Case Report

Dengue infections during pregnancy: case series from a tertiary care hospital in Sri Lanka

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Abstract

Introduction: Dengue is the most important mosquito-borne disease in Sri Lanka, leading to more than 340 deaths during the last outbreak (≈35,000 reported cases) starting in mid April 2009. The predominant dengue virus serotypes during the last few years have been DENV-2 and DENV-3. Dengue infection in pregnancy carries the risk of hemorrhage for both the mother and the newborn. Other risks include premature birth, fetal death, and vertical transmission.
We report clinical and laboratory findings and outcomes in pregnant women hospitalized with dengue infection during pregnancy.
Methodology: Clinical, laboratory, maternal/fetal outcomes and demographic data were collected from patients with confirmed dengue infections during pregnancy treated at De Soysa Maternity Hospital, Sri Lanka from 1 May 2009 to 31 December 2009.
Results: Fifteen seropositive dengue infected pregnant women were diagnosed in the period. Multiorgan failure leading to intrauterine fetal and maternal death occurred in one case of dengue hemorrhagic fever (DHF) IV. One patient with DHF III had a miscarriage at the 24th week of gestation. Perinatal outcomes of the other cases were satisfactory. One woman developed dengue myocarditis but recovered with supportive treatments. No cases of perinatal transmission to the neonate occurred.
Conclusion: Dengue in pregnancy requires early diagnosis and treatment. A high index of clinical suspicion is essential in any pregnant woman with fever during epidemic. Further studies are mandatory as evidence-based data in the management of dengue specific for pregnancy are sparse.

Introduction

Dengue infection is a febrile illness caused by four closely related dengue virus serotypes (designated DENV-1, DENV-2, DENV-3, and DENV-4) of the genus Flavivirus, family Flaviviridae. The clinical severity of disease has a wide spectrum and according to the World Health Organization (WHO) dengue classification scheme, there are four grades ranging from uncomplicated dengue fever (DF) to dengue hemorrhagic fever (DHF) and devastating dengue shock syndrome (DSS). Dengue is the most important mosquito-borne (by *Aedes aegyptii*) disease in Sri Lanka and epidemics have become more common, causing more than 340 deaths throughout the island up to now during the last outbreak, starting in mid April 2009, with ≈35,000 reported cases [1-3]. Significant outbreaks of dengue occur every few years due to the presence of all four viral serotypes [4]. The predominant serotypes during the last few years were DENV-2 and DENV-3 [5]. Infection by one serotype produces lifelong immunity to that specific serotype but only a few months of immunity to the others [6].

Dengue infection in pregnancy carries the risk of hemorrhage for both the mother and the newborn. In addition, there is a risk of premature birth and fetal death and vertical transmission causing neonatal thrombocytopenia that necessitates platelet transfusions [7-11].
Diagnosis of dengue infection affects management options and decisions of the obstetricians, particularly the mode of delivery due to the potential risk of hemorrhage secondary to thrombocytopenia. Elevated liver enzymes, hemolysis and low platelet counts may be confused with the diagnosis of hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, which occurs in women with pre-eclampsia and eclampsia.

Positive serology/viral PCR studies confirm dengue infections [12]. Few case reports on dengue infections during pregnancy have been published from the South Asian subregion. Systematic analysis

of data from many case reports will help establish evidence-based management recommendations for treatment of dengue in pregnancy in the future.

Methodology

We studied all serologically diagnosed pregnant women treated for dengue from 1 May 2009 to 31 December 2009 at De Soysa Maternity Hospital, a tertiary care hospital in Colombo, Sri Lanka. Demographic data, clinical and laboratory findings, and maternal and fetal outcomes were documented prospectively during the hospital stays. The cases were followed up daily for their clinical and laboratory parameters.

Grading of the severity of dengue infections was done according to WHO classification and case definitions (WHO, 1999). Based on the WHO dengue classification scheme, the key differentiating feature between DF and DHF is the presence of plasma leakage in DHF. We used the presence of thrombocytopenia with concurrent hemoconcentration to differentiate grades I and II DHF from DF. DHF was classified into four grades of severity as follows: Grade I: fever accompanied with non-specific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test and/or easy bruising; Grade II: presence of spontaneous bleeding manifestations, usually in the forms of skin or other hemorrhages. Grades III and IV (profound shock) are considered to be DSS (WHO, 1999).

Dengue viral specific antibodies were detected using the PanBio (Inverness Medical Innovations, Brisbane, Australia) dengue duo IgM and IgG rapid strip test on a serum sample taken between 5 and 10 days after the onset of the disease. The laboratory maintained quality control of the test according to the manufacturer's instructions. If only dengue-virus-specific IgM antibodies were detectable in the test sample, the patient was considered to have a primary dengue infection, whereas the presence of both IgM and IgG was considered to indicate a secondary infection.

The elements of the complete blood cell counts were analysed with a Sysmex KX-21N (Sysmex Corporation, Kobe, Japan) multichannel automated hematology analyser capable of being calibrated on approved standards. A comprehensive daily internal quality control of the Sysmex KX-21 was achieved by the laboratory. Quantitative determination of activity of serum aspartate and alanine aminotransferases (AST and ALT) were performed with the 3000 Evolution Semi-automatic photometer, (Biochemical Systems International, Arezzo, Italy). Biochemistry laboratory has its own internal quality control procedures. Approved standards were maintained during blood sample collection and transport.

Results

Fifteen pregnant women seropositive for dengue [age range: 22-41 years] were included. Their clinical and laboratory findings are shown in Table 1. Three of them presented in the second trimester of pregnancy and 12 in their third trimester. Six patients had only IgM dengue-specific antibodies (primary dengue infection) and nine had both IgM and IgG dengue-specific antibodies (secondary dengue infection). Three had DF, three had DHF grade I, and seven had DHF grade II. DSS developed in two women (one had DHF III and the other had DHF IV). Low platelet counts were seen in both primary and secondary infections.

Most of the patients presented with classical constitutional features such as fever and myalgia. All the referred or self-consulted women we analyzed were in the second or third trimester. Women in early pregnancy may have been managed by physicians.

In one case there was multiorgan failure leading to intrauterine death of the fetus and maternal death (Case #06). She was a 27-year old, second gravida at 35-week gestation who presented with high-grade fever, malaise and myalgia for one week. She was admitted to Colombo North Teaching Hospital-Ragama, had stable vital signs, and there were no bleeding manifestations. The investigations showed a platelet count of $18,000/mm^3$ and positive serology (IgM and IgG). Within two days, she developed bleeding manifestations, vascular leakage (pleural effusion and ascites) with hemoconcentration (hematocrit increased from 38% to 49% in the initial few days after admission) and rapidly developed hepatorenal and cardiac failure and respiratory distress which needed positive pressure ventilation with 100% oxygen. She received 20 units of platelet-rich plasma and 10 units of fresh frozen plasma and platelet count was maintained above $15,000/mm^3$. Intrauterine death was detected by routine ultrasound scan three days later. She was transferred to our hospital for specialized management, but expired two days later due to dengue shock syndrome while awaiting hemodialysis.

A 41-year-old woman (Case #11) who presented in her second trimester deteriorated to DHF III but

recovered. She had fetal demise (at 24 weeks) and expelled vaginally during the recovery phase. No external anomalies or hemorrhagic features were noted. Postmortem examinations could not be performed in either of the fetuses who died *in utero*, due to refusal of consent.

Another patient (Case #02) was delivered by caesarian section due to acute genital herpes in labour and 1,500 cc platelet-rich plasma (PRP) was transfused to cover the cesarean delivery. Her preoperative platelet count was $30,000/\text{mm}^3$.

Patient #09 developed severe pre-eclampsia and caesarian section was performed in the recovery phase of infection. Elevated liver enzymes and low platelet counts with hypertension were confusing initially as HELLP syndrome was considered as a differential diagnosis. There were no features of hemolysis in the blood picture and DHF was diagnosed with subsequent positive dengue antibodies (IgM: positive IgG: Negative). As her platelet counts were $114,000/\text{mm}^3$ preoperatively, platelets were not transfused. Neither Case #02 nor Case #09 developed peri/postpartum hemorrhage and fetal outcomes were normal in both. The other elective caesarean section was performed following recovery from dengue since the patient (Case #12) declined trial of vaginal birth after a past cesarean delivery. Pre-operative platelet count was $178,000/\text{mm}^3$.

Three other women (Cases #01, #03, and #08) in their late third trimester and a woman in the second trimester (Case #05) recovered with supportive management including the platelet transfusions. Uncommon bleeding manifestation of hematuria was seen in a woman (Case #15) with secondary dengue infection at the 29th week of gestation. Platelet transfusions were received by those patients who had bleeding manifestations and/or counts equal or less than $20,000/\text{mm}^3$.

None of them developed spontaneous labour during the acute illness or before the recovery from thrombocytopenia. Their perinatal outcomes were satisfactory (Table 1). Three women (Cases #10, #13 and #15) had ongoing pregnancies and were recovered from the acute illness.

The postpartum periods were not complicated with postpartum hemorrhage but one patient (Case #02) with a pre-operative platelet count of $30,000/\text{mm}^3$ had platelet transfusions at the time of caesarean delivery. All other women were in the recovery phase with a platelet count $>100,000/\text{mm}^3$ during the peripartum period.

Case #01 developed features suggestive of dengue myocarditis (cardiac arrhythmia and bradycardia) and Case #08 had a transient hyponatremia (both had DHF II). Raised serum hepatic transaminases (AST and ALT) levels were seen in all 15 patients. A markedly high level was seen only in the patient who had DSS-DHF IV, but in most of the others, enzyme levels were less than 250 IU/L.

Eight patients needed intensive care treatment, but due to limitation of beds were not admitted to an intensive care unit. All women received paracetamol as an antipyretic and intravenous fluid and electrolyte; 0.9% Sodium chloride solution as intravenous fluid and electrolyte replacement.

Three other patients (Cases #04, #07 and #14) with a milder clinical course of (*i.e.*: DF/DHF I) had uncomplicated vaginal births and uneventful hospitalizations.

Fetal outcomes were satisfactory in all but two of the pregnancies (Cases #06 and #11) that were complicated by DSS, who had fetal demise. There were no cases suggestive of vertical transmission causing anomalies or requiring platelet transfusions to the neonate due to bleeding manifestations. Routine screening using dengue-specific IgM antibodies in cord blood or serum for vertical transmission was not performed due to financial constraints. No spontaneous preterm deliveries or low birth weight ($< 2500g$) babies were born except for the iatrogenic prematurity due to caesarean delivery (Case #09) at 33 weeks of gestation due to pre-eclampsia.

The low birth weight (2,305 g) in this newborn was secondary to iatrogenic prematurity but it was within the two standard deviations for the gestational age. The baby was observed in the special baby care unit for 48 hours. The mean birth weight of babies born to mothers with dengue in this case series was 3,060 g (range 2,305 g to 3,600 g). Except the premature baby of Case #09, all the birth weights were more than 2,500 g).

None of the deliveries were complicated by postpartum hemorrhage.

All the women and newborns who were discharged from the hospital were reviewed after one month in antenatal/postnatal clinics and paediatrics clinics. None of the babies showed clinical evidence of ill health (including bleeding manifestations) or failure to thrive.

Table 1. Clinical and Laboratory characteristics with feto-maternal outcomes.

Patient	Age (years)	Gestational age (weeks)	Dengue IgM/IgG	Plt count*103/mm³	Haematocrit (highest)	AST / ALT IU/l	Presenting complaints	Haemorrhagic manifestations	Pleural effusion/ ascites	Severity	ICU admission	Platelet transfusion	Maternal outcome	MOD	Fetal outcome
01	26	36	IgM+ IgG-	14	43	158 58	Fever, myalgia	P	N	DHF II	Y	Y	Myocarditis	VD	Normal
02	32	38	IgM+ IgG-	30	42	154 116	Fever	P	N	DHF II	N	Y	Normal	CS#	Normal
03	27	35	IgM+ IgG+	20	45	83 52	Fever, myalgia	P	N	DHF II	Y	Y	Normal	VD	Normal
04	29	36	IgM+ IgG-	21	37	194 52	Fever, myalgia	H	N	DHF I	N	N	Normal	VD	Normal
05	28	22	IgM+ IgG+	9	38	273 146	Fever	P,G	N	DHF II	Y	Y	Normal	VD	Normal
06	27	35	IgM+ IgG+	8	49	8980 2195	Fever, myalgia	P,E	PE, Ascites	DHF IV	Y	Y	MOF Death	-	IUD
07	27	35	IgM+ IgG+	56	40	110 63	Fever, myalgia	N	N	DF	N	N	Normal	VD	Normal
08	37	36	IgM+ IgG+	6	40	148 55	Fever, myalgia,abd. pain	P	N	DHF II	Y	Y	Hyponatemia	VD	Normal
09	34	33	IgM+ IgG-	32	42	356 154	Fever	H	N	DHF I	N	N	Normal	CS ##	Normal
10	30	27	IgM+ IgG-	74	33	48 43	Fever	H	N	DHF I	N	N	Normal		Pregnancy continuing
11	41	24	IgM+ IgG+	10	40	76 48	Fever, myalgia	P,G	N	DHF III	Y	Y	Normal	VD	Fetal demise
12	34	35	IgM+ IgG+	35	36	78 41	Fever, cough	N	N	DF	N	N	Normal	CS *	Normal
13	33	30	IgM+ IgG+	58	33	206 88	Fever	E	PE	DHF II	Y	N	Normal		Pregnancy continuing
14	22	39	IgM+ IgG-	74	45	229 56	Fever, myalgia,abd. pain	N	N	DF	N	N	Normal	VD	Normal
15	23	29	IgM+ IgG+	7	39	228 63	Fever, back pain	P,E, hematuria	PE	DHF II	Y	Y	Normal		Pregnancy continuing

MOD-Mode of Delivery   **VD**- Vaginal Delivery   **CS**-Cesarean delivery   **Plt**-Platelet
P- Petechiae   **G**-Gum Bleeding   **E**-Epistaxis   **H**-positive Hess's test   **ab**-Abdominal
DF-Dengue Fever   **DHF**-Dengue haemorrhagic Fever   **PE** - Pleural effusion
MOF- Multi Organ Failure   **IUD**-Intra Uterine Death   **Y**- Yes   **N**-No
CS due to acute genital herpes in labour; platelet transfusion to cover cesarean delivery. Pre operative platelet count was 30,000/mm³.
Pregnancy was complicated by pre-eclampsia and CS done (initially HELLP was suspected)
* Elective CS done following recovery from dengue since patient refused vaginal delivery. Pre operative platelet count was 178,000/mm³.

Discussion

During the most recent outbreak of dengue fever in Sri Lanka we encountered 15 cases of seropositive dengue infection in pregnancy at a tertiary hospital in Colombo. It is important to consider dengue as a possible differential diagnosis of acute febrile illnesses in endemic regions. To date, several cases of dengue infection in pregnancy and its vertical transmissions have been published in the literature (Table 2).

Table 2. Summarized case reports of in pregnancies with dengue infection since year 2000.

Authors	Country	N	Maternal outcomes	Fetal outcomes
Phongsamart *et al.* [13]	Thailand	3	Thrombocytopenia, rash	Fever, petechiae, hepatomegaly
Sirinavin *et al.* [14]	Thailand	2	Thrombocytopenia, pleural effusion, elevated liver enzymes	Fever, thrombocytopenia, pleural effusion, elevated liver enzymes, rash, gastric bleeding
Petdachai *et al.*[15]	Thailand	1	Thrombocytopenia, fever	Thrombocytopenia, leucopenia, petechiae, hepatomegaly
Janjindamai and Pruekprasert [16]	Thailand	1	Postnatal dengue shock syndrome, fever	Thrombocytopenia, elevated liver enzymes
Choudhry *et al.* [17]	India	4	Not reported	Fever, thrombocytopenia, pleural effusion
Witayathawornwong [18]	Thailand	1	Thrombocytopenia, pleural effusion	Fever, thrombocytopenia, pleural effusion
Restrepo *et al.* [19]	Colombia	22	Not reported	Premature birth, fetal malformations, low birth weight
Fatimil *et al.* [11]	Bangladesh	1	Gum bleeding, bilateral pleural effusions	Fever, fetal distress, thrombocytopenia
Chotigeat *et al.* [8]	Thailand	2	Post-partum haemorrhage, shock	Thrombocytopenia, pleural effusion
Waduge *et al.* [20]	Sri Lanka	26	Thrombocytopenia, pleural effusion, hepatomegaly, myocarditis	Low birth weight, miscarriage
Kerdpanich *et al.* [21]	Thailand	1	DHF, platelets transfusion during labour	Fever, low platelets
Boussemart *et al.* [22]	West Indies	2	Fever	Rash, thrombocytopenia, leucopenia
Carles *et al.* [23]	Guiana	38	Premature delivery, post partum haemorrhage, abruptio placentae	Premature birth , fetal deaths, acute fetal distress
Phupong [24]	Thailand	1	No complications	Not reported
Basurko *et al.* [25]	French Guiana	20	premature labour, haemorrhage during labour, abruptio placentae	prematurity, intrauterine foetal death, late miscarriage, acute foetal distress during labour, neonatal death
Ismail *et al.* [26]	Malaysia	16	Maternal death	prematurity, intrauterine foetal death, acute foetal distress during labour, neonatal death
Rosado Leon *et al.* [27]	Mexico	8	premature labour, pleural effusion, oligohydramnion, postpartum haemorrhage,	Neonatal sepsis
Singh *et al.* [28]	India	2	postpartum hemorrhage	Foetal distress during labour, erythematous rash, hepatosplenomegaly

N = Number of cases   DHF = Dengue Haemorrhagic Fever

Similar to the results published in other papers, a higher percentage of women in our study were in their third trimester; and in contrast to a previous Sri Lankan study of dengue in pregnancy [20], our cohort showed that secondary infections were more common than primary (44% versus 62%). This pattern is similar to that of non-pregnant adults [5,29].

Symptoms of infected women vary among the reports published in the literature. In general, the most common symptoms include fever, myalgia and arthralgia [5]. Fluid leakage (elevated hematocrit, pleural effusion or ascites) and hemorrhagic manifestations are characteristic features of DHF. Twelve out of the 15 women met the WHO criteria for DHF [1]. In addition, the physiological hemodilution of normal pregnancy can mask the classical criteria of hemoconcentration in DHF [20]. Routine ultrasound examination for free fluid in abdominal or thoracic cavities may be supplementary and practical in pregnant women.

Elevated liver enzymes are common phenomena and values were higher in DHF than DF, similar to the observations in previous studies [5,20,30]. A markedly high level was seen in Case #06, who had DSS. Although the liver is not a primary target of dengue, hepatic involvement has been detected ranging from elevated transaminase levels to acute fulminant hepatitis leading to hepatic failure [30]. Aggravation of clinical or laboratory features suggestive of liver malfunction can be used to triage patients requiring intensive care admission.

The severity of the clinical picture varies among the previous publications, as evident in Table 2. Additionally, the differentiation from HELLP syndrome where thrombocytopenia and raised liver enzymes are universal features may be difficult [12,14,31]. Evidence of hemolysis and positive serology or viral PCR may aid delineation. Case #09 of our series initially confused diagnosis in a similar way. The woman who died (Case #06) of DSS was the only one who developed multiorgan failure, including acute respiratory distress syndrome (ARDS), similar to that described by Lum *et al.* [32].

It is well documented that sequential infection with different dengue serotypes predisposes to more severe forms of the disease (DHF/DSS). This is explained by enhancement of the cross-reactive cascade of amplified non-neutralising heterologous antibodies, cytokines (*e.g.*, interferon-gamma produced by specific T cells) and complement activation causing endothelial dysfunction, platelet destruction and consumptive coagulopathy [6,33-40]. The association between severity of disease and secondary dengue infection is not obvious in this case series due to the low number of cases. There are only a few studies or case reports available, especially from our region, and a systematic review in the future may show the association.

Adverse fetal outcomes may be attributed to the effects on placental circulation caused by endothelial damage with increased vascular permeability leading to plasma leakage [9,33]. In a prospective cohort, Tan *et al.* described the vertical transmission rate as 1.6% (one of 63) [31]. Basurko *et al.* reported a 5.6% rate of maternal-fetal transmission [25]. Two studies from Cuba and French Guiana showed four of 59 (6.8%) and two of 19 (10.5%) neonates were vertically infected by dengue [23,41]. However, a northern Indian study has shown no vertical infection in eight pregnancies [12]. It is possible that the vertical transmission rate might be dependent on the severity of maternal dengue.

Few case series with neonatal consequences have been reported that include cases in Asia (Thailand, Malaysia, Sri Lanka, India and Bangladesh), Europe (France) and Latin America (Colombia). The pathogenesis of neonatal effects is poorly understood. Watanaveeradej *et al.* suggested that maternal-fetal transferred dengue-specific IgG has a role in the pathogenesis of neonatal dengue hemorrhagic fever [42]. Fever, petechial rash, thrombocytopenia, leucopenia, elevated liver enzymes, hepatomegaly, pleural effusion, premature birth, fetal malformations, miscarriages, and low birth weight have been reported. The fetal and maternal consequences of the cases that have been reported since the year 2000 are analyzed in Table 2.

Sharma *et al.* reported an increase in the incidence of fetal neural tube malformation in women who had dengue in the first quarter of pregnancy [43], but such an association has been demonstrated following other febrile illnesses, due to pyrexia rather than to any teratogenic effect of the virus *per se* [44]. Chong *et al.* studied vertical transmission with amniocentesis/chorionic villi sampling and revealed that all chromosomal analyses were normal, and the level of alpha-fetoprotein in amniotic fluids and maternal sera were within normal range [38]. The cases we studied developed the infection in the latter half of pregnancy and fetal malformations or defects were not detected.

A review article including 38 severe cases registered in French Guiana evidenced five *in utero*

fetal deaths involving in-patients [23]. In our cohort of women, there was a fetal demise (at 24 gestational weeks) and an intrauterine death and both women had the secondary dengue infection.

Fernández *et al.* followed-up the first five years of life of four babies in Cuba who had vertical dengue infection and no long-term sequelae were seen [41]. Another one-year follow-up study of three vertically infected babies achieved similar results [13]. However, according to a literature review, there have been cases of vertical dengue transmission with life-threatening consequences in both the fetus and the newborn (Table 2).

In our case series, there were no cases suggestive of perinatal transmission causing anomalies or requiring platelet transfusions to the neonate although routine screening of cord blood or serum was not performed due to financial constraints. Except for one baby with iatrogenic prematurity and low birth weight (pre-eclampsia: Case #09), none of our patients had spontaneous preterm delivery or low birth weight in this cohort of women. This result contrasts with the detection of premature deliveries and low birth weight babies in previous studies [9,11,23,45] and only one woman had preterm labour in a previous Sri Lankan study [20]. The incidence of reported premature deliveries varies and in one study it was 55% [23].

Hydration and supportive care that includes antipyretics, platelet transfusions, and management in an intensive care unit reduce the mortality rate [1]. Ostronoff *et al.* suggested a therapeutic benefit of gamma globulins in severe thrombocytopenia in DHF. This was not evaluated in pregnant women [46].

Eight patients received intensive care management, but occasional non-availability of beds affected admission to an intensive care unit. Only three beds are available in the intensive care unit of De Soysa Hospital, and sometimes it is necessary to transfer a patient to other centers of Sri Lanka when the patient needs special care, particularly for mechanical ventilation.

The precise incidence of dengue infections during pregnancy is unknown. Serological studies are performed only on a high degree of clinical suspicion due to financial constraints; consequently, there could be many subclinical cases in the community since Sri Lanka is an endemic country.

Our study is subject to limitations. The widely available clinical diagnostic test (the method we used for the study) of investigating acute febrile illnesses

for dengue is the rapid strip test with a sensitivity and a specificity of ≈90%. The capture ELISA tests are comparatively more sensitive and specific (≈ 95% and 100% respectively) according to the manufacturers [47]. Therefore, our study might have underestimated the actual outcomes. None of the kits mentioned above has the ability to differentiate between the serotypes. At best, they can be used only for diagnosing acute dengue virus infection, not for serotyping. On the other hand, the gold standard, reverse transcriptase PCR using type-specific primers is highly sensitive and specific. It is only positive during the acute phase and becomes negative shortly after defervescence, so the detection window in the clinical setup to confirm infection is relatively narrow [48].

Conclusion

Dengue in pregnancy is associated requires early diagnosis and treatment. Health-care providers should consider dengue in the differential diagnosis of pregnant women with fever during epidemics in endemic areas, and be aware that clinical presentation may be atypical and confound diagnosis. Early diagnosis is made difficult by the ambiguity of clinical findings and physiological changes of pregnancy that may confuse the clinician. In the absence of associated feto-maternal complications, infection by itself does not appear to be an indication for obstetric interference.

Further studies and systematic reviews are mandatory as evidence-based data in the management specific for pregnant patients are inadequate and our study will contribute to the growing database and formulation of guidelines.

Acknowledgment

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