ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Comparison Of Epidemiological, Clinical And Laboratory Findings In Serologically Confirmed Icteric and Unicteric Leptospirosis.

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ABSTRACT

Leptospirosis is a seasonal zoonotic disease occurring in rainy seasons. Fever, chills, headache, severe myalgia, conjunctival suffusion, anorexia, nausea, vomiting, and malaise usually characterizes acute leptospirosis. This study was performed to compare the epidemiological, clinical and laboratory findings In serologically confirmed icteric & unicteric leptospirosis. A prospective study included 52 ELISA confirmed patients of above 18 years admitted from June 2012 to November 2014. Epidemiological, clinical and laboratory findings, complications were analysed & compared between icteric and unicteric leptospirosis. Out of 52 patients 35 were having icteric leptospirosis and 17 unicteric leptospirosis. In icteric group 22(63%) pts were between 21 to 40 years of age, 28 (80%) were males, 14(40%) farmers, 8(23%) labourers, 4(11%) carpenters & housewives each. Icteric leptospirosis affected rural population more. Jaundice Chills/rigors, calf pain, cough, dyspnoea, bleeding, altered sensorium, pallor, hepatomegaly, Thrombocytopenia, , hyperbilirubinemia, SGOT, SGPT, LDH, CPK rise, prolonged PT , hypokalemia are to be considered as clinical & laboratory pointers to icteric leptospirosis. All icteric patients suffer from complications & Hepatitis, AKI and Multiple organ failure, aseptic meningitis were the complications. Hepatitis is significant for icteric leptospirosis. Patients with Icteric leptospirosis may require hemodialysis & mechanical ventilation, hospital stay of > 7 days for case management & mortality may occur in icteric leptospirosis Our study may be helpful to health care physicians working in limited laboratory resource setting for identifying and treating patients of leptospirosis to improve outcome.
Keywords: Epidemiological, Clinical And Laboratory Findings, Serologically Confirmed Icteric

https://doi.org/10.33887/rjpbcs/2023.14.5.30

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ISSN: 0975-8585

INTRODUCTION

Leptospirosis is a worldwide seasonal zoonotic disease occurring in rainy seasons in tropical regions [3-4], like India caused by pathogen belonging to the Leptospira spp. genus comprising 250 serovars [5]. that affects predominantly men. The incidence of human infection is higher in the tropics [3, 4], mainly because of the longer survival of leptospires in warm and humid environments [6].

Transmission occurs by direct or indirect contact with urine, blood, water or tissue from an infected animal containing virulent leptospires. Leptospirosis is associated with occupational and recreational activities [7]. Leptospirosis is characterized by the development of vasculitis, endothelial damage and inflammatory infiltrates [4]. Fever, chills, headache, severe myalgia, conjunctival suffusion, anorexia, nausea, vomiting, and malaise usually characterizes acute leptospirosis [1, 2]. Two common forms of leptospirosis have been described: the anicteric (most common and mildest) and the icteric (Weil syndrome), which causes severe renal, hepatic, and vascular dysfunction. In the past though various investigators have studied epidemiologic al findings , clinical presentations , laboratory findings and complications in pts of leptospirosis. However, no study in the literature mentions about comparison of these findings in icteric vs unicteric leptospirosis hence an attempt is made to compare the epidemiological, clinical presentations and laboratory findings of serologically confirmed cases of leptospirosis admitted to the Sassoon General Hospital Pune, Maharashtra.

METHODS

A prospective study was conducted with 52 clinically suspected & ELISA IgM confirmed patients of above 18 years of age admitted in Sassoon General Hospital, Pune from June 2012 to November 2014.Lepto IgM ELISA was performed using Pan Bio diagnostics manufactured by Inverness Medical Innervation Australia. Demographic (age, sex, and occupation), Epidemiological data (type of contact, duration between onset of symptoms and admission to hospital, and place of residence), symptoms and findings related to the disease (fever, nausea, vomiting, diarrhea, headache, abdominal pain, muscle pain, jaundice, oliguria, hemorrhagic phenomenon, hypotension, tachypnea, cough, disturbance of consciousness, and neck stiffness), hepatomegaly, splenomegaly, meningism were recorded. Laboratory investigations included hemogram, Serum sodium, potassium, bilirubin, aspartate aminotransferase, alkaline phosphatase, Prothrombin time, creatinine, urea, creatine phosphokinase, LDH, and proteinuria. Duration of symptoms, length of hospital stays, supportive treatment, need of dialysis and complications were analyzed. Dialysis was indicated in those patients that remained oliguric after effective hydration and mechanical ventilation required with severe respiratory failure. The study protocol was reviewed and approved by the Ethical Committee of the Institution.

Statistical Analysis

The results were expressed through tables and summary measures (mean ± standard deviation) in the cases of quantitative variables. Statistical analysis was performed through the software's SPSS 10.0 (SPSS Inc. Chicago, IL, USA) and Epi Info, 6.04b, 2001 (Centers for Disease Control and Prevention, USA). The student's t test, Fisher's exact test and Wilcoxon test when appropriate. The descriptive values below 5% (p value < 0.05) were considered statistically significant.

RESULTS

A total of 52 (35 icteric & 17 unicteric) pts were included. In icteric group 22(63%) pts were between 21 to 40 years of age , 28 (80%) were males , 14(40%) farmers , 8(23%) labourers, 4(11%) carpenters, 4(11%) housewives ,onset of symptoms were < 5 days in 14(40%), 6- 10 days in 10(29%),> 10 days in 11(31%) , Environmental exposure in 17(49%) & 28(83%) resided in rural area while 6(17%) resided in urban area In unicteric group 10(59%) pts were between 21 to 40 years of age , 12(71%) were males , 4(24%) farmers , 4(24%) housewives ,5(29%) labourers, onset of symptoms were < 5 days in 3(18%), 6- 10 days in 7(41%),> 10 days in 7(41%) , Environmental exposure in 9(53%) & 6(35%) resided in rural area while 11(65%) resided in urban area. P value was statistically significant for Rural residence ($p< 0.001$) in icteric group.

In icteric group Main symptoms at admission were fever 35(100%), jaundice 35(100%), myalgia 31(89%), headache 13(76%), arthralgia 13(76%), GI symptoms 12(34%), chills/rigors 35(100%) calf

pains 35(100%), anorexia25(71%) ,oliguria 10(29%) , altered sensorium 8(23) while in unicteric group main symptoms at admission were fever 17(100%), arthralgia 13(76%), myalgia 12(71%), headache 3(18%), GI symptoms 4(24%), chills/rigors 8(47%) calf pains 8(47%), anorexia5(29%) ,oliguria 4(24%).Jaundice ($p < 0.0001$) ,Chills /Rigors ($p < 0.0001$), calf pain ($p<0.001$) ,cough($p< 0.05$) , dyspnoea ($p < 0.05$), bleeding manifestations($p< 0.01$) & altered sensorium ($p<0.005$) were statistically significant for icteric leptospirosis

In icteric group main signs at admission were Tachycardia 23 (66%), hypertension 3(9%), tacypnoea 2(6%), pallor 9(26%), dehydration 4(11%) , conjunctival suffusion 26(74%), petechie 11(33%), hepatomegaly 16(30.76%), splenomegaly 5 (14%) , while in unicteric group main signs at admission were Tachycardia 7(41%), hypertension 1(6%) ,pallor 1(6%), dehydration 1(6%), conjunctival suffusion 9(53%), petechie 1(6%), splenomegaly 2 (12%) . Pallor ($p<0.05$) & hepatomegaly ($p<0.0001$) was statistically significant for icteric leptospirosis.

In icteric group Hb was less than 11 in 18(51%), leucocytosis 33(94%), thrombocytopenia 28(80%) , acute kidney injury 18(51%), hyperbilirubinemia 35(100%), SGOT rise in 28(80%),SGPT rise in 29(83%),abnormal PT 15(43%), hyponatremia 5(14%), hypokalemia 17(49%),high LDH 20(57%) ,high CPK 17(49%) , proteinuria 5(14%), microscopic hematuria 2(6%) while in unicteric leptospirosis Hb was less than 11 in 6(35%), leucocytosis 17(100%), thrombocytopenia 8(47%) , acute kidney injury 5(29%), hyperbiliru binemia 6(35%) ,abnormal PT 1(2%), hyponatremia 3(18%), hypokalemia 3(18%),high LDH 3(18%), high CPK 3(18%), proteinuria 3(18%). Thrombocytopenia ($p<0.05$), hyperbiliru binemia ($p<0.001$),SGOT rise ($p<0.001$) &SGPT rise($p<0.001$),prolonged PT ($p<0.01$) , Hypokalemia($p<0.001$),high LDH ($p<0.01$),high CPK($p<0.05$) were statistically significant for icteric leptospirosis.

In icteric group complications were present in 35(100%) , AKI 18(51%), Hepatitis 35(100%), aseptic meningitis 2(6%), ARDS 1(3%) while in unicteric leptospirosis complications were present in 5(29%), AKI 5(29%), Hepatitis 1(6%). AKI ($p<0.0001$) was statistically significant for icteric leptospirosis. In icteric leptospirosis Hemodialysis required in 9(26%) pts and mechanical ventilation required in 2(6%), Death occurred in 2(6%) patients , Duration of hospital stay was < 7 days in 3(9%) & > 7 days in 32(91%) while in unicteric leptospirosis none required HD,MV or death occurred & duration of hospital stay was < 7 days in 9(53%) & > 7 days in 8(47%). Duration of hospital stay ($p<0.0001$) of > 7 days was statistically significant for icteric leptospirosis.

DISCUSSION

Leptospirosis is the most widespread zoonosis in the world, particularly in warm and humid places as in tropical countries like India. The transmission usually results from direct or indirect exposure to the urine of leptospiruric animals. Many cases of leptospirosis remain unrecognized because of the lack of specificity of signs and symptoms. Confirmation of the diagnosis is also difficult because of problems associated with isolating the organism and serological testing [8]. A better understanding of the clinical and paraclinical findings of leptospirosis is required to enhance its recognition and appropriate treatment.

It is important to identify the serovars associated with leptospires as clinical presentation may differ. Andrade et al [9] identified the serovars Icterohaemorrhagiae (71%) and Copenhageni (18%). Jauréguiberry et al [10]. Identified the serovars Grippotyphosa (30%), Icterohaemorrhagiae (15%) and Copenhageni (12%). We could not identify specific serovas as Lepto IgM ELISA test was performed however Lepto IgM ELISA is the test of choice for diagnosing current leptospiral infection [11] and is more easy to perform and sensitive than microscopic agglutination test but cannot determine the infecting serovar.[12]Various studies done in the past have studied clinical presentations [12-14] in leptospirosis however no study in the literature mentions about comparison of clinical presentations in icteric vs nonicteric leptospirosis Hence an attempt is made here to study the clinical profile and outcome of leptospirosis in general and comparison has been made in icteric and Nonicteric presentations. Our study included 52 patients & all were Lepto IgM positive.

Being a tertiary care teaching hospital the cases described here represent severe end of the spectrum of leptospirosis. The icteric leptospirosis (n=22 ,63%) as well as unicteric leptospirosis (n=10,59%) is common among young people between 21 to 40 years of age & is not statistically

significant for either group. Various investigators in the past have found leptospirosis in this age group only [2, 13, 15, 16]. The preponderance of cases between 21 and 40 years of age shows that leptospirosis is common in the working population who are most likely to be exposed to this organism. In our study though three fourth patients were males (n= 40,77%) as against females(n=12,23%), we did not find statistically significant association in gender distribution amongst icteric and unicteric leptospirosis. More preponderance of leptospirosis im males could be due active outdoor activities acquiring infection in male population. Male preponderance was reported by Muthusethupathi et al [12] in 88% of patients , by Singh et al in 86.2% [13].

Farming is classically an occupation at increased risk. Mansour- Ghanaei et al [2] found it in (60%). We observed disease preponderance in farmers in 34.61 %, followed by labourers (25%).However none of the occupation has statistically significant association for either icteric or unicteric leptospirosis.

Though 14(82%) patients with unicteric leptospirosis had duration of symptomatology > 6 days we could not find significant bearing for either icteric or unicteric leptospirosis(p=0.284). In our study, maximum (n=35, 83%) patients from rural area had icteric leptospirosis as against unicteric leptospirosis (n=6,17%) & has significant association with icteric leptospirosis (p< 0.001) and we attribute it to exposure of rural population to environmental factors as well as open shoe or barefoot walking.

Overall in pts of leptospirosis in the present study , main clinical findings were fever 52(100%), arthralgia 44(84.61%), chills/rigors 44(84.61%) calf pains 43(82.69%), myalgia 43 (82.69%), jaundice 35(67.30%), anorexia 30(57.69%), headache 16(30.76%), GI symptoms 16(30.76%), oliguria 14(26.92%), altered sensorium 8(15.38) , conjunctival suffusion 35(67%) , tachycardia 30(57.69%) , hepatomegaly 16 (30.76%), petechie 12(23%), pallor 10(19.23%), splenomegaly 7(17.30%) hypertension 4(7.69%), hypotension 2(3.84%), tachypnoea 2(3.84%) Overall these are the common clinical findings reported by various investigators in leptospirosis [1-3, 10, 12-14, 17-19]. However, there was statistically significant difference betwe en icteric and unicteric group. Jaundice (100 % vs 00% , p<0.0001), chills/rigors(100% vs 47%, p<0.0001),calf pain (100% vs 47% , p<0.001), cough (15% vs 00%, p < 0.05) , dyspnoea (15% vs 00% , p< 0.05) ,bleeding (31% vs 6% , p<0.01) , altered sensorium (14% vs 00% , p<0.001), pallor (26 % vs 6% ,p<0.05) & hepatomegaly(46% vs 00% ,p<0.001) had statistically significant association for icteric leptospirosis We conclude that chills/rigors,calf pain, cough, dyspnoea, bleeding , altered sensorium, pallor , hepatomegaly are to be considered as clinical pointers to icteric leptospirosis.

In our study hemoglobin less than 11 gm/dl was observed in 24(46.15%), .Leucocytosis in 50 (96.2%), thrombocytopenia in 36(69.23 %), serum creatinine after correcting dehydration was seen in 23(44.23%), hyperbilirubinemia 41(78.84%), SGOT rise in 28(53.54%), SGPT rise in 29(55.76%), ALK phosphatase rise in 2(3.80%), abnormal PT in 16(30.76%), hyponatremia 8(21.15%), hypokalemia 20(38.46%),high LDH 23(44.23%), high CPK in 20(38.46%) , microscopic hematuria 2(4%). Laboratory parameters in our study suggests hepatocellular inflammation, hypokalemia, acute kidney injury and probably skeletal muscle inflammation. Overall, these were the laboratory finding reported by various investigators in the past [6, 18]. However, there was statistically significant difference in laboratory findings in icteric vs unicteric leptospirosis. Thrombocytopenia (80% vs 47%, p<0.05) ,hyperbilirubinemia (100% vs 35% ,p <0.001),SGOT rise (80% vs 00%, p<0.001) , SGPT rise (83% vs 00%, p<0.001), prolonged PT(43% VS 3%, p<0.01), hypokalemia (49% vs 14% , p<0.01) , LDH rise (57% vs 18%, p<0.01),CPK rise (49% vs 18%,p<0.05) had statistically significant association for icteric leptospirosis. We conclude that Thrombocytopenia, hyperbilirubinemia, SGOT, SGPT, LDH, CPK rise, prolonged PT, hypokalemia can be considered as laboratory pointers for icteric leptospirosis. Abnormal chest radiographs were documented in 11% to 67% of leptospirosis cases in previous studies [20]. In our study only two patients from icteric group had abnormal XRC suggestive of ARDS & both required mechanical ventilation.

In our study 73.07% (n=38) patients had complications. All icteric patients 35 (100%) had complications as against in unicteric 5(29%) leptospirosis & is statistically significant for icteric leptospirosis (p<0.001). Overall MODS 17(32.69%), Acute kidney injury 23(44.23%) ,hepatitis 16(30.76)., aseptic meningitis 2(3.84%) , ARDS 1(1.92%) were the complications . Various investigators in the past have reported AKI (72%, 63%, 40%) [12, 21, 22], hepatitis (84%,71%) [14, 22]. In our study hepatitis (p<0.0001) was found to be statistically significant for icteric hepatitis. Out of 23 patients of acute kidney

injury in present study haemodialysis required in 9. (17.3%). patients & all 9 were from icteric group (23%) Our study differs from other studies Muthusethupathy et al reported dialysis in 40.35% [12]. Two patients (6%) with leptospirosis required mechanical ventilation due to ARDS & both had icteric leptospirosis. In a study by Muthusethupathi, MA, et al., 2% patients required ventilation [12]. Mortality in leptospirosis has ranged from 1% to 25% [23]. In our study 2 patients died of ARDS & both had icteric leptospirosis. Though statistically not significant we suggest that patients with icteric leptospirosis may require hemodialysis & mechanical ventilation for case management & mortality may occur in icteric leptospirosis hence physician should be very alert in patients with icteric leptospirosis. Hospital stay of < 7 days required in 9(53%) patients with unicteric & > 7 days in icteric 32(92%). Hospital stay of > 7 days is statistically significant for icteric hepatitis hence we suggest to inform patient and relatives about possible requirement of > days stay for icteric leptospirosis.

CONCLUSIONS

Though disease preponderance was found to be more in males between 21 to 40 yrs of age, in farmers & labourers,, age , gender , occupation was not found to be significant for icteric or unicteric leptospirosis. However icteric leptospirosis affects more rural population. The wide spectrum of nonspecific constitutional signs and symptoms associated with acute leptospiral infections necessitates a high degree of clinical suspicion for timely diagnosis. Jaundice Chills/rigors,calf pain, cough , dyspnoea, bleeding , altered sensorium, pallor , hepatomegaly, Thrombocytopenia, ,hyperbilirubinemia, SGOT, SGPT, LDH, CPK rise, prolonged PT, hypokalemia are to be considered as clinical & laboratory pointers to icteric leptospirosis. All icteric patients suffer from complications & Hepatitis, AKI and Multiple organ failure, aseptic meningitis were the complications. Hepatitis is significant for icteric leptospirosis. patient's Icteric leptospirosis may require hemodialysis & mechanical ventilation, hospital stay of > 7 days for case management & mortality may occur in icteric leptospirosis. Present study which elaborates on clinical, laboratory findings and complications, need for dialysis & mechanical ventilation may be helpful to health care physicians working in limited laboratory resource setting for identifying and treating patients of leptospirosis to improve outcome.

Limitations

Sample size is small. Being tertiary care referral hospital, milder forms are not getting admitted Similarly leptospirosis cases may not even reach tertiary care center for treatment as they can succumb to death without getting diagnosed. Hence sample do not include all types of patients of leptospirosis. As Lepto IgM ELISA test was used for diagnosing leptospira, conclusions do not apply for various serotypes. Liver biopsy & kidney biopsy was not performed for pathological diagnosis .

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