COMPARATIVE ANALYSIS OF BIOCHEMICAL PARAMETERS IN FETUSES WITH CONGENITAL MALFORMATIONS

Kalandarova A.N.[1],
Qurbonboyeva H.H.[2]
[1] Assistant of the Department of Obstetrics, Gynecology and Neonatology, Medical Institute of Karakalpakstan.
Email: amina_kan@mail.ru,
[2] 2nd-year Master's Student in Obstetrics and Gynecology, Medical Institute of Karakalpakstan.
Email: ircoinlist700@gmail.com.

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Relevance of the Topic

Congenital malformations are among the most critical complications leading to disability and mortality in fetuses and newborns. The incidence of children born with congenital and hereditary diseases is approximately 5% of all births. Annually, nearly 303,000 infants die within the first four weeks of life due to these defects. Hereditary factors account for about 15% of cases, aggressive environmental factors for 10%, and the combination of genetic and environmental influences for 20-25% of fetal congenital anomalies (Yangibayeva D.T., 2024. SYNAPSES: 191–197).

Congenital defects hold a leading position in the structure of perinatal mortality. Screening of pregnant women is conducted during the first and second trimesters. While the risk of pathologies such as Down and Edwards syndromes can be calculated in the first trimester, the risk of neural tube defects (NTDs) is primarily assessed starting from the second trimester. This is because alpha-fetoprotein (AFP), the primary marker for identifying such risks, is effectively determined during the second trimester of pregnancy.

Consequently, prenatal diagnostics plays a vital role in the early detection of congenital malformations and hereditary diseases.

Aim of the Research

To evaluate the effectiveness of measuring maternal serum alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG) levels in the prenatal detection of congenital malformations and hereditary diseases in the fetus.

Materials and Methods

Study Design and Setting: A comparative study was conducted at the Mother and Child Screening Center of the Republic of Karakalpakstan. The research focused on pregnant women whose fetuses were diagnosed with congenital malformations and hereditary diseases.Study Population: The study sample consisted of 29 pregnant women aged between 20 and 45 years. All participants in this group were identified as having pregnancies affected by congenital or genetic anomalies.Diagnostic Procedures: The evaluation was based on a comprehensive approach involving ultrasonography (USG) and the analysis of biochemical markers (specifically Alpha-fetoprotein and Human Chorionic Gonadotropin).Biochemical Analysis: The results of the biochemical marker analysis were interpreted using the MoM (Multiple of Median) indicator, which is a standardized measure used in prenatal screening to account for gestational age variations. For the purposes of this study, the normal reference range was defined as 0.5 to 2.0 MoM. Values falling outside this range were categorized as pathological indicators of potential fetal anomalies.

Results and Discussion

The analysis of the first and second-trimester biochemical and ultrasound screening results of 29 fetuses with congenital anomalies (CA) yielded the following findings. All cases were categorized into two primary groups: Chromosomal Abnormalities and Structural Defects.Chromosomal

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Abnormalities (Down Syndrome and others)This group (n=10) included fetuses identified with a high individual risk for Down syndrome and other chromosomal pathologies.Biochemical Markers: A distinct biochemical profile was observed in this cohort. The free beta-hCG levels were significantly elevated, with a mean value of 2.54 MoM. In contrast, PAPP-A levels remained within the normal range or were slightly decreased, averaging 1.14 MoM. During the second trimester, AFP levels were notably low, with a mean value of 0.38 MoM. Ultrasound Markers: The most significant finding was the nuchal translucency (NT) thickness, which averaged 3.94 mm. While the normal reference mean is approximately 2.06 mm, individual cases in this group reached as high as 5.49 mm. Notably, the nasal bone (NB) was present (NB+) in 90% of the cases, suggesting that this particular marker was less sensitive for screening within this specific study group.

Structural Defects (Central Nervous System, Cardiovascular, and others)This group (n=19) comprised fetuses with brain anomalies (hydrocephalus, Arnold-Chiari malformation), cardiac defects (atrioventricular canal defects), abdominal wall defects (omphalocele), and other structural anomalies.

Biochemical Markers: No specific unified biochemical profile was observed in this group. The mean values for PAPP-A (1.16 MoM) and free beta-hCG (1.28 MoM) remained close to the normal range. However, in cases associated with neural tube defects (NTDs) and other related anomalies, AFP levels were significantly elevated, reaching as high as 9.22 MoM. Ultrasound Markers: The mean NT value was 1.21 mm, which remained within the normal reference limits. The nasal bone (NB) was present in almost all cases (95%, NB+).

Cases Associated with Fetal Demise In instances of fetal loss, inconsistent deviations (both increases and decreases) were observed in PAPP-A and free beta-hCG markers. This suggests that the process of fetal demise

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exerts an unpredictable influence on biochemical screening results, complicating the diagnostic interpretation.

Table 1

Mean Values of Screening Markers in Fetuses with Various Congenital Anomalies (CA)

Group of Anomalies	Number of Fetuses (n)	PAPP-A	Free \beta-hCG (MoM)	NT(mm)	NB (%)	Normal Reference (Literature)
Chromosomal Abnormalities	10	1.14	1.84	1.94	90%	PAPP-A:1.0 MOM; hCG:1.0 MOM; NT; 2.5MM
Structural Defects	19	1.16	1.28	1.21	95%	PAPP-A:1.0 MOM; hCG:1.0 MOM; NT; 2.5mm
Normal		1.0	1.0	<2.5	100%	

Conclusion

The conducted analysis allows for the following key conclusions:

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1.Diagnostic Value Variability: There is a distinct difference in the diagnostic value of screening markers for the early detection of chromosomal abnormalities (particularly Down syndrome) and structural defects. For Down syndrome, the combination of elevated free \beta-hCG and relatively low PAPP-A levels constitutes a specific biochemical profile, confirming established global data. In contrast, structural defects often manifest without significant deviations in first-trimester biochemical markers.

2. Limitations of Ultrasound Markers: First-trimester ultrasound markers, such as Nuchal Translucency (NT) and Nasal Bone (NB), demonstrated relatively low isolated sensitivity. In our study, NT values in fetuses with chromosomal pathologies often remained within the normal range, and the nasal bone was present in nearly all cases. This indicates that these markers, when used independently, may fail to identify a substantial number of high-risk cases.

3. Necessity of a Combined Approach: Effective early prenatal diagnosis of congenital anomalies can only be achieved through a comprehensive approach. This requires a strict combination of biochemical screening (PAPP-A and free \beta-hCG) and detailed ultrasonography. No single marker used in isolation provides sufficient diagnostic reliability.

4. Impact of Fetal Demise: Fetal loss can cause significant deviations in biochemical markers, potentially distorting screening results and leading to an inaccurate assessment of risk. Consequently, the interpretation of biochemical risk parameters is clinically unreliable without concurrent ultrasound confirmation of fetal viability and development.

5. Methodological Validation: Although this study did not utilize a dedicated control group, a comparison of the obtained results with globally accepted reference values clearly demonstrates the clinical significance of comprehensive screening. The integration of various diagnostic modalities remains the most effective strategy for prenatal health management.

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