

**RELEVANCE OF ARTHROSCOPIC SYNOVIAL BIOPSY IN JOINT DISORDERS - A PROSPECTIVE STUDY**Kali Vara Prasad Vadlamani<sup>1</sup>, J. Satyanarayana<sup>2</sup>, Hari Prasad Rao<sup>3</sup>, G. V. S. Moorthy<sup>4</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: BACK GROUND:** Synovial biopsy is considered as the gold standard in the diagnosis of various joint disorders and synovial diseases. But sometimes the definitive diagnosis is elusive only by doing biopsy then clinical, hematological and x-ray examinations will help. The advantage with arthroscopic synovial biopsy is that it is easy to perform, minimal discomfort to the patient and can be done at intervals if the diagnosis cannot be made in the first examination. **MATERIAL & METHODS:** The present study was conducted in the Department of Orthopedics & Traumatology, Osmania General Hospital/ Medical College, Hyderabad. The duration of the study was from Sept 2012 to Sept 2014. **CONCLUSIONS:** Arthroscopic synovial biopsy is the mainstay in the management of Joint disorders and Synovial diseases. It is patient friendly and repeated procedures can be undertaken when the definitive diagnosis could not be established in the initial attempt, as is common in some cases of Non-specific synovitis, later being diagnosed either as Osteoarthritis or Rheumatoid Arthritis. This is the greatest advantage in using this procedure.

**KEYWORDS:** Arthroscopic synovial biopsy, Definitive diagnosis, Gold standard, repeat biopsy.

**INTRODUCTION:** The synovial membrane biopsy is of aid in the assessment of joint diseases and synovial disorders. It is the final diagnostic procedure. The synovial membrane behaves as a mirror to the joint diseases and examination of synovial membrane often reveals a myriad of features suggestive of specific disease entities. Jaffe, Lichenstein and Sutri,<sup>1</sup> (1941) regarded the synovium of tendon sheath, bursa and joint to be an anatomic unit that could give rise to a common family of lesions.

Diarthrodial or synovial (Paracelsus: first used the term synovia; viz; joint oil) joints are the joints most commonly affected by diseases in the human body. The joints are open tissue spaces communicating directly with periarticular tissues. The capsule is lined by synovial membrane, which also covers soft structures within the joints and forms bursa. The articular cartilage and menisci are not covered by synovial membrane.

The synovial membrane is composed of an inner secretory zone lined by a discontinuous layer of specialized cells with both secretory (Synovial fluid) and phagocytic function. Under certain circumstances it performs antigen-processing function similar to those of macrophages.

The symptom complex of pain, swelling and stiffness of joints is labeled as Arthritis and is a common problem often encountered in clinical practice. These are the afflictions of all age groups and are prevalent in both sexes. Arthritis may be classified as Mono-articular, Pauci-articular or Poly-articular when it involves one joint, four or less, or more than four joints respectively. Irrespective of the type of arthritis failure of timely institution of specific therapy, because of delay in diagnosis often leads to an increase in morbidity.

Common conditions such as rheumatoid arthritis rarely cause diagnostic problems with typical presentation. Difficulties arise when atypical clinical presentation is associated with noncontributory preliminary investigations. Sometime even fairly specific investigations which helps to differentiate between specific arthritis are unhelpful, e.g., rheumatoid factor (RF) may be negative in late cases of rheumatoid arthritis or RF is positive in 2 to 7% of patients with connective tissue disorders other than rheumatoid arthritis. Under such circumstances synovial membrane biopsy is of value in the diagnosis of joint disorders. This is especially so in chronic mono arthritis, where synovial biopsy is most useful as an aid to diagnosis or exclude potentially remediable conditions.

Different techniques are applied for synovial membrane biopsy. Open biopsy has an advantage of getting larger specimen, gross inspection of the joints and opportunity to obtain cartilage in addition to soft tissues. Before the era of advanced surgical techniques, pathological material for the study of joint was almost exclusively obtained from postmortem samples.

In addition to routine H & E stained sections under light microscopy, special staining techniques, electron microscopy and immuno-cytological techniques were evolved for accurate diagnosis of synovial lesions.

**Techniques & Equipment for Synovial Membrane Biopsy:** Arthroscopic biopsy and open biopsy procedures are having advantage of inspecting the joint and selection of biopsy site. Recently introduced MINI-ARTHROSCOPE (Needle arthroscope) with 1 to 1.9 mm diameter facilitated 80% of the joint cavity inspection in the evaluation of the minor joints and its application in visual guided synovial biopsies.

Arthroscopic biopsy has the advantage of being minimally invasive, less disturbance of normal tissues, resulting in quicker recovery and rehabilitation, minimal hospital stay and less infection rate.

Synovitis, the reaction of the synovial membrane to irritation, is effusion of fluid into the joint. The irritation can be mechanical, chemical or infection, in the form of local or general; exogenous or endogenous. Chronic unrecognized trauma is suggested as cause for synovitis, where the definite cause is not known.

#### **AIM & OBJECTIVES OF STUDY:**

**AIM:** To get specific diagnosis by arthroscopic guided synovial biopsy.

#### **OBJECTIVES:**

1. To assess the incidence of various synovial diseases.
2. To correlate the clinical findings with histopathological and laboratory findings in different diseases and to evolve a simple diagnosis.
3. To correlate the arthroscopic, clinical and histopathological studies in the diagnosis of the disease.
4. To evaluate the importance of arthroscopic synovial biopsy as a diagnostic aid in various joint diseases.
5. To minimize the number of lesions of nonspecific synovitis by histopathology as clinical findings of many diseases are similar.

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**MATERIALS & METHODS:** The material for the present study was collected from patients who attended our unit Out-patient department and were admitted in the Department of Orthopaedics, Osmania General Hospital, Hyderabad, having pain and swelling of the knee joint, with minimum study of 30 cases were taken and the patients were informed about study in all respects and informed written consent was obtained.

The period of the study was Two years i.e, from September 2012 to September 2014.

### **Inclusion Criteria:**

- a. Patients with swelling of the knee joint for which Biopsy is indicated.
- b. Patients of any sex and in the age group 10-60 years.
- c. Patients who are fit for biopsy under general or spinal anaesthesia.
- d. For confirmation of clinical and histopathological diagnosis when laboratory findings are not helpful.

### **Exclusion Criteria:**

- a. In traumatic conditions where there is bony injury of the joint occurred.
- b. Patients having poor general health.
- c. Patients whose skin condition over the joint is poor or not suitable for incision.
- d. Conditions where diagnosis is very obvious by other methods.
- e. Patients who are unfit for anaesthesia and Biopsy.

Cases were diagnosed on history, clinical examination and investigations (Histopathological findings and laboratory analysis). Statistical data included is name, age, sex, ward, occupation, chief complaint, history, general examination, local examination, investigations, biopsy technique, biopsy results.

Biopsy material for histopathological study consisted mainly of the synovial membrane obtained by arthroscopic biopsy. Specimens received were examined for gross findings like size, shape, color, consistency, fixed in 10% formalin and tissues were processed routine paraffin embedded technique. Routine H and E and special stains such as Touluidine blue, PAS. perl's and Ziehl nelson, Knyoun's method of stain for Acid fast bacteria were used where required.

The H&E stained sections of the specimen were each analyzed with regard to histological criteria of which synovial hyperplasia, fibrosis, proliferating blood vessels, perivascular infiltrates of lymphocytes, Focal aggregates of lymphocytes and diffuse infiltrates of lymphocytes as done by Goldenberg,<sup>2</sup> (1978) and cooper et al.,<sup>3</sup> (1981) in their studies. The remaining features like polymorphonuclear infiltration, surface fibrin and specific changes such as granulomatous type of giant cells, lymphoid follicles were noted. The changes in the each diagnostic category were then summarized and the clinical groups compared.

The other laboratory investigations were done were (Where ever necessary): Complete Blood picture, Urine analysis, Blood urea, serum creatinine, serum uric acid, serum rheumatoid factor, ASO titre, HIV, HBS Ag tests, synovial fluid analysis for biochemical findings and cytological analysis. X-ray of the involved knee joint.

**Procedure: (Fig 1, 2 & 3).**



**Anaesthesia:** Biopsy procedures were conducted under general and spinal anaesthesia depending on patients general conditions.

After anaesthesia, patient in supine position with prepared and draped limb angled of the lateral aspect of table. Precise entry portal location can be ensured best by carefully drawing the joint lines, soft tissue and bony land marks with skin marking pen before distention. Standard portals used for biopsy are anterolateral and anteromedial portals. We used the 1.9mm diameter 30 degree oblique forelens scope for visualization of joint. Biopsy material obtained with help of basket or punch biopsy forceps.

**OBSERVATIONS AND RESULTS:** This study was carried out for a period of two years between September 2012 to September 2014 at Department of Orthopaedics, Osmania General Hospital, Specimens of synovial membrane from 30 cases of various synovial disorders were obtained.

Sl. No.	Lesions	No. of patients	Percentage	Male	Female
1	Septic Arthritis	2	6.66%	1	1
2	Chronic nonspecific synovitis	9	30%	7	2
3	Tubercular synovitis	8	26.6%	7	1
4	Rheumatoid arthritis	6	20%	2	4
5	Gout	1	3.33%	1	0
6	Osteoarthritis	1	3.33%	1	0
7	Synovial Osteochondroma	1	3.33%	1	0
8	GCT Tendon Sheath	1	3.33%	0	1
9	Synovial sarcoma	1	3.33%	1	0
<b>TOTAL</b>		<b>30</b>	<b>100%</b>	<b>21</b>	<b>9</b>

Table 1: Incidence of Various Lesions of Synovial Membrane

**Male: Female Ratio-2.33: 1:** Of the 30 synovial biopsies studied, 8(26.6%) cases revealed characteristic features of tuberculosis. There were 2 cases (6.66%) of septic arthritis observed. Non-specific synovitis found in 9 cases (30%) and rheumatoid arthritis in 6(20%) of the Biopsies studied. There was 1 case of giant cell tumor (3.33%). There was one case each (1+1+1) of osteoarthritis, Gout and Synovial sarcoma with a view to discuss each clinical entity in detail each lesion will be discussed separately.

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**Septic Arthritis:** There were 2 cases (6.66%) of septic arthritis with synovitis encountered in the present study. One of them was a female patient of 50 yrs and other was male of 14 yrs old. Both cases presented as pain, swelling, joint effusion, there were restricted movements of joints. In one case there was evening rise of temperature.

**Non Specific Synovitis:** 9 cases (30%) in this study showed nonspecific changes in the synovial biopsy. Table No. 2 showing the age and sex wise distribution of these cases. Majority of the cases were in 20-30 years age group. Lower & upper limits of ages were 19 years in females & 52 years in males. Gender ratio (M: F): 3.5: 1.

**Tuberculous Synovitis:** 8 cases (26.6%) in the present study revealed features of tuberculosis in the synovial biopsy. (Fig 4.) The incidence of the tuberculous lesions in the present study is 26.6% and occurred more in the males in the age group of 10-20 yrs. The youngest were the 12 yr male while the oldest was the male aged 55 yrs. Their clinical parameters like ESR were found in the range from 10-25 mm per, 1st hr and 2nd hr to 70-120 mm per 1st and 2nd hr in the 4 cases observed.



Mantoux tests were done in 8 cases and was positive in two cases 25% (2/8) of cases. Ziehl Neelsen's method of staining were done for demonstration of acid-fast bacilli using positive control and the tests were negative for AFB in all (8/8) cases.

Sl. No.	Histopathological Parameters	No. of Cases	Percentage
1	Caseation	5	63.3%
2	Giant cells, Langhan's-type	5	63.3%
3	Epitheloid cells	6	75 %
4	Proliferation of synovial lining cells	4	16.6%
5	Fibrosis	5	50%
6	Perivascular inflammatory cell infiltrate	3	63.3%
7	Diffuse chronic inflammatory cell infiltrate	2	33.3%
8	Proliferating blood vessels	4	50%

**Histopathological Parameters of Tubercular Synovitis**

**RHEUMATOID ARTHRITIS (RA) Fig 5.**

There were 6 cases (20%) in the study revealed typical features of rheumatoid synovitis. Two cases are males and 4 are females. 5 cases referred as rheumatoid arthritis, but 6 cases were diagnosed as RA by histopathology one of them was positive for rheumatoid factor. Male: Female= 1:2.

**OSTEOARTHRITIS:** Though one of the commonest clinical disease affecting the joint there was only one case (3.33%) of osteoarthritis in this study and was confirmed by histopathology. The case was a 45yr old male with previous history of lt knee joint pain, locking episodes of the joint and intermittent swelling of the joint.

**GOUTY ARTHRITIS:** One case (3.33%) of gouty arthritis was encountered in the present study in a 48yr old male. The lesion occurred in the left knee joint. Gross examination synovium was multiple soft to firm bits, altogether measured 2 cm, gray - white in color.

**SYNOVIAL (OSTEO) CHONDROMATOSIS:** One case (3.33%) of synovial chondromatosis was encountered in this study. Patient was a male of 38yr age affecting the rt knee. Patient presented with pain and swelling of the joint and 2 palpable loose bodies with radiological findings and confirmed by biopsy.

**GIANT CELL TUMOR (GCT) OF TENDON SHEATH:** There was 1 (3.33) case of giant cell tumor in this study. Patient was a 32yr old female affecting rt knee. Biopsy revealed features typical of giant cell tumor of tendon sheath.

**SYNOVIAL SARCOMA:** Only one case (3.33%) in this study revealed typical features of synovial sarcoma from the lt knee of 26 yr old male patient. The patient was presented with pain and swelling of the left knee joint. X-ray of the region shows pathological fracture at lower end of left femur metaphysis with new bone formation and loose soft tissue shadow and displacement of patella.

**DISCUSSION:** Synovial and joint diseases are the commonest orthopaedic problems and affects both sexes and nearly all age groups without distinction. Usually a detailed clinical examination,



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radiological and serological aid is enough to diagnose the problems. However these findings are equivocal at times and therefore need arises for specific tests for confirmation of diagnosis. Review of literature and the present study have highlighted the usefulness of histological study of synovial membrane in the diagnosis of various joint diseases and correlation between the clinical and histopathological findings in disease diagnosis.

Among various disorders encountered in this study, the large group (30%) not fit into any specific diagnosis and hence they were grouped under non-specific synovitis. There were 2 cases of septic arthritis (6.6%). Among the specific lesions tuberculous synovitis was found to be the commonest 8 (26.6%) cases followed by rheumatoid arthritis 6 (20%) of 30 cases. There were 1 (3.33%) case of osteochondromatosis and 1 (3.33%) case of giant cell tumor, one case of each of gout (3.3%), osteoarthritis (3.3%) and synovial sarcoma (3.3%) present in this study. On histological examination of thirty cases of synovial membrane specimen, a definite histological diagnosis could be offered in 70% (21/30) of cases.

**NON SPECIFIC SYNOVITIS:** In the present study histopathological changes in 9 cases were not specific for any disease entity nor did they, when correlated with clinical findings to suggest a diagnosis. These cases showed varying degree of villous hypertrophy, proliferation of synovial lining cells, capillary proliferation, chronic inflammatory cell infiltrate and slight synovial or sub synovial fibrosis.

Various authors have given widely varying degree of lesions, which they have included under 'unclassified' category or under 'non-specific synovitis'. Misgar,<sup>4</sup> and Schumacher,<sup>5</sup> have reported figures of 22% and 27% respectively. Cooper and Abhayankar,<sup>6</sup> have given figures of 9% and 3%. The figures in the study are quite high and comparable to Schumacher study.

In order to find clear cut differences in the histopathological features of various chronic arthritis which did not exhibit histological features suggestive of specific diagnosis. A semi quantitative assay of histological changes were attempted as was done by Goldenberg and Cooper. However since the clinical diagnosis was not specific in most these cases (They were usually labeled as "chronic synovitis") and because of small number of cases sent with specific clinical diagnosis, no comparative study of significance of histological criteria could be carried out. Most of these cases may be earlier stages of Rheumatoid Arthritis or Osteoarthritis where the classical histological findings may be absent, in these repeat biopsies after a few months will clinch the diagnosis.

**RHEUMATOID ARTHRITIS:** The incidence of rheumatoid arthritis (synovitis) in present study is 20%. This differs from the previous studies of Abhayankar who quoted 27.5% in her cases. Goldenberg has given figures of 30%, western authors have also given similar figures of around 27%. The present study encountered 2 cases in males and 4 cases in females and peak incidence is 41-50 yrs age group. Silverberg (1990) has given the peak age group incidence between 30-45yrs Various studies have shown marked preponderance in females; Silverberg (1990) 3: 1, while Abhayankar has given figures of 2.5: 1.

Five cases were sent with clinical diagnosis of rheumatoid arthritis out of 6, but 6 cases were proved by histopathology and rheumatoid factor positive in 1 case.

**HISTOPATHOLOGICAL FEATURES:** Histopathological examination revealed proliferation of the synovial membrane in 100% and villous morphology in 50% of cases. This is correlated with the

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study of Kennedy,<sup>7</sup> Goldenberg and Cohen who found synovial cell hyperplasia in all the cases. Cooper et al found synovial lining hyperplasia in 60.8% of cases. All the other authors have found the hyperplasia is to the extent of moderate to marked diffuse infiltration of synovia by lymphocytes, plasma cells and mast cells were found in 100% of cases (23).

While Goldenberg and Cohen (1978) study showed 96%, and those of Kennedy showed 100% lymphocyte aggregate found in 100% of the cases in the present study, while Cooper's observation was 86.2% of the cases. There was a mild vascular proliferation in 50% of the cases in this study, while Goldenberg and Cooper have shown 98% and 97% of cases. Cytokines play important role in inflammation.

There was mild to moderate fibroblast proliferation in 100% of cases in this study. Misgar,<sup>4</sup> found fibrosis 75% of the cases, Cooper gave figures of 81.7% and Rooney,<sup>8</sup> reported fibrosis in 90% of cases. Foreign body type giant cells were found in 50% of the cases in the present study. While other reports were, Goldenberg 13.8% of cases, Cooper 15.6% cases special stains toluidine blue positive in 50% of the cases.

**OSTEOARTHRITIS:** The synovial membrane biopsy in one case (3.33%) was diagnostic of OA showing degenerating cartilage. This is less than the number of cases given by Misgar and Abhayankar who have reported figures of 16% and 12.5% in their studies respectively. The lower incidence is due to reluctance of the clinicians to subject patients for synovial biopsy. The patient is 45 yrs old male, while Goldenberg and Abhayankar found highest incidence in the 5th and 6th decades respectively. Rosenberg et al in their studies clearly defined to differentiate Osteo arthritis from rheumatoid arthritis taking nearly 37 parameters.

**HISTOPATHOLOGICAL FEATURES:** On microscopic examination there was mild proliferation of synovial membrane. Variable figures were given by different authors. Goldenberg, Cooper and Kennedy reported synovial lining cell hyperplasia in 70%, 64% and 25% cases respectively. Villi were not seen in the present study, which is clinically with the observations of Abhayankar, but differs from the study of Cooper 73% and Kennedy 100%. There was mild infiltration of chronic inflammatory cell infiltrate mainly lymphocytes and mononuclear cells in aggregates and in diffuse pattern. While Goldenberg and Kennedy also found no aggregates in their study. There were moderate increase in blood vessels and vascular dilatation. Cooper found only 5% of cases increase in blood vessels in 70% and 100% of cases in their study. Fibrosis was seen in very mild in the present study. Misgar and Cooper found 100% and 69% respectively. Spicules of cartilage and myxomatous degeneration was found in the present study.

**SYNOVIAL (OSTEO) CHONDROMATOSIS:** Nodules of metaplastic cartilage within the synovial membrane associated with loose bodies within the joint cavity were found in 1/1(100%) of the cases of present study.

In the present study patient is a male, 38yrs old. On gross examination there were 2 loose bodies, while other authors have reported 1 – 10 loose bodies.

The discrepancy may be due to small number of cases in the present study

**GIANT CELL TUMOR OF TENDON SHEATH (GCT):** Only one case of giant cell tumour was found in the present study. This is nodular. Patient is a 32 yr old female.



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Rao et al,<sup>9</sup> observed gender ratio (M: F) at 1: 4.9 and common during 5th decade.

Gross examination of the specimens showed nodular to globular gray-white to gray-yellow homogenous, while Myer and Masi<sup>10</sup>, Rao showed villous hypertrophy, gray – yellow with areas of hemorrhage and altered blood.

Microscopic examination revealed conspicuous round cell infiltration. This was in accordance with findings of Misgar, Myers and Masi who found similar conspicuous infiltrate of round to polygonal cells in their study. Mild proliferation of fibroblasts in the stroma were found in this case of present study.

Misgar and Rao found fibrosis of varying degree in 100% and 84% respectively. Giant cells osteoclast – type were seen in this case and mainly multinucleate. The giant cells were diffusely scattered.

These findings were in accordance with the findings of Rao who found such giant cells in 96% of his cases. There were no foamy histiocytes. Rao found similar observation in 61.8% of his cases per's stain revealed hemosiderin in the present study. Myer and Rao 28% and 86% respectively. Tissue spaces were seen in present study while Myer observed in 65% of his cases.

**SYNOVIAL SARCOMA:** One case (3.33%) in this study revealed typical features of synovial sarcoma from Lt. knee joint in a male 26 yrs (i.e. in 3rd decade of life). The patient presented with pain and swelling of Lt. knee joint. x-ray of the region showed pathological fracture at lower end of Lt femur at metaphysis with new bone formation and loose soft tissue shadow and displacement of patella

**CONCLUSIONS:** Synovial biopsy is an important adjuvant together with clinical details for giving a definite histo-pathological diagnosis. It is also evident that the synovial biopsy examination, at most of the times gives a conclusive diagnosis. But sometimes these are inconclusive. In these cases repeat biopsy at intervals of time will give the correct diagnosis and that is the greatest advantage with synovial biopsy. Arthroscopic synovial biopsy is indeed a gold standard in the diagnosis of Joint disorders and Synovial diseases and is here to stay.

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