

## 5. MATERNAL CIRCADIAN RHYTHM AND SLEEP DISORDERS AS A RISK FACTOR FOR AUTISM SPECTRUM DISORDER



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**Introduction.** The prevalence of Autism Spectrum Disorder (ASD) in the Republic of Moldova and Israel is 0.49 and 0.36, respectively, reflecting a global increase in ASD cases. According to current literature, the prevalence has increased by 2.5 times since the first Autism and Developmental Disabilities Monitoring (ADDM) Network study in 2000.

**Aim of study.** The exact causation of ASD remains unclear, but emerging research emphasizes the role of maternal factors during pregnancy, specifically disruptions in CR and sleep patterns. Maternal CR and SD may impact the complex mechanisms that underlie embryonic neurodevelopment. SD are reported to affect 46-78% of pregnant women, with sleep quality deteriorating in the third trimester. This review delves into the association between maternal CR disturbances and the development of autism in the fetus. The study aims to investigate if pregnant mothers' circadian rhythm (CR) and sleep disorders (SD) are cofactors for the development of Autism Spectrum Disorder (ASD) in their offspring. Keywords: maternal circadian rhythms, melatonin, autism, neurodevelopmental disorders in children

**Methods and materials.** This review synthesizes data from approximately 70 publications over the last decade, sourced from PubMed, PMC, and Google Scholar.

**Results.** ASD development involves a multifactorial interplay of genetics, hormones, gut microbiota, immune dynamics, neural connectivity, neurotransmitters, and environmental exposures. Another important group of factors, but still undersized, are maternal CR disruptions, especially during pregnancy, and sleep difficulties in the second trimester, both of which increase the risk of neurodevelopmental disorders in children. There are a few underlying mechanisms, the most important are disrupted maternal melatonin secretion and the impact of stress and cortisol levels, which influence fetal development. Also, the dysregulation of a pregnant mother's physical activity during 24 hours could play an important role in ASD development because during physical activity pregnant woman releases growth hormone and insulin-like growth factor-1, promoting fetal growth through improved nutrient supply, exercise enhances fetal blood flow, reduces inflammation, oxidative stress, and increases growth factor levels, which improve neurodevelopment. Moderate to high-intensity physical activity during pregnancy positively affects newborn neurodevelopment.

**Conclusion.** In summary, maternal circadian rhythm disruptions and pregnancy-related sleep issues pose risks to offspring with ASD. Melatonin's role in fetal circadian rhythm and the impact of maternal stress are crucial. Maintaining moderate to vigorous physical activity throughout pregnancy benefits newborn neurodevelopment. Despite these findings, further research is essential to understand these intricate connections fully, shaping future research and therapies for ASD and neurodevelopmental disorders.