

DIABETES AND IMPAIRED BONE HEALING: MECHANISMS LINKING HYPERGLYCAEMIA, OXIDATIVE STRESS AND SKELETAL REGENERATION

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RESUMO

Introduction: Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by insulin dysregulation and hyperglycemia, associated with increased fracture risk and impaired bone quality. Both T1DM and T2DM contribute to skeletal fragility. Hyperglycemia disrupts bone healing by altering the bone microenvironment, including immune imbalance, macrophage polarization, microvascular damage, advanced glycation end products (AGEs), and reactive oxygen species (ROS), leading to defective repair and increased risk of non-union fractures. **Objective:** The aim of this study is to investigate how Diabetes Mellitus (DM) affects bone regeneration by impairing the bone microenvironment and disrupting healing processes.

Methods: A narrative review was conducted using PubMed. The terms “diabetes mellitus”, “bone healing”, “bone repair”, “chronic inflammation”, and “bone” were used. Articles published between 2023 and 2026 in English were included and descriptively analyzed, focusing on metabolic, inflammatory, and oxidative mechanisms that affect bone regeneration.

Discussion: Diabetes negatively affects bone quality by altering mineral density and porosity, increasing fragility, and reducing mechanical properties. Impaired bone healing is driven by hyperglycemia, chronic inflammation, oxidative stress, AGEs, polyol pathway, protein kinase C (PKC) activity, and hexosamine biosynthesis pathways, disrupting repair and angiogenesis. Chronic inflammation increases IL-1 β and TNF- α , inhibiting osteoblast activity and promoting osteoclast formation, while prolonged M1 macrophage presence impairs tissue repair. Central to this process, excessive reactive oxygen species (ROS) and oxidative stress (OS) affect osteoblasts (OBs), osteoclasts (OCs), osteocytes, and bone-marrow mesenchymal stem cells (BMSCs), with ROS/AGE-RAGE signaling promoting adipogenesis and senescence. OS inhibits Wnt/ β -catenin and activates RANKL/RANK/OPG, NF- κ B, and MAPK pathways, favoring bone resorption, while AGEs impair bone matrix quality. These mechanisms disrupt the balance between bone formation and resorption, directly compromising bone healing and regeneration in diabetes. **Conclusion:** Diabetes impairs bone healing through interconnected effects of hyperglycemia, oxidative stress (ROS), and inflammation, which disrupt bone remodeling and skeletal regeneration. These mechanisms compromise the bone microenvironment and contribute to defective bone repair, highlighting their relevance for future therapeutic strategies.

Palavras-chave: Chronic Inflammation; Bone Healing; Diabetes Mellitus; Bone; Bone Repair.