MATERNAL STRESS AND OFFSPRING PANCREATIC PROGRAMMING: MORPHOLOGICAL, METABOLIC, AND IMMUNOLOGICAL DIMENSIONS

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Abstract. Maternal stress casts a shadow over offspring development, subtly reprogramming the pancreas—a guardian of metabolic health. This study, conducted in Uzbekistan, investigates how prenatal stress shapes pancreatic morphology, glucose metabolism, and immune responses in rat offspring, seeking clues to metabolic programming. Pregnant Wistar rats underwent chronic stress, with offspring assessed via histology, metabolic tests, and cytokine profiling. Findings revealed reduced beta-cell mass, impaired insulin release, and elevated pro-inflammatory cytokines, yet adaptive immune markers suggested partial resilience. In Uzbekistan’s youthful population (62% under 30), these insights highlight prenatal stress as a diabetes risk factor, urging global strategies for stress mitigation to protect future generations.

Keywords: maternal stress, pancreatic morphology, beta-cell programming, glucose metabolism, immune response, offspring health, metabolic disorders, developmental programming.

Introduction. Prenatal stress weaves a complex web, altering offspring organs like the pancreas, pivotal to glucose homeostasis, yet its role in pancreatic programming remains underexplored [1]. Globally, diabetes surges, with early-life stressors implicated, while in Uzbekistan, where 62% are under 30, maternal pressures amplify risks [2]. Stress hormones like glucocorticoids may disrupt islet development and immune balance, fostering metabolic vulnerability. Current research often overlooks the interplay of morphology, metabolism, and immunity, leaving gaps in understanding long-term outcomes. This study probes how maternal stress reprograms the offspring pancreas, integrating histological, metabolic, and immunological lenses to uncover mechanisms and inform interventions, resonating from Tashkent’s labs to global health forums.

Materials and Methods. Pregnant Wistar rats (n=25) endured restraint stress (2 hours/day, gestational days 8–18), while controls (n=25) remained unstressed.

Offspring were studied at postnatal day 55, reflecting metabolic maturity. Pancreatic tissues were processed for hematoxylin-eosin staining and immunohistochemistry (insulin, glucagon, PCNA) to evaluate islet structure and proliferation. Glucose tolerance tests (2 g/kg, intraperitoneal) monitored insulin and glucose over 120 minutes, with ELISA quantifying insulin and C-peptide levels. RT-PCR assessed glucocorticoid receptor (*NR3C1*), inflammatory (*IL-1α, IL-18*), and regulatory (*TGF-β*) gene expression. Serum cortisol and cytokine levels (IL-1α, IL-18) were measured via multiplex assays. Western blot analyzed pancreatic STAT3 signaling, linked to immune-metabolic crosstalk. Data were collected in Uzbekistan, leveraging local lab capabilities, with statistical analysis (ANOVA, $p<0.05$) ensuring rigor.

Results. Stressed offspring exhibited a 32% reduction in beta-cell mass and a 20% rise in alpha-cell ratio, with disrupted islet architecture versus controls [3]. Glucose tolerance tests showed a 40% lower insulin peak at 20 minutes and 25% slower glucose clearance, indicating metabolic strain [4]. Serum cortisol rose 20%, with IL-1α and IL-18 elevated 2.2-fold and 1.9-fold, respectively, signaling inflammation. *NR3C1* expression increased 2.4-fold, linking stress to programming, while *TGF-β* rose 1.8-fold, suggesting immune modulation [5]. STAT3 phosphorylation was 1.6-fold higher, hinting at adaptive signaling. Notably, 12% of stressed offspring maintained normal glucose responses, reflecting variable programming outcomes.

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