

Synovial biopsy: an underutilized diagnostic tool in clinical practice: an observational study

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ABSTRACT

Background: Synovial biopsy, an important diagnostic tool to evaluate chronic monoarthritis, undifferentiated inflammatory arthritis and neoplasms, remains underutilized in clinical practice due to perceived invasiveness and limited access to specialized techniques. This study evaluates the diagnostic utility and histopathological spectrum of synovial biopsies in a tertiary care centre.

Materials and Methods: This retrospective and prospective observational study was conducted over three years (June 2020–June 2023) in a tertiary care institute. Synovial biopsies obtained via needle biopsy or arthrotomy received in the Department of Pathology, were routinely processed and evaluated using Hematoxylin and Eosin (H&E) stain, with special stains wherever indicated.

Results: Total 148 synovial biopsies were analysed. The mean age was 49.9 years, M:F ratio was 1.7:1. The most common site was the knee joint (69.5%). Common histopathological diagnosis were chronic non-specific synovitis (46.6%), rheumatoid arthritis (RA) (16.2%), septic arthritis (12.8%), and tuberculous synovitis (11.5%). Diagnostic revision following histopathological examination occurred in 16 /148 cases (10.8%), significantly altering the clinical management. This included seven cases of tuberculosis (TB) initially presenting as acute synovitis, three cases of post-total knee replacement which were originally managed as bacterial infections but reclassified as TB following synovial biopsy and six cases of RA which were initially misclassified as osteoarthritis.

Conclusion: Synovial biopsy is a valuable investigation that can be incorporated into diagnostic algorithms for atypical presentations to improve patient outcomes and reduce clinical misclassification. In TB endemic regions, histopathological examination of synovial biopsy can prevent delayed diagnosis and suboptimal management.

Keywords: Synovium, tuberculosis, inflammatory, biopsy, rheumatoid arthritis.

INTRODUCTION

Chronic monoarthritis and undifferentiated inflammatory arthritis represent significant diagnostic challenges in clinical practice. Many patients remain undiagnosed after routine clinical, serological and radiological evaluation. In such diagnostically challenging cases, histopathological examination of synovial tissue can help to establish a diagnosis¹⁻¹⁰. Synovial biopsy allows microscopic assessment of synovial architecture, inflammatory infiltrate, vascular changes, granulomas, crystal deposition or tumor, thus playing a pivotal role in the diagnosis of degenerative, autoimmune arthritis, infectious arthritis like tuberculous arthritis, and neoplastic joint disorders²⁻¹². In regions endemic for

tuberculosis (TB), synovial biopsy has demonstrated superior diagnostic yield to detect TB as compared to synovial fluid analysis and microbiological tests^{9,11-17}. Synovial biopsy can also diagnose rare entities such as pigmented villonodular synovitis, synovial chondromatosis and malignancies¹⁸⁻²⁷. In inflammatory arthritides, histopathological evaluation of synovium not only reveals the diagnosis but also provides insight into disease mechanisms and potential therapeutic targets^{2,6,10,28}. Distinct synovial pathotypes have been described in rheumatoid arthritis (RA) and spondyloarthropathies, highlighting the emerging role of synovial biopsy in precision medicine^{5,6,10,28}. However, synovial biopsy should not be considered as the primary diagnostic modality for routine diagnosis of RA, where clinical evaluation, serology,

and imaging remain the cornerstone of establishing the diagnosis. Instead, biopsy is particularly valuable in atypical presentations, treatment-resistant disease, and cases with diagnostic uncertainty^{6,9,10}.

Despite its established diagnostic significance, synovial biopsy remains underutilized in routine clinical practice due to lack of awareness, perceived invasiveness, limited access to arthroscopic or ultrasound-guided techniques, and over-reliance on serological and radiological findings^{6,9,10}. In many centres, particularly in developing countries, biopsy is reserved for advanced or refractory cases, often resulting in delayed diagnosis and inappropriate treatment¹⁰. Recent advancements in minimally invasive techniques, like ultrasound-guided and needle arthroscopic synovial biopsy, have improved safety, feasibility, and patient acceptability, further supporting its integration into early diagnostic algorithms^{2,3,5-10}.

We have studied the histopathological spectrum of synovial biopsies in our tertiary care institute and highlighted the potential of synovial biopsy to establish a definite diagnosis and influence the treatment and further management.

MATERIALS AND METHODS

This was a retrospective and prospective observational study of all the synovial biopsies received in the Department of Pathology, of our tertiary care institute, during the study period of three years (16 June 2020–15 June 2023), to evaluate the histopathological spectrum of synovial biopsies. Synovial biopsy was generally performed after routine clinical evaluation, laboratory investigations like hemogram, routine biochemical tests, serological tests for autoimmune disorders, imaging studies, and synovial fluid analysis failed to establish a definitive diagnosis or when tissue diagnosis was considered necessary by the treating clinician. Histopathological findings were subsequently integrated with clinical, radiological, microbiological, and serological data to arrive at the final diagnosis.

Indications for synovial biopsy

1. **Undifferentiated Inflammatory Arthritis:** Cases presenting with persistent, unexplained monoarthritis where standard non-invasive investigations (including serology, radiography, and initial synovial fluid analysis) failed to yield a definitive diagnosis.

2. **Treatment-Resistant / Refractory Arthritis:** Patients with an established or suspected inflammatory

arthropathy who demonstrated an inadequate clinical response or resistance to standard first-line therapies (e.g., conventional NSAIDs), where tissue evaluation was required to assess ongoing disease activity, rule out secondary infection, or to explore the requirement of advanced therapeutic strategies.

3. **Postoperative and Prosthetic Joint Complications:** Patients undergoing debridement, revision arthroplasty, or spacer placement due to persistent postoperative symptoms, suspected mechanical failure, or suspected low-grade prosthetic joint infection (PJI).

4. **Suspected Infectious Pathology:** Patients presenting with acute or chronic joint symptoms with high clinical suspicion of bacterial or fungal etiology. Microbiological studies were also done simultaneously.

5. **Evaluation of Suspected Neoplastic or Proliferative Disorders:** Cases presenting with localized joint swelling or atypical imaging features suggestive of benign or malignant tumors, such as pigmented villonodular synovitis (PVNS).

Inclusion criterion – all synovial biopsies obtained either by needle biopsy or open arthrotomy, depending on clinical indication and surgeon preference.

Exclusion criteria - inadequate biopsy material and poorly preserved specimens.

Synovium biopsy specimens were fixed in 10% neutral buffered formalin, routinely processed, paraffin embedded, and sectioned at 2–3 µm. Hematoxylin and eosin (H&E) staining was performed for histopathological evaluation. Special stains such as Ziehl–Neelsen stain for acid-fast bacilli and Perl's Prussian blue stain for hemosiderin were applied wherever indicated.

Relevant clinical details, radiological findings, and laboratory parameters from the patients' records were correlated with histopathological diagnoses and results were expressed as frequencies, percentages, and descriptive statistics as appropriate. Diagnostic revision was defined as a change between the initial clinical impression and final histopathological diagnosis resulting in altered clinical management. Data was compiled and analyzed using Microsoft Excel and SPSS version 21.

RESULTS

A total of 148 synovial biopsy specimens were evaluated during the study period. The age of patients ranged from 12 to 85 years, with a mean age of 49.9 years. Majority of the cases were seen in the

40–60-years age group (50%). The male to female ratio was 1.7:1.

The knee joint was the most frequently sampled site (103 cases, 69.5%), followed by the shoulder (14.8%) and hip joints (11.4%). Unilateral joint involvement was more common than bilateral involvement across all sites. Among knee joint biopsies, 91 cases (88.3%) were associated with total knee replacement, with most samples obtained intraoperatively.

Histopathological examination revealed non-specific chronic synovitis as the most common diagnosis (69 cases, 46.6%) (Table I). It is defined by chronic synovial inflammation and hyperplasia without specific features of RA, TB, gout, pigmented villonodular synovitis, or septic arthritis. Septic arthritis accounted for 19 cases (12.8%), characterized by marked neutrophilic infiltration and necrosis. Seventeen cases were diagnosed as tuberculous synovitis based on combined clinicopathological

and microbiological correlation. Histopathological examination of all these cases demonstrated granulomatous inflammation with epithelioid cell granulomas, Langhans-type giant cells, and caseous necrosis. Ziehl–Neelsen stain identified Acid-fast bacilli (AFB) in four biopsies. CB NAAT (Cartridge based Nucleic Acid Amplification Test) was done in 11 cases but it could detect *Mycobacterium tuberculosis* in six cases only. Notably, seven of these 17 TB cases (41.2%) clinically presented as acute synovitis, characterized by joint pain, swelling, warmth, and restricted mobility, without strong clinical suspicion of TB. These patients were initially managed as inflammatory or nonspecific synovitis. However, due to persistent symptoms and lack of clinical improvement, synovial biopsy was performed, which subsequently demonstrated granulomatous inflammation (Figure 1a). Correlation of histopathological findings with clinical, radiological, and microbiological

Table I. — Histopathological spectrum of synovial biopsies in different studies in comparison with our study.

Lesion	Our Study (n=148)	Tevatia 2021 ¹⁷ (n=103)	Vijay PM 2011 ¹⁶ (n=83)	Kulkarni 2017 ¹⁹ (n=100)	Jayan-thi 2019 ²⁰ (n=214)	Panage 2018 ²² (n=46)	Keerthana 2019 ²⁴ (n=44)	Kumari 2024 ²³ (n=100)	Subrama-nian 2017 ²⁵ (n=10)	Patel 2023 (n=104) ¹⁸
INFLAMMATORY										
Chronic non-specific synovitis	46.6% (69)	25.2% (26)	71.0% (59)	49.0% (49)	73.4% (157)	32.6% (15)	80% (35)	18.0% (18)	20.0% (2)	14.42% (15)
Rheumatoid arthritis	16.2% (24)	13.6% (14)	4.8% (4)	14.0% (14)	6.1% (13)	19.6% (9)	2% (1)	6.0% (6)	10.0% (1)	1.92% (2)
Acute & chronic synovitis	6.8% (10)	—	—	—	—	—	2% (1)	—	—	—
INFECTIVE										
Tuberculous / granulomatous synovitis	11.5% (17)	1.0% (1)	18.1% (15)	10.0% (10)	7.0% (15)	10.9% (5)	7% (3)	6.0% (6)	20.0% (2)	1.92% (2)
Septic arthritis	12.8% (19)	2.9% (3)	6.0% (5)	9.0% (9)	6.5% (14)	—	7% (3)	10.0% (10)	10.0% (1)	0.96% (1)
CRYSTAL-INDUCED										
Gout	2.7% (4)	1.0% (1)	—	1.0% (1)	0.5% (1)	2.2% (1)	—	3.0% (3)	—	3.84% (4)
Pseudogout (CPPD)	1.4% (2)	1.0% (1)	—	1.0% (1)	0.9% (2)	1.1% (1)	—	3.0% (3)	—	—
TUMOR-LIKE / PROLIFERATIVE										
PVNS	1.4% (2)	1.9% (2)	—	2.0% (2)	0.9% (2)	2.2% (1)	—	4.0% (4)	—	0.96% (1)
Synovial chondromatosis	—	—	—	3.0% (3)	0.5% (1)	2.2% (1)	2% (1)	8.0% (8)	20.0% (2)	2.88% (3)
Lipoma arborescens	—	1.0% (1)	—	1.0% (1)	2.8% (6)	4.3% (2)	—	10.0% (10)	10.0% (1)	1.92% (2)
Giant cell tumor of tendon sheath	—	1.0% (1)	—	2.0% (2)	0.5% (1)	—	—	15.0% (15)	10.0% (1)	8.65% (9)
Hemangioma	0.7% (1)	—	—	—	—	—	—	—	—	—

†Panage et al.: Non-hemophilic hemosiderotic synovitis (2.17%) corresponds to PVNS spectrum.

‡Subramanian et al.: 2/10 cases were secondary chondromatosis (20%).

§ Patel et al: 2/104 (1.92%) cases were fibroma of tendon sheath, 1/104 (0.96%) case was chondrolipoma.

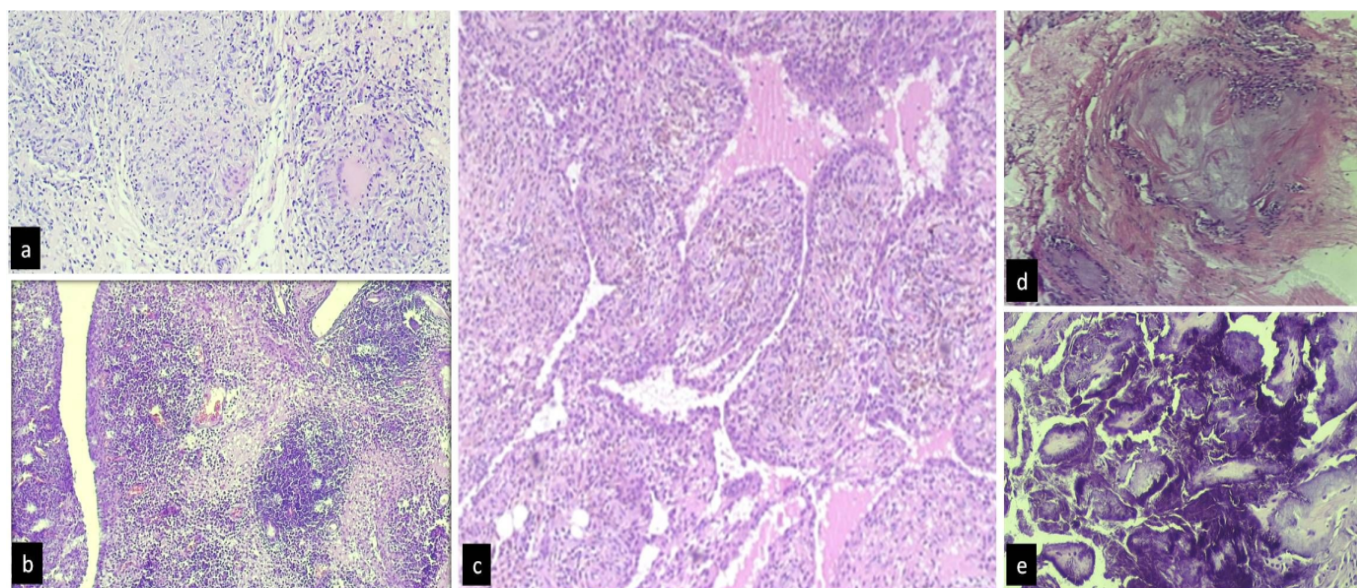


Fig. 1 — H&E stained sections showing a) Synovium containing epithelioid cell granulomas and Langhans giant cells in TB (100x); b) Pannus with lymphocytic infiltrate in RA (100x); c) Case of pigmented villonodular synovitis with hemosiderin laden macrophages; d) Gout showing oxalate crystals and multinucleated giant cell in periphery (40x); e) Pseudogout with basophilic crystals of Calcium pyrophosphate (40x).

investigations ultimately established the definitive diagnosis of TB. This finding highlights the deceptive and variable presentation of osteoarticular TB. Among the 17 TB cases, three other patients were initially managed as osteoarthritis and had undergone total knee replacement (TKR) for same. TKR may occasionally be performed in patients with underlying tuberculous joint disease that has initially been mistaken for osteoarthritis. These three patients presented with persistent pain, swelling, and clinical features suggestive of prosthetic joint infection (PJI) and were initially managed as bacterial PJI. Synovial biopsy was performed intraoperatively during debridement and placement of an antibiotic spacer. Histopathological examination surprisingly revealed granulomatous inflammation, resulting in revision of the initial diagnosis from bacterial PJI to TB, thereby significantly altering postoperative management and antimicrobial therapy (Tables II, III).

24 cases which were diagnosed as RA, showed characteristic histopathological features including synovial lining hyperplasia, dense lymphoplasmacytic infiltrate, focal lymphoid follicle formation, pannus formation and increased vascularity (Figure 1b). Six of these 24 cases (25%) were clinically suspected to represent osteoarthritis prior to biopsy. These patients presented with predominantly degenerative symptoms and radiologic findings overlapping with osteoarthritis, leading to initial misdiagnosis (Tables II, III). In addition, two of the 24 cases (8.3%) also had a prior history of TKR and presented with persistent

postoperative symptoms. Clinically, these cases were evaluated for mechanical failure or low-grade PJI but RA was not suspected. However, the histopathological examination of synovial biopsy revealed features of active RA, thereby identifying ongoing inflammatory disease activity as the underlying cause of persistent symptoms. Only after the synovial biopsy demonstrated features suggestive of RA, these patients underwent relevant serological and radiological investigations to establish the final diagnosis of RA. Subsequently, all these patients were found to have raised titres of anti CCP antibodies which established the hitherto missed diagnosis of RA.

Thus, histopathological examination of synovial biopsies led to revision of diagnosis in 16 out of 148 cases (10.8%).

Less frequent diagnoses included acute and chronic synovitis (6.8%), gouty arthritis (2.7%), pseudogout (1.4%), pigmented villonodular synovitis (1.4%), and synovial hemangioma (0.7%) (Table I) (Figure 1 c, d, e). Overall, chronic inflammatory conditions formed the predominant spectrum of synovial pathology in the present study. There was diagnostic revision in 58.8% of cases of TB and 25% of cases of RA; thus highlighting the diagnostic utility of synovial biopsy in establishing an accurate diagnosis (Table III).

DISCUSSION

The present study highlights the significance of synovial biopsy in evaluation of chronic monoarthritis

and undifferentiated joint disorders, particularly in TB endemic region. Microscopic examination of synovium resulted in revision of the initial clinical diagnosis in 16 of 148 patients (10.8%) as elaborated above (Tables II, III). These findings highlight the capacity of synovial biopsy to directly influence the course of treatment especially in infectious arthritis where routine serological investigations and synovial fluid analysis fail to establish a definite diagnosis^{4,6,7,9,10}. A proposed diagnostic algorithm has been illustrated in Figure 2 explaining the approach to manage patients with undifferentiated arthritis or atypical clinical presentation, refractory to conventional management strategies (Figure 2).

Tuberculous synovitis constituted 11.5% of cases in our series, a proportion higher than that typically reported in Western cohorts but comparable to

studies from TB endemic regions (Table I)^{17,20-22,24-27}. Bone and joint TB accounts for 10-15% of cases of extra pulmonary TB and commonly involves large joints¹¹⁻¹⁷. Osteoarticular TB has a variable and deceptive presentation, often mimicking septic arthritis, inflammatory arthritis, or prosthetic joint infection, resulting in frequent misdiagnosis¹¹⁻¹⁷. Besides, sometimes coexistence of early stages of knee joint TB with primary knee osteoarthritis may result in missing the diagnosis of TB altogether. In such scenarios, treating only the non infectious disease results in partial treatment, unresolving symptoms and further complications like TB osteomyelitis or disseminated TB^{12,14-17}. Prosthetic joint (PJ) TB is an under reported entity and is often misdiagnosed and sub optimally managed^{16,17}. Serological tests like elevated erythrocyte sedimentation rate (ESR), C

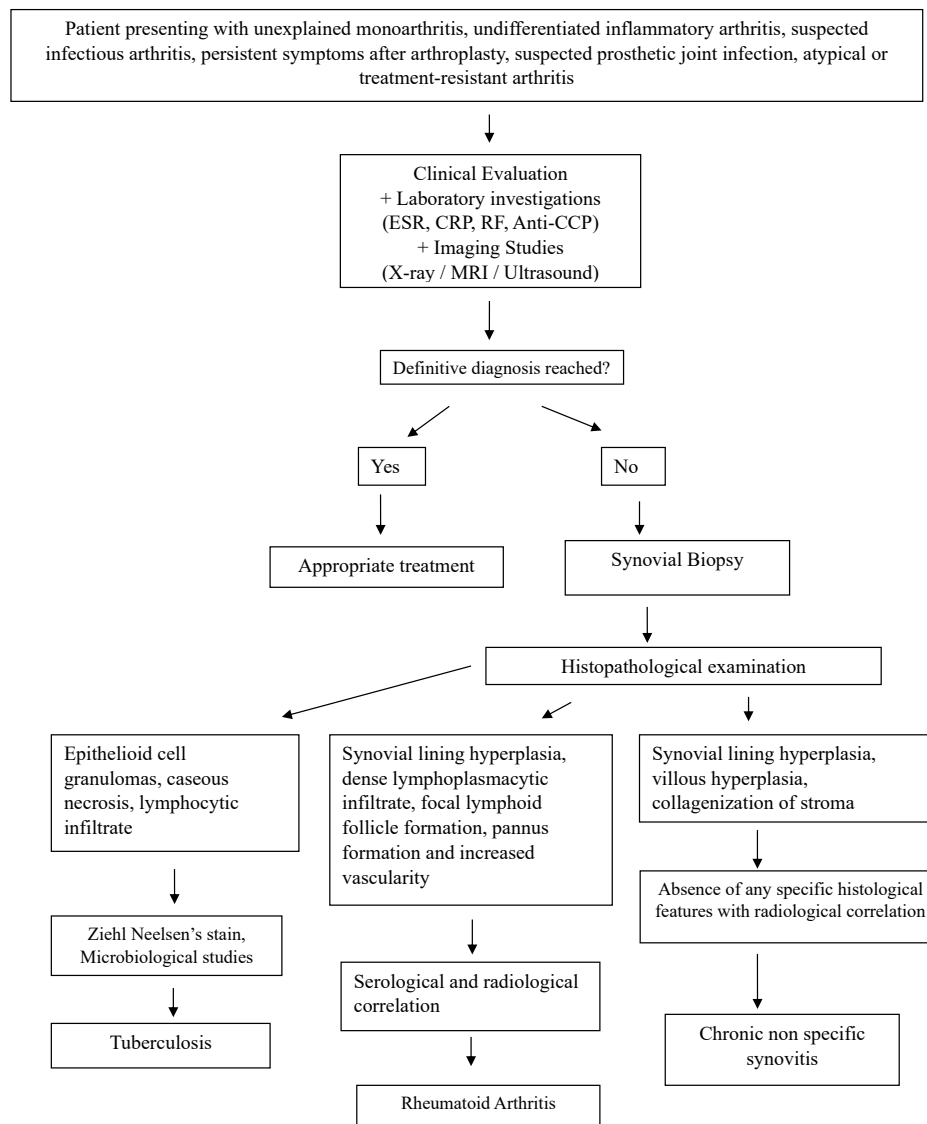


Fig. 2 — Diagnostic pathway demonstrating integration of synovial biopsy into the evaluation of chronic monoarthritis and undifferentiated arthritis.

reactive protein (CRP) have low specificity. Isolation of Acid fast bacilli (AFB) by culture using Lowenstein – Jensen medium is also time-consuming and may require several weeks, potentially delaying initiation of appropriate therapy when TB is not initially suspected¹³. If the sample has low bacillary load or if non representative area of synovium is sampled, then culture can also give false negative results¹⁴. Interferon gamma release assay (IGRA) cannot differentiate between active and latent infection, thus limiting its utility in acute infectious presentations¹³. In such challenging scenarios, combination of histopathological examination with molecular tests like Polymerase chain reaction (PCR) and Cartridge-Based Nucleic Acid Amplification Test (CB NAAT) can facilitate earlier identification of tuberculous prosthetic joint infections^{13,14,17}. The clinicians should have a high index of suspicion and always rule out TB either by histopathology or molecular tests like PCR and CB NAAT in TB endemic areas especially when managing patients with atypical symptoms refractory to conventional management strategies¹²⁻¹⁷. This is particularly important because TB often does not cause early prosthesis loosening, and timely diagnosis may allow successful treatment while preserving the prosthetic implant^{13,17}. In our study, CB NAAT could detect Mycobacterium in six cases only. Line probe assay is recommended in cases positive on CB NAAT. Therefore, molecular tests cannot substitute identification of granulomatous inflammation on histopathology^{15,17,18}. The reclassification of seven acute synovitis cases and three presumed bacterial PJI cases to TB underscores the importance of tissue diagnosis in endemic areas (Tables II, III). More than half (58.8%) of TB cases in our study could be diagnosed only after histopathology demonstrated caseating granulomas in the synovial tissue. Vijay PM et al have reported higher incidence of non caseating granulomas while Patel et al and Tevatia et al observed caseating granulomas in their studies^{18,20}.

The misclassification of RA as osteoarthritis in six of our cases is consistent with findings from other biopsy-based studies on undifferentiated monoarthritis, where synovial histopathology played a crucial role in identifying underlying inflammatory arthritides in diagnostically challenging cases^{3,4-11}. Synovial biopsy not only confirms the diagnosis but also demonstrates active inflammatory synovitis in patients with overlapping degenerative radiologic features where RA is not suspected clinically⁴⁻¹¹. Early and targeted interventions are critical to limit progression and improve long-term outcomes⁶.

Synovial biopsy is now evolving from a procedure performed in research settings to a feasible clinical tool that can bring RA management closer to personalized medicine. Modern ultrasound-guided techniques have standardized synovial sampling, making it a safe, accessible, and reproducible procedure even in multicenter frameworks⁴⁻⁷. By analyzing the diseased target tissue directly, clinicians gain unique insights into the biological heterogeneity of the disease, revealing distinct pathophysiological processes that peripheral blood-based assessments cannot detect^{6,28}.

However, synovial biopsy should not be used as primary diagnostic modality for RA, where clinical assessment, serology and imaging remain the cornerstone of diagnosis. Rather, biopsy is particularly useful in atypical presentations and cases with persistent postoperative symptoms where inflammatory synovitis may mimic degenerative disease or low-grade infection^{6,7}. Our study has demonstrated a relatively higher proportion of RA cases (16.2%) with marked bilateral involvement and strong serological correlation, including high anti-CCP positivity as compared to other studies where incidence varies from 2-19% (Table I)^{18,19-22,24-27}. Our observations are consistent with published literature demonstrating substantial diagnostic impact of synovial biopsy in clinical practice where inflammatory arthritis was misclassified as degenerative disease or where infection was not initially suspected^{4,9-11}. Romão et al. (2020) reported that ultrasound-guided synovial biopsy had a direct impact on diagnosis and management in approximately one-third of cases, particularly in undifferentiated arthritis and suspected infection⁷. Similarly, Soroosh et al. (2023) found that synovial biopsy established a definitive diagnosis in nearly 33% of patients with chronic undifferentiated knee monoarthritis, emphasizing its role in resolving diagnostic dilemmas⁸.

Chronic non-specific synovitis was another common histopathological diagnosis in our study, accounting for 69 out of 148 cases (46.6%) (Table I). The majority of patients were in the 40–60 year age group (50%), as also supported by other studies who have also reported peak incidence in middle-aged individuals¹⁸⁻²⁷. The knee joint was the most frequently involved site, seen in 71% of chronic synovitis cases, consistent with its weight-bearing role and high biopsy frequency. Many studies have reported similar knee predominance particularly in degenerative and chronic inflammatory conditions¹⁸⁻²⁷. Unilateral involvement was predominant (76.9%), supporting the understanding that non-specific synovitis, especially

secondary to osteoarthritis or trauma, is typically monoarticular, unlike autoimmune conditions such as RA¹⁸⁻²⁷.

Septic arthritis was diagnosed in 19 cases (12.8%) in our series, predominantly affecting individuals in the 40–60 year age group. This is comparable to findings by Kulkarni et al. (2017), who reported 9% of cases in middle-aged adults²¹. Vijay PM et al. (2011) reported fewer cases, but similarly recognized septic arthritis as an established though less frequent diagnosis compared to chronic synovitis¹⁸. Like chronic non specific arthritis, the knee was again the most commonly involved joint, consistent with other studies. Its large synovial cavity, superficial location, and vulnerability to trauma and procedures likely contribute to its increased susceptibility to infection¹⁸⁻²⁷.

Crystal deposition diseases were infrequent in our study, which is also corroborated by other studies¹⁸⁻²⁷. These conditions are rarely identified on synovial biopsy, as diagnosis is typically established through clinical features and synovial fluid crystal analysis. Biopsy is usually performed in atypical cases or when lesions mimic infection or neoplasm. The low frequency (~4%) aligns with previous studies. Across studies, the knee was the most commonly affected joint (Table I)¹⁸⁻²⁷. The low frequency (1.4%) of PVNS is also consistent with its rarity in general synovial biopsy series¹⁸⁻²⁷. Although some series report higher rates of tumor-like lesions, this likely reflects referral bias, especially inclusion of localized giant cell tumors of tendon sheath (Table I).

Our study showed male preponderance which is concordant with most series on synovial biopsies¹⁸⁻²⁰. However, Kumari et al have observed female preponderance in their study²⁵. Majority of the patients in our study belonged to 40 -60 years age group which is also similar to findings of other studies that have reported most of the cases in fifth, sixth and seventh decades^{18-22,25}.

Multicenter evaluations comparing arthroscopic and ultrasound-guided biopsy techniques have shown high safety, feasibility, and tissue adequacy rates, supporting earlier integration of synovial biopsy into diagnostic algorithms especially in diagnostically challenging cases with atypical presentations and refractory to conventional management^{2,3,6,7,10,28}. Our study has shown that in some cases, biopsy unmasked a diagnosis that would have been missed otherwise (e.g. an unexpected RA or TB). Thus, a recommendation is that whenever rheumatologists and orthopaedic surgeons have a high index of clinical suspicion for

TB or RA, they should opt for a synovial biopsy when faced with atypical presentations or treatment-refractory arthritis (Figure 2). Overall, our findings are consistent with existing evidence that a synovial biopsy can help in differentiating infectious from inflammatory and degenerative joint disorders^{2,4-10}. Although synovial biopsy is not the first line mode of investigation, yet its role is undisputed in cases where routine clinical, serological, radiological, and microbiological investigations remain inconclusive. Integration of minimally invasive biopsy techniques into earlier stages of diagnostic evaluation may improve patient outcomes and reduce misclassification.

Limitations of the study

Chronic synovitis can look remarkably similar whether it is due to low-grade rheumatoid arthritis, healed infection, osteoarthritis, or an idiopathic process. Without distinctive features, the pathologist must issue a broad descriptive diagnosis, which can be unsatisfying to both clinician and patient. This lack of specificity means that in such cases the burden falls on clinical correlation to arrive at a definite diagnosis.

Second, sampling error is a concerning issue. Synovitis can be patchy – for example, in tubercular arthritis, granulomas might be sparse and missed if the biopsy does not hit the right area. In our series, it is conceivable some of the non-specific cases could have had an occult granuloma or other feature in unsampled tissue. We tried to mitigate this by obtaining adequate tissue and examining multiple sections.

Third limitation is that histology provides mostly morphological information. In complex immune-mediated diseases, morphology may not differentiate between certain conditions like RA and psoriatic arthritis – yet the distinction is clinically important. Both conditions cause chronic synovitis, but require different treatments. In such scenarios, ancillary tests become important: immunohistochemistry or molecular analyses might help in the future. Our study did not employ advanced molecular diagnostics due to lack of availability in our centre.

Another limitation is the limited duration of the study. We analyzed biopsies obtained over 36 months, and while we correlated them with clinical data, the study design does not capture long-term outcomes.

Declarations of Interest: None.

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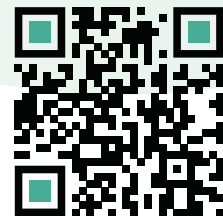
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