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## THE FEATURES OF CIRCULATORY DYNAMICS DURING PHYSIOLOGICAL PREGNANCY

**Summary.** *In the article the meaning of the gravitational orthostatic factor for blood circulation of the pregnant women is examined. According to the developed anthropophysiological approach of 147 pregnant women and of 230 nonpregnant women complex research central and peripheral blood circulation was carried out. The registration of the main hemodynamic of parameters was carried out with the help of univascular method of tetrapolar breast and regional rheography. The received data testify the expressed and increasing tension in cardiovascular systems functioning in the pregnant women. It is clear, that this tension is especially shown while standing and during trimester dynamics. It is reflected in characteristic changes of typological structure connected (by standing and laying) the characteristics of the circulatory dynamics.*

**Key words:** *pregnancy, circulatory dynamics, orthostatic, cardiovascular system, endothelium.*

### Introduction

Framework of clinical physiology and general pathology of human must surely be the notion that the distinctive human quality of biological species from other mammals with pronograde denote static and four locomotion is bipedal locomotion and the associated gravitational factor of particular importance in the functioning of the major physiological systems. In numerous studies conducted long ago set to hydrostatic redistribution of blood to regulate central and peripheral hemodynamic in orthostatic, defined now as gravitational circulation factor [Айламазян, 2007; Rang, Van Montfrans, et al., 2008; Sibai, 2008]. It should take into account the circumstances that orthostatic - is the basic physical condition of his life. It is advisable to once again focus on the following factors that a woman bears pregnancy in certain circumstances tag orthograde statics and walking upright. Moreover, during pregnancy effects of hydrostatic factor reinforced molded as a result of growth of the fetus and uterus characteristic biophysical conditions of regional and systemic circulation. All this justifies the question of absolute relevance to humans and especially for pregnant two normative characteristics of the basic functional state of cardiovascular system (CVS) - klinostatic and orthostatic. And related characteristics "standing-lying" is regarded as a reflection of the most characteristic hemodynamic situation for human beings as orthograde against which mainly sold CVS reactivity to various influences and the human condition [Белкания, Пухальска, 2006]. But especially it should be noted that the value of the gravitational factor - is the basic theory and practice in space biology and medicine. At the same time in a traditional clinical practice in all diagnostic studies characteristic of CVS is conducted under klinostatic rest, including lateral variations of this provision in pregnant women [Белкания, Пухальска, 2006; Rang, Van Montfrans, et al., 2008].

Although specific problems, such as hemodynamic assessment intralungs shunt, used body position while sitting and standing [DePaco, Kametas, 2008]. So, indeed, almost no need full regulatory hemodynamic characteristics, as in nonpregnant and in pregnant women in orthostatic - in the

most specific to pregnancy, denote conditions. At the same time arising in pregnancy is characterized by additional physical conditions (system uterine-placental blood flow, growth of the uterus and fetus, squeezing the large pelvic vessels and pressure gradient change in the ways of venous inflow to the right heart, especially in standing position) can affect the regulation of blood flow in gravitational factor [Понярева и др., 2008]. If a pregnancy is to be successful, it must have a normal developmental program and an efficient means of gaining access to and maintaining a nutrient pipeline derived from the maternal circulation. A continuous structural and functional development of the uteroplacental vasculature, including trophoblast invasion, spiral artery conversion, and constant adaptation to increasing levels of perfusion, is required. Trophoblast invasion proceeds by two different pathways: interstitial and endovascular. Both are derived from the proliferating tips of the anchoring villi. When the vessel is penetrated by interstitial trophoblast, the trophoblasts are termed endovascular and they proceed to migrate in a retrograde direction along the vascular lumen (opposite to the direction of arterial flow). Interstitial trophoblastic cells will fuse to form multinuclear giant cells at the end of their itinerary (either in the deeper decidua or myometrium). The endovascular trophoblast will remain essentially mononuclear during "burial" in an amorphous acidophilic "fibrinoid" material. In the very superficial endometrium, facing the intervillous space, the very distal venous segments can show replacement of endothelium by trophoblast [Айламазян, 2007].

Elaboration of vascular changes is restricted to the arteries with no apparent involvement of the veins. Physical (hemodynamic) flow-stress may be important to induce retrograde trophoblast migration in blood vessels. In general, insufficient synthesis and release of the relaxation factor nitric oxide (NO) by the vascular endothelium may result in generalized arterial vasoconstriction and increased resistance to flow in the uteroplacental circulation [Sibai, 2008]. NO, an endogenous vasodilator and inhibitor of vascular smooth muscle cell growth, is synthesized in the endothelium by a

constitutive NO synthase. Pregnancy appears to normally enhance acetylcholine-induced nitric oxide synthesis and release in the human uterine artery [Юпатов, Фаткулин, 2006]. NO antagonizes the effects of angiotensin II on vascular tone and growth and also down-regulates the synthesis of angiotensin-converting enzyme (ACE) and angiotensin II type I receptors. In the absence of NO antagonism, angiotensin II increases prostacyclin production by the uterine artery endothelium via the angiotensin type I receptor.

Vascular endothelium in this circulation primarily serves to assure blood-supply to every organ according to physiological needs. The mechanisms underlying the alterations in vascular resistance and the role of endothelium in human pregnancy have been investigated intensively, yet we still lack knowledge for primary noninvasive diagnostic test for adequate blood-supply of pregnancy [Макаров, Николаев, 2004]. The urgency of research in this direction is determined according to the regulation of blood flow in a gravitational factor in CVS reactivity on the development of arterial hypertension [Серов, Стольников, 2006]. Especially given the circumstances, that pregnancy is a provoking factor in the development of hypertension in women [Батюшкин, Заяц, 2003].

To clarify the role of adequate blood-supply of pregnancy in pregnancy-related obstetric disorders, we studied the hemodynamic effects from normal pregnant women and from gravidas with various obstetric complications of pregnancy.

### Materials and methods

The study was performed between September 2008 and December 2011 in the 1-st Vinnitsya clinical maternity home following a study protocol approved by the institutional review board. All of the patients gave their informed consent. Investigation of the CVS in klinostatic and orthostatic conducted in clinically healthy nonpregnant women younger than 35 years (n=230). These anthropo-physiological characteristics of the cardiovascular system in women of reproductive age were required regulatory framework for the analysis of the dynamics of basic indicators of central and peripheral circulation in women during the first, second and third trimesters of pregnancy. Functional status of CVC was investigated in 122 women with physiological pregnancy and in 25 women with fetal growth restriction, and preeclampsia.

Preeclampsia was defined by one of the following: hypertension  $>140/90$  mm Hg, 24-hour proteinuria  $>0,3$  g per 24 hours, oliguria  $<500$  mL per 24 hours, cerebral or visual disturbances, epigastric or right-upper-quadrant pain, or impaired liver function and thrombocytopenia developing after 20 weeks of gestation in a previously normotensive woman [Sibai, 2008]. Fetal growth restriction was defined by a birth weight below the 10th percentile for the gestational age.

Obesity, overweight, chronic hypertension, diabetes, renal and CVDs, and multiple pregnancies in the index pregnancy were exclusion criteria for case and control subjects, because these conditions increase the incidence and the severity of

obstetric complications. Smokers were also excluded, because in them the risk of preeclampsia seems to be reduced and, in postpartum, they alter markers of endothelial function. Subjects with thrombophilia were excluded. None used hormonal or intrauterine contraceptives or received medications.

A detailed parental history of cardiovascular disorders was obtained using a structured interview questionnaire. As significant end points of CVD, hypertension and premature atheromatous arterial disease (cerebral, carotid, coronary, aortic, and peripheral) were considered positive. All of the study subjects had 10 years of education and belonged to the middle-income groups.

Comprehensive registration of the main parameters of central and peripheral hemodynamic was conducted by standard tetrapolar chest and of regional rheography [Kubicek et al., 1966, Ronkyn, 1997] in a state of active orthostatic (immediately after preparation of the patient in standing position) and klinostatic rest (15-20 minutes after the transition in the supine position). It should emphasize the use of special relevance as a rheography developed non-invasive method in studies of pregnant women. The default method registered and identified the following basic parameters of central hemodynamic: mean arterial pressure (BP), heart rate (HR), stroke volume of the heart (SVH), minute volume of blood (MVB), and indexed by body weight value of impact (WV) and minute (CO) cardiac output. Contractile function (CF) (on the right of heart) was estimated by the amplitude of the differential thoracic rheograms ( $\Delta Z/\Delta t$ ,  $\text{cm}\cdot\text{s}^{-1}$ ). Determined by the ratio  $\text{BP}/\text{CO}$  (units) As equivalent to the well-known for total peripheral vascular resistance, and calculated overall arterial perfusion

$$\text{OAP} = \text{BP} \times \text{SVH} \text{ (units).}$$

Regional head circulation, abdomen and pelvis, thigh and shin were assessed in terms of blood flow, BF (amplitude differential rheograms) regional resistance arterial flow - RRF (the ratio of SVH and BF) deposition of blood - DB (reverse rate base impedance Z0) and venous outflow - VF (the ratio of BF and DB). Characteristics held anthropo-physiological based approach that takes into account the typological diversity of hemodynamic disorders during the transition from a state klinostatic rest in the upright posture [Белкания, Пухальська, 2006].

The latter reflected in the identification of three types of blood circulation in orthostatic that fundamentally differ in orientation changes cardiac output for its size in the prone position, adopted by 100%. Relative (in %) change in MVB in orthostatic determined on 95% percentile zone fluctuations of individual values about the mean in klinostatic MVB. This range of representative sample studied was 94-106%. Hypokinetic (hypodynamic) diagnosed with Type I in terms MVB orthostatic below 94%, eukinetic (II) - 94-106% and hyperkinetic (III) type - while quantities MVB in excess of 106%. Selected types of qualitative differences are determined by the associated characteristics of hemodynamic in klinostatic. However, as it was found that

the types of circulation in orthostatic determine qualitatively different CVS reactivity to various effects (physical and mental stress, pharmacological agents), such as depending on body position (standing, lying down) and the type of regulation of blood circulation in orthostatic. It is possible to determine the type of hemodynamic in orthostatic CVS reactivity as a marker.

Data are presented as mean $\pm$ SEM. Data were analyzed by Student t-test, and 2 test, using Sigma Stat software (Sigma). A P value <0.05 was considered significant.

### Results and their discussion

Patients from groups of healthy women clearly identified three types of hemodynamic in orthostatic: hypokinetic (I), eukinetic (II) and hyperkinetic (III). This is determined by the ratio of age dynamics of these types. In our study demonstrates that the structure typologies hemodynamic in orthostatic women before 30 years- age group predominates hypokinetic representation type, respectively, in 67% ( $p < 0.01$ ) and 60% of cases ( $p < 0.05$ ). A marked reduction (50%) representation of type I observed in women whose age corresponds 30-35 years. In parallel, the award-age dynamics of type I increased the total representation of types II and III - from 33% in the women before 30 years-age group, and to 50% in the group of women in the 30-35 years-age. Clearly defined typological direction of blood flow in orthostatic and marked the first, second and third trimesters of pregnancy.

Typological structure hemodynamic in the first trimester is quite identical with that in nonpregnant women. Further, representation of type I progressively decreased from 67% in the first trimester to 55% in the second and 44% in the third trimester. Parallel to this representation type III expressed grew from 21% in the first trimester to 28% in the second and up to 46% in the third trimester. Hyperkinetic hemodynamic in orthostatic was observed absolute prevalence among patients with pathological pregnancies ( $p < 0.01$ ). The latter was marked in 92% of pregnant women while I type all in 4% of cases. Such dynamics of the ratio between type I and III indicates that the basis of adaptation of blood circulation in pregnant women is hyperkinetic orientation. Last, as noted above, is based on age and dynamics among nonpregnant women during pregnancy but this focus is much more pronounced character. If age orientation in hyperkinetic circulatory adaptation in orthostatic realized for several decades, the pregnancy is much shorter adaptation period is only 9 months, and the most active typological alteration in hemodynamic orthostatic sold mainly in the second half of pregnancy. Molded in the process of pregnancy trimesters types are characterized by varying degrees of stability.

The greatest stability was characterized by Type I, which initially established during the second study during the first trimester played in 69% of cases. The uncertainty in this respect characterized type II (50%) and low stability in the first trimester of different type III hemodynamic in orthostatic.

However, already since the 2nd trimester and then in the 3rd trimester, hyperkinetic type of stability is progressively increased, according to 50% and 80%. After I type in the second trimester remained sufficient stability (58%), significantly decreased in the III trimester to 14%. In our study of the longitudinal sample is determined by a progressive increase from first to third trimester it is this orientation transitions (I-II-III). Thus, in the first trimester of this orientation was determined in 57% ( $p < 0.05$ ) in the second trimester - 75% ( $p < 0.01$ ) in the third trimester - in 88% ( $p < 0.01$ ) cases. Reverse direction (III-II-I), on the contrary, in the first trimester was determined in the prevailing inadequate number of cases (43%), and thereafter progressively decreased, respectively, in the second trimester to 20% in the third trimester to 12% of cases.

These data suggest that in a pregnancy that develops over a relatively short period of time formed strongly marked above in the analysis of age differences in ontogenetic orientation typological manifestations of adaptation hemodynamic in orthostatic. This is evidence that the functional conditions, molded pregnancy synergistic hemodynamic mechanisms, ensure the adaptation of blood flow to the hydrostatic factor in orthostatic. In this regard, the undoubted interest are the data obtained that the abnormal pregnancy is associated with almost full advantage of hyperkinetic (III) type of hemodynamic in orthostatic - 92% of cases ( $p < 0.01$ ). While, the I-st or type hypokinetic state of hemodynamic in orthostatic identified only 1 case of 25 pregnant women with pathology (4%). Similarly, a single detection was in the group with pregnancy pathology of intermediate type II or eukinetic (4%). This confirms the above representation of the hyperkinetic direction of development during pregnancy, increasing tensions in the functioning of CVS and emphasizes the clinical importance of identifying the type of hyperkinetic circulatory state as adverse signs in the prognosis of pregnancy.

Interaction of hydrostatic blood factor and additional hemodynamic conditions is the basis anthropo-physiological circulatory dynamics in pregnant and is reflected in specific changes typological structures and appropriate hemodynamic disorders in klinostatic and in orthostatic. Found in our study overall changes in basic parameters of central and peripheral circulation during pregnancy in a klinostatic in general compliance with this and other researchers. As shown in our investigations, in pregnant women during all three trimesters in the state klinostatic resting (supine) systolic, diastolic and medium BP decreased and heart rate increased. Increase systolic indicators of cardiac activity (SVH CF) in the first trimester of changing their decline in the third trimester. CF significantly increased during the first two trimesters and decreases in the third trimester.

Changes in peripheral circulation in a prone position is a clear asymmetry index of blood flow between the vascular pools located above (head) and lower (abdomen, thigh, shin) the heart. Thus, cerebral blood flow in klinostatic, increased throughout pregnancy, is characterized by its relative decline

from first to third trimester. This is likely to have decreased in 1 trimester blood flow of the lower limbs (by thigh and shin) in the future, as well as blood flow to the head, progressively decreases. On abdominal blood flow can be noted only a tendency to reduce it without expressive dynamics throughout pregnancy. Such stability of flow abdominal expressly provided by other regions and peripheral vascular disease, especially as seen from the data, by reducing blood flow in the vessels of the lower limbs and in 3 trimester - and cerebral blood flow. The feasibility of such redistribution is obvious and reflects the orientation of the relevant regulatory mechanisms for maintaining the stability of abdominal and pelvic blood flow, which provides the core for pregnancy hemodynamic request from the growing uterus and fetus.

The general direction of changes in orthostatic pressure in pregnant women is the same as in klinostatic, and is characterized by significantly reduced levels during all three trimesters. As in conditions of calm in a prone position, relative to the lowest level of blood pressure is defined in orthostatic in the first trimester. It should be noted that when comparing the basic cardio-dynamical parameters which, at first glance, unidirectional change in orthostatic are much more pronounced changes. Firstly, it is - a preliminary increase of systolic cardiac performance, and, secondly, a more stable maintenance of them at this level throughout pregnancy trimester dynamics. This applies to the pulmonary circulation.

This focus was reflected the formation of a new hemodynamic profile, which fully corresponds to the restructuring of the typological structure trimester blood flow in pregnant women and aims to ensure optimum life for the most relevant physical conditions. The possibility of identifying such a reorganization emphasizes the importance of diagnostic related anthropo-physiological (standing, lying down) the characteristics of circulation.

Comparison of changes in central circulation and peripheral arterial circulation shows that the basis adjustment is celebrated cardio-dynamical centralization of circulation. A reflection of this was increased in peripheral vascular resistance, especially expressed in orthostatic. It identifies significant differences in the dynamics of blood flow rate between the different vascular regions. Thus, the arterial blood flow of the head in orthostatic significantly lower in a trimester, and during the subsequent trimesters were significantly higher compared to non-pregnant ones. The opposite is the dynamics of arterial blood flow in the abdominal cavity. It is important to note that the orthostatic decrease BP in abdominal region in the second half of pregnancy is a reliable and significantly more pronounced than klinostatic. In orthostatic changes in blood circulation to the lower limbs does not differ from klinostatic, except for a significantly more pronounced reduction in his leg in the 1-st trimester. We should pay attention to the significant and progressive BP decrease in the thigh and shin in both postural conditions. Accordingly, the orthostatic decrease in arterial blood flow and arterial vascular resistance was significantly higher

compared to non-pregnant ones, in almost all areas of the body below of heart, during pregnancy, and characterized by a clear directional dynamics. Its can use like indicator for progressive increase of resistance peripheral vascular.

It should be noted that the comparison of the dynamics of changes in regional vascular resistance indices in klinostatic, so especially in orthostatic sufficient evidence of the use of conditionality in the peripheral vascular resistance as an indicator of total peripheral vascular resistance. As for cardiodynamics and peripheral arterial circulation changes in the venous circulation during pregnancy were more pronounced in comparison between orthostatic and klinostatic. Trimester general direction of the dynamics of venous circulation was decreased of regional venous drainage, which, along with a decrease in blood flow, followed by reduction of regional blood volume. This, apparently, is the mechanism required to maintain blood volume in order to ensure as stable blood of mother and fetus. That is the venous dynamics can be taken as equivalent, and circulatory mechanism, which prevents pregnancy by physiological, as manifestations of failure of the peripheral venous circulation and edema.

First of all, it is characteristic that takes into account the standard and natural for orthograde human situation stereotyped daily change in body position, revealed a marked gain in pregnant women standing influence of the hydrostatic factor in venous circulation areas below of the heart. It is in this situation - the transition from a prone position in the standing position in the lower extremities, while growing up on the pelvis and legs, increases the deposition of blood.

As noted above, the basic anthropo-physiological related (standing, lying) was a characteristic typological structure of circulation in orthostatic. At the same time a number of hemodynamic parameters was revealed not only expressed in quantitative but also qualitative differences between the conditions principally for pregnancy when I (hypokinetic) and III (hyperkinetic) types of blood circulation.

General and typological analysis of hemodynamic characteristics, in our study, was indicated very substantial voltage operation of CVS in pregnant women. This tension could caused by typical hormonal changes in pregnant women, remodeling of blood vessels, the formation of the utero-placental blood flow and complex biophysical environment formed by the progressive enlargement of the uterus with the fetus, which significantly affects the functioning of the abdomen and pelvis and a mechanical effect on the circulation of blood in the vessels.

Our data provide further evidence of functional cardiovascular risk markers that may contribute to later obstetric complications. Moreover, it adds women with pregnancy-related inadequate blood supply as a potential population at preeclampsia and IUGR. The need to identify whether this association may be extrapolated to perinatal lost deserves to be addressed.

In conclusion, pregnancy-related disorders circulation of the blood, characterized by a insufficient blood supply

abdominal and pelvic regions is present in a significant number of subjects with a history of preeclampsia and spontaneous recurrent abortions. We suggest that endothelial dysfunction may be a triggering mechanism for majority of pregnancy-associated complications. The presence of the vascular abnormalities in women with obstetric complications, who were not exposed to the vascular damage, supports the hypothesis that, in a subgroup of women, endothelial dysfunction constitutes a cause of placental defect, which in obstetric complications is latter aggravated by the factors liberated by the ischemic placenta into the maternal circulation.

### Perspectives

The findings of the present study lead to the exciting hypothesis that correction of the endothelium-related hemodynamic disorders early in pregnancy may help prevent obstetric complications derived from placental-related disorders and eventually may modify the cardiovascular risk later. We need to pursue studies to test whether gestational endotheliopathy represents a cause of placental defects, identify obstetric patients who present intragenerationally or in previous pregnancies with clinical signs of a defective placental, and introduce interventions to improve endothelial function.

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#### ОСОБЕННОСТИ ГЕМОДИНАМИКИ ПРИ ФИЗИОЛОГИЧЕСКОЙ БЕРЕМЕННОСТИ

**Резюме.** В статье рассматривается влияние гравитационного ортостатического фактора на циркуляцию крови у беременных женщин. Используя антропофизиологический подход, проведено комплексное исследование центрального и периферического кровообращения у 147 беременных женщин и 230 небеременных женщин. Регистрация основных параметров гемодинамики проводилась с помощью метода неинвазивной тетраполярной грудной и регионарной реографии. Полученные данные свидетельствуют о выраженном повышении напряжения в сердечно-сосудистой системе у беременных. Это отражается в изменениях типологической структуры (стоя и лежа) характеристики гемодинамики.

**Ключевые слова:** беременность, гемодинамика, ортостатика, сердечно-сосудистая система, эндотелий.

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#### ОСОБЛИВОСТІ ГЕМОДИНАМІКИ ПРИ ФІЗІОЛОГІЧНІЙ ВАГІТНОСТІ

**Резюме.** У статті розглядається вплив гравітаційного ортостатического фактора на циркуляцію крові у вагітних жінок. Використовуючи антропофізіологічний підхід, проведено комплексне дослідження центрального та периферичного кровообігу у 147 вагітних жінок і 230 невагітних жінок. Реєстрація основних параметрів гемодинаміки проводилася за допомогою методу неінвазивної тетраполярної грудної та регіонарної реографії. Отримані дані свідчать про виразне підвищення напруги в серцево-судинній системі у вагітних. Це відбивається у змінах типологічної структури (стоячи і лежачи) характеристики гемодинаміки.

**Ключові слова:** вагітність, гемодинаміка, ортостатика, серцево-судинна система, ендотелій.

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## ПРОЦЕСИ ГОРМОНАЛЬНОЇ ДЕЗАДАПТАЦІЇ У ПАЦІЄНТІВ З ІДІОПАТИЧНИМ ПРОЛАПСОМ МІТРАЛЬНОГО КЛАПАНУ