# PATHOMORPHOLOGICAL ASSESSMENT OF THE MORPHOGENESIS OF CHRONIC PLACENTAL INSUFFICIENCY IN TORCH INFECTIONS (BASED ON KARAKALPAKSTAN MATERIALS)

**Sharap Iskanderovich Mamutov**
Candidate of Medical Sciences, Department of Pathology, Karakalpakstan Medical Institute, Nukus, Uzbekistan
**Azizbek Amangalievich Atazhanov**
Master's Student of Pathological Anatomy, Karakalpakstan Medical Institute, Nukus, Uzbekistan
**Ziyuar Khojabay qizi Alauatdinova**
Master's Student of Pathological Anatomy, Tashkent Medical Academy, Tashkent, Uzbekistan Abstract

**Annotation**

**Aim:** To evaluate the pathomorphological changes and the morphogenesis of chronic placental insufficiency (CPI) triggered by TORCH infections among pregnant women residing in the Republic of Karakalpakstan.

**Material and Methods:** A macroscopic, histological, and morphometric analysis was conducted on 100 placentas from pregnancies complicated by TORCH infections and CPI, alongside 30 control placentas from uncomplicated physiological pregnancies. Tissue sections were stained using Hematoxylin and Eosin (H&E), Van Gieson, and PAS reaction.

**Results:** The study revealed that TORCH infections lead to profound microcirculatory disorders and inflammatory alterations, notably productive villitis and intervillositis. The structural morphogenesis of CPI in this cohort is characterized by the rapid exhaustion of compensatory-adaptive angiogenesis, giving way to progressive pathological changes including avascular terminal villi, massive fibrinoid necrosis, and severe stroma sclerosis.

**Conclusion:** The synergistic impact of viral/bacterial insults and the underlying environmental stressors in Karakalpakstan accelerates the morphogenetic transition from placental adaptation to decompensation. Early screening and targeted microvascular therapies are highly recommended to mitigate fetal growth restriction.

**Key words:** chronic placental insufficiency, TORCH infections, pathomorphology, morphogenesis, placenta, Karakalpakstan, histology, compensatory-adaptive reactions, fetal growth restriction.

## Introduction

TORCH infections constitute a group of vertically transmitted infectious agents that are primarily responsible for severe congenital morbidity, fetal death, and long-term neurodevelopmental sequelae (Lynn et al., 2023). These pathogens disrupt the delicate fetal-maternal interface, frequently leading to chronic placental insufficiency (CPI). CPI is defined as the functional and structural failure of the placenta to deliver an adequate supply of oxygen and nutrients to the developing fetus, which is a leading cause of fetal growth restriction (FGR) (Zhang et al., 2015).

The morphogenesis of CPI involves a complex sequence of structural alterations at the tissue and cellular levels. In regions characterized by ecological tension and environmental degradation, such as the Republic of Karakalpakstan, pregnant women frequently present with compounding variables such as chronic anemia and hypoxia. These environmental exposures can synergistically exacerbate inherent developmental or infectious defects in the placenta (Maslen, 2018). Therefore, understanding the specific histopathological patterns of the placenta in this geographical cohort is essential. The aim of this research is to conduct a detailed pathomorphological and morphometric assessment of the morphogenesis of CPI caused by TORCH infections based on materials collected in Karakalpakstan.

## Material and Methods

The study was conducted on a sample of 130 afterbirths delivered at maternity facilities in the Republic of Karakalpakstan. The main study group consisted of 100 placentas from women with serologically confirmed TORCH infections whose pregnancies were complicated by clinically diagnosed CPI and FGR. The control group comprised 30 placentas from healthy women with uncomplicated physiological pregnancies resulting in the delivery of healthy, full-term neonates.

Standard procedures were utilized for the pathomorphological investigation. Macroscopic evaluation included the assessment of placental weight, volume, maternal and fetal surface integrity, and the identification of visible infarcts or calcifications. For histological examination, tissue samples were excised from the central, paracentral, and marginal zones of the placental disc. The tissues were fixed in 10% neutral buffered formalin and embedded in paraffin blocks. Thin sections (4–5 μm) were prepared and subjected to the following histological staining techniques:

- **Hematoxylin and Eosin (H&E):** For general morphological and structural assessment.
- **Van Gieson's stain:** For the differential evaluation of connective tissue proliferation (sclerosis and fibrosis).
- **Periodic Acid-Schiff (PAS) reaction:** For the detection of glycogen deposits and the evaluation of the syncytio-capillary basement membrane thickness.

Morphometric analysis was performed using digital light microscopy to quantify the density of syncytial knots, the percentage of avascular villi, and the extent of fibrinoid deposition within the intervillous space.

**Result and Discussion**

Macroscopic examination of the placentas in the TORCH-infected group frequently revealed hypoplasia, lobular asymmetry, and a high incidence of dense, chalky calcifications and diffuse white infarcts, which were significantly less prevalent in the control group. The placental weight-to-birth-weight ratio was notably altered, reflecting the morphological adaptations and subsequent failure of the organ to support optimal fetal growth.

Histological analysis illuminated the detailed morphogenesis of CPI. In the early stages of the infectious process, signs of compensatory-adaptive reactions were evident. These included terminal villous hyperplasia, the formation of syncytioplasmic sprouts, and localized angiogenesis aimed at restoring the transplacental oxygen gradient. However, under the persistent influence of TORCH pathogens, these adaptive mechanisms underwent rapid exhaustion.

The dominant microscopic findings in the pathological phase were severe microcirculatory and inflammatory disruptions. Pathognomonic signs included focal and diffuse productive villitis, chorioamnionitis, and intervillositis. The activation of inflammatory cells, such as CD68+ macrophages in the intervillous space, is known to be heavily associated with the disruption of the vascular and stromal components of the villous chorion during FGR (Berezhna et al., 2021). Consequently, the villous stroma in the main group exhibited pronounced fibrotic and sclerotic changes (readily visualized via Van Gieson staining).

Furthermore, extensive fibrinoid necrosis of the chorionic villi was observed, leading to the functional exclusion of large placental territories. The PAS reaction highlighted a marked thickening of the basement membranes of the fetal capillaries and the trophoblastic epithelium. This thickening drastically increases the diffusion distance, critically impeding gas exchange. The combination of avascular terminal villi,

excessive connective tissue proliferation, and syncytial knotting confirms the transition into the decompensated stage of CPI. The accelerated rate of this fibrosing morphogenesis observed in the Karakalpakstan cohort suggests that chronic environmental hypoxia acts as a catalyst, exacerbating the endothelial damage initiated by the infectious agents.

**Conclusion and Recommendation**

The pathomorphological assessment demonstrates that the morphogenesis of chronic placental insufficiency in TORCH infections among women in Karakalpakstan is characterized by a rapid and severe transition from compensatory angiogenesis to pathological decompensation. The histological triad of persistent inflammation (villitis), microvascular obliteration, and progressive stromal sclerosis highlights the profound disruption of the maternal-fetal interface. The regional ecological factors likely contribute to the early exhaustion of adaptive reserves, accelerating fibrinoid necrosis and the functional failure of the placenta.

**Recommendations:**

1. **Clinical Practice:** It is highly recommended to implement stringent preconception and early-trimester screening protocols for TORCH infections specifically tailored for the population of Karakalpakstan.
2. **Therapeutic Intervention:** Obstetric management should actively incorporate early interventions focused on endothelioprotection, improving microcirculation, and mitigating hypoxia to prolong the compensatory-adaptive phase of the placenta.
3. **Future Research:** Further immunohistochemical studies are recommended to quantify the specific inflammatory cytokine profiles in the placental tissue of this geographically distinct cohort.

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