DOI: 10.14260/jemds/2014/3738

ORIGINAL ARTICLE

CLINICAL IMPACT OF LEPTOSPIROSIS ON PREGNANCY: AN ANALYSIS

Madhu Udawat[1], G. Sumathi[2], J. Nithyalakshmi[3], Mohana Krishnan[4]

HOW TO CITE THIS ARTICLE:
Madhu Udawat, G. Sumathi, J. Nithyalakshmi, Mohana Krishnan. "Clinical Impact of Leptospirosis on Pregnancy: An Analysis". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 58, November 03; Page: 13071-13078, DOI:10.14260/jemds/2014/3738

ABSTRACT: BACKGROUND: Leptospirosis is one of the most widespread zoonotic diseases in the world. Infection may range from subclinical infection to death of the patient, although majority of the cases are mild and self-limited. **AIMS & OBJECTIVES:** The present study was carried out to determine the clinical impact of leptospirosis in pregnant women attending antenatal clinic of our tertiary care hospital. **METHODS & MATERIALS:** In this case control study, blood samples from pregnant women who attended routine antenatal check- up during March 2008 to March 2010 were included the study. A total of 33 cases and 237 controls were compared during the study period. The diagnosis was made by performing the two serological tests: (i) The rapid screening test – Macroscopic Slide Agglutination Test (MSAT) and the other (ii) the confirmatory test – Microscopic Agglutination Test (MAT). **RESULTS:** Out of 270 patients, 33 (17.9%) were found to be positive for leptospirosis by Microscopic Agglutination Test (MAT) and 35 (19%) by Macroscopic Slide Agglutination Test (MSAT).The biochemical parameters like SGPT, SGOT were found to be elevated. Increased awareness among pregnant women is of utmost important for early detection & treatment of the disease and thus, for the safety of the fetus.

KEYWORDS: Leptospirosis, stillbirth, pregnancy, fever.

INTRODUCTION: Leptospirosis is one of the most widespread zoonotic diseases in the world. Infection may range from subclinical infection to death of the patient. It may occur endemically in tropical countries, showing seasonal incidences following heavy rainfall. As the diagnosis is difficult due to vague clinical symptoms, laboratory investigations are essential for the confirmation of the disease. (1)

The core determinants of transmission of leptospiral infection are the presence of carrier animals, suitability of the environment for the survival of leptospires and interaction between man and animals & environment. The mode of transmission of leptospirosis is categorized as direct or indirect depending upon the immediate source of infection. When the immediate source of infection is animal tissue, body fluids or urine, the transmission is termed as direct. Cattle and pig farmers, veterinarians, butchers, laboratory personnel who handle laboratory animals etc are at high risk for contacting leptospirosis by direct transmission.

When the immediate source of infection is environment contaminated with the urine of the carrier animals, the transmission is termed as indirect. Agricultural workers, Sewage workers, people walking bare foot in water logged areas, sportspersons who participate in water related sports such as rafting, canoeing, swimming etc are at the high risk of contracting the disease through indirect transmission. However the specific risk factors of infection vary from one epidemiological setting to another.(2)

Many places in South India are known to be endemic to leptospirosis. These include Chennai in the state of Tamil Nadu. (3) Leptospirosis has been reported from Chennai since 1980's.(4)

DOI: 10.14260/jemds/2014/3738

The rate of maternal-fetal transmission is not known but leptospirosis could not be uncommon cause of prenatal deaths in endemic areas.[5] It appears that women are more likely to spontaneously abort if leptospirosis occurs in the early months of pregnancy.[6]

Very little is currently known regarding the true incidence of Leptospirosis. The incidence rate ranges from 0.1 – 1/100, 000 per year in temperate climates to 10- 100/100, 000 in tropical countries. During outbreak the incidence may reach over 100/100, 000. Hospital based data on clinical manifestations confirmed by laboratory tests (Rapid tests / MAT) are usually needed to obtain the incidence rates.

In a recent study of 500 cases of fever at government Stanley hospital, leptospirosis was the second common cause of fever contributing to 17%, following malaria which was 27 %.[7]

Coinfection of leptospirosis (48 cases) with malaria (220 cases) occurred in 22% of cases.[8]

Co-infection of Malaria and Leptospirosis has been reported from Chandigarh. A sero survey in Chennai revealed a seroprevalence rate of 32.9% (Range 17.8% - 40.5%).[9]

Serology is the most frequently used diagnostic approach for leptospirosis.[10] MSAT is a valuable and simple screening test. The Sensitivity of this test is enhanced by adding locally prevalent serovars.[11] Rapid diagnosis of leptospirosis is therapeutically important and is effective only when administered early in the course of illness.[12]The Microscopic agglutination test (MAT) is the reference test for serological diagnosis of leptospirosis, because of its high sensitivity and specificity.[10]

MATERIALS & METHODS:

METHODS: Study area: This study was carried out in our tertiary level referral and teaching hospital, which is serving the population of Chennai.

Study Design: In this case control study, blood samples from pregnant women who attended routine antenatal check- up during March 2008 to March 2010 were included. The study group was thoroughly investigated and clinically assessed.

Diagnostic Criteria:

Cases: Pregnant women with clinical symptoms suspicious of leptospirosis as defined by clinical criteria, history of fever for more than seven days accompanied with any of the following manifestations i.e. severe headache, prostration, severe myalgia, conjunctival suffusion, uveitis, arthralgia, rash, hepato-splenomegaly, evidence of hemorrhage, renal failure, icterus, aseptic meningitis, acute respiratory distress syndrome (ARDS) and pulmonary hemorrhage along with single high titre of MAT were included in this study as cases.[12]

Inclusion Criteria:

1. All possible infectious causes leading to serious obstetric complications were ruled out by doing appropriate test during routine antenatal checkup. Those who found to be negative were included.
2. Pregnant women without any lethal congenital malformation or maternal factors like uterine abnormalities, cervical insufficiency, trauma, hypertension, Diabetes mellitus or any other chronic disease that can lead to abortion, stillbirth and premature rupture of membranes were included in this study.

DOI: 10.14260/jemds/2014/3738

Exclusion Criteria:

1. Pregnant women who had symptoms suggestive of leptospirosis but low titre by MAT were excluded. We excluded all pregnant women who had visited antenatal clinic during the study period, with clinical features suggestive of leptospirosis but negative by MAT.

Healthy Controls: Control group comprised of pregnant women who have visited our hospital during the same study period and presented without any history suggestive of leptospirosis and whose serum samples had not shown any titre by MAT.

A total of 33 cases and 237 controls were compared during the study period. The blood serum samples from these 270 pregnant women were collected and subjected to two serological tests:

i. The rapid screening test – Macroscopic Slide Agglutination Test (MSAT) and the other
ii. The confirmatory test – Microscopic Agglutination Test (MAT).

The MAT was performed with eight live leptospiral strains as antigens which include L. icterohaemorrhagiae, L. australis, L. canicola, L. grippotyphosa, L. louisiana, L. pomona, L. hebdomadis and L. sejroe. MAT was done using doubling dilutions starting from 1:20. The patient's serum was initially doubly diluted in phosphate buffer saline solution up to the dilution of 1 in 640.

Live leptospira cell suspension were added to serially diluted serum specimens in 96 well flat bottomed microtiter plates and incubated at 37^0C for 2 hours. Agglutination was examined by dark field microscopy at a magnification of 100X. The reported titer was calculated as the reciprocal of the highest dilution that agglutinated at least 50% of the cells for each.[12]

The significant titre for the MAT was 1 in 80 dilution. Positive samples were titrated upto end titres. It has been shown that 1:50 is the ideal cut off for nonendemic areas and titre of 1:80 is ideal for highly endemic area like Chennai in various previous study conducted in chennai. A titre of 1:80 was considered positive.[11,13,14]

MSAT was performed by adding one drop of patient serum and one drop of polyvalent antigen together. A 4+ agglutination titre by MSAT was considered to be a significant titre. [11,15,16]

Statistical Analysis: Odds ratios (OR) of leptospirosis and 95% confidence intervals (95% CI), according to fever history, were calculated.

RESULTS: Among the 270 cases studied, 33 cases (17.9%) were reported positive for leptospirosis by the confirmatory serological test MAT and 35 cases (19.0%) were reported to be positive by screening test Macroscopic Slide Agglutination Test (MSAT).

All the women had fever and vomiting; one had diarrhea; one had polyarthralgia and facial puffiness and one had polyhydramnios [Table-I].The laboratory tests showed a slight elevation in the serum creatinine level (>1µ/dl) in the positive cases, while all the control individuals had less than 1µ/dl. The SGPT and SGOT levels were found to be high in the positive cases when compared to the control individuals. The hemoglobin level was decreased in positive cases when compared to the normal controls. The platelet parameters were normal in all the cases. There were no traces of albumin and sugar deposits in all the patients [Table-II].

DOI: 10.14260/jemds/2014/3738

Out of these 33 positive cases 6 cases had stillbirth, one had pre-term baby, two women had premature rupture of membranes and 24 cases were uneventful [Table-III].

Among the 237 controls, 16 had premature rupture of membrane. Except for them, delivery was uneventful in all pregnant women. Both mother and child were found to be healthy after delivery in all the control female. In this study, a five- fold increase in risk was associated with MAT positive leptospirosis cases than negative patients (OR = 5.7: 95% CI 2.06 to 12.9)

L. australis was found to be the predominant serogroup in this study by affecting 18 pregnant women among the 33 probably causing 2 still births and 1 premature rupture of membranes. L. icterohaemorrhagiae was found have played a vital role by affecting 11 pregnant women among the 33 positive cases and probably causing 4 still births and 1 premature rupture of membrane. While, L. grippotyphosa were found among 4 pregnant women and those were uneventful.1 preterm women was found to be serologically positive for by L. australis.

SYMPTOM	NUMBER OF PATIENTS	PERCENTAGE (%)
Fever	33	100
Vomiting	20	60.6
Bodyache	17	51.5
Headache	12`	36.3
Rigors	9	27.2
Diarrhea	1	3.0
Facial Puffiness	1	3.0
Polyhydramnios	1	3.0

Table 1: Clinical frequency

CATEGORY	SERUM CREATININE	HEMOGLOBIN	SGPT[1]	SGOT[1]	URINE ALBUMIN SUGAR DEPOSIT
Controls (n=237)	< 1.0µ/dl	12.0-14.0 gm%	10-35 IU/ml	10-40	Nil
Cases (n=33)	1.0-1.5 µ / dl	8.0 – 10.0 gm%	100-150IU/ml	90-110	Nil

Table 2: Bio-Chemical Tests

[1] Normal Value: SGPT/SGOT: 6-40IU/ml

TOTAL POSITVE CASES	OUTCOME/CLINICAL COURSE	NUMBER OF CASES	MAT SEROGROUPS
	Stillbirth	6	L.icterohaemorrhagiae(4) L.australis(2)
	Premature rupture of	2	L.icterohaemorrhagiae(1)

DOI: 10.14260/jemds/2014/3738

33	membrane		L.australis(1)
	Pre-Term	1	L.australis(1)
	Uneventful	24	L.icterohaemorrhagiae(6) L.australis(14) L.grippotyphosa(4)

Table 3:Outcome and MAT Distribution

DISCUSSION: Leptospirosis has protean clinical manifestations. It is classically presents as a biphasic illness both icteric and anicteric form of leptospirosis. The clinical manifestations of leptospirosis ranging from inapparent infection to fulminant disease. The incidence of leptospirosis, a widespread anthropozoonosis, is underestimated due to variable clinical presentations.

The majority of the patients in this study had nonspecific signs and symptoms. Fever was the most common symptom followed by vomiting and bodyache. The clinical findings of our study are similar to the observation reported by Alora et al. In his review study, prominent features described were fever, myalgia, headache, pharyngitis, abdominal pain, nuchal rigidity, conjunctival suffusion.[17]

The clinical findings of this study can be compared with Philippine retrospective studies in which fever, calf tenderness and conjunctival suffusion were the most prominent features.[18]

Consistent with previous reports of leptospirosis the disease usually presents with fever as the most common presenting symptom. Fever was a consistent finding; therefore, a diagnosis of leptospirosis in an afebrile patient may make the diagnosis doubtful.[19,20]

In the earlier studies, Jaundice used to be prominent but in our study among pregnant women, none of the positive cases had jaundice. This is consistent with the recent study in a general population from Chennai that Anicteric leptospirosis was the common clinical presentation.[21] A similar observation was also reported from Vietnam.[22] This could be due to screening all pregnant women at the early stage, admitted with fever for leptospirosis utilizing MSAT and MAT.

Biochemically, the characteristic features of biochemical profile showed a slight elevation in aminotransferases and serum creatinine. [Table 2].

This is in accordance with the findings by Ahmed et al., who reported a slight elevation in aminotransferases in active leptospirosis at the early week of illness.[23] Elevated serum creatinine (82.7%), and elevated liver function tests were the notable common laboratory abnormalities in the study signifying the involvement of major organs like the liver and kidneys among the Leptospirosis cases.[24] In studies done by Sulit (1963) and Reyes (2001) elevated liver function test, albuminuria and pyuria were also found.[25] Sulit et al., also reported that one of the outstanding feature of the disease was ARF and all the cases seen had oliguria and azotemia.

This is in contrast to our study where no patients suspected or positive for leptospirosis found to have jaundice or oliguria. A similar study about leptospirosis in pregnant woman, also reported a mild elevation in liver enzymes. [26]

In Table 3, clinical outcome of active leptospirosis on pregnant women were shown. Titre was found to be positive in 1:1280, in all these 9 cases, which is significantly very high and this would suggest that the probable cause for the serious obstetric complication could be due to active leptospirosis in this study group.

Leptospirosis is an important cause of abortion in animals; however data regarding its occurrence and its impact on human fetus is scanty. These findings are in accordance with the study reported by Shaked et al., who found that eight women with active leptospirosis had abortion. [27]

An another study in French Guyana in 11 cases of leptospirosis in pregnant women, more than 50% were associated with abortion.[28] Similarly in another case of leptospirosis in a pregnant woman at 23 weeks gestation had flu like illness, an intrauterine fetal death was confirmed by ultrasound. Serology demonstrated positive IgM for leptospira and for Microscopic agglutination test & the infecting serovar was Leptospira hardjo. [29] Bal M et al., also observed leptospirosis, early in pregnancy often leads to abortion. [30]

CONCLUSION: It is imperative that high index of suspicion should be maintained particularly in endemic areas like Chennai. Clinicians need to be aware of the possibility of leptospirosis especially in pregnant women as they usually present with nonspecific symptoms.

REFERENCES:

1. Jagadish Chandra K, Prathb AG, Rao SP. Clinical and Epidemiological correlation of Leptospirosis among patients attending KMCH, Manipal. Indian Journal of Medical Science. 57:101-104.
2. Sehgal SC. Epidemiological patterns of leptospirosis. Indian Journal of Medical Microbiology. 24:310-311
3. Kalimuthusamy Natarajseenivasan, Marimuthu Boopalan, Krishnaswamy Selvanayagi, Sudalaimuthu Raja Suresh, Sivalingam Ratnam. Leptospirosis among rice mill workers of Salem, South India. Japan Journal of infectious diseases 55:170-173.
4. Ratnam S, Subramanian S, Madanagopalan T. Isolation and demonstration of antibodies in human leptospirosis in Madras, India. Transactions of the Royal Society of Tropical Medicine and Hygiene 77:455-458.
5. Carles G, Montoya E, Joly F, Peneau C. Leptospirosis and Pregnancy. Eleven Cases in French Guyana. Journal of Gynaecology Obstetrics Biological reproduction (Paris) 24(4):418-421.
6. Shaked Y, Shpilberg O, Samra D, Samra Y. Leptospirosis in pregnancy and its effect on the fetus: Case report and review. Clinical infectious diseases 17(2):241-243.
7. Loganathan N, Shivakumar S, Ravishankar D. Co-infection of Malaria and Leptospirosis – A Study of 48 cases (Abstract).62nd Annual Conference of Association of Physicians of India 2007.Goa.
8. Srinivas R, Agarwal R, Gupta D. Severe sepsis due to severe Falciparum Malaria and leptospirosis co-infection treated with activated Protein C. Malaria Journal 2007.6:42.
9. Ratnam S, Evarard COR, Alex JC et al. Prevalence of leptospiral agglutinins among conservancy workers in Madras City, India. Journal Of Tropical Medicine and Hygiene 1993; 96:41-45.
10. Cumberland P, Everard CO, Levette PN. Assessment of the efficacy of IgM ELISA and Microscopic agglutination test (MAT) in the diagnosis of leptospirosis. American Journal of Tropical Medical Hygiene 61:731-734.
11. Sumathi G, Pradeep Kumar Subudhi CH, Helen PS Manuel, Kalpana, Shivakumar S, Suguna Rajendran, Muthusethupathi MA. Serodiagnosis of leptospirosis – A Madras study. Indian Journal of Medical Microbiology 13(4):192-195.

12. Faine S. Guidelines for the control of Leptospirosis. Geneva: World Health Organization publication 67.
13. Vijayachari P, Suganan AP, Sehgal SC. Role of microscopic agglutination test (MAT) as a diagnostic tool during acute stage of leptospirosis in low and high endemic areas. Indian J Med Res 2001; 114: 99-106.
14. Mazonelli J, Dorta DC, Mazonelli G, Mailloux M. Possibilite de diagnostic serologique Macroscopic des leptospires a paide d'un antigene unique Medicine et maladies infectieusues 4:252-254.
15. Muthusethupathi MA. Shivakumar S. Sumathi G. Pradeep Kumar Sumathi et al. Serodiagnosis of leptospirosis – A Madras study (1994-5). Indian J Med Microbiology 1995; 13(4), 192-195.
16. Sumathi G, Chinari Pradeep KS, Shivakumar S. MSAT – A Screening test for leptospirosis Indian Journal of Medical Microbiology 15 (2):84.
17. Alora B, Nambayan A, Perez J, Famatiga E, Tan Alora A. Leptospirosis in Santo Tomas University Hospital: analysis of 17 cases, 1967-71. Phil J Microbiol Infect Dis 1973; 2: 11-22
18. Manaloto CR, Alora AT, Alora BD. Leptospirosis: an analysis of 29 cases (Jan 1974-Dec 1975). Phil J Microbiol Infect Dis 1980; 9: 75-81.
19. Casiple L. Thrombocytopenia and bleeding in leptospirosis. Phil J Microbiol Infect Dis 1998; 27: 18-22.
20. Cordero C, Valdez J. The impact of the algorithm for the diagnosis and treatment of cases of acute renal failure secondary to leptospirosis at the UP-PGHMC. Phil J Intern Med 2000: 249-64.
21. Muthusethupathi MA, Shivakumar S. Leptospirosis in Chennai. A clinical & serological study. J. Assoc. phys. India. 1995; 43: 456-58.
22. Steven J Berman. Che-chang Tsai. Sporadic Anicteric leptospirosis in South Vietnam. Annals of Internal medicine. 1973; 79:167- 73.
23. SN Ahmad, S Shah, FM H Ahmad. Laboratory diagnosis of leptospirosis 2005; vol 51. Issue: 3; 195-200.
24. Gaurang Parmar, Dilip Kava, Shreyash Mehta, Kallol Mallick, Rachana Prasad, RK Bansal, Mihir Rupani. Socio-Demographic, Clinical And Laboratory Profile Of Leptospirosis Cases Registered At Smimer, Surat. National Journal of Community Medicine; Jul-Sep2013, Vol. 4 Issue 3, p507.
25. Sulit Y. Features of Weil's disease. A review of cases seen in the Philippine General Hospital with comments from the literature. Acta Medica Philippina 1963; 19 (4): 1-22
26. Gaspari R, Annetta MG, Cavaliere F, Pallavicini F, Grillo R, Conti G, Antonelli M, Tafani C, Proietti R. Unusual presentation of leptospirosis in the late stage of pregnancy 2007 jul-aug; 73 (7-8): 429-32.
27. Shaked Y, Shpilberg O, Samra D, Samra Y. Leptospirosis in pregnancy and its effect on the fetus: Case report and review. Clinical infectious diseases 17 (2): 241-243
28. Carles G, Montoya E, Joly F, Peneau C. Leptospirosis and Pregnancy. Eleven Cases in French Guyana. Journal of Gynaecology Obstetrics Biological reproduction (Paris) 24 (4): 418-421.
29. Aker N, Elizabeth B James, Johnston AM, Pasvol G. Leptospirosis and pregnancy: An Unusual relatively unrecognized and cause of intrauterine death in man. Journal of Obstetrics and Gynaecology 16: 163-165.
30. Bal AM. Unusual clinical manifestations of leptospirosis. Journal of Post graduate Medicine 51 (3): 179-183.

DOI: 10.14260/jemds/2014/3738

ORIGINAL ARTICLE

AUTHORS:

1. Madhu Udawa
2. G. Sumathi
3. J. Nithyalakshmi
4. Mohana Krishnan

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Obstetrics and Gynaecology, SMMCRI.
2. Professor and HOD, Department of Microbiology, SMMCRI.
3. Associate Professor, Department of Microbiology, SMMCRI.
4. Professor, Department of Microbiology, SMMCRI.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. J. Nithyalakshmi,
5/7, Sethammal Colony,
Varalakshmi Apartments,
Alwarpet, Ch-18.
Email: nithya.smmcri@gmail.com

Date of Submission: 12/10/2014.
Date of Peer Review: 14/10/2014.
Date of Acceptance: 29/10/2014.
Date of Publishing: 31/10/2014.