CLINICAL AND PARACLINICAL CHARACTERISTICS OF DENGUE HEMORRHAGIC FEVER DURING PREGNANCY AT MILITARY HOSPITAL 103 IN 2023

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Abstract

Objectives: To describe clinical and paraclinical characteristics of Dengue hemorrhagic fever (DHF) during pregnancy at the Department of Infectious Diseases, Military Hospital 103 in 2023. ***Methods:*** A cross-sectional descriptive study was conducted on 162 pregnant patients diagnosed with DHF and treated at the Department of Infectious Diseases during the 2023 epidemic (from January 2023 to December 2023). ***Results:*** The average age was 28.92 ± 5.64 years old, and the average gestational age was 18.98 ± 16.75 weeks. Clinical characteristics: Fever was 84.4%; headache and eye socket pain was 76.5%; bleeding gums was 8.6% and abnormal vaginal bleeding was 2.5%; pleural or peritoneal effusion was 7.4%. Paraclinical characteristics: Decreased white blood cell (WBC) (< 4 G/L) was 28.4%, decreased platelet (< 150 G/L) was 69.1%. The first-trimester group had the highest average hematocrit (HCT) (%) and WBC ($p < 0.05$), and the second-trimester group had the lowest average platelet ($p < 0.05$) compared to other groups. Blood biochemistry tests showed increased AST (≥ 40 U/L) and ALT (≥ 40 U/L) in 46.7% and 49.3% of cases, respectively. The third-trimester group had the highest average AST and ALT compared to other groups ($p < 0.01$). Disease severity was classified as DHF with warning signs in 24.7% of cases and severe DHF in 1.8% of cases. The third-trimester group had the highest rate of DHF with warning signs and severe DHF ($p < 0.05$). ***Conclusion:*** Pregnant women with DHF exhibit different clinical and paraclinical characteristics depending on the stage of pregnancy. The third-trimester group experienced more severe liver injury and disease severity compared to the first and second-trimester groups.

Keywords: Pregnancy; Dengue hemorrhagic fever; Clinical and paraclinical characteristics.

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INTRODUCTION

Southeast Asia is among the regions most affected by Dengue, and Vietnam is one of the five countries in this region with the highest burden. In 2022, the country recorded 367,729 DHF cases and 140 deaths, and as of December 17, 2023, the country recorded 166,619 infections, including 42 deaths. Dengue fever can occur in all subjects, including pregnant women. Dengue during pregnancy increases the risk of pre-eclampsia, severe DHF, fetal distress, preterm delivery, caesarean delivery, and maternal mortality [1]. In addition, physiological changes during pregnancy, according to the stages of pregnancy, have been shown to have certain effects on the progression and prognosis of the disease [2]. Currently, in Vietnam, the number of studies on Dengue fever in pregnant women published in medical literature is limited. Therefore, we conducted this study to: *Describe the clinical and paraclinical characteristics of DHF in pregnant women. At the same time, we compared some clinical and paraclinical differences between stages of pregnancy.*

MATERIALS AND METHODS

1. Subjects

Including 162 pregnant patients diagnosed with DHF and treated at the Department of Infectious Diseases, Military Hospital 103 in 2023.

* *Inclusion criteria:* Pregnant patients diagnosed with DHF according to the Vietnamese Ministry of Health's standards in 2019 - Decision No. 3705/QD-BYT, with positive Dengue - NS1 or Dengue - IgM test results [3].

* *Exclusion criteria:* Patients who did not agree to participate in research.

* *Time and location:* From January 1, 2023 to December 30, 2023 at the Department of Infectious Diseases, Military Hospital 103.

2. Methods

* *Study design:* A cross-sectional descriptive study.

* *Sample size:* Purposive convenience sampling method, all eligible patients were included in the study.

* *Research content:*

General information: Characteristics of age, gestational age.

Group division by pregnancy stage: First 3 months, middle 3 months, and last 3 months of pregnancy.

Clinical characteristics: Symptoms and signs at the time of admission.

Paraclinical tests: Red blood cells (RBC), Hemoglobin (Hb), HCT, WBC, platelets (PLT), AST, ALT; Abdominal and pleural ultrasound assessed at the time of admission.

Assessment of disease severity: According to the 2019 Ministry of Health guidelines, divided into levels of DHF, DHF with warning signs and severe DHF [4].

* *Data collection and processing:* Data was collected from unified research medical records, entered into Excel 16.0 software, and processed with SPSS 22.0 software.

3. Ethics

The research data does not impact testing rights or expenses and is gathered from patient data that is regularly tested throughout hospital inpatient treatment. All patient data is kept private and confidential. The Department of Infectious Diseases, Military Hospital 103 granted permission for the use and publication of the research data. The authors declare to have no conflicts of interest.

RESULTS

Through a study of 162 pregnant patients diagnosed with DHF, the average age was 28.92 ± 5.64 years old. The age group of 21 - 30 years old accounted for the highest percentage (51.9%), followed by the 31 - 40-year-old group at 29.0%.

The average gestational age was 18.98 ± 16.75 weeks, with the smallest being 6 weeks and the largest being 39 weeks. According to the trimesters, the middle 3 months accounted for the largest proportion with 39.5% (64 pregnancies); the first 3 months and the last 3 months accounted for 32.1% (52 pregnancies) and 28.4% (46 pregnancies), respectively.

1. Clinical characteristics at the time of admission

Table 1. Symptoms and signs of DHF in pregnant women.

Symptoms and signs		Number (n = 162)	Percentage (%)
Systemic	Fever	136	84.0
	Headache, eye pain	124	76.5
	Muscle and joint pain	98	60.5
Digestive	Nausea and vomiting	76	46.9
	Liver pain	12	7.4
	Epigastric pain	32	19.8
	Diarrhea	10	6.2
Hemorrhage	Nose bleeding	8	4.9
	Gum bleeding	14	8.6
	Vaginal bleeding	4	2.5
	Gastrointestinal bleeding	0	0.0
Other	Pleural/peritoneal effusion	12	7.4

Some common symptoms include fever (84.4%); headache and eye pain (76.5%); nausea and vomiting (46.9%); epigastric pain (19.8%); bleeding gums (8.6%) and abnormal vaginal bleeding (2.5%); pleural or peritoneal effusion (7.4%).

2. Paraclinical characteristics at the time of hospitalization

Table 2. Characteristics of some hematology tests.

Results		First 3 months (n = 52)(1)	Middle 3 months (n = 64)(2)	Last 3 months (n = 46)(3)	p	Number (n = 162)	Percentage (%)
RBC (T/L)	$\overline{X} \pm SD$	4.67 ± 0.65	4.53 ± 0.86	4.52 ± 0.92	> 0.05	4.58 ± 0.75	
Hb (g/L)	$\overline{X} \pm SD$	118.94 ± 12.30	118.32 ± 13.68	116.34 ± 10.12	> 0.05	117.21 ± 12.34	
	< 110	10 (19.2)	14 (21.9)	10 (21.7)	> 0.05	34	21.0
	≥ 110	42 (80.8)	50 (78.1)	36 (78.3)		128	79.0
HCT (%)	$\overline{X} \pm SD$	46.23 ± 8.64	43.67 ± 6.06	44.26 ± 5.25	$p_{(1-2.3)} < 0.05$	44.56 ± 6.45	
	< 47	45 (86.5)	53 (82.8)	35 (76.1)	> 0.05	133	82.1
	≥ 47	7 (13.5)	11 (17.2)	11 (23.9)		29	17.9
WBC (G/L)	$\overline{X} \pm SD$	6.38 ± 3.23	6.06 ± 3.38	5.78 ± 4.34	$p_{(1-3)} < 0.05$ $p_{(1-2.\ 2-3)} > 0.05$	6.21 ± 4.03	
	< 4	20 (38.5)	16 (25.0)	10 (21.7)		46	28.4
	4 - 10	29 (55.8)	40 (62.5)	25 (54.4)	< 0.05	94	58.0
	> 10	3 (5.7)	8 (12.5)	11 (23.9)		22	13.6
PLT (G/L)	$\overline{X} \pm SD$	56.78 ± 62.43	42.65 ± 52.65	48.87 ± 56.34	$p_{(2\ -1.3)} < 0.05$	50.02 ± 58.39	
	< 50	8 (15.4)	18 (28.1)	11 (23.9)		38	23.4
	50 - 149	28 (53.8)	36 (56.3)	27 (58.7)	> 0.05	74	45.7
	≥ 150	16 (30.8)	10 (25.6)	8 (17.3)		50	30.9

Pregnant women with DHF had a rate of decreased Hb (< 110 g/L) of 21.0%, increased HCT (≥ 47%) of 17.9%, decreased WBC (< 4 G/L) of 28.4%; decreased PLT with < 50 G/L and 50 - 149 G/L of 23.4% and 45.7%, respectively. The first 3-month group had a higher average HCT (%) and WBC than the other groups ($p_{1-2.3} < 0.05$ and $p_{1-3} < 0.05$). The middle 3-month group had the lowest average number of WBC among the comparison groups ($p < 0.05$).

Table 3. Characteristics of some liver function tests.

Results		First 3 months (n = 49)(1)	Middle 3 months (n = 61)(2)	Last 3 months (n = 40)(3)	p	Number (n = 150)	Percentage (%)
AST (U/L)	$\overline{X} \pm SD$	85.67 ± 125.64	96.76 ± 234.45	126.56 ± 326.76	< 0.01	102.16 ± 267.58	
	< 40	33 (67.3)	27 (44.3)	20 (50.0)	> 0.05	80	53.3
	40 - 399	15 (30.7)	30 (49.2)	15 (37.5)		60	40.0
	400 - 999	1 (2.0)	3 (4.9)	3 (7.5)		7	4.7
	≥ 1000	0 (0.0)	1 (1.6)	2 (5.0)		3	2.0
ALT (U/L)	$\overline{X} \pm SD$	96.54 ± 106.43	93.34 ± 156.76	145.56 ± 289.70	< 0.01	121.13 ± 206.23	
	< 40	30 (61.2)	30 (49.2)	16 (40.0)	> 0.05	76	50.7
	40 - 399	17 (34.7)	26 (42.6)	17 (42.5)		60	40.0
	400 - 999	2 (4.1)	4 (6.6)	5 (12.5)		11	7.3
	≥ 1000	0 (0.0)	1 (1.6)	2 (5.0)		3	2.0

(Exclude pregnant women with a history of chronic liver disease)

The rates of increased AST and ALT (≥ 40 U/L) were 46.7% and 49.3%, respectively. Of these, increased AST ≥ 1000 U/L and ALT ≥ 1000 U/L both accounted for 2.0%. In the last 3 months of pregnancy, the average AST and ALT enzyme activity increased more than the other two groups ($p < 0.01$).

Table 4. Classification of disease level of study subjects.

Disease severity	First 3 months (n = 52)(1)		Middle 3 months (n = 64)(2)		Last 3 months (n = 46)(3)		p	Number (n = 162)	Percentage (%)
	n	%	n	%	n	%			
DHF	46	88.5	47	73.4	26	56.6		119	73.5
DHF with warning signs	6	11.5	16	25.0	18	39.1	< 0.01	40	24.7
Severe DHF	0	0.0	1	1.6	2	4.3		3	1.8

The rates of DHF with warning signs and severe DHF in pregnant women accounted for 24.7% and 1.8%, respectively. The last 3-month group had a higher rate of DHF with warning signs and severe DHF than the other two groups, with $p < 0.05$.

DISCUSSION

1. Clinical and paraclinical characteristics of Dengue fever in pregnant women

** Characteristics of age and gestational age:*

According to our study results, pregnant women were all of childbearing age, with an average age of 28.92 ± 5.64 years old. The results are similar to Nguyen Thi Thu Huyen (2018), with an average age of 27.9 ± 4.8 [4]; and Trinh Tien Dat, with an average age of 24.8 ± 3.7 [5].

The average gestational age in the study was 18.98 ± 16.75 weeks, of which the middle-trimester group accounted for the highest proportion at 39.5%, followed by the first- and last-trimester groups. The studies by Machain-Williams C (2018) in Mexico [6] and Nguyen Thi Thu Huyen (2018) [4] also noted that the middle 3-month group had a higher rate than the other groups.

** Clinical characteristics:*

Some clinical symptoms include fever (84.4%), headache and eye pain (76.5%), nausea and vomiting (46.9%),

and epigastric pain (19.8%). These are common symptoms similar to those of patients with common Dengue fever.

Abnormal vaginal bleeding in our study accounted for 2.5%, lower than the research results of Nguyen Thi Thu Huyen (2018) at 11.8% [4], but similar to Hoang Xuan Cuong (2022) at 4.1% [7]. The difference can be explained by the research subjects, stage characteristics, and severity of the disease. In addition, the progression, severity, and complications of DHF change every year according to the characteristics of each epidemic.

The rate of peritoneal and pleural effusion in our study accounted for a significant proportion of 7.4%. This is one of the signs included in the diagnostic criteria for DHF, indicating hospitalization and close monitoring and treatment for these subjects. Physiological changes in the cardiovascular system of pregnant women have been mentioned in some studies, such as decreased systemic vascular resistance, increased capillary permeability leading to decreased plasma volume, and increased risk of preeclampsia. Placental ischemia in the first 3 months can occur secondary to increased vascular permeability and fluid leakage from interstitial spaces [1].

2. Paraclinical characteristics of Dengue fever in pregnant women

** Complete blood count:*

According to a report by Hoang Xuan Cuong (2022) on 727 subjects with Dengue fever in 2022, the rate of PLT reduction was 96.3%, in which PLT < 50 G/L ranged from 70 - 80%; HCT increase (≥ 47%) accounted for about 20 - 30% [7]. Compared to our study, the rate of HCT increase was lower, accounting for only 17.9%. As mentioned above, the physiological process of pregnancy is often accompanied by vasodilation, so changes in hematological status and blood concentration due to plasma leakage are often not as obvious as in normal subjects.

Comparing the stages of pregnancy, the first-trimester group had a higher average HCT than the other two groups ($p < 0.05$). This can be explained by the physiology of pregnancy. In the first trimester, plasma volume often decreases, then gradually increases and stabilizes in the last 3 months of pregnancy. According to the guidelines for diagnosis and treatment of DHF in pregnant women in Sri Lanka, special attention is required, as pregnant women with Dengue fever in the first 3 months face an increased risk of plasma leakage from the blood vessels, trapped blood pressure, preeclampsia, and acute pulmonary edema [8].

Regarding PLT, the overall PLT reduction rate in the study was 69.9%. Comparing between pregnancy stages, the second-trimester group had a significantly lower PLT reduction than other stages in pregnancy ($p < 0.01$). During pregnancy, the second-trimester period is often accompanied by hypercoagulability, and gestational thrombocytopenia can occur in 4.4 - 11.6% [9]. Therefore, the group of pregnant women in this period with DHF may have a combination of physiological and pathological thrombocytopenia.

Regarding the WBC index, in the guidelines for diagnosing Dengue fever, leukopenia or leukopenia is one of the common signs. However, in pregnant women, leukopenia is rarely recorded. In our study, the overall rate of leukopenia was 28.6%. Comparing the pregnancy groups, the first-trimester group had a higher leukopenia count than the other two groups, with a clear difference recorded when comparing the first and last trimesters of pregnancy ($p < 0.05$). This is explained by the fact that pregnant women often have increased leukocytes, especially in the first trimester of pregnancy. Therefore, the guidelines for Dengue fever in pregnant women also noted that leukopenia may not be recorded, especially in the first trimester of pregnancy [8].

** Liver function test:*

In pregnant women with Dengue fever, Machain-Williams C (2018) reported elevated ALT and AST with the following rates: 92.6% and 46.3% in the DHF group; 93.3% and 66.7% in the DHF with warning signs; and 92.3% and 92.3% in severe DHF [6]. The results of our study were lower, the rate of increased AST and ALT in pregnant women (> 40 U/L) accounted for only 46.7% and 49.3%, respectively. The difference can be explained by the time of test assessment. Our study chose a cross-sectional time point upon admission, the above studies chose a time point when the tests changed most clearly during the hospital follow-up, so the rate was different.

Comparing between gestational age groups, we noted that in the last 3 months of pregnancy, elevated AST and ALT were significantly higher than in the first 3 months and the middle 3 months of pregnancy ($p < 0.05$). Currently, there is no study that addresses changes in liver function during pregnancy. In our opinion, in addition to the mechanisms of liver damage caused by the Dengue virus (the virus directly attacks liver cells and Kupffer cells, cytotoxicity through T lymphocytes, cytokines such as IL-2, IL-6, TNF-α, and IFN-γ, ...); there are

also mechanisms of increased liver enzymes in pregnant women such as cholestasis in the liver, HELP syndrome, fatty liver, etc. Pathological liver enzyme elevation disorders in pregnant women are often concentrated in the last months of pregnancy, so when infected with Dengue virus, it will aggravate liver cell damage.

** Characteristics of disease severity:*

In our study, the rates of DHF with warning signs and severe DHF were 24.7% and 1.8%, respectively. The last 3-month group had higher rates of DHF with warning signs and severe DHF than the other two groups ($p < 0.05$). Our results were similar to those of Machain-Williams C (2018), the rates of DHF with warning signs and severe DHF were 18.3% and 15.9%, respectively. No cases of DHF with warning signs and severe DHF were recorded in the first 3 months of pregnancy. The last 3-month group also had the highest rate of severe Dengue fever compared to the other groups [6]. Thus, the rates of DHF and severe DHF may be slightly different, possibly due to different standards and guidelines for classifying disease severity according to the regulations of each research country. However, our results and some studies mentioned above show that the last 3-month group was at high risk of DHF with warning signs and severe DHF when compared with subjects in other stages of pregnancy.

CONCLUSION

Compared to the other two groups, the average HCT (%) and WBC count of the first-trimester group was higher ($p < 0.05$). On the other hand, the last-trimester group showed an increase in the liver enzymes AST and ALT ($p < 0.05$), whereas the middle-trimester group had the lowest average platelet count ($p < 0.05$). The percentages of DHF with warning signs and severe DHF were 24.7% and 1.8%, respectively, in relation to the disease's severity. When compared to the other two groups, the last-trimester group had the highest percentage of DHF with warning signs and severe DHF ($p < 0.05$).

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