Melatonin Modulates Immunometabolic Signaling Associated with Macrophage Polarization in the Colostrum of Obese Mothers

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Abstract:

Maternal obesity is associated with chronic low-grade inflammation and metabolic dysregulation, potentially affecting the immunobiological composition of human colostrum and early-life programming mechanisms. Despite increasing interest in nutrigenomics and immunometabolism, little is known about the endocrine-enzymatic regulation of macrophage polarization in the colostrum of obese mothers. This study investigated melatonin-associated immunometabolic signaling, including macrophage phenotypes, inflammatory cytokines, and the L-arginine metabolic pathway, in human colostrum. Colostrum samples were obtained from eutrophic mothers (BMI 18.5–24.9 kg/m²) and obese mothers (BMI ≥30 kg/m²). Macrophages were isolated by density gradient and treated with melatonin. M1/M2 macrophage phenotypes and cytokine concentrations (IL-6, IL-10, TNF-α, and IL-17) were evaluated by flow cytometry. Melatonin levels, inducible nitric oxide synthase (iNOS), and arginase were quantified by ELISA. Colostrum from obese mothers exhibited increased endogenous melatonin concentrations associated with an altered immunometabolic profile characterized by reduced M1/M2 macrophage expression, increased iNOS activity, and elevated IL-6 and IL-17 levels. Melatonin treatment restored macrophage polarization profiles and modulated the enzymatic balance between iNOS and arginase, approaching values observed in eutrophic mothers. These findings demonstrate that maternal obesity disrupts immune-endocrine-metabolic signaling networks in colostrum, suggesting potential nutrigenomic implications for neonatal immune and metabolic programming. Melatonin appears to act as a key immunometabolic regulator, modulating inflammatory pathways, macrophage plasticity, and L-arginine metabolism at the maternal-infant interface.

Keywords:

Immunometabolism, nutrigenomics, melatonin, macrophage polarization, colostrum, maternal obesity, metabolic programming, cytokines.