



Document heading doi: 10.1016/S1995-7645(14)60316-3

Dengue in pregnancy: an under-reported illness, with special reference to other existing co-infections

Nidhi Singla^{1*}, Sunita Arora², Poonam Goel², Jagdish Chander¹, Anju Huria²

¹Departments of Microbiology, Government Medical College Hospital, Chandigarh, India

²Departments of Obstetrics & Gynaecology, Government Medical College Hospital, Chandigarh, India

ARTICLE INFO

Article history:

Received 15 November 2014

Received in revised form 20 January 2015

Accepted 15 February 2015

Available online 20 March 2015

Keywords:

Dengue
Pregnancy
Females
Coinfections

ABSTRACT

Objective: To keep the level of awareness high as far as incidence of dengue among pregnant women is concerned. **Methods:** A total of 300 blood samples of patients with fever in pregnancy were received in the Department of Microbiology to rule out dengue infection (January 2011 to December 2012). The samples were put up for presence of dengue IgM antibodies and NS1Ag by ELISA. The patients who turned out to be positive for dengue serology were retrospectively analysed with respect to patient's age, gestational age, clinical presentation, complications, platelet counts and maternal as well as foetal outcomes. **Results:** Out of 300 females tested, 22 (7.3%) were found positive for dengue infection during the said time period. Out of them 9 were positive for IgM antibodies against dengue and 10 were found to be positive for NS1Ag, while 3 were positive for both IgM antibody and NS1Ag. Five patients presented with dengue in first trimester, 9 in second trimester and 8 in third trimester. Two patients had coinfections. Patient with coinfection of dengue with malaria had intrauterine death of fetus at 37 weeks while the second one having dengue with typhoid had a preterm vaginal delivery at 35 weeks. **Conclusions:** Establishing diagnosis of dengue infection in pregnancy is important for effective management by the obstetricians particularly the mode of delivery due to the potential risk of hemorrhage for both the mother and the newborn. Coinfections seen in endemic areas may be more common than usually reported.

1. Introduction

Dengue has always been one of the most important arboviral infections affecting mankind. Recent frequent epidemics has made it a serious public health problem. The disease is traditionally caused by bite of *Aedes aegypti* mosquito and the illness can vary from merely asymptomatic one to life-threatening dengue hemorrhagic fever. There are four serotypes of dengue and presumably infection with one serotype does not lead to immunity against the other. Rather the chances of developing a severe form of the disease are more if prior sensitization has occurred with a different serotype.

This may occur even with a primary infection, depending on the infecting serotype[1].

Dengue infection in pregnant women is under suspected, under diagnosed hence underreported. The available literature is not clear regarding increased maternal or fetal morbidity in the form of increased pre-term deliveries, low-birth weight, pre-eclampsia and caesarean sections, etc[2]. Chances of vertical transmission have been discussed resulting in neonatal dengue[3]. With the recent resurgences of the disease tremendously increasing the number of people affected, there is an overall increase in pregnant women predisposed to infection during pregnancy. Frequent international travel to endemic areas also increases the exposure to pregnant women. It is estimated that the risk of exposure is almost 1% during a given pregnancy in a highly endemic area[1]. In this retrospective study, we have tried to clinically correlate the maternal and fetal

*Corresponding author: Dr Nidhi Singla, Assistant Professor, Department of Microbiology, Government Medical College Hospital, Chandigarh-160030, India.
Tel: 91-172-2665253 Ext-1061
E-mail: nidhisingla76@gmail.com

outcome with serologically confirmed cases of dengue fever in pregnancy. The main purpose for this documentation is to keep the level of awareness high as far as prevalence of dengue among pregnant women is concerned and also not to ignore the potential chances of its vertical transmission.

2. Materials and methods

A total of 300 blood samples of patients with fever in pregnancy were received in the Department of Microbiology to rule out dengue infection over a period of two years from January 2011 to December 2012. The sera from these samples were separated and the test was put up for detection of dengue IgM antibodies and NS1Ag by PanBio ELISA, supplied by Inverness Medical Innovations Pvt Ltd, Australia. The test was performed as per the instructions of the manufacturer, the sensitivity and specificity of the test being 94% and 100%, respectively.

Of these 300 patients, 22 turned out to be positive for dengue serology, who were retrospectively analyzed with respect to patient's age, gestational age of pregnancy, clinical presentation, any complications at presentation, platelet counts and treatment provided along with maternal mortality and morbidity. Outcome of pregnancy like abortion, pre-term delivery and term delivery were noted along with weight and condition of fetus at birth.

3. Results

Out of 300 females tested for dengue serology, 22 (7.3%) were found to be positive for dengue infection during the said time period. Out of them 9 were positive for IgM antibodies against dengue and 10 were found positive for NS1Ag, while 3 were positive for both IgM and NS1Ag. So, thirteen patients had been diagnosed early during the period of illness when NS1Ag could be detected.

Maximum number of cases were in age group 20-25 years (11 cases) followed by 26-30 years (9 cases). One patient was less than 20 years and one was more than 35 years age.

In this study 5 patients presented with dengue in first trimester, 9 in second trimester and 8 patients in third trimester. Out of the 5 patients in first trimester, two patients continued normal pregnancy while 2 patients had incomplete abortions with one patient presenting with missed abortion. Among 9 patients in second trimester, 3 had normal ongoing pregnancy, 2 underwent elective lower segment caesarean section (LSCS) at term and two patients were lost on follow up. However, other two patients had adverse outcome with one patient undergoing preterm delivery at 26 weeks (fetus did not survive) and other had abortion at 22 weeks. Among 8 patients in third trimester, 3 had preterm vaginal deliveries with healthy babies and one patient

had preterm LSCS for twins with breech presentation in first twin. Two were term normal vaginal deliveries while 2 patients had intrauterine death of the fetus at the time of reporting. One patient with gestational diabetes, controlled on insulin, presented with foetal hydronephrosis and oligohydramnios was lost on follow up.

Two patients were having coinfection with malaria and typhoid respectively with the first one having the worst fetal outcome in form of intrauterine death of fetus at 37 weeks while the second one had a preterm vaginal delivery at 35 weeks.

Of the 22 patients, 7 patients had platelet count more than 1.5 lac/mm^3 , 9 patients had platelet count more than $40\,000/\text{mm}^3$ but less than 1.5 lac/mm^3 . In 6 patients platelet count was less than $40\,000/\text{mm}^3$ and among them, three patients required platelet transfusion apart from antipyretics as a part of management. Two of them were those who presented with hemorrhagic fever and one patient presented with fever and petechiae with platelet count of $25\,000/\text{mm}^3$.

4. Discussion

The pregnant patients with dengue fever are mostly diagnosed clinically with the diagnosis later being confirmed by laboratory tests[1]. An early diagnosis is usually difficult due to the ambiguity of clinical findings and also the various physiological changes of pregnancy that may mislead the clinician. As per Wiwanitkit, the triad of high fever, haem concentration and thrombocytopenia can be the clue for diagnosis of dengue haemorrhagic fever in pregnancy[4]. The available data clearly shows that pregnancy as such does not increase the incidence or severity of dengue, however, dengue may predispose to certain complications related to pregnancy. There is a possibility of transplacental infection but at the same time protective antibodies crossover transplacentally[5]. Perrett *et al* has concluded that serious dengue disease occurs only when the mother is at or near term and there is insufficient time for the maternal production of protective antibodies[6]. However, Watanaveeradej *et al* suggested that maternal-fetal transferred dengue-specific IgG play a role in the pathogenesis of dengue hemorrhagic fever in neonates[7]. Generally, the severe forms of the disease are thought to occur more commonly after prior sensitization with a different serotype. Adverse fetal outcomes are considered to be due to the effects on placental circulation caused by endothelial damage with increased vascular permeability leading to plasma leakage[8]. The general consensus is that transplacental maternal antibodies are protective to the newborn if the titres are high usually for about 6 months in neonates but after that, the lower titres result in immunological enhancement and predispose the infant to dengue haemorrhagic fever or dengue shock syndrome[1].

The presence of dengue virus in fetal and cord blood samples

indicates intrauterine infection of the neonate[9]. Different studies have reported the rate of vertical transmission to vary from 1.6%-10.5%[10,11]. However, one study from northern India did not report any vertical infection in eight pregnancies[12]. It is possible that the vertical transmission rate might be dependent on the severity of maternal dengue. Fever, petechial rash, thrombocytopenia, leucopenia, elevated liver enzymes, hepatomegaly, pleural effusion and low-birth weight has also been observed by various authors[13]. Moreover, published reports also indicate premature birth (the incidence varies and in one study it was as high as 55%), fetal malformations, miscarriages and several fetal and newborn adverse effects but clearer evidence is still needed to attribute these problems to the dengue infection per se[14].

In the native endemic areas, the seropositivity rate in females increases with advancing maternal age, indicating that younger women are more at risk to contract the disease during pregnancy while older patients are more likely to have preexisting protective immunity[6]. It is pertinent to establish an early diagnosis of dengue infection as it affects management options taken by the obstetricians particularly the mode of delivery due to the potential risk of hemorrhage, secondary to thrombocytopenia. Dengue infection in pregnancy carries the risk of hemorrhage for both the mother as well as the newborn.

Co-infections can be seen in the endemic areas and may be more common than usually reported. We had two cases of co-infections, one was dengue with malaria and other dengue with enteric fever (Widal titres high 1: 160 for both TO and TH, although blood culture was sterile for *Salmonella*). In co-infections, overlapping sign and symptoms make the diagnosis and management difficult for the clinician together with the stress of pregnancy on body. In case of co-infection of dengue with enteric fever, the outcome was preterm vaginal delivery at 35 weeks with 2.2 kg baby, while in case of co-infection of dengue with malaria (*Plasmodium vivax*) there was intrauterine death of fetus at 37 weeks. 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.

Conflict of interest statement

We declare that we have no conflict of interest.

References

- [1] Carroll ID, Toovey S, Van Gompel A. Dengue fever and pregnancy - A review and comment. *Travel Med Infectious Dis* 2007; **5**: 183-188.
- [2] Adam I, Jumaa AM, Elbashir HE, Karsany MS. Maternal and perinatal outcomes of dengue in Port Sudan, Eastern Sudan. *Virology* 2010; **7**: 153-157.
- [3] Janjindamai W, Pruekprasert P. Perinatal dengue infection: a case report and review of literature. *Southeast Asian J Trop Med Public Health* 2003; **34**: 793-796.
- [4] Wiwanitkit V. Dengue haemorrhagic fever in pregnancy: appraisal on Thai cases. *J Vect Borne Dis* 2006; **43**: 203-205.
- [5] Ventura AK, Ehrenkranz NJ, Rosenthal D. Placental passage of antibodies to dengue virus in persons living in a region of hyperendemic dengue virus infection. *J Infect Dis* 1975; **131**: S62-S68.
- [6] Perret C, Chanthavanich P, Pengsaa K, Limkittikul K, Hutajaroen P. Dengue infection during pregnancy and transplacental antibody transfer in Thai mothers. *J Infect* 2005; **51**: 287-293.
- [7] Watanaveeradej V, Endy TP, Samakoses R, Kerdpanich A, Simasathien S, Polprasert N, et al. Transplacentally transferred maternal-infant antibodies to dengue virus. *Am J Trop Med Hyg* 2003; **69**: 123-128.
- [8] Phongsamart W, Yoksan S, Vanaprapa N, Choekhephaibulkit K. Dengue virus infection in late pregnancy and transmission to the infants. *Pediatr Infect Dis J* 2008; **27**: 500-504.
- [9] Balmaseda A, Hammond S, Perez L, Tellez Y, Saborio SI, Mercado C, et al. Serotype-specific differences in clinical manifestations of dengue. *Am J Trop Med Hyg* 2006; **74**: 449-456.
- [10] Tan PC, Rajasingam G, Devi S, Omar SZ. Dengue infection in pregnancy: prevalence, vertical transmission, and pregnancy outcome. *Obstet Gynecol* 2008; **111**: 1111-1117.
- [11] Fernández R, Rodríguez T, Borbonet F, Vázquez S, Guzmán MG, Kouri G. Study of the relationship dengue- pregnancy in a group of Cuban-mothers. *Rev Cubana Med Trop* 1994; **46**: 76-78.
- [12] Malhotra N, Chanana C, Kumar S. Dengue infection in pregnancy. *Int J Gynaecol Obstet* 2006; **94**: 131-132.
- [13] Kariyawasam S, Senanayake H. Dengue infections during pregnancy: case series from a tertiary care hospital in Sri Lanka. *J Infect Dev Ctries* 2010; **4**: 767-775.
- [14] Ismail NAM, Kampan M, Mahdy ZA, Jamil MA, Razi ZRM. Dengue in pregnancy. *Southeast Asia J Trop Med* 2006; **37**: 681-683.