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INTEGRATED BIOMECHANICAL ASSESSMENT OF TRABECULAR BONE MICROARCHITECTURE AND MECHANICAL INTEGRITY IN TYPE 2 DIABETES MELLITUS

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Abstract

Type 2 Diabetes Mellitus (T2DM) negatively impacts bone quality by modifying its microarchitecture and mechanical strength, resulting in an elevated fracture risk despite normal or increased bone mineral density (BMD). Traditional densitometric assessments frequently overlook these qualitative alterations. This work combines high-resolution micro-computed tomography (micro-CT) and biomechanical compression testing to thoroughly evaluate trabecular bone integrity in Indian persons with T2DM.

Micro-CT analysis was conducted on trabecular bone specimens from two healthy controls and three patients with type 2 diabetes mellitus. Quantitative morphometric metrics, such as trabecular thickness (Tb. Th), trabecular number (Tb. N), trabecular separation (Tb. Sp), structural model index (SMI), and degree of anisotropy (DA), were calculated utilising ImageJ and MATLAB. Samples from T2DM demonstrated diminished trabecular thickness (Tb.Th) and trabecular number (Tb.N), augmented trabecular separation (Tb.Sp) and degree of anisotropy (DA), alongside an enhanced structural model index (SMI), signifying a transition from plate-like to rod-like trabecular configurations and a decline in structural connectivity.

Complementary uniaxial compression tests were performed on cylindrical trabecular bone specimens from matched groups to assess yield strength. T2DM specimens exhibited a 24% decrease in average yield strength (3.66 ± 0.32 MPa) relative to healthy controls (4.8 ± 0.14 MPa). In the diabetic group, increased HbA1c and BMI levels were linked to diminished mechanical performance, indicating a robust association between microstructural degradation and impaired mechanical integrity.

The consolidated data affirm that T2DM induces microarchitectural deterioration and mechanical compromise of trabecular bone, which together result in diabetic bone fragility. These findings underscore that bone mineral

Keywords: Micro-computed tomography, Trabecular bone, Type 2 Diabetes Mellitus, Bone microarchitecture, Biomechanics, Compression testing, Bone fragility, Structural model index, Anisotropy.

1. Introduction

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Bone is a dynamic tissue that perpetually undergoes remodelling due to mechanical loads and systemic influences. It is crucial to human physiology by facilitating movement, safeguarding internal organs, and acting as a vital metabolic reservoir. Trabecular bone is notably important among skeletal components because of its extensive surface area, metabolic activity, and vulnerability to pathological changes. It consists of a porous, fragile lattice structure of interconnecting plates and rods designed to withstand intricate mechanical loads.

Systemic illnesses like T2DM can significantly affect this fragile structure, resulting in compromised bone integrity and an increased risk of fractures. Type 2 Diabetes Mellitus (T2DM), a persistent metabolic condition marked by hyperglycemia and insulin resistance, is becoming more common in ageing populations, particularly in India. Multiple studies have demonstrated that persons with T2DM had an increased fracture risk, even with normal or higher BMD. This contradiction indicates that bone fragility in diabetes is influenced not only by bone quantity but also by microarchitectural and material integrity.

Conventional densitometric methods, including dual-energy X-ray absorptiometry (DEXA), frequently do not adequately represent bone quality [1][2]. Consequently, sophisticated analytical instruments that evaluate microstructural and mechanical properties are crucial for comprehending diabetic bone fragility. Hence, high-resolution micro-CT has become the benchmark for three-dimensional, non-destructive assessment of trabecular bone architecture [2][3]. It facilitates the determination of essential morphometric indicators, including Tb. Th, Tb. N, Tb. Sp, SMI, and DA, each acting as a determinant of bone strength and mechanical competency [4][5].

Research employing micro-CT has demonstrated that diabetic bone has diminished trabecular thickness and quantity, augmented separation, and modified anisotropy, indicating a shift from plate-like to rod-like morphology [6][7]. This architectural degeneration leads to quantifiable decreases in bone mineral density and results in diminished load-bearing capacity. Micro-CT provides a sensitive diagnostic method for identifying modest, clinically significant alterations in trabecular architecture linked to T2DM.

Imaging-based structural assessment yields information on bone geometry, whereas biomechanical testing delivers direct measurements of bone strength and stiffness—factors that influence functional capability under physiological loads. Uniaxial compression testing is especially appropriate for assessing trabecular bone due to its anisotropic and porous characteristics [8]. Prior biomechanical investigations have indicated substantial decreases in yield strength and stiffness in diabetic bone relative to healthy controls, frequently ascribed to the buildup of advanced glycation end-products (AGEs), diminished osteoblast activity, and modified collagen cross-linking [9][10].

Notwithstanding this findings, there is a paucity of data about the mechanical performance of trabecular bone in T2DM among ethnically distinct groups, including Indian cohorts. Genetic, nutritional, and lifestyle variations necessitate region-specific research to more accurately define diabetic bone fragility.

Due to the multiple aspects of bone degeneration in diabetes, a combined assessment of microstructural and mechanical analyses is essential for a thorough understanding. The current work seeks to

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- Quantitatively evaluate trabecular bone microarchitecture in both healthy and diabetic individuals utilising high-resolution micro-CT.
- Assess the biomechanical integrity of trabecular bone by uniaxial compression testing.
- Establish a correlation between microstructural characteristics and mechanical performance to clarify the structure–strength link in T2DM. This dual-modality technique connects imaging-based morphology with load-bearing behaviour, improving the diagnostic comprehension of diabetic bone fragility. The results are anticipated to yield significant insights into the early identification of skeletal deterioration and guide future approaches for risk assessment and therapeutic intervention in metabolic bone disease.

2. Assessment of Bone Characteristics

The experimental methodology was designed to assess the morphological and mechanical properties of trabecular bone in diabetic and healthy states using micro-CT imaging and uniaxial compression testing.

2.1 Collection and Preparation of Samples

Trabecular bone specimens were collected from five Indian individuals—two healthy controls (HC1, HC2) and three patients diagnosed with Type 2 Diabetes Mellitus (T2DM). Ethical approval was acquired before sample collection, and informed consent was obtained from all individuals or their legal representatives.

Bone biopsies were obtained from the iliac crest for microstructural evaluation and from cadaveric femoral heads for mechanical testing. All donors were of Indian descent, and diagnoses of T2DM were validated through medical history and increased HbA1c readings. Samples were meticulously cleansed of soft tissue under sterile circumstances and maintained in 0.9% isotonic saline at 4°C for micro-CT analysis, and at 37°C prior to compression testing to ensure hydration and physiological consistency. Cylindrical trabecular bone cores were fabricated with approximate dimensions of 6 mm in diameter and 8–10 mm in length for micro-CT analysis, and 10 mm in diameter and 15 mm in height for compression testing, in accordance with ASTM F1839-08 standards [3].

Cores were affixed to Acrylonitrile Butadiene Styrene (ABS) rods with cyanoacrylate adhesive for imaging and subjected to mechanical loads under displacement control. A laser-guided alignment mechanism guaranteed consistent orientation of the trabecular longitudinal axis.

2.2 Micro-Computed Tomography (Micro-CT) Imaging

Microstructural characterisation was conducted via a Phoenix Nanotom S micro-CT system (GE Measurement and Control, Germany). The scanning parameters were modified for enhanced resolution and artefact reduction. Figure 1 illustrates the configuration of the Phoenix Nanotom S micro-CT Scanner. The scanning parameters are as follows:

- Voxel size: 10 μm
- X-ray tube voltage: 45 kV
- Tube current: 250 μA
- Integration time: 250 s
- Total projections: 400

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System calibration was performed via a standard phantom with established geometry. The scan generated 2D cross-sectional slices that were rebuilt into 3D volumetric models utilising GE Phoenix datos|x software.

Figure 1. Phoenix Nanotom S Micro-CT Scanner Setup

Post-processing and morphometric analyses were conducted utilising ImageJ with the BoneJ plugin, alongside the development of supplementary algorithms in MATLAB R2023a. Segmentation was accomplished by a global thresholding method to differentiate between bone and marrow sections.

The subsequent morphometric characteristics were quantified [1][11]:

- Trabecular Thickness (Tb. Th)
- Trabecular Number (Tb. N)
- Trabecular Separation (Tb. Sp)
- Structural Model Index (SMI)
- Degree of Anisotropy (DA)

Morphometric analysis utilised a three-dimensional sphere-fitting and distance transformation methodology [13].

Visual models of reconstructed samples were created for both healthy and diabetic cohorts to examine qualitative disparities in trabecular orientation and connection. Figure 2 illustrates the trabecular bone model of the HC1 sample utilised for the assessment of trabecular morphometric characteristics.

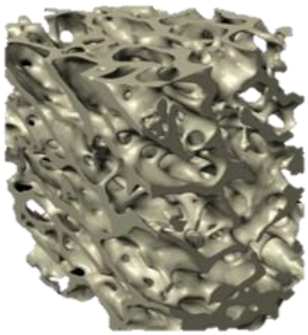

Figure 2. 3-D Model of Trabecular bone of HC1 Sample

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2.3 Biomechanical Compression Assessment

Mechanical testing was conducted to assess the yield strength and deformation characteristics of trabecular bone under quasi-static loading conditions.

Cylindrical specimens (10 mm diameter × 15 mm height) were evaluated using a servo-controlled Universal Testing Machine (UTM) fitted with a 10 kN load cell (Figure-3), in accordance with ASTM F1839-08 standards [3].

Compression was executed under displacement control at a rate of 0.5 mm/min. Force and displacement were measured at a frequency of 50 Hz, and stress-strain curves were generated. The yield strength (σy) was ascertained with the 0.2% offset method appropriate for porous trabecular materials [14].

A bespoke cylindrical alignment jig guaranteed precise axial loading to reduce bending effects. Each test was performed in triplicate to ensure repeatability.

Figure 3: Universal Testing Machine (UTM) setup for compression testing

3. Results and Discussion

3.1 Demographics and Clinical Data of Participants

The study had five participants: two healthy controls (HC1, HC2) and three individuals diagnosed with Type 2 Diabetes Mellitus (DM1, DM2, DM3). Their demographic and clinical characteristics are encapsulated in Table 1.

Table 1: Demographic and Clinical Attributes of Participants

Sample	Age (years)	Sex	BMI (kg/m²)	HbA1c (%)	Health Status
HC1	40	M	22.5	5.3	Healthy
HC2	42	F	23.1	5.5	Healthy
DM1	40	M	27	7.8	T2DM

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DM2	45	F	28.4	8.2	T2DM
DM3	42	M	26.7	7.5	T2DM

Healthy individuals demonstrated normal Body Mass Index (BMI) and HbA1c levels, while diabetic people presented higher BMI (26.7–28.4 kg/m²) and HbA1c (7.5–8.2%), aligning with the metabolic characteristics of T2DM. These physiological changes provide the foundation for assessing structural and mechanical variances in trabecular bone.

3.2 Microarchitectural Assessment using Micro-CT

Quantitative study of trabecular morphology via micro-CT demonstrated significant disparities between the healthy and diabetic cohorts. Representative 3D reconstructions exhibited significant architectural degradation in diabetes samples.

Figure 4 illustrates a quantitative morphometric investigation conducted by micro-CT, which uncovered notable architectural disparities.

Significant trends were observed in key morphometric parameters:

- Trabecular Thickness (Tb. Th): Reduced in T2DM samples, signifying a decline in bone mass and mineralised connection.
- Trabecular Number (Tb. N): Decreased in diabetic bone, indicating a reduction in trabecular network density.
- Trabecular Separation (Tb. Sp): Significantly increased, resulting in enlarged marrow gaps and compromised load distribution.
- Structural Model Index (SMI): Increased in diabetes samples, signifying a transition from a plate-like to a rod-like structure.
- Degree of Anisotropy (DA): Elevated in T2DM, indicating a directionally biassed and less isotropic bone architecture.

These microstructural changes collectively signify a decline in trabecular connection, heightened porosity, and diminished load-bearing efficacy [3}[12].

The transition from plate-like to rod-like morphology diminishes the surface area for stress distribution, hence compromising the structural integrity of the bone framework [1].

Figure 3 demonstrates that T2DM samples consistently display reduced Tb. Th and Tb. N values in comparison to controls, although Tb. Sp and DA are heightened. These results align with prior research connecting hyperglycemia and collagen glycation to impaired trabecular organisation [5,6]. Chronic hyperglycemia mechanistically facilitates the buildup of advanced glycation end-products (AGEs), which rigidify the collagen matrix and hinder remodelling. Decreased osteoblast activity and modified cytokine signalling additionally exacerbate trabecular thinning and loss of connection [2].

The micro-CT data indicate that, despite minimal BMD loss, diabetic bone has significant qualitative degradation identifiable using morphometric indices.

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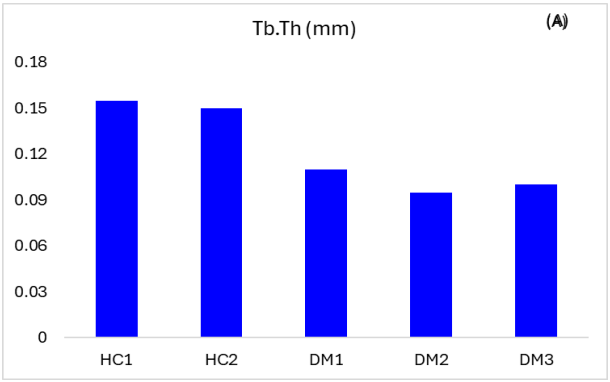

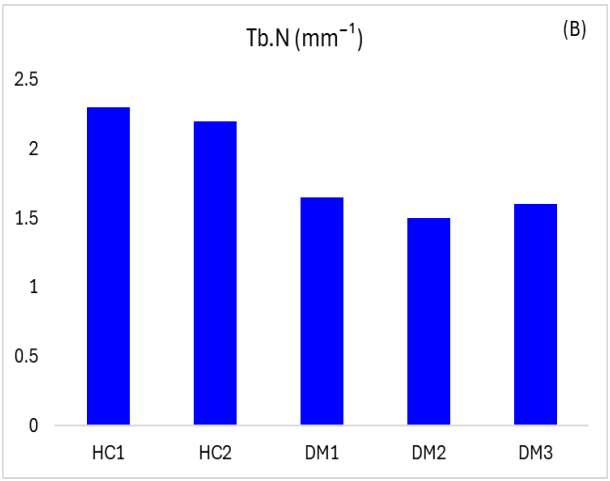

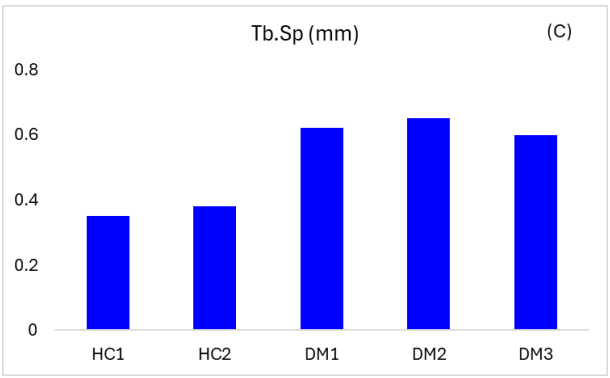

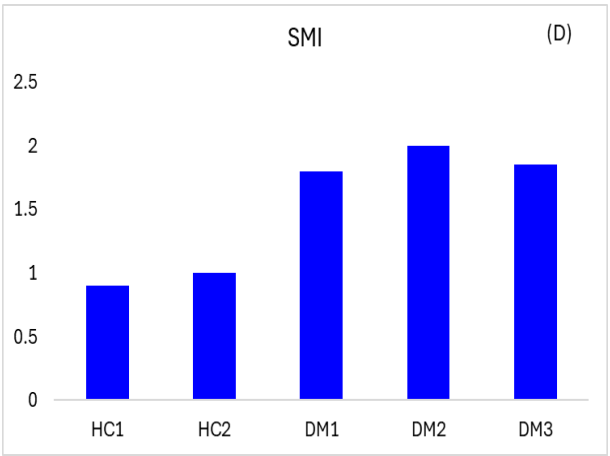

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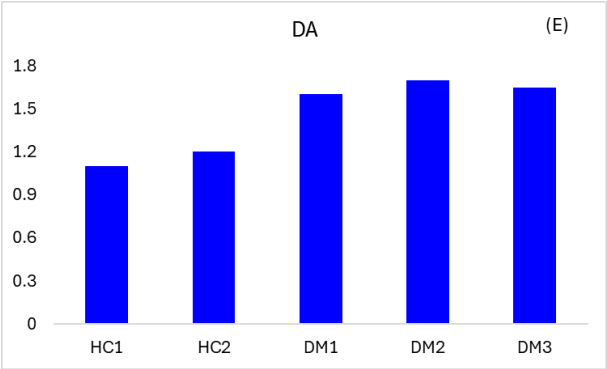

Figure 4. Comparison of trabecular morphometric parameters with different samples

3.3 Mechanical Properties Assessed via Compression Testing

Compression tests of femoral trabecular specimens demonstrated a significant reduction in mechanical strength in diabetic samples. Figure 5 shows stress–strain curves from both Control and T2DM groups

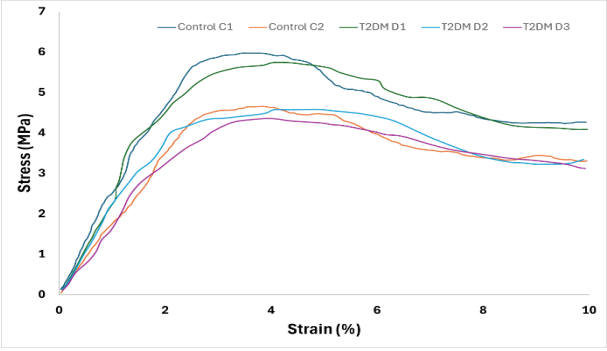

Figure 5: Stress–strain curves from both Control and T2DM groups

The mean yield strength for T2DM specimens was 3.66 ± 0.32 MPa, indicating a 24% decrease relative to the 4.8 ± 0.14 MPa recorded in healthy controls.

This reduction strongly correlated with increased HbA1c and BMI levels (Table 1), both markers of metabolic dysregulation.

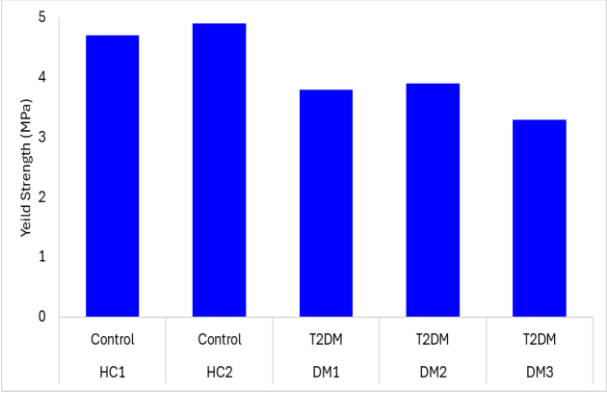

Figure 6: Comparison of yield strength between Control and T2DM specimens

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Control specimens demonstrated a triphasic stress-strain response characterised by a steep beginning slope, signifying elevated stiffness and elastic modulus. Diabetic samples exhibited earlier yield points and sudden post-yield failure, aligning with the principles of brittle fracture mechanics [4][15].

Observations following failure indicated certain fracture modes:

- Controls: Distributed microcracking accompanied by progressive crushing, preserving partial trabecular connection.
- T2DM samples exhibit abrupt vertical fissuring and localised subsidence, indicating compromised connections and deficient load redistribution [10].

The mechanical findings validate that T2DM markedly undermines trabecular bone integrity, supporting the morphological degradation shown with micro-CT.

AGE-induced collagen cross-linking, marrow fat infiltration, and inhibited remodelling combined result in rigid yet fragile bone, susceptible to fractures even from low-energy impacts [6][16].

3.4 Correlation between Structure and Strength

A significant association was noted between microstructural characteristics (Tb.Th, Tb.N, SMI, DA) and mechanical performance (yield strength).

Samples exhibiting elevated Tb.Th and diminished SMI demonstrated enhanced compressive strength, corroborating that microarchitectural deterioration directly results in mechanical frailty.
This correlation between structure and strength underscores that bone mineral density (BMD) alone is inadequate for evaluating fracture risk in type 2 diabetes mellitus (T2DM) [7][8]. The integration of high-resolution imaging and mechanical assessment provides a more precise and physiologically pertinent evaluation of bone competency.

3.5 Clinical Implications

The results of micro-CT and compression testing highlight that T2DM causes multifaceted decline in bone quality, impacting both structure and strength.

Conventional BMD-based diagnostics may undervalue fracture risk in diabetic groups.

Utilising integrated diagnostic methodologies, such as micro-CT, finite element modelling, and mechanical testing, can enhance fracture risk assessment and inform therapy methods focused on restoring trabecular connection and collagen integrity [9][10]. Such analyses could facilitate the assessment of the effectiveness of anti-diabetic drugs or lifestyle treatments on skeletal health, especially in ageing populations.

The comparative study of trabecular bone between healthy and T2DM groups demonstrated continuous structural and mechanical deterioration in diabetic specimens. Both trabecular thickness (Tb.Th) and trabecular number (Tb.N) exhibited significant declines, signifying a reduction in bone mass and connectivity within the trabecular framework. Conversely, trabecular separation (Tb.Sp) and degree of anisotropy (DA) were markedly elevated in diabetic samples, indicating enhanced porosity and anisotropic architecture that compromises overall stability. The structural model index (SMI) displayed high values, indicating a

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morphological transition from plate-like to rod-like trabecular structures that possess reduced mechanical efficiency. Yield strength exhibited an average decrease of around 24% in T2DM specimens compared to controls, indicating reduced mechanical integrity and increased vulnerability to fracture.

These results collectively demonstrate that T2DM causes both microarchitectural and mechanical degradation in trabecular bone. The deterioration of structural connection, heightened anisotropy, and diminished compressive strength collectively highlight the vulnerability of diabetic bone and its increased fracture risk, despite bone mineral density being within normal ranges.

4. Conclusions

High-resolution micro-CT and uniaxial compression tests collectively offer a thorough assessment of trabecular bone integrity in persons with type 2 diabetes mellitus. This study's integrated findings indicate that T2DM causes substantial degradation in both the microarchitecture and mechanical integrity of trabecular bone, despite BMD remaining within normal ranges.

Micro-CT examination demonstrated significant deterioration in trabecular architecture, indicated by diminished trabecular thickness and number, increased trabecular separation and density anisotropy, and heightened structural model index. These values collectively signify a morphological shift from plate-like to rod-like structure, leading to reduced load distribution capacity and mechanical strength.

Complementary compression tests verified a 24% decrease in yield strength in diabetes specimens relative to healthy controls. This mechanical deterioration correlates with increased HbA1c and BMI levels, indicating the effects of chronic hyperglycemia, the buildup of advanced glycation end-products (AGEs), and modified collagen cross-linking on bone quality. The noted structural alterations immediately resulted in diminished mechanical strength and heightened fragility of diabetic bone.

The findings highlight that BMD alone is inadequate for evaluating fracture risk in people with T2DM. Assessing both microstructural and mechanical factors yields a more precise depiction of bone health. The amalgamation of micro-CT imaging, mechanical testing, and finite element modelling may facilitate the early identification of skeletal fragility and enhance the therapeutic management of diabetic bone problems.

Future research should encompass bigger cohorts and investigate relationships among micro-CT-derived parameters, mechanical strength, and computer simulations to improve predictive models of fracture risk. Multimodal techniques can enhance early intervention efforts and increase diagnosis accuracy for metabolic bone disorders.

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