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HYPOTHYROIDISM IN PREGNANT RATS AFFECTS PROLIFERATION AND CELL DEATH OF GROWTH PLATE CHONDROCYTES IN PUPS

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Overt and subclinical maternal hypothyroidism affects cartilage and bone extracellular matrix formation during fetal endochondral bone development. Less is known about the effect maternal hypothyroidism has on cell proliferation and death of growth plate chondrocytes.

This study aimed to evaluate the expression of proliferation (Ki67), autophagy (LC3) and apoptosis (caspase 3) markers in the epiphyseal cartilage of the tibia in pups from subclinical and overt hypothyroid does, in their early postnatal development.

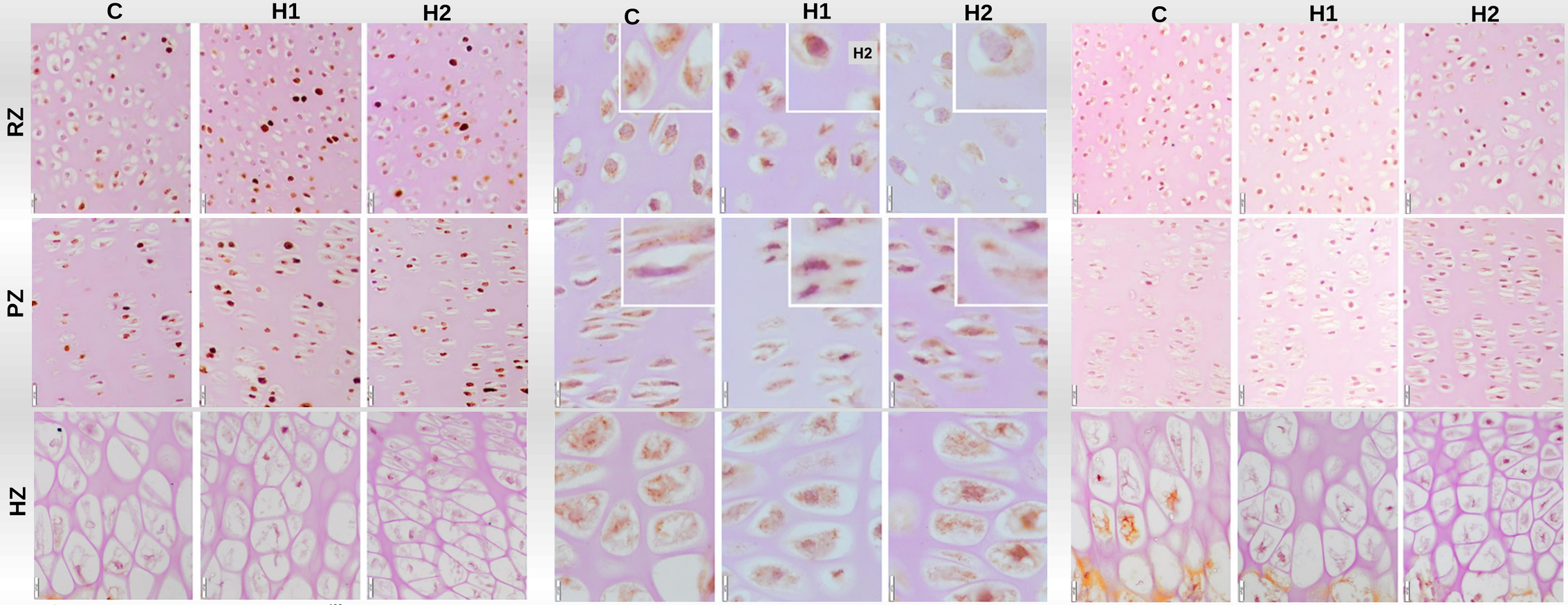
Material and metods: **Hypothyroidism was induced with propylthiouracil using low (1.5 mg/L) for subclinical (H1) and high dose (150 mg/L) for overt (H2) form. Propylthiouracil was administered through drinking water in pregnant Albino Oxford does from the first day of gravidity and during lactation. Control (C) group was not treated. Six, seven-day-old male pups from each group were euthanized. Histological examinations were performed on paraffin sections of the proximal tibial growth plate. Immunohistochemistry was used to assess the expression of Ki67, LC3 and caspase 3. The number of Ki67 positive chondrocytes was evaluated in the resting and proliferating zone using Image J. The expression of LC3 was performed by counting the number of positive dots in chondrocytes.**

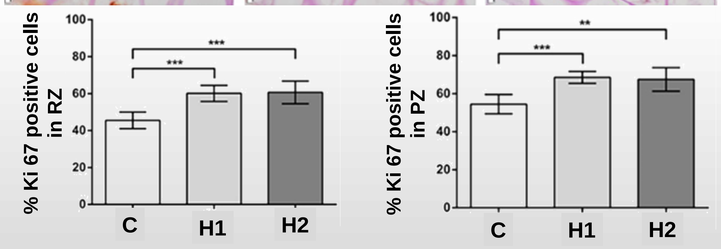
Results: **The number of Ki67 positive chondrocytes was higher in both hypothyroid groups, while the number of LC3 positive dots per cell was lower indicating that the chondrocyte cell cycle in hypothyroid animals is faster and that the basal level of autophagy is reduced due to frequent mitosis. Compared to controls, caspase 3 expression in the terminal hypertrophic chondrocytes was reduced in H1 and completely absent in H2 pups which might indicate impaired differentiation.**

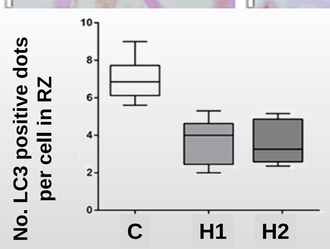
Expression of Ki 67

Expression of LC 3

Expression of Caspase 3







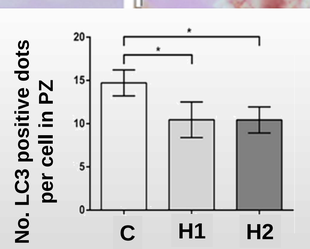


Figure legend:

C - Control group

H1 - Subclinical hypothyroid group

H2 – Overt hypothyroid group

RZ – Resting zone

PZ – Proliferating zone

HZ - Hypertrophic zone

Conclusion: **We conclude that both forms of maternal hypothyroidism in rats lead to accelerated proliferation, slowed autophagy and compromised apoptosis of terminal hypertrophic chondrocytes in the early infantile period and a delay in cartilage to bone transition.**

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