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# IMPROVING THE CRITERIA FOR EARLY DIAGNOSIS OF HYDATIDIFORM MOLE AND RISK STRATIFICATION IN THE ARAL SEA REGION.

**Abstract:** Recent advances in cellular biology and diagnostic technology have improved gynecological disease management and fertility preservation. Early detection of conditions like hydatidiform mole is linked to better outcomes, while appropriate treatment and careful monitoring increase the chances of a successful pregnancy and healthy childbirth.

**Aim:** To evaluate the role of immunohistochemical analysis in detecting malignant transformation of hydatidiform mole in women residing in the Aral region and to develop a comprehensive management algorithm for these patients.

**Study design:** An open-label, independent prospective study.

**Materials and methods:** A total of 70 endometrial aspirate samples from women diagnosed with hydatidiform mole were analyzed. The samples were collected between 2019 and 2022.

**Conclusion:** Successful pregnancy outcomes require precise regulation and interaction between specific hormones and their respective receptors. Dysregulation or aberrant expression within any of these pathways may lead to implantation failure or pregnancy loss.

**Keywords:** hCG antibodies, hormonal receptors, immunohistochemistry, endometrium, hydatidiform mole.

**Funding:** The study had no sponsorship support.

**Conflict of interest.** The authors declare no conflict of interest.

Progress in cellular biology and the introduction of advanced diagnostic methods have greatly enhanced gynecological disease treatment and increased fertility preservation options for women. Early detection of conditions like hydatidiform mole, a type of gestational trophoblastic disease, is linked to a positive prognosis. Proper therapeutic approaches and diligent follow-up care improve the chances of conception, a full-term pregnancy, and the delivery of a healthy baby [2,4].

Hydatidiform mole, a pregnancy-associated condition, is distinct among gynecologic oncological disorders. Epidemiological research highlights considerable geographic disparities in its prevalence, influenced by ethnicity, socioeconomic factors, and lifestyle. While the incidence in Europe and North America ranges from 0.5 to 1.84 per 1,000 pregnancies, it is reported to be up to ten times higher in Latin America, the Middle East, and East Asia [5,6].

Several predisposing factors contribute to its development, including early first pregnancy, pregnancy parity, immune system disorders, deficiencies in vitamins A and C, protein malnutrition, pelvic inflammatory diseases, and genetic predisposition [1, 3, 4, 8].

Timely implementation of preventive measures reduces recurrence rates and ensures favorable outcomes for subsequent pregnancies [1, 7, 9, 10].

Currently, the genetic theory is considered the most relevant hypothesis for the pathogenesis of hydatidiform mole:

1. The condition arises due to chromosomal aberrations that disrupt embryonic development.
2. A predominance of paternal chromosomes in the embryonic karyotype, which may result from fertilization of an ovum by multiple spermatozoa or by a single diploid sperm cell, leads to developmental abnormalities and deformities [2, 4, 11].

Hydatidiform mole is a trophoblastic disorder characterized by edematous swelling of chorionic villi and trophoblastic proliferation. However, it lacks invasive trophoblastic cell infiltration into the myometrium or blood vessels.

Both forms are associated with hypertrophy and hyperfunction of the chorionic villi. In complete hydatidiform mole, human chorionic gonadotropin (hCG) levels are significantly elevated, serving as a primary clinical marker of the disease.

Pathogenetic Mechanisms

Key pathogenetic alterations include: severe vasculogenic insufficiency. Delayed angiogenesis. Fluid accumulation and cystic cavity formation (cystic spaces) within chorionic villi

Diagnostic Methods

The primary diagnostic modalities include ultrasound imaging (US) and serum hCG measurement. Complete hydatidiform mole is characterized by generalized hyperplasia on ultrasound. Partial hydatidiform mole presents with focal cystic changes in the placenta, and an increase in the size of the gestational sac by 1.5 times, indicative of triploidy.

Additional morphological and immunohistochemical techniques are essential for evaluating the expression of molecular markers:

Immunohistochemical Markers: p53: Regulates cell cycle control and apoptosis, preventing mutation accumulation. Ki-67: A marker of proliferative activity, used to assess the biological potential of malignant tumors. CD34: An intercellular adhesion molecule involved in early hematopoiesis. hCG: Elevated levels serve as a key diagnostic criterion for hydatidiform mole [2, 10, 12].

This comprehensive approach to diagnosis, incorporating both conventional imaging and advanced molecular profiling, enables precise differentiation of hydatidiform mole subtypes and facilitates timely therapeutic interventions.

**The aim of the study:** the study aims to assess the significance of immunohistochemical analysis in diagnosing the malignant transformation of hydatidiform mole in women residing in the Aral region and to develop a clinical management algorithm for these patients.

**Materials and Methods.** The research was conducted from 2022 to 2024 at the Department of Obstetrics, Gynecology, and Oncology of the Urgench Branch of the Tashkent Medical Academy.

**Clinical Material.** The study utilized clinical specimens obtained from the Khorezm Branch of the Republican Specialized Scientific-Practical Center for Maternal and Child Health and the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology. Histopathological evaluations were conducted in the Department of Pathomorphology of this center, while immunohistochemical (IHC) analyses were performed at the FBC NGS MEDICAL laboratory.

**Data and Study Groups.** Retrospective Phase: Analysis of 70 endometrial aspirate samples from women diagnosed with hydatidiform mole collected between 2019 and 2022. Among these, 40 samples underwent IHC staining for the expression of Ki-67, CD34, hCG, and p53 markers. Prospective Phase: The study included 94 women, with an average age ranging from 25.8 to 38.2 years, residing in the Khorezm region and the Republic of Karakalpakstan (44.6% urban residents and 55.4% rural residents).

Participants were divided into three groups: primary group (n = 44): Women diagnosed with hydatidiform mole. Comparison group (n = 30): Women with non-viable pregnancy. Control group (n = 20): Clinically healthy women seeking elective pregnancy termination.

**Research Methods.** Survey assessment: Patient-reported symptoms, medical history, lifestyle factors, menstrual function, and reproductive health were recorded. Clinical and laboratory evaluations: Included biochemical and hormonal assays, ultrasound imaging (USG), and diagnostic testing. Therapeutic interventions and outcomes were systematically analyzed.

Statistical evaluation included calculation of mean values (M), standard errors of the mean (m), and relative proportions (%) to ensure accurate comparison across study groups.

**Results and Analysis.** Analysis of medical history among study participants revealed that anemia was the most prevalent comorbidity across all three groups: **p**rimary group: 50±2.2% (n = 22)**.** Comparison group: 46.7±2.0% (n = 14)**.** Control group: 45±2.2% (n = 9)

Other common comorbidities included: cholecystitis: 27.3±1.5% (primary group), 26.7±0.9% (comparison group), 10±1.4% (control group). Gastritis: 43.2±1.3% (primary group), 36.7±0.5% (comparison group), 10±1.1% (control group). Varicose veins: 18.1±1.6% (n=8, primary group), 15±0.8% (n=15, comparison group), 15±0.9% (n=3, control group).

These findings highlight the high prevalence of anemia and gastrointestinal disorders in women diagnosed with hydatidiform mole, emphasizing the need for comprehensive clinical evaluation and targeted management strategies for affected patients.

**Table №1**

**Frequency of somatic diseases in the examined women**

| **Disease** | Main group, n= 44 | Comparison group, n=30 | Control group, n=20 |
|---|---|---|---|
| Anemia | 2 2 / 50±2.2 | 1 4 / 46.7 ±2.0 | 9 / 45 ±2.2 |
| Cholecystitis | 12 / 2 7.3 ±1.5 | 8 / 26.7 ±0.9 | 2 / 10.0±1.4 |
| Varicose veins | 8 / 1 8.1 ±1.6 | 15 / 50 ±0.8 | 3 / 15 ±0.9 |
| Gastritis | 19 / 43.2 ±1.3 | 1 1 / 36.7 ±0.5 | 1 / 10.0 ± 1.1 |

Data analysis revealed no significant differences between the study groups in these parameters. The absence of statistically significant variations confirms the appropriateness of cohort selection and the representativeness of the study groups.

In addition to systemic comorbidities, the prevalence of gynecological disorders among the study population was also assessed and analyzed. The findings are presented in Table 2.

**Table № 2**

**Gynecological diseases in comparative groups**

| Disease | Main group, n= 44 | Comparison group, n=30 | Control group, n=20 |
|---|---|---|---|
| Chronic endometritis | 12 / 2 7.3 ±1.5 | 15 / 50 ±0.8 | 1 / 5.0 ±1.1 |
| Cervical ectopia | 6 / 13 ,6 ±1,3 | 1 1 / 36.7 ±0.5 | 2 / 10.0±1.4 |
| Vulvovaginitis | 12 / 2 7.3 ±1.5 | 15 / 50 ±0.8 | 2 / 10.0±1.4 |
| Endocervicitis | 6 / 13 ,6 ±1,3 | 8 / 26.7 ±0.9 | 2 / 10.0±1.4 |

The prevalence of gynecological disorders in the medical history of women from both study groups was approximately equal. However, when comparing all three groups, it was observed that chronic endometritis, vulvovaginitis, endocervicitis, and cervical ectopia were more frequently diagnosed in women from the second group. These findings resulted in statistically significant differences between the groups ($p<0.01$) (Table 2).

The study also analyzed data on menstrual cycle characteristics and sexual history, as these parameters play a crucial role in the management of hydatidiform mole and in assessing the hormonal status of the body.

The results showed that in most women from the first group, menarche occurred at ages 10–13 and 14–16 years.

The duration of the menstrual cycle among the participants was within the physiological norm (3–5 and 6–7 days). However, dysmenorrhea (painful menstruation) was significantly more common in the first group: 27.3±1.5% in the first group, 6.7±1.2% in the second group, and 0% in the control group.

One of the indicators of the representativeness of the study groups was anthropometric measurements of the participants. Notably, the mean height and body weight across all groups were statistically comparable.

Additionally, the Body Mass Index (BMI) was calculated using the Quetelet formula: BMI = body weight (kg) / (height ($m^2$)).

The BMI values across the study groups were similar, with the normal BMI range being the most frequently observed category. No significant intergroup differences in this parameter were detected, confirming the validity of group selection and their representativeness.

Data Analysis. In line with the research objectives, a total of 94 pregnant women underwent medical examination. The distribution of professional activity among the study groups was approximately the same. No significant differences in occupational affiliation were observed between the healthy women group and the hydatidiform mole group, further supporting the homogeneity of the study sample.

**Table №3**

**Distribution of women by pregnancy parity**

| Parameter | Main group, n= 44 | Comparison group, n=30 | Control group, n=20 | p |
|---|---|---|---|---|
| 1st pregnancy | 26 (59%) | 12 (40%) | 8 (40%) | p1<0.05<br>p2<0.05<br>p3>0.05 |
| Repeated pregnancies | 18 (40.1%) | 18 (60%) | 12 (60%) | p1>0.05<br>p2>0.05<br>p3>0.05 |
| One birth | 5 (11.4%) | 8 (26.7%) | 5 (25%) | p1<0.05<br>p2>0.05<br>p3>0.05 |
| Two or more births | 10 (22.7%) | 6 (20%) | 7 (35%) | p1>0.05<br>p2>0.05<br>p3>0.05 |
| Twins in this pregnancy | 1 (2.27%) | - | - | - |
| History of twins | 3 (6.8%) | - | 1 (5%) | p2<0.05 |
| Repeated non-viable pregnancy | 3 (6.8%) | 4 (13.3%) | - | p1<0.05 |

Analysis of pregnancy parity revealed that for the majority of women diagnosed with hydatidiform mole, it was their first pregnancy, which significantly differed from both the comparison and control groups ($p_1$, $p_2 < 0.05$).

In the first group, recurrent pregnancy was observed in 18 women (40.1%), but no statistically significant differences were found when compared with the other groups.

Singleton births were more frequent in the second group, whereas recurrent pregnancies were more prevalent in the third group. However, this parameter did not exhibit statistically significant differences across the study groups ($p_1$, $p_2$, $p_3 > 0.05$).

A particularly noteworthy finding was the incidence of multiple pregnancies, which was primarily observed in women from the first group. However, none of these pregnancies resulted in a live birth.

TORCH screening was conducted in all participants across the three study groups during pregnancy, given the established role of infectious diseases in the etiology of spontaneous miscarriage, fetal growth restriction, and perinatal mortality. The analysis revealed no significant differences among the groups, suggesting that pregnancy complications cannot be exclusively linked to TORCH infections.

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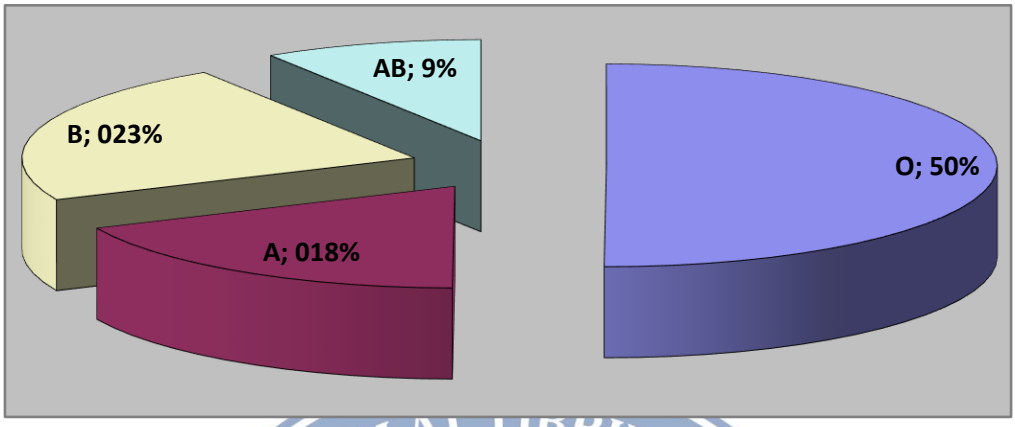


**Figure 1. Blood group analysis in women with hydatidiform mole**

An analysis of blood group distribution among women diagnosed with hydatidiform mole revealed the following distribution: blood group I (O) – 22 women (50%). Blood group II (A) – 8 women (18.1%). Blood group III (B) – 10 women (22.7%). Blood group IV (AB) – 4 women (9%)

These findings suggest that women with blood group I (O) demonstrate the highest predisposition to developing hydatidiform mole.

The majority of patients sought medical attention due to vaginal bleeding. In many cases, this symptom was initially misinterpreted as a threatened miscarriage, leading to hospital admission in gynecological departments for hemostatic management and uterine evacuation. However, the definitive diagnosis of hydatidiform mole was frequently established only after histopathological examination.

Given these observations, a comparative analysis of clinical manifestations among affected patients was conducted (Table 4).

**Table No. 4.**

**Comparison of clinical and ultrasound data between groups**

| Parameter | Main group, n= 44 | Comparison group, n=30 | Control group, n=20 | p |
|---|---|---|---|---|
| Asymptomatic | 3 (6.8%) | 14 (46.7%) | 8 (40%) | p1<0.05<br>p2<0.05<br>p3>0.05 |
| Amenorrhea | 3(6.8%) | 4 (13.3%) | 20 (100%) | p1>0.05<br>p2<0.05<br>p3<0.05 |
| Bloodbath | 16 (36.4%) | 8 (26.7%) | - | p1<0.05 |
| Bleeding from the genital tract | 25 (56.8%) | 4 (13.3%) | - | p1<0.05 |
| Pain in the lower abdomen | 11 (25%) | 9 (30%) | 3(15%) | p1>0.05<br>p2<0.05<br>p3<0.05 |
| Nausea and vomiting in pregnancy | 18(40.1%) | 3(10%) | 12 (60%) | p1<0.05<br>p2<0.05<br>p3<0.05 |

| | | | | |
|---|---|---|---|---|
| Hypertension in pregnancy | 4 (9.1%) | - | - | - |
| Increased heart rate | 11 (25%) | - | - | - |
| An increase in the size of the uterus that does not correspond to the gestational age | 26 (59.1%) | - | - | - |
| The appearance of luteal cysts | 5 (11.4%) | 3(10%) | - | p1>0.05 |
| Echographic picture of a "snow storm" in the uterine cavity | 9 (20.5%) | - | - | - |

In all study groups, cases of asymptomatic pregnancy progression were observed. However, this was more frequently noted in the group of healthy pregnant women (40%) and in women with fetal growth restriction (46.7%), with no statistically significant differences between these two groups ($p_3 > 0.05$). In the hydatidiform mole group, the condition was incidentally detected on ultrasound in 3 women (6.8%) ($p_1 < 0.05$; $p_2 < 0.05$) and subsequently confirmed through histopathological examination. Brown vaginal discharge lasting 3–8 days was reported in 36.4% of cases in the first group and 26.7% in the second group ($p_1 < 0.05$), representing a statistically significant finding. The most prevalent clinical symptom in patients diagnosed with hydatidiform mole was uterine bleeding, observed in 25 women (56.8%), which was 6.25 times more frequent than in the second group ($p_1 < 0.05$). Lower abdominal pain was recorded in the first and second groups without significant intergroup differences; however, its incidence was substantially higher compared to the control group ($p_2 < 0.05$, $p_3 < 0.05$). Unlike other symptoms, nausea and vomiting were less frequent in women with fetal growth restriction (10%), whereas in healthy pregnant women, this symptom occurred in 60% of cases ($p_2 < 0.05$, $p_3 < 0.05$). Hypertension (elevated blood pressure) before 16 weeks of gestation was recorded exclusively in the first group. Tachycardia (increased heart rate) was observed in 25% of women in the first group, likely associated with a sharp elevation in human chorionic gonadotropin (hCG) levels, which modulates metabolic processes similarly to thyroid hormones.

Ultrasound Findings in Women with Hydatidiform Mole:

- Enlarged uterine size– 26 women (59.1%)
- Presence of lutein cysts – 5 women (11.4%)
- Characteristic "snowstorm" pattern on ultrasound – 9 women (20.5%)

These findings confirm that sonographic changes can serve as key diagnostic markers of hydatidiform mole (Table 4).

Laboratory Investigation Results: a complete blood count (CBC) revealed varying hemoglobin levels across the three study groups; however, no significant intergroup differences were observed. The highest leukocyte count was recorded in the second group, with the following values: first group – 7.533 ± 0.123 × $10^9$/L. Second group – 10.127 ± 0.221 × $10^9$/L. Third group – 5.783 ± 0.1127 × $10^9$/L

**Table № 5.**

**Hormonal analysis results**

| Indicator | Main group, n= 44 | Comparison group, n=30 | Control group, n=2 0 | P |
|---|---|---|---|---|
| Prolactin 11.2-90ng/ml | 9 1.729 ± 4.05 55 | 85.56±2.56 | 5 4 ,729±3,059 | p1>0.05 p2<0.05 p3<0.05 |
| TTG 0.3-4.0 ng/ml | 4.9±0.02 | 3.9±0.05 | 2.24±0.08 | p1>0.05 p2<0.05 p3<0.05 |
| T3 free | 1.2±0.2 | 1.4±0.22 | 1.82±0.048 | p1>0.05 |

| | | | | |
|---|---|---|---|---|
| 1.4-4.2 ng/ml | | | | p2<0.05<br>p3<0.05 |
| T4 free<br>0.8-2.2 ng/ml | 0.7±0.019 | 0.9±0.02 | 1.7±0.023 | p1>0.05<br>p2<0.05<br>p3<0.05 |

To identify the potential etiological factors contributing to the development of hydatidiform mole, an analysis of hormone levels that could influence fetal development was conducted.

Key Hormonal Alterations: prolactin levels in the first group were 1.7 times higher than in normal pregnancy and 1.6 times higher in cases of fetal growth restriction ($p_2$, $p_3 < 0.05$). Thyroid-stimulating hormone (TSH) was significantly elevated in the primary study group, indicating a high predisposition to hypothyroidism (4.9 ± 0.02 ng/mL). Triiodothyronine (T3) and thyroxine (T4) levels were reduced in the first group, representing a clinically significant finding ($p < 0.05$).

**Table № 6.**

**Human chorionic gonadotropin (hCG) levels in comparative groups**

| Indicator | Main group, n= 4 4 | Comparison group, n=30 | Control group, n=20 | P |
|---|---|---|---|---|
| HGCh <50,000 ME/l | 9 (20.5%) | 27 (90%) | 5 (25%) | p1<0.05<br>p2>0.05<br>p3<0.05 |
| 50,000-100,000 | 26 (59%) | 3 (10%) | 15 (75%) | p1<0.05<br>p2<0.05<br>p3<0.05 |
| >100,000 | 9 (20.5%) | - | - | - |

One of the key diagnostic markers of hydatidiform mole is an elevated serum level of human chorionic gonadotropin (hCG). In the first group (hydatidiform mole), hCG levels exceeded 100,000 IU/L. In the second group (fetal growth restriction), 90% of women had hCG levels below 50,000 IU/L, which is a statistically significant finding ($p_1 < 0.05$; $p_3 < 0.05$). Thus, a reduced hCG level in cases of fetal growth restriction suggests insufficient functional activity of the chorionic villi, whereas an elevated hCG level in hydatidiform mole indicates excessive trophoblastic activity and villous hyperplasia. The gold standard for diagnosing hydatidiform mole remains histological examination of endometrial aspirate obtained from the uterine cavity.

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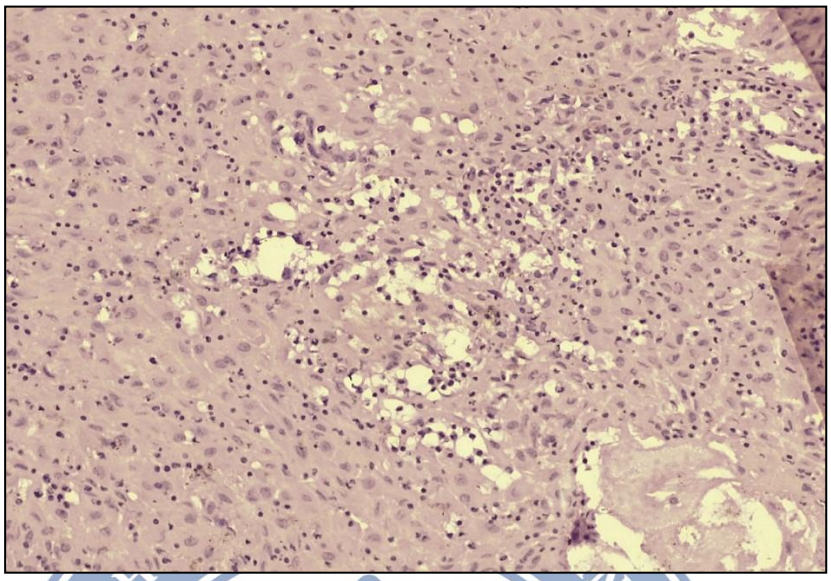

Figure No. 2. **Microscopic picture of decidual tissue in normal pregnancy. Surrounding heme-eosin. Ob10xok40.**

In the control group (normal pregnancy), the following histopathological findings were observed: dystrophically altered decidual tissue; A moderate presence of angiomatous tissue; Focal areas of endometrial hyperplasia; Blood vessels of varying calibers with moderate lymphocytic infiltration

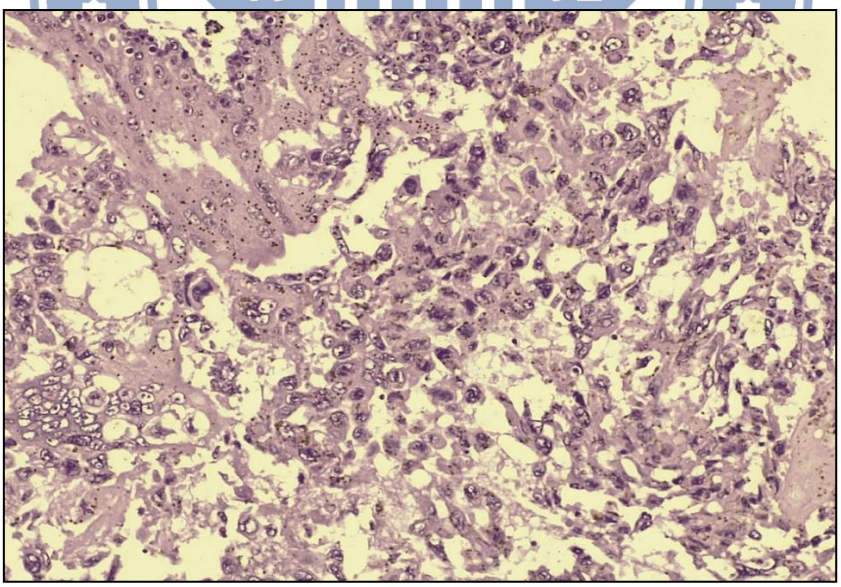

**Figure №3. Microscopic picture of decidual tissue in invasive hydatidiform mole. heme-eosin. Ob10xok40.**

Hydatidiform mole is classified into two morphological types: complete hydatidiform mole – involves all chorionic villi, with the absence of embryonic tissue. Partial hydatidiform mole - characterized by the presence of both normal chorionic villi and decidual cells, but with pathological alterations.

Macroscopic Features of Complete Hydatidiform Mole: edematous, hydropic villi; Translucent cystic structures; A characteristic “grape-like” appearance with reddish, hyperemic masses; Microscopic Features of Complete Hydatidiform Mole: Trophoblastic hyperplasia and

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cellular polymorphism; Prominent angiomatous changes; Perivascular inflammatory infiltration composed of lymphocytes

Immunohistochemical analysis enables the quantification of hCG expression and other protein markers, facilitating both diagnostic accuracy and disease prognosis.

**Table №7.**

**Immunohistochemical indices in the study groups**

| Indicators<br>1. < 10% low positive reaction<br>2. 10-20% average positive reaction<br>3. > 20% highly positive reaction | **Main group, n= 20** | **Comparison group, n= 1 0** | **Control group, n= 10** | p - |
|---|---|---|---|---|
| HGC<br>min – max | 23 ,6±0,1 32<br>[ 1 8 - 30] | 16.6±0.1265<br>[ 11-20 ] | 18.8±0.1785<br>[ 16-20 ] | p1<0.05<br>p2<0.05<br>p3>0.05 |
| With D -34<br>min – max | 1 3.2 ±0.1 42<br>[7 - 18] | 8.525±0.1625<br>[ 7-15 ] | 15.5±0.349<br>[ 10-18 ] | p1<0.05<br>p2>0.05<br>p3<0.05 |
| Ki- 67<br>min – max | 18,75 ±0,1 78<br>[ 1 1 - 28] | 10.275±0.1421<br>[ 8-15 ] | 16.2±0.3703<br>[ 10-19 ] | p1<0.05<br>p2>0.05<br>p3<0.05 |
| wp-53<br>min – max | 1 6 ,5±0, 22 9<br>[8 -25 ] | 6,675 ±0,169<br>[ 16-25 ] | -<br>[-] | p1<0.05 |

The sensitivity of hCG receptors in cases of hydatidiform mole was found to be 1.4 times higher than in the control group. This increase is associated with chorionic villous hypertrophy and hyperfunction, leading to excessive secretion of hCG into the bloodstream.

The Ki-67 marker, an indicator of cellular proliferation, was significantly elevated in the study group compared to the control group (18.75±0.178 vs. 10.275±0.1421; p<0.05). While proliferative activity is also observed in normal pregnancy, its intensity remains lower than in hydatidiform mole. No statistically significant differences were detected between the first and third groups (p>0.05).

The tumor suppressor marker p53, which is specific to oncogenic processes, was significantly upregulated in patients with hydatidiform mole (16.5±0.229), indicating a potential risk of malignant transformation (p<0.05).

**Table № 8.**

**Dynamics of hCG levels in the blood after evacuation of a hydatidiform mole**

| HCG amount / Weeks | 0 | 2 | 4 | 6 | 8 | 10 | 12 |
|---|---|---|---|---|---|---|---|
| 1000ME/L | 0 | 5 | 10 | 26 | 10 | 5 | 0 |
| 2000 | 4 | 5 | 8 | 10 | 5 | 0 | 0 |
| 3000 | 6 | 4 | 10 | 4 | 5 | 4 | 0 |
| 4000 | 4 | 20 | 8 | 2 | 0 | 0 | 2 |
| >5000 | 30 | 10 | 8 | 2 | 0 | 0 | 2 |

After the removal of the hydatidiform mole, human chorionic gonadotropin (hCG) levels in the blood of the studied women were monitored every two weeks. The primary observations indicated that by week 8, hCG levels had decreased below 3000 IU/L. By week 10, four women exhibited hCG levels of approximately 4000 IU/L, suggesting a prolonged hormonal normalization process. Subsequent follow-up revealed that in two of these cases, hCG levels doubled, which may indicate persistent trophoblastic tissue and an increased risk of malignant transformation (choriocarcinoma).

**Conclusion:** Thus, histological examination remains the gold standard for diagnosing hydatidiform mole, while immunohistochemical analysis aids in assessing the aggressiveness of the disease and guiding optimal patient management strategies. Elevated hCG levels serve as a key diagnostic marker for hydatidiform mole. Women with blood type I (O) appear to have the highest predisposition to developing this condition. Overexpression of p53 may indicate a high risk of neoplastic transformation, necessitating close follow-up. Post-evacuation hCG levels must be closely monitored until complete resolution, as persistent or recurrent hCG elevation may suggest residual trophoblastic disease or malignant transformation. A rational diagnostic approach helps minimize unnecessary testing and treatment, thereby reducing patient burden.

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