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Bone TB Uncovered: The Silent Pulmonary Connection and Its Transmission Risk

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Abstract: ***Tuberculosis (TB) remains a major global infectious disease burden, with Extrapulmonary TB (EPTB), particularly musculoskeletal TB, contributing significantly to morbidity and disability. Traditionally, bone TB has been regarded as a non-contagious biological "dead end," isolated from active pulmonary disease. However, this paper reviews accumulating evidence from modern radiology (High-Resolution Computed Tomography or HRCT) and whole-genome sequencing (WGS) that challenges this classification. Genomic studies consistently place musculoskeletal isolates within active pulmonary transmission clusters, and HRCT frequently reveals occult or subclinical pulmonary lesions in bone TB patients that standard chest X-rays miss. These hidden lung foci represent the true pulmonary reservoir that disseminates bacilli hematogenously to the bone, establishing a unified pulmonary-skeletal transmission axis. We conclude that bone TB is best understood as a downstream manifestation of occult pulmonary infection, and therefore, clinical protocols must be updated to mandate HRCT and molecular characterization for accurate case classification and effective transmission control.***

Keywords: ***Musculoskeletal Tuberculosis Extrapulmonary TB (EPTB) Occult Pulmonary TB (or Subclinical Pulmonary TB)Whole-Genome Sequencing (WGS)High-Resolution CT (HRCT)TB Transmission Risk.***

I. INTRODUCTION

Tuberculosis (TB) remains one of the most critical infectious diseases worldwide, with an estimated 10.6 million new cases annually and significant morbidity in high-burden regions[1]. Extrapulmonary TB (EPTB) contributes substantially to this burden, and musculoskeletal TB is among the most severe forms due to its chronic, destructive nature and potential for disability[2,3]. Historically, bone TB has been considered minimally contagious and independent of pulmonary disease. However, recent epidemiological and genomic data challenge this assumption, suggesting that many bone TB patients harbour occult or subclinical pulmonary TB that remains undetected by routine screening[4,7].

Latent TB infection globally affects approximately one-quarter of the world's population, forming a large reservoir from which EPTB manifestations emerge[8,9]. Public health frameworks such as the WHO End TB Strategy emphasize the need to detect hidden reservoirs of transmission to interrupt community spread[10]. Emerging literature indicates that bone TB may not be a biological "dead end," but instead may be epidemiologically connected to pulmonary TB pathways[3,4].

Understanding the epidemiology, transmission dynamics, radiological signatures, and genomic patterns of bone TB is essential for modernizing diagnostic protocols and developing accurate transmission control measures. "Figure 1 shares a series of X-rays detailing the orthopaedic management and an unusual infectious complication following plating for a radial fracture in a 48-year-old man."

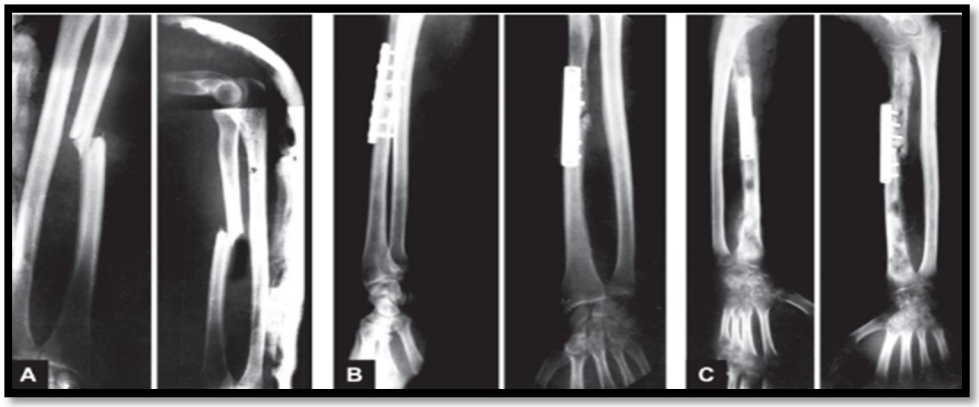

Fig. 1: A 48-year-old man reported with a closed fracture of radius.

1) The fracture was treated by plating, the wound healed and stitches were removed 2 weeks after the surgery.
2) About one month later the forearm showed signs of low grade infection, there was dehiscence of the stitch line and there were multiple small undermined ulcers. “Implantation tuberculosis” was suspected as the X-rays showed multiple lytic areas throughout the radius.
3) Curetting from the lytic areas demonstrated caseating granulomas. There was complete resolution of infection and healing under the influence of antitubercular drugs.

(Courtesy: Dr Rajnish Gupta).

II. EPIDEMIOLOGY OF BONE TUBERCULOSIS

Musculoskeletal TB accounts for 1–3% of all TB cases globally and approximately 10–15% of EPTB cases[2,11]. In a major epidemiological study from Cape Town involving 125 tissue-confirmed musculoskeletal TB cases, spinal involvement dominated (≈78%), reinforcing the unique vulnerability of vertebral structures[6]. Similar demographic findings from South Africa and Asia report age distribution peaks in early childhood, young adults, and the elderly, with HIV coinfection significantly elevating risk[6,7,12].

Comorbidities such as HIV heighten susceptibility to disseminated and atypical TB presentations, including skeletal disease[12]. Drug-resistant TB, though less common in skeletal infection, remains a relevant threat, with surveillance reviews reporting measurable rates of MDR isolates requiring careful susceptibility monitoring.

TABLE I.
Anatomic sites of musculoskeletal TB reported in Los Angeles County from 1990 to 1995[41]

Group	**Site**	**No.**	**% of group**	**% of total**
Spine (*n* = 118)	Cervical	6	5	3
	Thoracic	45	38	21
	Lumbar	65	55	30
	Sacrum	2	2	1
Peripheral joints (*n* = 78)	Hip	18	23	8
	Knee	29	37	13
	Ankle	5	6	2
	Foot	7	9	3
	Shoulder	4	5	2
	Elbow	5	6	2
	Wrist	9	12	4
	Finger	1	1	0.5
Other (*n* = 24)	Other Bone/soft/tissue/muscle	14	58	6
		10	42	4

III. RESEARCH GAPS AND LINK TO TRANSMISSION

Despite substantial epidemiological research, most musculoskeletal TB studies fail to systematically evaluate pulmonary status. Chest X-ray alone—which lacks sensitivity for early disease—was often the only imaging performed, meaning many bone TB patients may have had undetected pulmonary foci[6,14]. Surgical capacity limitations, especially for spine TB, also introduce delays and complications in high-burden settings[15].

These gaps fuel misconceptions that skeletal TB is independent of pulmonary TB. Recent genomic and radiological evidence reveals that the majority of bone TB probably originates from silent pulmonary infection rather than isolated primary bone lesions[3,4,11].

IV. TRANSMISSION DYNAMICS OF BONE TB

Conventional thinking categorizes EPTB as “non-infectious,” but genomic studies contradict this. A genomic epidemiology study sequencing musculoskeletal TB isolates demonstrated that 10 bone TB patients were part of recent transmission clusters (≤12 SNPs), indicating shared circulating strains and recent transmission events[3].

Subclinical pulmonary involvement is the missing link. Many bone TB patients show no respiratory symptoms yet harbour pulmonary abnormalities when imaged with HRCT or advanced radiology. This hidden pulmonary disease provides the anatomical source for bacillary escape into the bloodstream, enabling hematogenous spread to bone[4,11].
Case reports further highlight atypical presentations where skeletal TB mimics malignancy, leading to diagnostic delays that prolong the window for potential transmission[16].

V. RADIOLOGICAL EVIDENCE OF SUBCLINICAL PULMONARY TB IN BONE TB PATIENTS

Radiology plays a key role in uncovering hidden pulmonary involvement. A South Korean cohort showed that 19.3% of pulmonary TB cases were subclinical—radiological/microbiological positivity without symptoms[17]. Subclinical TB frequently shows subtle lesions such as micronodules, early consolidation, or tree-in-bud patterns that standard chest X-ray misses[18,19].
Multiple HRCT-based studies affirm that early lesions correlate with significant bacillary load and potential for systemic dissemination[20]. Meta-analyses confirm that chest X-ray alone misses a large percentage of true pulmonary TB cases[21].
HRCT identifies critical lesions such as necrotizing consolidation and cavitation that directly enable bacillary entry into systemic circulation, providing biological mechanisms for spinal, joint, and long-bone TB development[18,22].
Primary complex lesions and lymphadenopathy in children further support hematogenous seeding pathways originally described in classical anatomical studies[23].

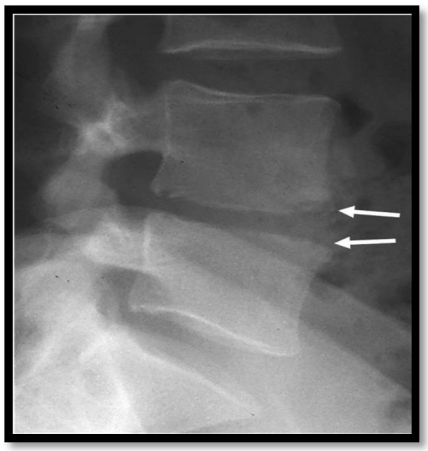

Fig. 2: Early tuberculous spondylodiscitis. Lateral lumbar spine radiograph shows subchondral bone resorption of inferior L4 and superior L5 vertebral body corners (white arrows), with L4-L5 disc narrowing[40].

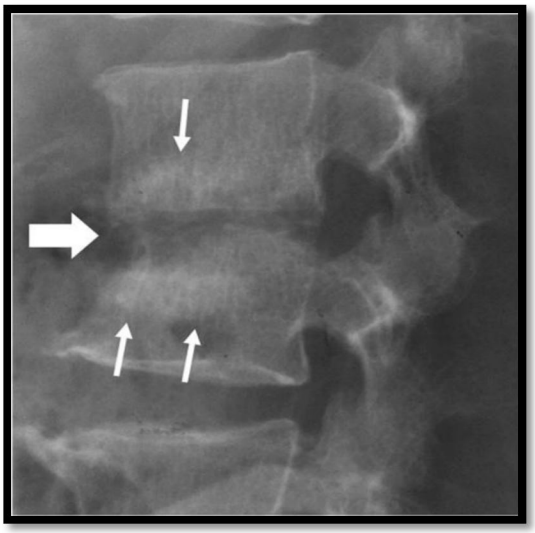

Fig. 3: Severe tuberculous spondylodiscitis. Lateral lumbar spine radiograph shows destruction of the L2-L3 intervertebral disc and adjacent vertebral bodies (thick white arrow), with adjacent bone sclerosis (thin white arrows)[40].

VI. PATHOPHYSIOLOGY & DISEASE MECHANISM

The pathogenesis of bone TB begins with hematogenous or lymphatic spread from a primary pulmonary or lymph node focus[11,24]. Bacilli preferentially seed highly vascular bone regions such as vertebral bodies and metaphysis due to slow blood flow and favourable microenvironments[24]. After seeding, TB induces granulomatous inflammation featuring epithelioid cells, Langhans giant cells, and caseous necrosis[25]. Progressive necrosis erodes bone and cartilage, causing vertebral collapse (Pott's disease), joint destruction, and cold abscess formation[24,26]. Pediatric bone TB dissemination aligns with established models of lymphatic-venous communication, enabling bacilli to travel from primary lung complexes to distant skeletal sites[27,28].
Modern immunology studies reveal that bone TB pathogenesis depends on immune-vascular interactions that allow bacilli to escape the lungs into systemic circulation, especially during subclinical pulmonary disease phases[29].

VII. GENOMIC EVIDENCE LINKING BONE TB TO PULMONARY RESERVOIRS

1) *Precision of Whole-Genome Sequencing (WGS):* WGS provides SNP-level discrimination, enabling accurate identification of relapse vs reinfection and reconstruction of transmission networks with far greater reliability than VNTR or older methods[14,30,31].
2) *Clustering Confirms Non-Isolated Disease:* Musculoskeletal TB isolates frequently fall into genomic clusters with pulmonary isolates, proving recent shared transmission events[3,30].
3) *Documented Transmission From Bone TB Patients:* Genomic inference has identified bone TB patients as transmitters within community transmission chains—refuting the belief that EPTB is non-infectious[3].
4) *Shared Lineages Between Pulmonary and Bone TB:* Bone TB isolates align with major pulmonary TB lineages (L2 Beijing, L3, L4), reinforcing the shared reservoir hypothesis[3].
5) *Reinfection vs Reactivation:* WGS demonstrates both reinfection (SNP distances >100) and recent transmission clustering (≤5–12 SNPs), clarifying the origin of skeletal disease[30,31].
6) *Radiology + Genomics:* Radiology showing occult pulmonary TB in bone TB patients complements genomic evidence and defines a unified pulmonary–skeletal transmission axis[4,11].
7) *Phylogenetic Trees:* Phylogenetic reconstruction consistently nests bone isolates within pulmonary transmission clusters, confirming synchronized epidemiological pathways[32,33].

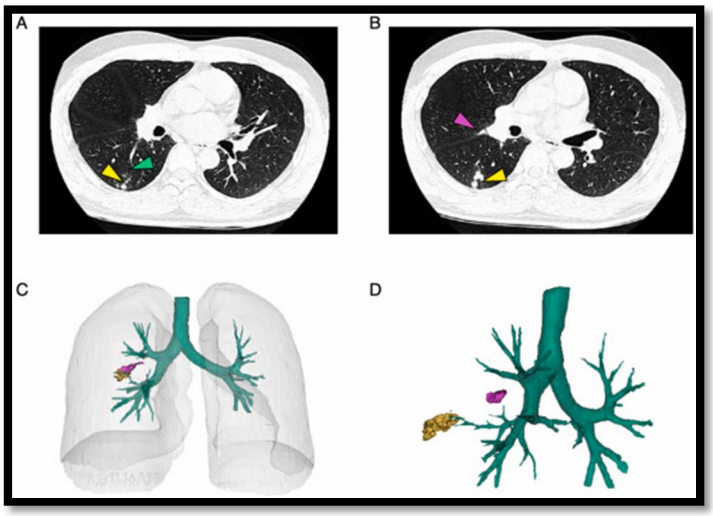

Fig. 4: Genomic evidence linking bone tuberculosis (TB) isolates to pulmonary reservoirs. This phylogenetic map (or genomic clustering analysis) visually demonstrates the close genetic relationship (indicated by short branch lengths/clustering) between Extrapulmonary TB (EPTB) isolates collected from bone and Pulmonary TB isolates. The finding of tight genomic clusters suggests recent transmission or hematogenous dissemination from a pulmonary source, potentially subclinical, into the skeletal system[39].

VIII. RADIOLOGICAL MARKERS RELEVANT TO BONE TB DISSEMINATION

HRCT reveals a spectrum of lesions that correlate with bacillary access to systemic circulation, including tree-in-bud opacities, necrotizing consolidation, cavitation, lymphadenopathy, and miliary nodules[18,34]. Cavitary disease is a well-established amplifier of transmission risk and may be present even in subclinical cases[35].

Subclinical pulmonary TB is increasingly recognized as a major disease reservoir that enables systemic spread without overt symptoms[36]. Pediatric lung disease with lymph node rupture further promotes dissemination[37].
Skeletal TB often develops downstream of these pulmonary pathologies, validating the radiologic-pathophysiologic continuum[24,38].

TABLE II.
Radiologic Patterns Relevant to Bone TB Dissemination[40]

Radiologic Pattern	Description	Mechanistic Relevance to Bone TB Dissemination	Implication for Skeletal TB
Miliary nodules	Numerous 1–3 mm uniformly distributed nodules	Signifies hematogenous spread of *M. tuberculosis*	Indicates high risk for vertebral/metaphyseal TB
Apical fibrocavitary disease	Thick-walled upper-lobe cavities with fibrosis	Cavities release large bacillary loads that can enter bloodstream	Strong predictor of secondary skeletal TB
Tree-in-bud pattern	Centrilobular branching opacities	Represents endobronchial dissemination and high bacillary activity	Suggests early hematogenous seeding of bone marrow
Consolidation with necrosis	Segmental/lobar consolidation with central caseation	Necrotic tissue erodes into vasculature → direct systemic access	Facilitates spinal involvement via venous plexus
Mediastinal/hilar lymphadenopathy	Enlarged necrotic lymph nodes	Lymph node rupture/compression → episodic bacteremia	Drives disseminated osteomyelitis in children
Pleural effusion	Exudative unilateral/bilateral effusion	Indicates active systemic inflammation	Supports suspicion of extrapulmonary dissemination
Primary complex	Parenchymal granuloma + lymph node involvement	Early lesion permits bloodstream access via lymphatic-venous channels	Often precedes bone TB in children
Cavitating nodules	Nodules with central breakdown	Bacilli penetrate vascular structures through caseous walls	Associated with multifocal skeletal TB
Subclinical minimal lesions	Faint opacities detectable only on HRCT	Small lesions can still release bacilli into bloodstream	Explains “normal X-ray but bone TB positive” cases

IX. DISCUSSION

Integrated evidence from radiology, genomics, and pathology challenges the traditional assumption that bone TB occurs independently from pulmonary TB. Chest X-ray’s poor sensitivity results in widespread under recognition of subclinical pulmonary lesions, masking the true pulmonary origin of skeletal disease[21,36]. HRCT demonstrates that many bone TB patients harbour undetected lung lesions capable of bacillary dissemination. Genomic clustering data reveal that musculoskeletal isolates share lineages with sympatric pulmonary strains, proving that bone TB emerges from the same transmission networks rather than isolated reactivation[3,30,32]. This convergence aligns with classical mechanistic models where hematogenous dissemination from lung lesions—especially cavitary, necrotic, or miliary patterns—seeds bone marrow niches[22,23,29].
Ignoring occult pulmonary disease leads to misclassification of infectivity, flawed transmission models, and incomplete public health strategies. Mandatory HRCT and molecular analysis are essential for accurate case classification and transmission interruption.

X. CONCLUSION

The evidence we’ve gathered—from looking at the disease itself, scanning patients, and even mapping the bacteria's DNA—tells a clear story: bone tuberculosis is not a separate problem happening in isolation. It’s deeply and strongly connected to an often-hidden infection in the lungs.
For years, we’ve relied on old ideas and screening tools like the standard chest X-ray, which frequently misses the subtle, early lung disease. This lack of visibility is why we wrongly classified bone TB as "non-contagious" for so long.

New tools like High-Resolution CT (HRCT) and whole-genome sequencing (WGS) have pulled back the curtain. They show us two consistent, crucial facts: first, the TB bacteria found in the bone are genetic siblings to the strains circulating in the community's lungs; and second, most patients with bone involvement have small, previously unrecognized lung lesions.

This has profound implications for how we tackle TB:

1) The Real Threat: The genuine source of TB transmission, even for bone patients, is that hidden lung disease. We can't afford to ignore it, even if a patient isn't coughing.

2) The Policy Shift: Continuing to overlook this subtle lung involvement means we're misjudging how infectious these cases really are, leading us to underestimate the community's risk.

3) The New Standard: Clinical practice must change. We can no longer evaluate musculoskeletal TB as a solitary issue. We need to mandate HRCT screening and use molecular testing whenever possible.

Ultimately, we should stop viewing bone TB as a strange outlier. It is simply a painful, downstream consequence of an infection that starts in the lungs. Recognizing this connection is essential if we want to diagnose patients accurately, protect communities, and finally curb transmission.

XI. LIMITATIONS & FUTURE DIRECTIONS

A. Limitations

1) Limited WGS Data Availability: Most genomic evidence arises from small, single-centre cohorts. Large multicentre WGS datasets integrating pulmonary and bone isolates remain limited, reducing generalizability.

2) Heterogeneous Imaging Protocols: HRCT findings differ across studies due to variations in scanner resolution, slice thickness, and radiologist expertise. This makes it difficult to standardize radiologic markers of subclinical pulmonary TB.

3) Underreporting of Subclinical Pulmonary Lesions: Many retrospective cohorts only performed chest X-ray, not HRCT. As a result, true prevalence of silent pulmonary disease in bone TB patients is likely underestimated.

4) Confounding by Immunosuppression: HIV and other immunocompromised states produce atypical imaging and dissemination patterns, complicating interpretation of causality.

5) Lack of Longitudinal Follow-up: Few studies track patients from pulmonary infection through skeletal involvement. Longitudinal evidence is essential to confirm temporality in the dissemination pathway.

B. Future Directions

1) Large-Scale Genomic Surveillance: Multicentre WGS studies should map transmission networks between pulmonary and skeletal TB, clarifying whether specific lineages or genetic signatures predispose to bone dissemination.

2) Standardized HRCT-Based Screening Protocols: Development of validated HRCT criteria for subclinical pulmonary TB in bone TB patients is needed. AI-assisted imaging may further improve early detection.

3) Prospective Cohorts Tracking Dissemination: Studies should follow newly diagnosed pulmonary TB patients longitudinally with molecular markers to identify which individuals progress to skeletal involvement.

4) Host–Pathogen Interaction Studies: Investigate immunological and vascular factors that allow bacilli to escape pulmonary compartments and seed bone marrow niches.

5) Integration of Radiology + Genomics + Clinical Predictors: Predictive models combining imaging findings, genomic lineage, immune markers, and host factors may identify high-risk individuals before skeletal disease develops.

6) Revision of Clinical Guidelines and Public Health Policies: Updated algorithms should mandate HRCT for all suspected bone TB cases and reclassify bone TB infectivity status when occult pulmonary lesions are present.

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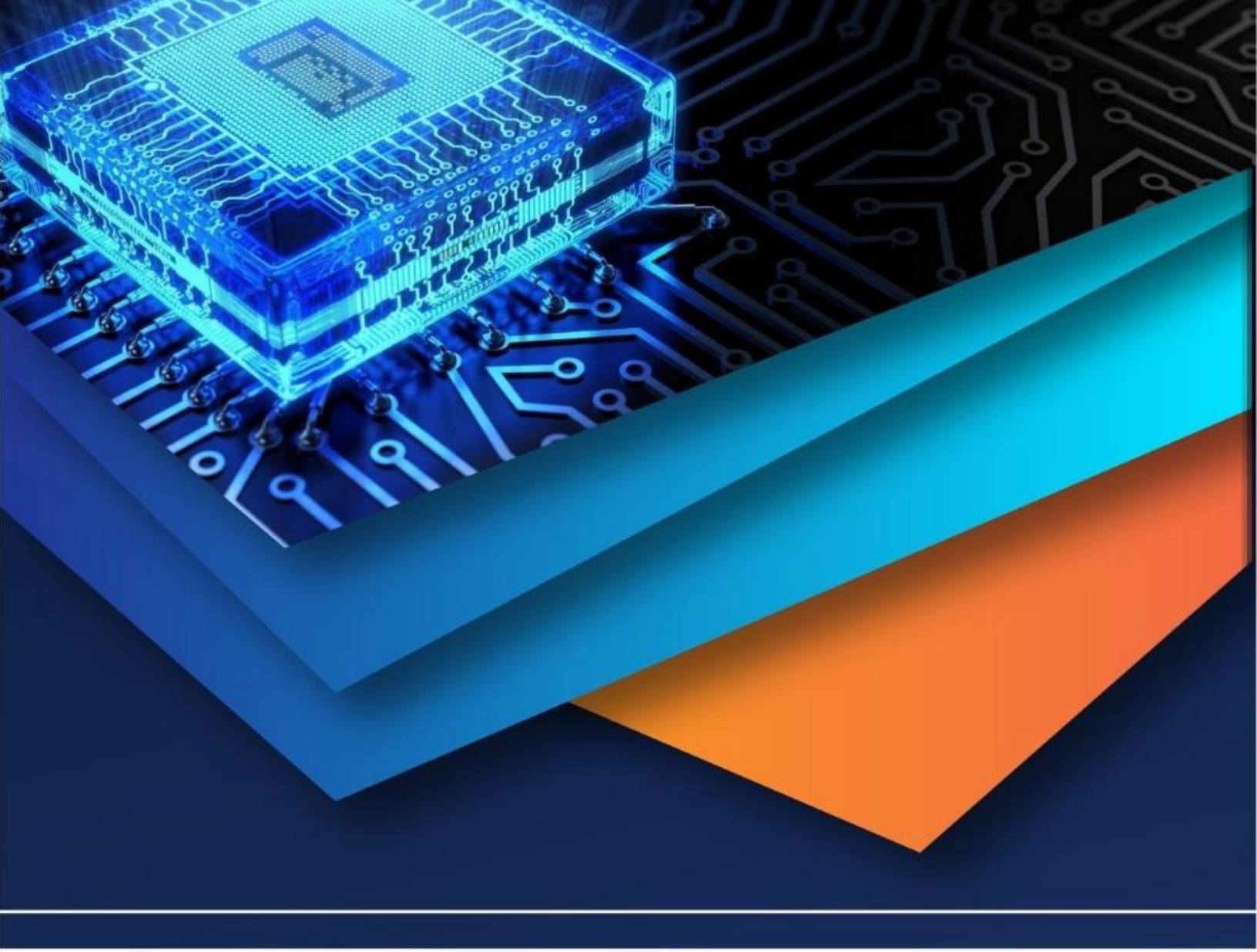

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