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# Role of enoxaparin on fetal loss associated with genital infection (bacterial vaginosis and cytomegalovirus)

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**Fetal loss is one of the most important problems of the woman's health, which significantly affects her psychological status. It has different causes, so there is no unique method for its diagnosis and treatment.**
***The objective:*** **to evaluate the enoxaparin effect in pregnancy with recurrent fetal loss related to genital infections.**
***Materials and methods:*** **a cross-sectional study 205 included pregnant women with fetal loss in the history who were managed at Hospital from January 1st, 2022, to October31st, 2023. Serodiagnosis of IgG and IgM against cytomegalovirus (CMV) was performed by using ELISA. Bacterial vaginosis (BV) was diagnosed by microscopic examination of vaginal discharges. Also, fibrinogen level was determined. Enoxaparin (low molecular weight heparin) was prescribed to all infected patients.**
***Results*****. It was found that the largest proportion of the study population was women aged 21–25 years, 70.65% of patients lived in rural areas. Among 205 women with a history of fetal loss, 81% were diagnosed with BV and CMV infection, and 19% had no infectious diseases. 95.8% of patients with CMV infection and BV responded positively to enoxaparin therapy, which was manifested by normalization of fibrinogen level and a favorable course of pregnancy. At the same time, 4.19% of women did not have an adequate response to treatment, which was associated with lower fibrinogen level.**
***Conclusions*****. The presence of an infectious process leads to an increased level of inflammatory cytokines in the placenta, which can lead to the formation of blood clots, atherosclerotic changes with or without increased blood clotting factors, in particular fibrinogen, which reduce blood transport to the fetus. This, in turn, can lead to miscarriage, preeclampsia and premature birth. Enoxaparin is a safe and effective medication for preventing fetal loss in pregnant women with genital infectious diseases. Furthermore, it helps to reduce the frequency of fetal loss. However, studies on the effectiveness and safety of enoxaparin for the prevention of thromboembolic complications and thrombosis are currently insufficient, which requires further scientific observations.**
***Keywords:*** *abortion, cytomegalovirus, enoxaparin, fetal loss, genital infections.*

## Роль еноксапарину в запобіганні утраті плода, пов'язаній з інфекцією статевих органів (бактеріальний вагіноз і цитомегаловірус)

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Утрата плода є однією з найважливіших проблем, пов'язаних зі здоров'ям жінки, що суттєво впливає на її психологічний стан. Це явище має різні причини виникнення, тому не існує універсального методу діагностики та лікування.
***Мета дослідження:*** оцінка ефективності застосування еноксапарину під час вагітності в жінок із рецидивами утрати плода, пов'язаних з інфекцією статевих органів.
***Матеріали та методи.*** У перехресне дослідження включено 205 вагітних жінок з утратою плода в анамнезі, які перебували в стаціонарі з 1 січня 2022 р. до 31 жовтня 2023 р. Серологічне дослідження для визначення рівнів IgG та IgM до цитомегаловірусу (ЦМВ) проводили за допомогою імуноферментного аналізу (ІФА). Для діагностики бактеріального вагінозу проводили мікроскопічне дослідження вагінальних виділень. Також оцінювали рівень фібриногену. Еноксапарин (низькомолекулярний гепарин, НМГ) призначали усім інфікованим пацієнткам.
***Результати.*** Встановлено, що найбільшу частку досліджуваних становили жінки віком 21–25 років, 70,65% пацієнток проживали в сільській місцевості. Серед 205 жінок із втратою плода в анамнезі у 81% було діагностовано бактеріальний вагіноз і цитомегаловірусну (ЦМВ)-інфекцію, а 19% не мали інфекційних захворювань. 95,8% пацієнток із ЦМВ-інфекцією та бактеріальним вагінозом позитивно відповіли на терапію еноксапарином, що проявлялося нормалізацією рівня фібриногену й сприятливим перебігом вагітності. Водночас у 4,19% жінок не було належної відповіді на лікування, що асоціювалося з нижчим рівнем фібриногену.
***Висновки.*** Наявність інфекційного процесу зумовлює підвищення рівня запальних цитокінів у плаценті, що може призводити до утворення тромбів, атеросклеротичних змін із підвищеними факторами згортання крові або без них, зокрема фібриногену, що зменшують транспорт крові до плода. Це, своєю чергою, може призводити до викидня, прееклампсії та передчасних пологів. Еноксапарин є безпечним та ефективним засобом для запобігання утраті плода у вагітних жінок з інфекційними захворюваннями статевих органів. Крім того, він сприяє зниженню частоти втрат плода. Однак досліджень щодо ефективності та безпеки еноксапарину для профілактики тромбоемболічних ускладнень і тромбозу наразі недостатньо, що потребує подальших наукових спостережень.
***Ключові слова:*** *викидень, цитомегаловірус, еноксапарин, утрата плода, статеві інфекції.*

Maternity infections can pass from the vagina to the fetus by way of the cervical canal, and then reach the placenta and amniotic fluid through an ascending infection or by blood spread because the mother may be infected with viruses, bacteria, or parasites. These microorganisms produce infections via the rising route, and then they cause inflammatory alterations in the amniotic and chorionic tissues, which they are calling chorioamnionitis. All of them may result in early rupture of the fetal membranes and premature labor. Significant infections in pregnancy often occur at an earlier gestational age [1]. The risk of fetal loss is increased by viral, bacterial, and parasitic infections. There is evidence that infections like bacterial vaginosis (BV) and cytomegalovirus (CMV), dengue fever, brucellosis, and malaria can have unfavorable pregnancy consequences [2]. Infective factors like TORCH (Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes) cause about 10–15% loss of fetus, while CMV remains a common virus that infects people of all ages. About 40–100% of all adults are carrying the virus worldwide [3].

Enas Alwaily R. et al. presented the fungal infection as *Candida* 52% of cases, which was divide into *Candida albicans* 30%, *Candida krusei* 8%, and *Candida parapsilosisas* 5.6% [4]. During pregnancy, the usual bacterial infection is BV which is comprised about 30% per year. This is an increased hazard due to changes in the hormones during pregnancy. BV may cause current miscarriage and early delivery [5]. Another study reported a postpartum patient presenting with a left-sided ovarian vein thrombus (OVT), likely precipitated by a lower urinary tract infection and possibly vaginitis. A high clinical index of suspicion and expeditious diagnosis are necessary to avoid the more serious squeal of OVT, and extensive patient counseling is imperative to ensure appropriate compliance with treatment and follow-up [6]. In addition to that, toxoplasmosis has a considerably high rate in pregnancy, so the detection of *Toxoplasma gondii* infection is important during pregnancy [7]. Z. A. Ahmed et al. mentioned that pregnant women with toxoplasmosis had slightly higher IL-37 level. This cytokine, IL-37, is important in the regulation of immunity in pregnancy, while a high level of Dectin-1, which acts on fetal loss [8]. Other reports noticed that there was a link between elevated cytokine levels and their elevated levels in the milk. The level of tumor necrosis factor alpha increases in the milk of mothers with *Toxoplasma* infection compared with non-infected mothers [9]. E. F. Turkey et al. have demonstrated that there is no association between genotype of prothrombin level frequency and abortion in CMV-infected women [10]. While there is a highly significant association between A and G allele combinations and abortion in CMV-infected women. The most virally dangerous connect to vascular, placental, specific infective pathogens, pregnancy age at presentation, and female fetal condition [11]. Patients with several microthrombosis resulted from CMV infection. In addition, they proposed that CMV infection has be considered a different diagnosis for immunosuppressed persons who already have thrombosis of an unspecified cause [12]. The acute CMV infection should add to the list of thrombosis triggers [13]. Abduljalil Alsaad R. K. thought that the risk of toxoplasmosis increased with pregnancy (84.23%) [14]. There are different species of coccidian parasites that may be present in the soil in local areas and cause infections in humans and animals [15]. They may enhance the danger of venous thromboembolism in inmates showing factor V Leiden mutation heterozygosis [16]. In the present study, we thought that infections would increase the inflammatory cytokines strictly in the placenta and produce clots and atherosclerosis with or without elevated clotting factors like fibrinogen, which decrease blood transport to the fetus, which is leading to miscarriage, pre-eclampsia, and preterm labor.

**The objective** of the study is to determine the effect of enoxaparin in pregnancy with recurrent fetal loss related to genital infection (BV and CMV) and fibrinogen level.

## MATERIALS AND METHODS

**Collection of specimens.** The study population was a cross-section for the period from January 1st, 2022, to October 31st, 2023. The collected samples were 205 pregnant women at ages 15–40 in the first, second, and third trimesters who were attending the Teaching Hospital and obstetric clinic in City, Iraq. Most pregnant women were suffering from loss of fetus with a history of abortion, preterm labor, stillbirth, and congenital abnormalities. A structural interview would use a standard maternal questionnaire, which would include age, parity, gestational age, mode of delivery, gynecologic and medical history of abortion, and residence. Enoxaparin doses 2000 IU daily were given subcutaneously from the first month of pregnancy until seventh months.

**Exclusion criteria**. All patients had subjected to clinical examination and laboratory investigations to exclude other causes of fetal loss, such as hypertension, diabetes mellitus, Rh (rhesus) incompatibility, and physical causes of abortion. In addition, we excluded the patients who had taken medications, such as antibiotics, for any infection for four weeks previously.

**Blood collection**. About 4–5 milliliters of blood from an intravenous puncture had collected from patients. We put blood into two sterilized tubes, and then sent them for centrifugation at (2000 rounds/minute) for ten minutes to get serum, which it had insulated from the clot, then it preserved in screwed tubes very closely, and stored, at –20 °C.

**Vaginal swab**. Vaginal swabs had collected, which have characteristics of being gray in color with a fishy odor. BV (*Gardenella vaginalis*) was diagnosed using microscopic examination of vaginal swab samples for clue cells cultured on selective media such as Colombia blood agar base with FD 056 supplement (Gentamicin sulfate 2 mg, Nalidixic acid 15 mg, and Amphotericin B 1 mg) (HiMedia/India). Also, API RapID™ NH Remel System (USA) for diagnosis of *Gardnerella vaginalis* and β-galactosidase test.

**Serology test**. Using kits for estimating the concentration of specific CMV-IgM and CMV-IgG markers performed the enzyme-linked immune sorbent assays (ELISA) method. The kits had brought from Sigma Diagnostics (USA), and the techniques had performed according to the manufacturer's instructions.

We examine the frozen serum for the accessibility of anti-CMV IgM and IgG antibodies using an ELISA kit. The positive result was > 0.9 IU, while the negative result was < 0.9 IU according to the kit to the manufacturer's instructions and reading of the O.D. at 450 nm within 15 min.


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*Table 1*

**Distribution of infections (BV and CMV) in women with recurrent fetal loss**

| Causes of abortions in studied group | Frequencies No. (%) | $\chi^2$ square test (p-value) |
|---|---|---|
| Infections (BV and CMV) | 167 (81) | 112.13 (< 0.001)*HS |
| Other causes | 38 (19) | |
| Total | 205 (100) | |

*Note:* *HS – high significant difference between groups (p-value < 0.001); Chi-square test has been used.

*Table 2*

**Frequency of CMV and BV in pregnant patients with recurrent fetal loss**

| Types of Infections | Frequencies No. (%) | $\chi^2$ square test (p-value) |
|---|---|---|
| BV | 13 (7.78) | 131.035 (< 0.001)*HS |
| CMV | 154 (92.22) | |
| Total studied infection | 167 (100) | |

*Note:* *HS – high significant difference between groups (p-value < 0.001); Chi-square test has been used.

*Table 3*

**Frequency of BV and CMV in pregnant women based on age**

| Age (yr) | Infected pregnant women with BV and CMV | |
|---|---|---|
| | No. | % |
| 15–20 | 24 | 14.37 |
| 21–25 | 66 | 39.52 |
| 26–30 | 27 | 16.17 |
| 31–35 | 35 | 20.96 |
| 36–40 | 15 | 8.98 |
| Total No. | 167 | 100 |

*Table 4*

**Infected pregnant with recurrent fetal loss related to residence***

| Residence | Pregnant with infections (BV and CMV) | |
|---|---|---|
| | No. | % |
| Rural area | 118 | 70.65 |
| Urban area | 49 | 29.34 |
| Total | 167 | 100 |

*Table 5*

**Distribution of Infected pregnant women with BV & CMV according to gestational age**

| Gestational age (week) | Frequencies No. (%) |
|---|---|
| First Trimester (≤ 12) | 83 (49.70) |
| Second Trimester (13–27) | 57 (34.13) |
| Third Trimester (28–40) | 27 (16.17) |
| Total | 167 (100) |

*Table 6*

**Frequency of infected pregnant women with previous loss of fetus**

| Previous adverse outcome pregnancy (complications) | Frequencies No. (%) |
|---|---|
| Abortions | 97 (58.08) |
| Preterm labor | 23 (13.77) |
| Stillbirth | 14 (8.38) |
| Congenital abnormalities (spinal bifida and encephalopathy) | 33 (19.76) |
| Total | 167 (100) |

*Table 7*

**Frequency of CMV antibody in pregnant women based on chronicity**

| CMV antibody | Frequencies No. (%) |
|---|---|
| Elevated CMV (IgM) | 52 (33.77) |
| Elevated CMV (IgG) | 74 (48.05) |
| Elevated CMV (IgM and IgG) | 28 (18.18) |
| Total | 154 (100) |

The steps to check the samples were according to the manufacturer's instructions. In addition, we examine the fibrinogen level. The normal level of fibrinogen was between 200 and 400 mg/dL, while the high level was > 400 mg/dL.

**Ethical approval.** This research was ethically approved by the Research Ethical Committees of the Ministry of Higher Education and Scientific Research, Iraq, and the approval is numbered (No. 119 dated 16.03.2022).

**Statistical analysis.** The results had presented as numbers and percentages for categorical variables and analyzed using the computer statistical analysis system. Chi-square and T-tests had performed to assess the statistical significance of the data values. Where descriptive statistics had used. The significant comparison between percentages had calculated using Chi-square test. Probability value (p-value) was calculated with the levels of 0.05 and 0.01; the significant difference was considered at p-value < 0.05.

## RESULTS AND DISCUSSION

The age of women was from 15 till 40 years old. In the history they had recurrent fetal loss, about 167 (81%) cases had infections, including BV and CMV infections, while 38 (19%) cases may have other causes of fetal loss with a high significant statistical difference (p-value < 0.001) (Table 1). There were 154 (92.22%) women with fetal loss in the history who were infected by CMV and 13 (7.8%) women with fetal loss who were diagnosed BV(p-value < 0.001) (Table 2). The most infected age group of pregnant women with previous fetal loss and suffering from BV and CMV infections were women from 21 till 25 years old (66 (39.52%) cases). Most of them lived in rural areas (118 (70.65%); p < 0.05) (Tables 3, 4).

From 167 infected pregnant women with BV and CMV, the most of them had previous loss of fetus (abortion, stillbirth, preterm labor) presented within first trimester – 83 (49.70%) cases (Table 5). In addition, the most infected pregnant women had previous abortion – 97 (58.08%) cases (Table 6).

From 154 infected pregnant women with CMV, 74 (48.05%) cases had elevated CMV-IgG antibody, while 52 (33.77%) cases had elevated CMV-IgM antibody (Table 7).


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*Table 8*

**Response of infected pregnant women to enoxaparin according to fibrinogen level***

| Response to drug | Infected pregnant = 167 (treated with enoxaparin) | | | | Total No. | |
|---|---|---|---|---|---|---|
| | Normal fibrinogen level | | High fibrinogen level | | | |
| | No. | % | No. | % | No. | % |
| Respond to enoxaparin (No loss of fetus & good outcome) | 110 | 96.49 | 50 | 94.33 | 160 | 95.81 |
| Not respond to enoxaparin (with loss of fetus) | 4 | 3.51 | 3 | 5.66 | 7 | 4.19 |
| Total No. 167 | 114 | 100 | 53 | 100 | 167 | 100 |

*Notes:* * – Hypothesized Mean Difference = 0.05; T-test = 0.002471118458; Degree of freedom = 1; p-values < 0.05 = significant results.

The present study included 205 pregnant women who had recurrent fetal loss. Of them 167 women with BV and CMV infection received treatment with enoxaparin. 160 (95.81%) cases respond positively to treatment, while 7 (4.19%) cases do not respond to treatment regardless of the level of fibrinogen, with a significant statistical difference (p = 0.05) (Table 8). 167 patients with BV and CMV received enoxaparin and investigated fibrinogen levels previously. From 167 patients, there were 114 patients had a normal fibrinogen level (200–400 mg/dL), while the remaining 53 of the 167 cases had a high fibrinogen level (> 400 mg/dL).

Fetal loss is a major health problem that has unfavorable pregnancy consequences. Treatment during subsequent pregnancies with unfractionated heparin improves pregnancy outcomes [17]. The aim of the current study was to estimate the effect of enoxaparin on fetal-loss women with BV and CMV infection who had a normal or high fibrinogen level and to confirm that enoxaparin was an effective anticoagulant and improved pregnancy outcome. From 205 pregnant women between the ages of 15 and 40 who were suffering from recurrent fetal loss, 81% had infections, including CMV and BV, while 19% of cases without infection may have other causes of fetal loss, like other diseases. We can see that the ratio of 81% of infection (Table 1) includes CMV 92.22% and BV 7.78% (Table 2) related to recurrent fetal loss in Iraq, which corresponds with Qabas N. Al-Hajjar and Haider T. Al-Mousawi reporting that 89% of aborted patients possess positive CMV IgG, while 93% of patients were positive CMV IgM in Babylon City [18].

Turkey E.F. et al. observed the pregnant women were suffering CMV infection, 87.8% of such patients had IgG-Ab and 4.1% – IgM-Ab, that is accepted our results [10]. The current research corresponds with a systematic review done by Mhandire D. et al, who investigated the epidemiology of CMV among pregnant women in Africa and found that the prevalence of anti-CMV IgG and IgM antibodies ranged from 60 to 100% [19]. In addition, data from a Malaysian study demonstrated that 84% of well-pregnant females had IgG-Ab against CMV, and 17 persons had abortions [20]. In addition, other studies confirm that infected pregnant women with bacteria will have infants with congenital infections who were symptomatic at birth have a worse prognosis than asymptomatic ones [21]. This finding means the CMV infection is a major health problem in pregnant women more than BV in Iraq, and they need therapeutic treatment before and during pregnancy to avoid bad outcomes of pregnancy such as microcephaly, intracranial calcifications, cerebrospinal fluid abnormalities, chorioretinitis, or sensory-neural hearing impairment. Thus, the frequency of IgM antibodies to CMV indicates that latent CMV are infections or re-infections with a new strain of the virus.

Mahmood H. M. and Al-Moayad H. A. mentioned that there is no significant difference in the presence or absence of infection by BV between groups with pre-labor rupture of the membrane [22]. In the current study, the most infected age group of gravid females with previous fetal loss suffered from BV and CMV at 21–25 years old was 39.52% of the cases, and most of them were from rural areas and were 70.65% of the cases. These results come from other studies that observed that the rate of fetal loss in pregnant women associated with CMV infection was 47.3% at female's ages 22–28 years [10]. As well, it was corresponded with other results, who found elevated Abs against CMV at the rate of 26.6% in the age groups of 20–29 years [18]. This may be owing to the fact that the age of 21–25 years is active sexual period and that pregnant women are more susceptible to infection in addition to altering their immune defense during pregnancy and because of their more probable chance of pregnancy than elderly age groups.

The majority of primary CMV and BV occur in early adulthood, with elevated CMV seropositivity in younger women. Because CMV has found everywhere, people are usually susceptible to the risk of a primary viral infection, especially during pregnancy, who are serologically negative. Secondary infection and reactivation can happen, especially in communities with a high prevalence. In order to do that, the diagnosis of CMV is very important, as is the treatment and tracking of the infected child [23]. Our results, corresponding with Francesca R. et al, mentioned that 40% of immunocompetent adults had negative results for CMV infection, while infected adults presented with fever, lymphadenopathy of the neck, mild hepatitis, splenomegaly, and a decreased platelet count. CMV infection and BV are asymptomatic during childhood. Acute CMV infection and BV in pregnancy cause venous thromboembolism [24].

**Response of patients with recurrent fetal loss to treatment with enoxaparin**

In the present study, of 205 pregnant women who had recurrent fetal loss, 167 persons with BV and CMV infection received treatment with enoxaparin; 160 (95.81%) women responded positively to treatment, while seven (4.19%) cases did not respond to treatment regardless of


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fibrinogen level. This finding had attributed to increasing the inflammatory cytokines strictly in the placenta, which will produce clots and atherosclerosis with or without elevated clotting factor levels such as fibrinogen and cytokines, which decrease blood transport from mother to fetus, that can lead to the fetal loss. Enoxaparin acts as prophylactic therapy for repeated abortions.

Our explanation of the results corresponds with the study done by D'Ippolito S. et al, who found that the heparin/heparin sulfate glycosaminoglycans (HSGAGs) are important binding sites for many viruses [25]. Adherence to HSGAGs helps in the binding of a virus to target cells and its consequent entrance into the cell. Therefore, soluble heparin and heparin sulfate compounds have successfully utilized in various cases as antivirals by professionally attaching the virus to the endogenous heparin attached to the cell membrane. Therefore, enoxaparin has an anti-viral effect. Moreover, it accepted other studies that mentioned enoxaparin was as the low-molecular-weight heparin (LMWH) used as a prophylactic drug for thromboembolism, so the global guidelines assist in its usage [25]. However, this is an up-to-date cohort study and systematical revision explaining the efficiency and assurance of enoxaparin as a therapy for thromboembolism and as a prophylactic drug in pregnancy to avoid mortality and morbidity during and after pregnancy [26]. The coagulation system gets stronger in pregnant women; however, the inflammatory process due to toxoplasmosis, CMV, or BV results in a prothrombin state situation is associated with increased fibrinogen levels, which increases the risk of thromboembolism that causes placental infarction and fetal loss. In this condition, if the woman had infected with one of the infections during pregnancy, the excessive elevation of coagulation factors may increase the risk of thromboembolism [27].

The current study shows positive responses to enoxaparin (low molecular weight heparin) intake in 96.49% of the cases with normal fibrinogen levels and 94.33% of cases with high fibrinogen levels (Table 5). In addition, of the 114 cases with a normal fibrinogen level, 110 (96.49%) respond to enoxaparin treatment, while four (3.51%) cases not respond to treatment. Moreover, of 53 patients with high fibrinogen levels, 50 (94.33%) responded to enoxaparin treatment, while three (5.67%) patients not respond. This result may confirm the view that enoxaparin acts as an anti-CMV infection in addition to being a being an anticoagulant agent and is more effective than other aspirins. This finding goes with other studies, such as Bates S. M. et al. found that pregnant women with previous fetus losses often used anticoagulant drugs to avoid thromboembolism in their mothers and decrease the dangers of abortions [28].

Some of the health problems in pregnancy and the puerperium are venous thromboembolism, which can induce morbidity and death since this case had treated with LMWH such as enoxaparin [29]. However, other studies have observed the benefits of aspirin at high doses that might be associated with some side effects. The elevation of prostaglandin and the aggregation of platelets have inhibited by using aspirin; in addition to that, it has anticoagulant effects [30, 31]. Elif G. Y. et al. has mentioned in the case report, that thrombosis which is associated with CMV, has reported sporadically in the medical literature. Therefore, we need more research on this subject to understand it [32]. In the current study, we noted that enoxaparin, regardless of fibrinogen level, considerably enhanced survival at birth, compared with aspirin, by decreasing abortions, intrauterine growth retardation, preterm delivery, and pre-eclampsia, and proved to be effective. Jinfeng Xu. et al, reported that the usage of LMWH might markedly enhance the fetal and neonatal consequences in pregnant females while lowering the hazard of intrauterine fetal death [33]. Hertz-Picciotto I. et al., mentioned the fetal malformation occur by using the high dose of aspirin (600 mg/day) [34]. While, there is no effect on the fetal status by using aspirin (< 150 mg/day), in addition to other side effects of aspirin like peptic ulcer, and the fetal birth weight can be increased when using aspirin [35].

In addition to that, the use of enoxaparin has no significant effects on the pregnancy progression, like in a study done on the efficiency the usage of low molecular heparin in pregnant women with a history of abortions, and there was no information about the risk of enoxaparin on the fetus [36].

**Relationship between CMV infection, fibrinogen level, and response to enoxaparin treatment**

In our study from 167 women with previous fetal loss and BV and CMV infection who had received enoxaparin during current pregnancy 114 patients had a normal fibrinogen level, while the remaining 53 cases had increased fibrinogen level. This is because of alterations in hormones, which occur in pregnancy in addition to changes in the hemostasis system, and hemodynamics, which cause disorders in coagulation factors and fibrinolysis, which then increases the risk of thrombosis. Thrombosis will produce abnormalities in the hemodynamic vascularization of the placenta and uterus and decrease the blood perfusion of the placenta, resulting in fetal loss and a bad outcome of pregnancy [37, 38]. In a meta-analysis study, about 1.9% and 9.1% of patients with venous thromboembolism had acute CMV infection. This is because of the transient formation of anti-phospholipid antibodies, the transient formation of antibodies targeting CMV capsule phospholipids properties, and direct infection of the endothelial cells [39]. Anti-thrombin deficiency, mutations in the prothrombin gene, and hereditary thrombophilia may be associated with unfavorable pregnancy outcomes [40]. Korchynska O. and Baloga O. demonstrated the necessity for further research of pregnancy management in case of intrauterine infection, as well as the features of newborn' conditions in the presence of intrauterine infection [41]. The late and less effective prophylactic antiretroviral therapy, defects in the effectiveness of standardization of health care for the prevention of mother-to-child transmission of human immunodeficiency virus with the participation of primary healthcare specialists, the main representative of which is a general practitioner – family medicine [42].

## CONCLUSIONS

Our data demonstrate that enoxaparin is safe and effective for the prophylactic management of pregnant patients with BV and CMV infection, who are at risk for fetal loss. In pregnant women with CMV and BV have the risk of increasing inflammation. There is an increased fibrinogen level, which leads to adverse obstetrical complications,

and CMV infection leads more severe complications than BV. In addition, we have established that enoxaparin has linked to decreasing the problems of fetal loss. In spite of this, the literature on the efficiency and safety of enoxaparin for thromboembolic disease and preventive treatment of thrombosis remains insignificant.

**Ethical clearance**. Researchers have a responsibility to perform their studies with honesty and transparency.

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**Authors' contributions**. All authors contributed to the study's conception and design, material preparation, data collection, laboratory investigations, and analysis. All authors reviewed and commented on previous versions of the manuscript and approved the final version.

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