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Study of Incidence of Acalculous Cholecystitis In dengue Patients of Southern Odisha

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Abstract

Background: Dengue is an acute febrile disease of viral etiology common in tropics and subtropics. In recent years, dengue has become a global public health concern. There are certain rare atypical presentations in dengue like encephalopathy, encephalitis, hepatitis, AKI, cardiomyopathy, ARDS, GBS, rhabdomyolysisand acalculous cholecystitis. Acute acalculous cholecystitis accompanying dengue fever has beenunderreported.

Aims and Objectives: To study incidence and prognosis of acalculous cholecystitis in dengue and tocorrelatea calculouschole cystitis with severity of dengue.

Materials and Methods: 200sero positive dengue patients admitted to dengue ward of MKCG medical college hospital, Berhampur, Odisha, India, were studied during the period Oct 2016-Oct 2018. Acalculous cholecystitis was diagnosed on basis of clinical feature and ultra sound findings.

Results: Out of 200 patients, 170 (85%) were classified as dengue fever, 19 (9.5%) as dengue hemorrhagic fever and 11 (5.5%) as dengue shock syndrome. Fever was the main presenting symptom (100%) in all our patients followed by headache(98.5%), myalgia(92.5%),rash(24.5%), retro-orbitalpain (22%), arthralgia (21.5%), pain abdomen(19%) and bleeding manifestation (15%). The clinical examination revealed pallor (2%) and icterus (0.5%). Features of shock was present in 5.5%. 19 out of 200 patients of dengue had acalculouschole cystitis. The incidence was found tobe9.5%.Outofthe19cases of acalculouschole cystitis, theincidencein Dengue fever (DF), Dengue hemorrhagic fever (DHF)andDengue shock syndrome(DSS)groupswere5.88%, 26.31% and 36.36% respectively. Outo f the19acalculouschole cystitis patients, 18 patients (94.7%) recovered with conservative treatment.

Conclusion: Dengue patients with multiorgan dysfunction have poor clinical outcome. Acalculouschole cystitisin dengue is notun commonan disusually self limiting and resolves with conservative management. It is more often manifested in severe forms of dengue.

Keywords : Acalculous chole cystitis, Dengue fever (DF), Dengue hemorrhagic fever(DHF), Dengue shock syndrome(DSS).

Introduction : Dengue is an acute febrile disease of viral etiology commonintropic sand subtropics. Theetiologic agent belongsto flaviviridae family and flavi virus genus . The viruses of this family are arbo virus and are

transmitted by Aedes mosquito.[1] Dengue virus has 5 serotypesi.e.DEN1,DEN2,DEN3,DEN4andDEN5.Thefifth serotype has been isolated in October 2013 .[2]In recent years, dengue has become global public health concern. Approximately 2.5 billion people (40% of world's population) living mainly in urban areas of tropical and subtropical regions are estimated to be at risk of acquiring dengue infection.[3]

Dengue fever has been known to been demicin India for more than 20 years as a benign self limited disease. However, during recent years, the severe form is manifesting more frequently[4]. In Odisha, increasing number of cases are reported since 2010. Several outbreaks have been reported from various parts of the state mainly from the coastal districts.

Dengue fever is usually a non specific and self limiting biphasic febrile illness but the presentation may range from asymptomatic to dengue fever, DHF and DSS. Dengue is characterised by high grade fever, headache, musculoskeletal pain, retro-orbital pain, joint pain, abdominal pain, nausea , vomiting and morbiliform rash[5,6,7] . Severe dengue is defined by one or more ofthe following:**1**.Plasmaleakagethat may lead to shock(dengue shock) and/or fluid accumulation with or without respiratory distress, and/or **2**. Severe bleeding , and/or **3**. Severe organ impairment.[8] There are certain rare atypical presentations in dengue . Eg, encephalopathy, encephalitis, seizures, liver damage, cardio myopathy, severe GI hemorrhage, GBS, rhabdo my olysis and acalculous cholecystitis [6,7,9]. In these cases, a high clinical suspicion is required to make an early diagnosis and initiate prompt treatment.

Acute acalculous chole cystitis accompanying dengue fever has been underreported. The complication may be more common than previously suspected. AretrospectivestudyinTaiwanof131patientshas shown that acalculous cholecystitis occurred in about 7.63% of cases[10]. Aprospective study by Sharma etalshowed 14outo f27patients(51.8%) of dengue fever with acalculous cholecystitis[7]. The exact patho physiology in the development of acalculous cholecystis in dengue is unknown. Some experts in this field suggested cholestasis and increase dbileviscosity from pro longed fasting,spasm soft heampullaof vater, infection ,end otoxemia , micro angiopathy and ischemia- reperfusion injury[11,12]. The main path physiologic change in dengue fever could be increased vascular permeability causing plasma leakage and serous effusion with high protein content, which then induces thick eningofgallbladderwall. Acalculous cholecystitisin dengue patients present with upper abdominal pain, dyspepsia , fever, positive Murphy sign, abnormal LFT and thickened gallbladder without stone. Course is generally self limiting and thickened gall bladder wall returns to normal.

Aims And Objectives: To study incidence and prognosis of acute acalculous chole cystitis in dengue and to correlate it with severity of dengue.

Materials Andmethods :200 seropositive dengue patients admitted to dengue ward of MKCG medical college hospital, Berhampur were studied during the period Oct 2016-Oct2018. This observational study was conducted after the study protocol was approved by the Institutional Ethics Committee of MKCG Medical College Hospital, Berhampur, Odisha, India. Informed consent was obtained from all participants. All patients with dengue fever with either NS1 antigen or dengue IgM antibody positive and aged more than 15 years were included. Patients with malaria, known positive viral serology for viral hepatitis, chronic liver disease, diabetes mellitus with nephropathy,

cardiomyopathy, chronic kidney disease, collagen vascular diseases like SLE, Mixed Connective Tissue Disease and calculous cholecystitis were excluded from the study. Patients were classified in to dengue fever(DF),dengue hemorrhagic fever (DHF) and dengue shocks ssyndrome (DSS). Acalculous cholecystitis was diagnosed on the basis of clinical features and ultrasound findings.

Ultra sonography of abdomenand pelvis was doneinall patients included in the study. The diagnosis of acalculous chole cystitis was done on the basis of ultra sono graphic findings along with clinical features.

Sonographicevidenceforacalculouscholecystitisinclude– thickenedgall bladder wall(defined as wall thickness >3.5 mm), a positive sonographic Murphy's sign(defined as maximum tenderness of the sonographicallylocalised gall bladder), pericholecystitic fluid collection and no stone(s) in gall bladder. In the present study, patients with thick enededematous gallbladder wall in USG along with clinical features like fever, right upper quadrant pain, positive Murphy's sign, etc. were diagnosed to have acalculous cholecystitis. These patients were treated with antibiotics, intravenous fluids, analgesics, with regular monitoring for development of any complications. The patients were followed till they recovered completely and discharged.

Statistical data analysis was done using SPSS version 17. Inferential statistical tools like Chi square test and student's unpaired t-test were used. P value < 0.05 was considered significant.

Results : In the present study, out of 200 cases, total no of males were 131(65.5%) while females were69(34.5%). Maletofemaleratiowas1.89:1.Outofthe200patients, 170(85%) were classified as dengue fever, 19(9.5%) as dengue hemorrhagic fever and 11(5.5%) as dengue shock syndrome.(Table1)

Table 1: Clinical category of patients with dengue infections

Total patients	DF(%)	DHF(%)	DSS(%)
200	170(85%)	19(9.5%)	11(5.5%)

Clinical findings

Fever was the main presenting symptom(100%) in all the patients followed by headache(98.5%), myalgia(92.5%), rash(24.5%),retro-orbital pain(22%), arthralgia (21.5%), pain abdomen(19%) and bleeding manifestation(15%). Table 2 shows the clinical findings of patients with denguefever.

Table 2: Clinical characteristics of Dengue Patients at the time of admission

Clinical Presentation	No. Of Patients(N=200)
Fever	200(100%)
Headache	97(98.5%)
Retro-Orbital Pain	44(22%)
Myalgia	185(92.5%)
Arthralgia	43(21.5%)
Rash	49(24.5%)
Pain Abdomen	38(19%)
Bleeding Manifestation	30(15%)
Hepatomegaly	31(15.5%)
Pleural Effusion	24(12%)
Ascites	25(12.5)
Shock	11(5.5%)
Icterus	1(0.5%)
Pallor	4(2%)

Total no. of dengue patients found to have acalculous cholecystitis was 19 out of which 10 were from DF category, 5 were from DHF category and 4 were from DSS category. Incidence of acalculous cholecystitis in DF,DHF and DSS category was 5.88%, 26.31%, and 36.36%

respectively. This shows that the incidence of acalculous cholecystitis was significantly more in severe forms of dengue(DHF and DSS).

Overall incidence of acalculous cholecystitis in dengue was found to be 9.5%(Table 3).

Table 3: Incidence of acalculous cholecystitis in DF,DHF and DSS

	DF(n=170)	DHF(n=19)	DSS(n=11)	TOTAL(n=200)
Acalculous cholecystitis	10(5.88%)	5(26.31%)	4(36.36%)	19(9.5%)

Symptoms of dengue patients with acute acalculous cholecystitis: Fever and headache were present in 100% cases of dengue patients with acalculous cholecystitis. Myalgia was present in 94.73% . Pain abdomen and positive murphy sign was found in 89.47% and 73.68% respectively. 52.63% cases had retro-orbital pain. Arthralgia and rash were present in 5% cases(Table 4).

Table 4: Symptoms of dengue patients with a calculous cholecystitis:

Symptoms	No. Of Cases	%
Fever	19	100%
Pain Abdomen	17	89.47%
Murphy Sign	14	73.68%
Myalgia	18	94.73%
Arthralgia	5	26.31%
Rash	5	26.31%
Headache	19	100%
Retro-Orbital Pain	10	52.63%

USG findings of dengue patients with acalculous cholecystitis: In the present study, thickened edematous gall bladder wall in USG was used to diagnose acalculous cholecystitis in suspected cases. Other associated USG findings in patients with acalculous cholecystitis were ascites(94.7%), hepatomegaly (52.63%), pleural effusion (26.31%) and splenomegaly (15.78%). (Table 5)

Table 5: USG findings of dengue patients with acalculous cholecystitis:

USG finding	No of patients	%
Thickened edematous gall bladder wall	19	100%
Pleural effusion	5	26.31%
Ascites	18	94.7%
Hepatomegaly	10	52.63%
Splenomegaly	3	15.78%

Table 6: Association of acalculous cholecystitis with severity of dengue:

Acalculous cholecystitis / Severity of Dengue	YES	NO
Severe Dengue(DHF,DSS)	9	21
Dengue Fever	10	160

The odds ratio was found to be 6.8, which shows that the odd of having acalculous cholecystitis among severe dengue (DHF and DSS) patients was approximately 7 times higher than that of dengue fever patients.(Table 6)

Table 7: Prognosis of patients with acalculous cholecystitis in dengue:

Survival	Non survival
18/19(94.7%)	1/19(5.3%)

Out of 19 dengue patients with acalculous cholecystitis, survival was seen in 94.7% cases . No complications of acalculous cholecystitis were reported in these patients. Most patients recovered with conservative treatment. Death occurred only in 1 patient(5.3%). So acalculous cholecystitis in dengue has an overall good prognosis.

Discussion: This prospective study was conducted to find the incidence of acalculous cholecystitis in dengue patients of southern Odisha. Out of 200 denguepatients, 19 had acalculous cholecystitis. The incidence was found to be 9.5%. Similar studies have been conducted in various parts of the world. **Keng liana wu et al.**found the incidence of acalculous cholecystitis to be 28%.[13] In another study done by **S Khanna et al**,the incidence was 16.36%.[14] A retrospective study from **Taiwan** of 131 patients with dengue fever has shown that acalculous cholecystitis occurred in about 7.63% of cases[16]. A prospective study by **Sharma et al.** showed 14 out of 27 patients(51.8%) of DF with acalculous cholecystitis[7]. Out of the 19 cases of acalculous cholecystitis in our study, the incidence in DF, DHFand DSS groups were 5.88%, 26.31% and 36.36 % respectively. This showed that there was a significant association of acalculous cholecystitis with severe dengue(DHF and DSS). The exact pathophysiology in the development of acalculous cholecystis in dengue is unknown. Some experts in this field suggested cholestasis and increased bile viscosity from prolonged fasting , spasms of the ampulla of vater, infection ,endotoxemia , microangiopathy and ischaemia- reperfusion injury[11,12].The main pathophysiologic change in dengue fever could be increased vascular permeability causing plasma leakage and serous effusion with high protein content, which then induces thickening of gall bladder wall.

Out of the 19 acalculous cholecystitis patients, 18 (94.7%) recovered with conservative treatment. No complications of acalculous cholecystitis were reported in these patients. Death occurred only in 1 patient(5.3%). So acalculous cholecystitis in dengue has an overall good prognosis. A study conducted by **Sreeramulu et al** in **Sri Devaraj medical college in Kolar, India** showed that all the dengue patients with acalculous cholecystitis recovered fully with conservative line of management with none requiring any surgical intervention.[15]

Conclusion: In dengue patients, acalculous cholecystitis is not uncommon and is usually self-limiting and resolves with conservative management only .Conservative treatment is required in the form of adequate hydration, antipyretics, antibiotics and platelet transfusion in cases of severe thrombocytopenia. Cholecystectomy is not required in cases of dengue fever complicated by acalculous cholecystitis. Role of ultrasonography has a supporting role in dengue fever. Abdominal ultrasound should be mandatory in cases of dengue fever as it helps in clinical diagnosis as well as for early detection of complications. In dengue endemic areas, it is important that typical and atypical presentations of dengue fever are recognized early before the development of complications.

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