart rate and electrocardiographic changes associated with dengue fever. A major challenge for public health officials in all tropical areas of the world is to develop and implement sustainable prevention and control programs that will reverse the trend of emergent dengue hemorrhagic fever.[9]

METHODS

This a prospective comparative study of relative bradycardia as clinical finding in paediatric patients admitted in PICU and ward as suspected dengue fever and later was confirmed by either NS1 antigen or IgM antibodies test. Total 40 patients were studied from 20 August 2020 to 20 November 2020. 20 patients were taken from PICU and 20 from general ward, 5 to 15 years of age, who were admitted at Atal Bihari Vajpayee Government Medical College Vidisha (MP) with complaint of highgrade fever (>38C) for more than 3 days along with malaise, headache and abdominal pain as suspected dengue fever. Their symptoms and signs were recorded at the time of admission and followed daily till discharge or death. Clinical signs included general appearance, vitals including heart rate, pulse, blood pressure, temperature; capillary refill time, urine output and signs of shock were identified and recorded for 5 days. Stable patients were admitted in general ward and sick patients were admitted in PICU. Their serum sample for NS1 antigen detection by ELISA along with IgM and IgG antibodies were sent for laboratory confirmation along with CBC, CRP and liver function test. Other viral and bacterial causes were also ruled out. Chest X-ray was done in all PICU to look for pulmonary oedema. Dengue is characterised by microangiopathic capillary leak and thrombocytopenia so daily CBC was followed. Patient was closely monitored for bradycardia (HR less than 60), hypotension (BP less than 5th centile), wide or narrow pulse pressure, oligouria (less than 0.5 ml/kg/hr), and CRT, low pulse volume and cold peripheral extremities. Daily ECG was recorded in patients with bradycardia. Only those patients who reported positive for dengue fever was included in the study. The patient was followed up till discharge or death/referral. Their age group, gender, clinical features, signs, lab findings, ECG findings and outcome were compared. Statistical analysis was done and p-value was calculated. This was an observational prospective study; Chi square was used as statistical tool to calculate the p-value for the data using IBM SPSS software version 20.

No tool or technique was used to calculate the sample size. It was completely observational and all the patients fulfilling the inclusion criteria was included in the study.

RESULTS

In this study among 40 patients taken, 50% patients were from ward and 50% PICU (1:1) ratio. There was no significant difference between age and gender distribution between ward and PICU.

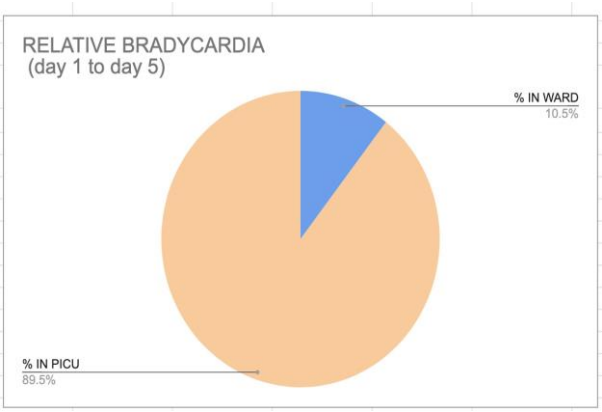

Figure 1: Relative bradycardia PICU and ward (day 1 to day 5).

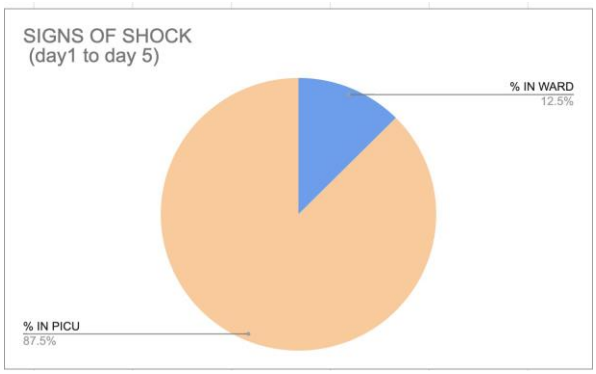

Figure 2: Signs of shock PICU and ward (day 1 to 5).

There is significant difference between the incidence of relative bradycardia between the ward and PICU patients. It was observed that the critical patients who were admitted in PICU had HR <60/min rather than tachycardia (as patients were febrile and had impending shock). Relative bradyacrdia was seen in 89.5% PICU patients whereas it was seen only in 10.5% ward patients making it a significant finding. There was significant difference seen between incidence of hypotension in patients admitted in PICU and ward. Patients admitted in PICU were critical and had hypotension along with bradycardia. There was a significant difference between incidence of shock in form of hypotension, bleeding manifestation, reduced urine output, increased capillary refill time in patients admitted in PICU. They should have tachycardia as it is the 1st sign of shock but instead the patient presented with bradycardia.

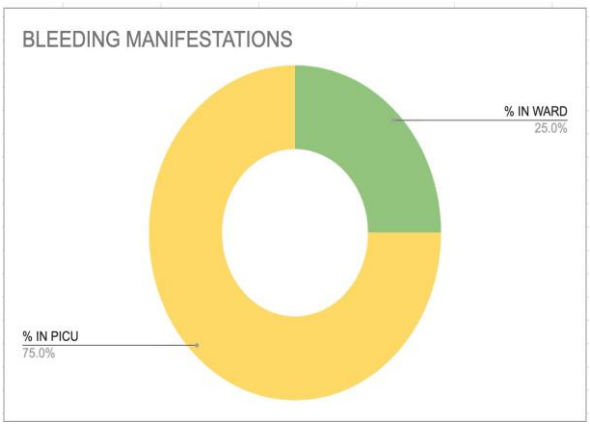

Figure 3: Bleeding manifestations PICU and ward (day 1 to 5).

Table 1: Relative bradycardia PICU vs ward.

Relative bradycardia (day 1)	No. of patients in ward	No. of patients in PICU	% in ward	% in PICU
>60 beats/min	18	03	90	15
<60 beats/min	02	17	10	85
P value	0.001			

Table 2: Hypotension incidence PICU vs ward.

Blood pressure (day 1 to 5)	No. of patients in ward	No. of patients in PICU	% in ward	% in PICU
≤5th centile	00	07	0	35
50th-75th centile	08	07	40	35
≥75th centile	12	06	60	30
P value	0.03			

Table 3: Incidence of shock PICU vs ward.

Signs of shock (day 1 to 5)	No. of patients in ward	No. of patients in PICU	% in ward	% in PICU
Present	02	14	10%	70%
Absent	18	06	90%	30%
P value	0.001			

Table 4: Thrombocytopenia incidence PICU vs ward.

Platelet count	% in ward	% in PICU
0-20000	-	40%
20000-50000	55%	45%
50000-100000	45%	15%
P value	0.001	

Table 5: ECG findings PICU vs ward.

ECG finding	Ward	PICU
Sinus bradycardia	02,10%	15.75%
Myocarditis	00,0	01.5%
Arrythmia	01,0	01.1%
P value	0.001	

Table 6: Outcome of PICU vs ward patients.

Outcome	No. of patients in ward	No. of patients in PICU	% in ward	% in PICU
Discharge	18	14	90%	70%
Death	-	06	-	30%
Shifted to PICU	02	-	10%	-
P value	0.006			

Signs of shock was present in 87.5% PICU patients whereas present in only 12.5% patients. There was significant thrombocytopenia with bleeding manifestations in form of petechiae, malena, epistaxis and hemetemesis in patients with platelet count less than 20000 admitted in PICU, whereas only 25% patients in ward presented with bleeding manifestation. 75% patients in PICU presented with bleeding manifestations in form of petechiae, epistaxis, hemetemesis and malena. They had impemding shock and bradycardia which was contradictory.

ECG was suggestive of sinus bradycardia in maximum patients who presented with bradyacrdia which suggests that it is a temporary finding. The virus causes ventricular hypokinesia in active and convalescent phase resulting in bradycradia which caused no permanent damage to the myocardium. 30% mortality was reported in PICU patients who initially presented with bradycardia due to shock and bleeding manifestations. Therefore, bradycardia should be taken as initial clinical sign to foresee further morbidity and mortality.

DISCUSSION

From 20th August 2020 to 20th November total 40 dengue fever positive patients were studied, 20 patients were from PICU (50%) and 20 from general ward (50%). The mean age of patients in PICU was 12.5years and in ward was also 12.5 years. It is similar to study done by Aisha Lateef et al in which relative bradycardia was observed in adult patients with admitted with dengue fever with mean age group 32years.[7] The study was done in Singapore in 2005.

Out of total 40 patients, 25 were male (62.5%) and 15 patients were female (37.5%). There is no gender correlation with the clinical findings.

Relative bradycardia was seen in 85% patients in PICU which proves that bradycardia can be taken as a clinical marker to assess and foresee the severity of illness as maximum of these PICU patients later presented with shock or had bleeding manifestations unlike in ward where only 10% patients presented with HR less than 60/min. They remained quite stable throughout the illness. There is a significant difference (p-value 0.001) in heart rate of patients admitted in PICU and ward. It is similar to the study done by B. A. Cunha at Infectious disease division, Winthrop-University Hospital, Mineola, New York, USA, and, SUNY School of Medicine, New York USA, where patients above 13 years were studied for pulse-temperature deficit as early diagnostic marker in infectious diseases like typhoid, enteric, dengue fever and legionella infection and further morbidities can be prevented.[10] A similar study was done by Meenaxi Sharda et al at GMC Kota department of medicine where 48 patients were admitted with ELISA IgM/IgG positive for dengue fever and out of them 8 cases of dengue fever with sinus bradycardia were reported. They concluded that bradycardia in dengue fever may not only be a relative phenomenon and should be looked at carefully during both acute and convalescence period.[11]

70% patients from PICU reported hypotension (35% had BP less than 5th centile and 35% had from 50-75th centile) within 5 days of admission who also had bradycardia from the day of admission whereas 40% patients from ward had BP reported between 50-75th centile and 60% had blood pressure within normal limits and they never heart rate less than 60 beats/min.

70% patients from PICU who had hypotension also landed in shock later within 5 days of admission whereas only 10% patients from ward showed signs of shock and had to be shifted to PICU. Considering other complications like thrombocytopenia and bleeding manifestations, 50% PICU patients had platelet count less than 50000 from day 1 to day 5 of admission and 60% patients presented with bleeding manifestations and they all had bradycardia as initial presentation from day 1 of admission which is significant compared to ward patients (p-value 0.001).

ECG was done in all 40 patients and despite having bradycardia, 75% patients had sinus rhythm in ECG, and only 2 patients had cardiac pathology. It proves that relative bradycardia is not causing any permanent damage to the myocardium; the virus only results in ventricular hypokinesia as seen in study done by Khongphatthanayothin A et al, where ECG was done in 24 patients were studied during convalescent and recovery phase where reduced cardiac output and contractility was temporary due to virus.[4] A significant number of patients of dengue developed asymptomatic involvement of heart as evidenced by electrocardiography changes, raised cardiac enzymes (CPK-MB, S.trop.T, LDH and SGOT). Myocardial involvement was subclinical as 2-D echo and ECG was normal.[12]

In one study of 913 school children with dengue, a wide variety of complications were observed: hepatitis (27%), neurological alterations (25%), renal impairment (7%), cardiac involvement (8%), pulmonary changes (9%), acalculous cholecystitis (9%), hemophagocytic syndrome (2.5%), and acute abdominal pain (11%).[13] Clinical manifestations of cardiac involvement can from silent disease to severe myocarditis resulting in death. Rhythm abnormalities, hypotension, arrhythmias, myocarditis, myocardial depression with symptoms of heart failure and shock, and pericarditis have been reported.[14]

A total 70% patients from PICU were discharged after 7-10 days and 6 patients (30%) died due to shock and bleeding manifestations. All these patients had bradycardia as initial clinical finding. 18 patients were discharged from ward and 2 were shifted to PICU due to complications.

CONCLUSION

Relative bradycardia can be taken as initial clinical marker of severity of dengue fever. Patients in PICU who initially had bradycardia later presented with shock and bleeding manifestations. Therefore, when a patient presents with bradycardia as initial symptom, he/she should be admitted in PICU to manage the morbidities as early as possible as WHO urges all dengue endemic countries to enhance surveillance and implement effective vector measures to prevent and control the spread of the disease.[15]

Limitation of the study were total number of patients is less as due to COVID both IPD and OPD load reduced. As dengue fever is endemic during rainy seasons in India study was conducted only for 3 months from August to November.

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