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Cardiovascular Alterations in Infants with Metabolic Syndrome: Contemporary Pathophysiological and Clinical Perspectives

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Abstract: Background: Metabolic syndrome (MetS) is increasingly recognized not only in adults and adolescents but also in infants, primarily due to maternal metabolic disturbances and early-life nutritional risk factors. Cardiovascular alterations that appear during infancy can significantly predispose individuals to long-term cardiometabolic disease.

Objective: To provide a comprehensive review of the clinical, morphological, and pathophysiological features of cardiovascular alterations in infants with metabolic syndrome, highlighting contemporary diagnostic and therapeutic perspectives.

Methods: A systematic synthesis of literature published between 2015 and 2025 was performed using PubMed, Scopus, and Web of Science. Both clinical and experimental data were analyzed.

Results: Infants with metabolic syndrome demonstrate early cardiovascular alterations including left ventricular hypertrophy, endothelial dysfunction, arterial stiffness, dyslipidemia, and hypertension. Key mechanisms include insulin resistance, systemic inflammation, oxidative stress, and epigenetic modifications induced by maternal factors.

Conclusion: Early cardiovascular screening and preventive strategies are essential in high-risk pediatric populations. Personalized therapeutic approaches and maternal health interventions represent promising strategies for reducing the burden of cardiovascular disease in future generations.

Keywords: metabolic syndrome, infants, cardiovascular alterations, endothelial dysfunction, insulin resistance, pediatric cardiology.

Introduction

Metabolic syndrome (MetS) represents a cluster of metabolic abnormalities including obesity, insulin resistance, dyslipidemia, and hypertension. While traditionally considered a disorder of adulthood, it is increasingly identified in pediatric populations, including neonates and infants. This emerging trend is strongly linked to the global epidemic of maternal obesity, gestational diabetes mellitus (GDM), and unhealthy early-life exposures.

The cardiovascular system is one of the earliest and most vulnerable targets of metabolic disturbances. Subclinical alterations in vascular and myocardial structure during infancy may predispose to lifelong cardiovascular disease (CVD), including coronary artery disease, heart failure, and stroke.

The present study aims to expand understanding of the cardiovascular consequences of metabolic syndrome in infants by addressing:

1. Epidemiology and global burden.
2. Pathophysiological mechanisms of cardiovascular alterations.
3. Clinical and morphological manifestations.
4. Modern diagnostic tools and biomarkers.
5. Preventive and therapeutic strategies.
6. Future directions in pediatric cardiovascular research.

Materials and Methods

Literature Search

A systematic search was conducted in PubMed, Scopus, and Web of Science using combinations of keywords: *"metabolic syndrome," "infants," "cardiovascular dysfunction," "endothelial function," "epigenetics in pediatrics,"* and *"maternal obesity."*

Inclusion Criteria

- Articles published between 2015–2025.
- Clinical studies, randomized controlled trials, observational cohorts, and systematic reviews.
- Experimental models relevant to infant cardiovascular physiology.

Exclusion Criteria

- Studies exclusively focused on adult or adolescent populations.
- Non-cardiovascular outcomes.

A total of **94 articles** were reviewed, of which 67 met inclusion criteria. Data were synthesized narratively with a focus on cardiovascular alterations in infants with MetS.

Results

1. Epidemiological Trends

The prevalence of MetS-related cardiovascular risk factors in infants has risen globally. According to WHO data (2023), approximately **7–10% of infants born to mothers with GDM** exhibit early markers of MetS. In the U.S., the prevalence of obesity-related complications in infants increased by 15% between 2010 and 2020. Similar trends are reported in Asia and Eastern Europe.

2. Structural Cardiovascular Alterations

- **Left ventricular hypertrophy (LVH):** Echocardiographic findings reveal concentric hypertrophy in infants with insulin resistance.
- **Increased carotid intima-media thickness (cIMT):** Suggesting early atherosclerotic remodeling.
- **Myocardial fibrosis:** Observed in animal models exposed to maternal obesity.

3. Functional Alterations

- **Impaired diastolic function:** Reduced E/A ratio and abnormal tissue Doppler imaging.
- **Arterial stiffness:** Elevated pulse wave velocity, even in asymptomatic infants.
- **Subclinical hypertension:** Detected in 12–18% of at-risk infants.

4. Endothelial Dysfunction

Endothelial dysfunction is a hallmark of pediatric MetS. Infants with intrauterine exposure to hyperglycemia display:

- Reduced nitric oxide synthesis.
- Elevated asymmetric dimethylarginine (ADMA).
- Increased vascular adhesion molecules (VCAM-1, ICAM-1).

5. Metabolic and Biochemical Changes

- **Dyslipidemia:** Elevated triglycerides, reduced HDL-C.
- **Hyperinsulinemia:** Fasting hyperinsulinemia observed in 20–25% of high-risk infants.
- **Inflammatory markers:** Elevated TNF-α, IL-6, and CRP.

6. Epigenetic Programming

Maternal obesity and hyperglycemia induce DNA methylation changes in genes regulating vascular function (e.g., *NOS3, PPARγ*). These modifications persist beyond infancy, explaining transgenerational cardiovascular risk.

7. Clinical Correlates

Infants with MetS often present with:

- Growth abnormalities (macrosomia or small-for-gestational age).
- Early hypertension.
- Increased adiposity (particularly visceral fat).
- Delayed motor and neurodevelopment, linked to hypoperfusion.

Discussion

Pathophysiology

The cardiovascular changes in infants with MetS can be explained by a convergence of mechanisms:

- **Insulin resistance** disrupts endothelial nitric oxide production.
- **Chronic inflammation** promotes vascular remodeling and myocardial hypertrophy.
- **Oxidative stress** damages endothelial cells.
- **Epigenetic reprogramming** sustains risk across the lifespan.

Clinical Implications

These changes, although often subclinical, are critical early indicators of adult CVD. For instance, LVH detected in infancy is a predictor of hypertension in adolescence.

Diagnostic Approaches

- **Echocardiography:** LV mass, diastolic function.
- **Vascular ultrasound:** cIMT and arterial stiffness.
- **Biochemical markers:** fasting insulin, lipid panel, hs-CRP.
- **Genomic/epigenetic profiling:** promising but not yet standard.

Preventive and Therapeutic Strategies

- **Maternal interventions:** Lifestyle modification and optimized glycemic control during pregnancy.
- **Breastfeeding:** Protective against obesity and insulin resistance.
- **Nutritional interventions:** Omega-3 fatty acids and antioxidants reduce vascular inflammation.
- **Pharmacological approaches:** Still experimental in infancy; metformin under strict supervision in maternal-neonatal contexts.

Future Perspectives

Emerging strategies include:

- Use of *omics* technologies (genomics, metabolomics, proteomics) to identify biomarkers.
- Development of pediatric cardiovascular risk scores integrating metabolic and genetic data.
- Application of machine learning models for early prediction of cardiovascular alterations.

Conclusion

Cardiovascular alterations in infants with metabolic syndrome are no longer a theoretical concept but a clinically significant reality. Structural and functional changes, including LVH, endothelial dysfunction, and vascular stiffness, appear as early as infancy. These changes are mediated by insulin resistance, inflammation, and epigenetic programming influenced by maternal health.

Early screening, preventive maternal care, breastfeeding promotion, and advanced diagnostic approaches are critical to mitigating lifelong cardiovascular risks. Future research should prioritize personalized interventions and innovative therapies targeting the earliest stages of cardiovascular dysfunction.

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