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THE EFFECT OF PRECONCEPTION CARE ON PERINATAL OUTCOMES OF THE MOTHER-PLACENTA-FETUS SYSTEM

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Abstract

Relevance. Examining the placenta could provide valuable insights into the effectiveness of preconception care, inform pregnancy management strategies, and aid in planning future pregnancies.

Objective: comparative clinical and morphological characteristics of the "mother-patient-fetus" system in women with preconception care and women without preconception care.

Methods. A prospective study compared maternal, perinatal and placental outcomes in a group of women who received preconception 6 months prior to their current pregnancy and women who did not receive preconception prior to their current pregnancy, provided that they also had placental histology. Clinical data were obtained from the medical records of the mother and newborn in a comprehensive health information system. The examination of the placenta and the collection of placental tissue fragments were carried out in accordance with the consensus recommendations of the Amsterdam Placental Workshop Group.

Results. Women with preconception care suffered less from serious pregnancy complications, such as Preeclampsia (4.3% vs. 11.6%; p=0.015) or gestational hypertension (7.9% vs. 15.2%; p=0.039). In the group of newborns from women with preconception care, young children for gestational age are less common (10.4% vs. 19.5%; p=0.021), newborns have fewer respiratory complications (14.0% vs. 23.8%; p=0.025) and antenatal fetal mortality (0.6% vs. 6.1%; p=0.006). Histopathological results of maternal vascular malperfusion (12.8% vs. 29.9%; p<0.01), acute inflammation of the placenta (4.9% vs. 11.6%; p=0.028) and chronic inflammation of the placenta (5.5% vs. 12.8%; p=0.022) are rare in the placentas of women with preconception care, as well as macrophages are rare. chorial with meconium in the lamina and amniotic membranes (7.9% vs. 16.5%; p=0.019).

Conclusion. Preconception care, aimed at improving the health of the mother, leads to a decrease in histopathological findings in the placentas and an improvement in the perinatal outcome. Morphological examination of the placenta should be an integral part of the strategy aimed at mitigating the adverse outcomes of current and subsequent pregnancy and childbirth in women without preconception care.

Keywords: *preconception care, placenta, perinatal outcome.*

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Резюме

ВЛИЯНИЕ ПРЕГРАВИДАРНОЙ ПОДГОТОВКИ НА ПЕРИНАТАЛЬНЫЕ ИСХОДЫ СИСТЕМЫ «МАТЬ-ПЛАЦЕНТА-ПЛОД»

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Актуальность. Исследование плаценты может дать ценную информацию об эффективности подготовки к зачатию, помочь в разработке стратегий ведения беременности и планировании будущих беременностей.

Цель исследования: сравнительная клиническая и морфологическая характеристика системы «мать-пациента-плод» у женщин с прегравидарной подготовкой и женщин без прегравидарной подготовки.

Методы. В проспективном исследовании сравнивали материнский, перинатальный исход и морфологические данные плаценты группы женщин у которых за 6 месяцев до текущей беременности была проведена прегравидарная подготовка и женщин, не проходивших прегравидарную подготовку до наступления текущей беременности, при условии, что у них также проводилось гистологическое исследование плаценты. Клинические данные были получены из медицинских записей матери и новорожденного в комплексной медицинской информационной системе. Исследование плаценты и отбор фрагментов ткани плаценты проводились в соответствии с рекомендациями консенсуса Amsterdam Placental Workshop Group.

Результаты. Женщины с прегравидарной подготовкой реже страдали от таких тяжелых осложнений беременности как преэклампсия (4.3% против 11.6%; p=0.015) или гестационная гипертензия (7.9% против 15.2%; p=0.039). В группе новорождённых от женщин с прегравидарной подготовкой реже встречалась малые для гестационного возраста новорожденные (10.4% против 19.5%; p=0.021), реже наблюдались респираторные осложнения у новорожденных (14.0% против 23.8%; p=0.025) и случаи антенатальной гибели плода (0.6% против 6.1%; p=0.006). В плацентах женщин с прегравидарной подготовкой реже встречались гистопатологические находки материнской сосудистой мальперфузии (12.8% против 29.9%; p<0,01), острого воспаления плаценты (4.9% против 11.6%; p=0,028) и хронического воспаления плаценты (5.5% против 12.8%; p=0,022), а также реже обнаруживались макрофаги с меконием в хориальной пластинке и амниотических оболочках (7.9% против 16.5%; p=0,019).

Выводы. Прегравидарная подготовка, направленная на улучшение здоровья матери, приводит к уменьшению гистопатологических находок в плацентах и улучшению перинатального исхода. Морфологическое исследование плаценты должно составлять неотъемлемую часть стратегии, направленной на смягчение неблагоприятных исходов текущей и последующей беременности и родов у женщин без прегравидарной подготовки.

Ключевые слова: *прегравидарная подготовка, плацента, перинатальный исход.*

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Түйіндеме

ПРЕГРАВИДАЛЬДЫ ДАЙЫНДЫҚТЫҢ "АНА-ПЛАЦЕНТА-ҰРЫҚ"ЖҮЙЕСІНІҢ ПЕРИНАТАЛДЫҚ НӘТИЖЕЛЕРІНЕ ӘСЕРІ

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Өзектілігі. Плацентарлы зерттеу жүктілікке дейінгі күтімнің тиімділігі туралы құнды ақпарат бере алады, жүктілікті басқару стратегияларын жасауға және болашақ жүктілікті жоспарлауға көмектеседі.

Зерттеудің мақсаты: прегравидальды дайындығы бар әйелдерде және прегравидальды дайындығы жоқ әйелдерде "ана-пациент-ұрық" жүйесінің салыстырмалы клиникалық және морфологиялық сипаттамасы.

Әдістері. Перспективалық зерттеуде қазіргі жүктіліктен 6 ай бұрын прегравидарлық дайындықтан өткен әйелдер тобы мен қазіргі жүктілікке дейін прегравидарлы дайындықтан өтпеген әйелдердің, егер олар плацентаға гистологиялық зерттеу жүргізген болса, аналық, перинаталдық және плацентарлы морфологиялық нәтижелерін

салыстырды. Клиникалық деректер кешенді медициналық ақпараттық жүйедегі ана мен жаңа туған нәрестенің медициналық жазбаларынан алынды. Плацентаны зерттеу және плацента тінінің сынықтарын таңдау Amsterdam Placental Workshop Group консенсусының ұсыныстарына сәйкес жүргізілді.

Нәтижесі. Преэклампсия (4.3% қарсы 11.6%; p=0.015) немесе гестациялық гипертензия (7.9% қарсы 15.2%; p=0.039) сияқты жүктіліктің ауыр асқынуларынан прегравидальды дайындығы бар әйелдер аз зардап шекті. Прегравидальды дайындығы бар әйелдерден шыққан жаңа туған нәрестелер тобында гестациялық жасқа арналған кішкентай нәрестелер сирек кездеседі (10.4% қарсы 19.5%; p=0.021), жаңа туған нәрестелерде респираторлық асқынулар (14.0% қарсы 23.8%; p=0.025) және ұрықтың антенатальды өлімі жағдайлары (0.6% қарсы 6.1%; p=0.006) аз байқалды.

Прегравидальды дайындығы бар әйелдердің плаценталарында аналық тамырлы малперфузияның гистопатологиялық нәтижелері (12.8% қарсы 29.9%; p<0,01), плацентаның жедел қабынуы (4.9% қарсы 11.6%; p=0,028) және плацентаның созылмалы қабынуы (5.5% қарсы 12.8%; p=0,022) сирек кездеседі, сонымен қатар хориальды пластинада және амниотикалық қабықшаларда (7.9% қарсы 16.5%; p=0,019) меконийі бар макрофагтар аз кездеседі.

Қорытынды. Ананың денсаулығын жақсартуға бағытталған прегравидарлы дайындық плацентадағы гистопатологиялық нәтижелердің төмендеуіне және перинаталдық нәтиженің жақсаруына әкеледі. Плацентаның морфологиялық зерттеуі прегравидарлы дайындықсыз әйелдерде ағымдағы және кейінгі жүктілік пен босанудың қолайсыз нәтижелерін азайтуға бағытталған стратегияның ажырамас бөлігі болуы керек.

Түйін сөздер: *прегравидальды дайындық, плацента, перинаталдық нәтиже.*

Дәйексөз үшін:

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Introduction

Making sure both the mother and newborn stay healthy is a key focus for public health systems around the world. The preconception period—before or between pregnancies—provides a crucial window of opportunity to improve women's health, promote healthy lifestyles, and identify risk factors for targeted interventions. Growing evidence suggests that the health status of both partners during this period plays a significant role in fertility and perinatal outcomes [3, 29, 32, 30, 28]. However, adverse birth outcomes remain a major global public health challenge, contributing to increased morbidity, mortality, and healthcare costs.

Preconception care has been shown to reduce the risk of preterm birth, low birth weight, congenital anomalies, and intrauterine growth restriction. However, most previous studies have focused on clinical characteristics rather than investigating the impact of preconception preparation on placental histopathology in relation to maternal and fetal conditions. Examining the placenta in this context could provide valuable insights into the effectiveness of preconception care, inform pregnancy management strategies, and aid in planning future pregnancies.

This study aims to compare the clinical and morphological characteristics of the Maternal-Placental-Fetal system in women who underwent preconception preparation versus those who did not.

Materials and methods

Study design

This prospective study included women who received medical care for delivery - either by vaginal birth or cesarean section - at the Regional Clinical Hospital in Karaganda, Kazakhstan, between January 1, 2018, and January 1, 2023. The study was approved by the Bioethics Committee of Karaganda Medical University (06.02.2022 №6) and written informed consent was obtained from all participants for the use of their clinical and placental morphological data for research purposes.

In accordance with the study objectives, participants were divided into two groups: "with preconception preparation" and "without preconception preparation."

The preconception preparation group included women who had undergone preconception care at least six months before their current pregnancy and whose placentas underwent histological examination.

The non-preconception preparation group included women who had not undergone preconception care before their current pregnancy, but whose placentas were also subjected to histological examination.

Placentas were sent for histological examination based on the following indications:

1. Maternal factors: Thyroid disorders, autoimmune diseases, hypertensive disorders, hypothyroidism, kidney disease, coagulopathies chronic and conditions such as diabetes.

2. Pregnancy complications: Gestational hypertension, Gestational diabetes and preterm birth.

3. Fetal/newborn factors: Antenatal fetal death or early neonatal death, birth weight below the 10th percentile, suspected infection or sepsis, an Apgar score of ≤6 at 5 minutes, or the need for respiratory support beyond 10 minutes.

4. Placental abnormalities: Deviations in placental mass or umbilical cord length, marginal or membrane insertion of the umbilical cord, and structural abnormalities of the placenta.

Exclusion Criteria: women with multiple pregnancies, chromosomal abnormalities, or congenital malformations of the newborn were excluded from the study.

Collection of clinical and morphological data

Clinical data were obtained from maternal and neonatal medical records within an integrated medical information system.

Obstetric data included gestational age at delivery, mode of delivery, and the presence of pregnancy-related pathologies. Maternal conditions assessed included hypertensive disorders and diabetes mellitus, while fetal and neonatal conditions included small for gestational age (SGA) and macrosomia.

Neonatal data encompassed clinical diagnoses of perinatal asphyxia and neonatal infections requiring intensive care, as well as antenatal fetal demise and neonatal death.

Morphological data were obtained from perinatal pathologists who conducted histopathological examinations of the placentas.

A summary of the clinical data for the study groups is presented in Table 1.

Table 1.

Demographic and clinical characteristics of the study groups.

Variables	Preconception preparation n (%) (n=164)		Non-preconception preparation n (%) (n=164)		P-value
Women's age, year	18-30	106 (64.6)	18-30	121 (73.8)	0.106
	31-40	48 (29.3)	31-40	39 (23.8)	
	41-45	10 (6.1)	41-45	4 (2.4)	
BMI, kg/м^2	<18.5	24 (14.6)	<18.5	32 (19.5)	0.136
	18.5-24.9	89 (54.3)	18.5-24.9	79 (48.2)	
	25-30	39 (23.8)	25-30	48 (29.3)	
	>30	12 (7.3)	>30	5 (3.0)	
Systolic blood pressure/ Diastolic blood pressure before pregnancy	>129 / >84	11 (6.7) / 9 (5.5)	<129 / <84	9 (5.5) /6 (3.7)	0.413 /0.603
	120-129 / 80-84	79 (48.2) /114 (69.5)	120-129 / 80-84	91 (55.5) / 121 (73.8)	
	<120 / <80	74 (45.1) /41 (25.0)	<120 / <80	64 (39.0) / 37 (22.5)	
Smoking	yes	4 (2.4)	yes	10 (6.1)	0.102
	no	160 (97.6)	no	154 (93.9)	
Alcohol consumption before pregnancy (≥2 times per month)	yes	3 (1.8)	yes	5 (3.0)	0.475
	no	161 (98.2)	no	159 (97.0)	
Mother's education	school	25 (15.2)	school	37 (22.6)	0.091
	higher	139 (84.8)	higher	127 (77.4)	
Gestation period, weeks	<28	8 (4.9)	<28	17 (10.4)	0.128
	28-31	14 (8.5)	28-31	11 (6.7)	
	32-36	42 (25.6)	32-36	51 (31.1)	
	>36	100 (61.0)	>36	85 (51.8)	
Prelabor rupture of amniotic membranes	yes	19 (11.6)	yes	11 (6.7)	0.204
	no	145 (88.4)	no	153 (83.5)	
Placental abruption	yes	6 (3.7)	yes	5 (3.0)	0.760
	no	158 (96.3)	no	159 (97.0)	
Delivery	vaginal birth	133 (81.1)	vaginal birth	129 (78.7)	0.573
	planned CS	14 (8.5)	planned CS	12 (7.3)	
	emergency CS	17 (10.4)	emergency CS	23 (14.0)	
Gender of the newborn	male	89 (54.3)	male	85 (51.8)	
	female	75 (45.7)	female	79 (48.2)	

Abbreviations: CS – cesarean section.

** p1<0.05 statistically significant differences between the group with pregravid preparation and the group without pregravid preparation.*

Definitions

Preconception care refers to a set of interventions designed to identify and modify biomedical, behavioral, and social risk factors that may impact a woman's health or pregnancy outcome. These interventions focus on prevention and management, emphasizing factors that should be addressed before conception to improve maternal and fetal health [7, 34].

Definitions of Maternal Conditions

Preeclampsia was defined as blood pressure ≥140/90 mmHg after 20 weeks of gestation, accompanied by

proteinuria (>0.3 g per day) or severe symptoms in a previously normotensive woman [9].

Chronic arterial hypertension (CAH) was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two separate occasions before 20 weeks of gestation [20].

Gestational hypertension was defined as newly diagnosed systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, measured at least twice, 4 hours apart, after 20 weeks of gestation, persisting up to one week postpartum, in the absence of systemic maternal organ damage [20].

Pregestational diabetes mellitus was diagnosed before pregnancy, based on a glycosylated hemoglobin (HbA1c) level >6.5% [44].

Gestational diabetes mellitus was diagnosed in pregnant women without a prior history of diabetes if at least two of the following criteria were met during a 3-hour, 100 g oral glucose tolerance test conducted between 24 and 28 weeks of gestation: fasting glucose ≥95 mg/dL, 1-hour glucose ≥180 mg/dL, 2-hour glucose ≥155 mg/dL, or 3-hour glucose ≥140 mg/dL [44].

Definitions of Neonatal and Perinatal Outcomes

Gestational age was determined based on the last menstrual period and confirmed by ultrasound. If first-trimester ultrasound dating differed by more than one week from menstrual dating, ultrasound measurements were used exclusively [15].

Small-for-gestational-age (SGA) neonates were defined as having a birth weight below the 10th percentile for gestational age at delivery.

Macrosomia is when a baby is born with a weight that is significantly higher than average of ≥4000 g at birth [5, 8].

Perinatal asphyxia was defined as a clinical diagnosis of birth asphyxia in the neonatal intensive care unit (NICU).

Birth asphyxia was characterized by progressive hypoxemia, hypercapnia, metabolic acidosis, and multiple organ failure.

Neonatal infection was defined as a clinical diagnosis of infection in the NICU.

Early neonatal death refers to the death of a newborn within the first seven days after birth.

Antenatal fetal death was defined as fetal demise occurring after 20 weeks of gestation, confirmed via ultrasound before delivery [2, 50].

Early neonatal death was defined as the death of a live-born infant within the first seven days of life.

Placental abruption was diagnosed based on clinical findings, including vaginal bleeding, abdominal pain, and the presence of a retroplacental blood clot unrelated to placenta previa or uterine rupture [10].

Placental Histopathology

Placental injury patterns were categorized based on the Amsterdam criteria [24]:

Maternal vascular malperfusion (MVM) was diagnosed based on histopathological findings indicative of impaired maternal blood flow to the placenta. These included:

- Central or peripheral infarctions affecting >10% of placental villi
- Acute atherosis of the basal plate or decidual arteries
- Hypertrophy of the muscular layer of basal plate arteries
- Thickening of arteriolar walls in the amniotic membranes [18, 38, 42].

Fetal vascular malperfusion (FVM) refers to a condition where there is reduced or no blood flow to the fetal part of the placenta. Diagnostic criteria included:

- Two or more medium-to-large areas of avascular villi or villi with stromal-vascular karyorrhexis
- Three or more small areas of avascular villi or villi with stromal-vascular karyorrhexis
- Thrombosis within large fetal vessels and/or vascular obliteration in stem villi [39, 37, 40, 48, 49].

Acute inflammatory placental injury was diagnosed by the presence of neutrophilic infiltration in the chorionic plate, fetal membranes (chorioamnionitis), or fetal vessels (funisitis) [24].

Chronic inflammatory placental damage is a lesion of the chorionic villi, characterized by the accumulation of small lymphocytes with a stromal reaction in the terminal chorionic villi and an increased number of fetal macrophages [16, 22].

Histological examination of the placenta

Placental examination and tissue collection were conducted in accordance with the Amsterdam Placental Workshop Group consensus recommendations [24]. Immediately after delivery, placentas were submitted for examination and processed following standard biosafety protocols.

Placentas were fixed in 10% formalin for 24–48 hours before undergoing routine histological processing. Each placenta was systematically evaluated, including:

- Photographic documentation of both the maternal and fetal surfaces
- Measurement and weighing (excluding amniotic membranes)
- Macroscopic examination of sectioned surfaces

For histological examination, the following tissue samples were collected:

- Two rolls of amniotic membranes
- Two umbilical cord fragments
- Two full-thickness placental sections
- Representative samples of any identified lesions

All tissue samples were processed using standard histological techniques and stained with hematoxylin and eosin (H&E) according to a standardized protocol.

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics 22. Group differences were assessed using the Mann–Whitney U test and the χ^2 test. A p-value < 0.05 was considered statistically significant.

Results

A comparison of the maternal part of the Maternal-Placental-Fetal system

The clinical conditions found in women from the study groups are summarized in the table 2.

In the preconception preparation group, hypertensive disorders were diagnosed in 29 (17.7%) cases, including preeclampsia in 13 (44.8%), chronic arterial hypertension in 9 (31%), and gestational hypertension in 7 (24.2%). Diabetes mellitus was observed in 15 (9.2%) women, of whom 6 (40%) had pregestational diabetes mellitus (type 1 or type 2), and 9 (60%) had gestational diabetes mellitus. Other chronic

conditions, such as chronic pyelonephritis and thyroid disease, were reported in 27 (16.5%) cases. The postpartum period was complicated by bleeding in 3 (1.8%) cases, but there were no maternal deaths in this group.

In the non-preconception preparation group, hypertensive disorders were more prevalent, affecting 50 (38.0%) women. Among them, preeclampsia occurred in 19 (38%), CAH in 6 (12.0%), and gestational hypertension in 25 (50.0%). Diabetes mellitus was diagnosed in 16 (9.8%) women, equally distributed between pregestational diabetes mellitus (8 cases, 50%) and gestational diabetes mellitus (8 cases, 50%). Other chronic conditions, including chronic pyelonephritis and thyroid disease, were recorded in 34 (20.7%) cases. Postpartum bleeding was observed in 5 (3.0%) cases. Notably, there was one maternal death in this group, attributed to bilateral purulent-necrotic pyelonephritis with abscess formation, complicated by the development of a systemic inflammatory response.

Comparative Analysis of the Fetal Compartment in the Maternal-Placental-Fetal System

The diagnoses of newborns and cases of perinatal mortality in the study groups are presented in Table 2.

Table 2.

The clinical and morphological characteristics of the maternal, fetal, and placental compartments of the «Maternal – Placental – Fetal» system.

	Clinical and morphological characteristics, n (%)	Preconception preparation (n=164)	Non-preconception preparation (n=164)	P-value
«Mother»	Preeclampsia	7 (4.3)	19 (11.6)	**0.015***
	Chronic arterial hypertension	9 (5.5)	6 (3.7)	0.428
	Gestational hypertension	13 (7.9)	25 (15.2)	**0.039***
	Pregestational diabetes mellitus	6 (3.7)	8 (4.9)	0.585
	Gestational diabetes mellitus	9 (5.5)	8 (4.9)	0.804
	Other chronic conditions[1]	27 (16.5)	34 (20.7)	0.321
	Postpartum hemorrhage	3 (1.8)	5 (3.0)	0.475
	Maternal death	0	1 (0.6)	0.317
«Fetus/ newborn»	SGA	17 (10.4)	32 (19.5)	**0.021***
	Macrosomia	14 (8.5)	23 (14.0)	0.117
	Perinatal Asphyxia	8 (4.9)	19 (11.6)	**0.028***
	Neonatal Infection	14 (8.5)	25 (15.2)	0.061
	Respiratory Problems[2]	23 (14.0)	39 (23.8)	**0.025***
	Antenatal Fetal Death	1 (0.6)	10 (6.1)	**0.006***
	Early Neonatal Death	3 (1.8)	2 (2.4)	0.653
«Placenta»	Maternal Vascular Malperfusion	21 (12.8)	49 (29.9)	**<0,01***
	Fetal Vascular Malperfusion	12 (7.3)	18 (11.0)	0.251
	Acute Inflammatory Lesions	8 (4.9)	19 (11.6)	**0.028***
	Chronic Inflammatory Lesions	9 (5.5)	21 (12.8)	**0.022***
	Meconium[3]	13 (7.9)	27 (16.5)	**0.019***

Abbreviations: SGA – Small for Gestational Age (SGA)

1 – Chronic diseases of the kidneys (e.g., pyelonephritis), thyroid gland (e.g., hypothyroidism, hyperthyroidism, and autoimmune thyroiditis).

2 – Respiratory complications in newborns, including transient tachypnea of the newborn, meconium aspiration, respiratory distress syndrome, asphyxia, and the need for oxygen therapy or intubation.

3 – Macrophages containing meconium in the chorionic plate and amniotic membranes.

p1<0.05 – Statistically significant differences between the group with preconception care and the group without preconception care.

In the group with preconception care, there were 17 (10.4%) cases of fetal growth restriction and 14 (8.5%) cases of macrosomia. Perinatal asphyxia was diagnosed in 8 (4.9%) cases. Neonatal infection was identified in 14 (8.5%) newborns. Respiratory problems, including transient tachypnea of the newborn, meconium aspiration, respiratory distress syndrome, asphyxia, and the need for oxygen therapy or intubation, were observed in 23 (14.0%) newborns. There was 1 (0.6%) case of antenatal fetal death and 3 (1.8%) cases of early neonatal mortality in this group.

In the group without preconception care, there were 32 (19.5%) cases of FGR and 23 (14.0%) cases of macrosomia. Perinatal asphyxia was diagnosed in 19 (11.6%) cases. Neonatal infection was identified in 25 (15.2%) newborns. Respiratory problems were observed in 39 (23.8%) newborns. There were 10 (6.1%) cases of antenatal fetal death and 2 (2.4%) cases of neonatal mortality.

Comparative analysis of placental findings

Histopathological findings in the placentas are presented in Table 2.

In the group that received preconception care, maternal vascular malperfusion was found in 21 (12.8%) placentas, while fetal vascular malperfusion was found in 12 (7.3%) placentas. Acute inflammatory issues, such as chorioamnionitis, funisitis, and inflammation of the blood vessels in the chorionic plate, were present in 8 (4.9%) placentas. Chronic inflammation was observed in 9 (5.5%)

placentas. Macrophages containing meconium in the chorionic plate and amniotic membranes were observed in 13 (7.9%) placentas.

In the group without preconception care, maternal vascular malperfusion was detected in 49 (29.9%) placentas. Signs of fetal vascular malperfusion were found in 18 placentas (11.0%). Acute inflammation was present in 19 placentas (11.6%), while chronic inflammation was observed in 21 placentas (12.8%). Macrophages containing meconium were found in the chorionic plate and amniotic membranes of 27 placentas (16.5%).

Discussion

This study presents a comparative clinical and morphological analysis of the "Maternal-Placental-Fetal" system in women who underwent preconception care at least six months before the current pregnancy and those who did not receive preconception care before the current pregnancy.

The clinical data showed that women who didn't receive preconception care were more likely to experience severe pregnancy complications compared to those who did. Specifically, they had higher rates of preeclampsia (11.6% vs. 4.3%; p=0.015) and gestational hypertension (15.2% vs. 7.9%; p=0.039). These results align with other studies that link preconception care to a lower risk of maternal complications. Our findings are consistent with those of other studies that associate preconception care with a reduced risk of maternal complications [1, 14, 17, 36].

Secondly, we found that women without preconception care were more likely than those who underwent preconception care to give birth to SGA newborns (19.5% vs. 10.4%; p=0.021). Additionally, respiratory complications in newborns, including transient tachypnea of the newborn, meconium aspiration, respiratory distress syndrome, asphyxia, and the need for oxygen therapy or intubation, were more frequently observed (23.8% vs. 14.6%; p=0.025), along with perinatal asphyxia (11.6% vs. 4.9%; p=0.028) and antenatal fetal death (6.1% vs. 0.6%; p=0.006). These findings are consistent with previously published studies indicating that the absence of preconception care is associated with increased neonatal morbidity and mortality, stillbirth, and low birth weight [19, 33, 45, 47]. We believe that this is primarily due to maternal health conditions, which serve as a predisposing background factor in the antenatal period, increasing the vulnerability of the fetal nervous and cardiovascular systems in postnatal life. Birth and the transition from intrauterine to independent existence are significant stressors for the fetus and newborn. In the presence of maternal infections, these stressors may disrupt compensatory-adaptive mechanisms, leading to episodes of sudden neonatal asphyxia and postnatal collapse of the vascular and respiratory systems.

Furthermore, we observed a significant increase in the frequency of maternal vascular malperfusion (MVM) in the placentas of women without preconception care (29.9% vs. 12.8%; p<0.01). Notably, preconception blood pressure did not differ between the groups, indicating that the observed maternal vascular malperfusion in the group without preconception care was not related to any preexisting hypertensive condition that could have influenced the results.

Maternal vascular malperfusion represents a placental abnormality affecting maternal vascular function and blood circulation, often associated with an increased risk of adverse fetal outcomes [6, 18, 35, 41] as well as maternal hypertensive disorders and cardiovascular diseases [43, 46]. As expected [11, 13, 27, 31], our study found that women with placental signs of maternal vascular malperfusion were more likely to have chronic diseases, develop preeclampsia, and give birth to preterm babies.

It's important to note that not all women with maternal vascular malperfusion developed these complications. Also, in the group without preconception care, placental signs of maternal vascular malperfusion were more commonly seen in pregnancies where no maternal diseases were diagnosed. This suggests that, in some cases, the vascular abnormalities in this group may indicate a specific vascular susceptibility phenotype and/or undiagnosed maternal cardiovascular risk factors before or during pregnancy.

We also observed an increased frequency of acute placental inflammation in the group without preconception care (11.6% vs. 4.9%; p=0.028), which in some cases may be attributed to undiagnosed infections prior to conception. Additionally, we found a higher frequency of chronic inflammatory placental lesions of unknown etiology in women without preconception care (12.8% vs. 5.5%; p=0.022). The etiology of chronic placental inflammation remains unclear; however, it is believed to involve chronic microbial infection and the maternal immune response to fetal antigens [26]. We hypothesize that, in some cases in our study, the increased frequency of chronic inflammatory placental lesions in women without preconception care may be linked to pre-pregnancy maternal health conditions that affect the body's ability to adapt adequately to pregnancy. This idea is indirectly supported by the trend we observed, where smoking was more common in the group without preconception care. Smoking may contribute to increased systemic inflammation [4, 12, 21]. Further research is needed to better understand the pathophysiological links between maternal preconception care and chronic placental inflammation.

In this study was found an increased frequency of placentas with macrophages containing meconium in the chorionic plate and amniotic membranes in women without preconception care (16.5% vs. 7.9%; p=0.019). This may be associated with fetal distress, such as hypoxia or infection, as demonstrated in previous studies [23, 25].

Taken together, these findings suggest that placental morphological examination should be an integral part of strategies aimed at mitigating adverse pregnancy and birth outcomes in women without preconception care.

The strengths of this study include the comparative analysis of clinical and morphological factors within the "mother-placenta-fetus" system in the context of preconception care versus its absence. An additional advantage is the systematic data collection and placental sample examination conducted in accordance with a strict protocol.

A limitation of this study is that, although we applied the criteria of the Amsterdam Consensus Statement [24], which include sub classification by stage and/or severity, we only assessed the presence or absence of each pathological feature without considering its stage or severity. A more detailed evaluation of the impact of the stage and/or

severity of each placental pathological finding on adverse outcomes is an important objective for future research.

Thus, we found that women without preconception care were more likely to experience severe pregnancy complications such as preeclampsia and gestational hypertension. In the newborns of women without preconception care, there was a higher incidence of small-for-gestational-age babies, respiratory complications, and cases of antenatal fetal death. Taken together, these results confirm that preconception care leads to improved perinatal outcomes.

We also identified that women without preconception care were at increased risk for maternal vascular malperfusion, chronic placental inflammation, and more frequent presence of macrophages containing meconium in the chorionic plate and amniotic membranes, which indicates chronic or prolonged fetal hypoxia and placental dysfunction. These findings complement and expand the understanding of the impact of preventive medical interventions prior to pregnancy on structural placental changes.

The results of the study confirm that preconception care aimed at improving maternal health reduces histopathological findings in placentas and improves perinatal outcomes.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions *YP: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. LS: Conceptualization, Supervision, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. DK: Conceptualization, Writing – review & editing. YK: Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Writing – original draft. ZA: Data curation, Writing – original draft. RS: Supervision, Writing – original draft, Writing – review & editing. OZ: Writing – original draft, Writing – review & editing, Formal analysis, KN: original draft, Writing – review & editing.*

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Data Availability *Statement Data is unavailable due to ethical restrictions.*

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