INTRODUCTION
The majority of clinical studies have proved the fact that multiple pregnancy is accompanied by a significant number of perinatal complications, namely premature abortion, feto-placental dysfunction with delayed fetal growth, as well as pre-eclampsia, which in turn contributes to an increase in perinatal morbidity and mortality [1, 2, 6, 7]. Perinatal mortality in multiple pregnancies around the world remains higher than with single pregnancy, and the probability of antenatal death of a fetus with twins or triplets is ten times higher [2, 6, 7]. The course of pregnancy with multiple pregnancies is predicted and in the future depends on the process of implantation of the fetal egg, the type of placenta, the adaptation of the mother’s body to the pregnancy, and the influence of external factors on the pregnant woman during the critical periods of the developing fetus.

According to statistics, the incidence of pre-eclampsia in multiple pregnancy is 3 to 4 times higher than that of single-femoral pregnancy. The risk of pre-eclampsia in multiple pregnancies increases in connection with hyperplacenta, as a result of violation of the placenta perfusion capacity, placental dysfunction develops with the blood flow violation [4, 8, 13]. One of the most common hypotheses concerning the pathogenetic mechanisms of pre-eclampsia is the primary utero-placental blood flow violation and concomitant violation of cytotrophoblastic invasion in spiral arteries myometrium, superficial trophoblastic invasion with subsequent incomplete remodeling of vascular structures in which there is a slowing of blood flow due to increased vascular resistance. Incomplete invasion, in turn, leads to a violation of placentation angiogenesis and thus plays a key role in the development of pre-eclampsia. Dysplasia of chorionic villi is known to be observed when the concentration of placental growth factor in the blood of the mother decreases, which is related to a number of endothelial growth factors [3, 4, 9, 10, 11]. Gene coding for the synthesis of this factor is proved to be localized in...
the fourteenth chromosome, on its long shoulder. PlGF is produced by trophoblast, namely endothelial cells of trophoblastic and placental macrophages [5, 6]. Placental growth factor promotes angiogenesis, with a pronounced angiogenic potential. (PlGF) is essentially a glycosylated homo dimer whose biological effect is realized by activating the vascular receptors with subsequent stimulation of vascular genesis and angiogenesis. Reducing the concentration of PlGF in tissues of trophoblast undoubtedly leads to disturbance of the developing the villi of chorion, reducing the transport of oxygen and nutrients of the fetus, creating a model of feto placental dysfunction with subsequent delay in fetal growth [3, 12]. In the mother’s bloodstream, the placental growth factor enters through active transport along with numerous hormones and peptides that are secreted by the cyto- and syncytiotrophoblast [4]. In this regard, the placental growth factor should be considered as a marker for a number of gestational diseases, in particular, pre-eclampsia, feto placental dysfunction and growth retardation of the fruits. Slow blood flow provokes damage to the endothelium, promotes micro thrombosis in the vessels, and development of heart attacks in the placenta. As a result of increased vascular wall sensitivity, a cascade of hemodynamic disturbances is triggered, which leads to the disruption of regulatory mechanisms and contributes to the development of chronic DIC and syndrome of decompensating placental dysfunction. In turn, the generalizing the process of endothelial dysfunction is associated with the release of cytokines, the formation of free radicals, acidosis [4, 10, 14].

The study of immunological processes that ensure the normal course of pregnancy, as well as the detection of pathogenetic mechanisms that lead to violations of its physiological course, is one of the primary tasks of reproductive immunology [5]. For the physiological course of the gestation process, it is necessary to ensure the normal functioning of the feto-placental complex. At the stage of forming the placenta, the growth factors of the placenta play a major role in the regulation processes, ensuring the normal functioning of the mother-placenta-fetus system. Placental growth factors contribute to cyto-trophoblast invasion, angiogenesis and invasion processes of the spiral arteries; they are directly related to their insufficiency and provoke the development of gestational complications: the formation of feto-placental dysfunction, miscarriage of pregnancy and the progression of pre-eclampsia [1, 6].

A prospective study of pregnancy and childbirth in 320 females with multiple pregnancies constituted the main group of examined 144 (Group I): pregnant with monchorus di-amniotic twins, 176 (group II) , patients with dihorionic di-amniotic twins. The control group consisted of 40 healthy women with unipolar pregnancy. The groups under study were homogeneous in composition and presentable. The average age of pregnant women in the main group was 29.8 ± 4.5 years, in the control group 27.6 ± 3.2 years. Differences in age, somatic pathology, frequency of complications in obstetric history between control and main groups were not revealed. Laboratory research was carried out on the basis of the clinical laboratory of the Sumy Clinical Regional Perinatal Center, the Synevo Laboratory, and the Medical-Genetic Laboratory of the Sumy State University.

The level of PlGF in serum was determined by solid-phase immunoassay analysis using monoclonal antibodies and standard R & D systems reagents in the first trimester of pregnancy. The evaluation of the state of the feto-placental complex was carried out with the help of modern sonoDIAGNOST-360 ultrasound devices from Philips (Netherlands) and Aloka SSD-2010 (Japan), in real time using the early transvaginal sensor of 6.5 MHz, in more late terms of convection sensors 3, 5 and 5 MHz in two-dimensional echo modes; it included definition of chorality, placenta metry, feto metry, determination of the state and number of amniotic fluid, dopplerometry. Dopplerometry of placental and fetal blood flow was performed in uterine arteries (MA), arteries (PA) and umbilical cord veins (PV), middle cerebral artery (SMA) fetuses. The following parameters were measured: the maximum blood flow velocity during systole, early ventricular diastole, average blood flow velocity throughout the cardiac cycle, pulsation and resistance index and systole diastolic ratio. Indicators of the hemostasis system (vascular platelets and coagulation link) were evaluated according to generally accepted methods.

Statistical processing and analysis of the data were carried out using Microsoft Excel programs using the methods of mathematical statistics and software package Statistics 8.0. Charts and diagrams were built using Microsoft Excel.

RESULTS AND DISCUSSION
According to the results of the research conducted on the progress of multiple pregnancy and the development of gestational complications, not only the presence of chronic inflammatory diseases in the history, but also the exacerbation of infections in the first trimester of pregnancy had a significant impact, as it is during this period of pregnancy undergoing implantation processes, trophoblast invasion, further development and normal functioning of the feto-placental complex. According to our data, only 43 (13.4%) women with multiple pregnancies had a physiological course of gestational process. Interruption of pregnancy up to 12 weeks was observed in 17 (5.3%) patients with multiple pregnancies, and reduction of one of

THE AIM
The purpose of the research: is to study the effect of the placental growth factors on the gestational process in multiple pregnancies.

MATERIAL AND METHODS
The study was conducted on the basis of the Sumy Regional Clinical Perinatal Center and the Department of Obstetrics and Gynecology Sumy State University during 2012-2017.
the fruits was observed in 8 (2.5%) pregnant women. The course of multiple pregnancies was accompanied by the symptoms of a recurring threat of abortion in 180 (56.2%) cases, which resulted in inpatient treatment in the period of 8-12, 14-16, 18-22 and 24-28 weeks of gestation. Among the main etiologic factors that provoked the threat of early termination of pregnancy, 107 (33.4%) of the pregnant women in the first place had a history of chronic endometritis, in the control group this was observed in 24 (7.5%) pregnant women. In the microscopic examination of excretions from the cervical canal and vagina in 168 (52.6%) patients of the main group, the conditionally pathogenic micro flora was detected, while the control group was 5 (12.5%). A combined bacterial and viral infection (Epstein-Barr virus in combination with Urea plasma urea licitum) was detected in cervical canal sows in 107 (33.4%) patients in the main group, and in 3 (7, 5%) control women, pathogenic staphylococcus and streptococcus in 60 (18.7%) of the pregnant women in the main group and 2 (5.0%) in the control group.

The study of the hemostasis of the examined pregnant women has shown that during multiple pregnancies changes were noted in the first trimester of pregnancy. These abnormalities were manifested by the characteristic changes of the vascular platelet unit: the platelet count was 181.2 ± 8.7 × 109 / l, with a control group of 236.4 ± 8.7 × 109 / l, and there was also an inhibition of the ADF-induced platelet aggregation and its decrease by 1.2 times (32.4 ± 1.7%) in almost half of the pregnant women in the main group compared to the average control group, which was 56.2 ± 2.6% (p < 0.01). Investigation of the coagulation link of hemostasis showed an increase in the level of fibrinogen in the main group to the level of 5,5 ± 0,6 g / l, with a control group of 12, 0 ± 1.2 mg / 100 ml in the main group, with a control group of 418.2 ± 10.4 pg / ml (p <0.01), the development of severe forms of pre-eclampsia - in 56 (17.5%) cases, (p <0.01), the control group, this indicator was 3 (7.5%) and 1 (2.5%) respectively.

The study of the hemostasis of the examined pregnant women was at risk of developing gestational complications - premature births in 67.8%
BASIC CLINICAL AND PATHOGENETIC ASPECTS OF DEVELOPING THE COMPLICATIONS DURING MULTIPLE PREGNANCIES

1. Low levels of PlGF in serum of pregnant women with multiple pregnancies in the case of premature delivery, feto-placental dysfunction and preeclampsia (111.23 ± 8.4, 203.24 ± 6.4 and 305.86 ± 7.4 pg / ml) in compared with the corresponding indicators for single-pregnancy (418.2 ± 10.4 pg / ml) is a prognostic marker for the development of gestating complications, which is reliably confirmed by the study (p <0.01).

2. The revealed violations of vascular thrombocyte and coagulation homeostasis in the first trimester of pregnancy are the main risk factors for premature abortion.

3. Timely medical correction of gestational complications during multiple pregnancies with using the micronized progesterone, low molecular weight heparins, angio protectants allowed prolonging the pregnancy with monochoric type of placentation by 3.2 weeks (up to 34.2 ± 2.4 weeks), and in the case of dichoric twins - to full-term pregnancy.

REFERENCES


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Authors’ contributions:
According to the order of the Authorship.
Conflict of interest:
The Authors declare no conflict of interest.

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