

## Original Research Article

# A prospective study for diagnosing joint diseases by synovial fluid analysis and percutaneous needle biopsy of synovium

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### ABSTRACT

**Background:** Arthritis is an important cause of morbidity, presenting as monoarticular or polyarticular lesion. Percutaneous synovial aspiration and biopsy can help in identifying specific aetiological diagnosis. The study was conducted with the objective to evaluate the efficacy of percutaneous synovial biopsy as a diagnostic aid and study the characteristics of synovial fluid in various joint diseases.

**Methods:** Percutaneous synovial biopsy along with synovial fluid analysis was studied in all the 100 enrolled cases arthritis. The fluid was subjected to physical, biochemical, and cytological analysis.

**Results:** Of the 100 cases, monoarticular joint involvement predominated over polyarticular (n =80; 80%), knee joint (60%) was most commonly affected in monoarticular and polyarticular arthrititis. Rheumatoid arthritis (RA) (n =33; 33%) is the most common aetiology followed by tuberculosis (n =22). Males predominated over females in this study (n =61; 61%).

**Conclusions:** The evaluation of synovial fluid and synovial biopsy in joint diseases will stimulate its use as routine investigative procedure in the diagnosis of various puzzling joint disorders. Both these procedures can be done simultaneously through the same site of aspiration by the same needle.

**Keywords:** Joint diseases, Synovial fluid, Synovial biopsy

### INTRODUCTION

Rheumatoid arthritis (RA) is an inflammatory arthritis that affects nearly 1% of the world's adults. It is characterized by symmetric polyarticular inflammation of the synovium, typically of the small joints of the hands (MCP and PIP), wrists and feet. This inflammation results in pain and stiffness, and can lead to progressive joint damage resulting in deformities and loss of function.<sup>1</sup> The clinical examination can disclose synovial thickening and swelling, indicators of joint inflammation. At the time of presentation, nearly 70% of radiographs can be normal, but MRI and ultrasound with power Doppler have higher sensitivity to detect smaller erosions

and synovial inflammation, and may reveal changes even when X-rays are normal.<sup>2</sup>

Arthritis is an important cause of morbidity, affecting all ages and both sexes. It may present as a monoarticular or polyarticular lesion. Monoarticular lesion often follows trauma or infective etiology, while polyarticular lesion is commonly seen in rheumatoid pathology.<sup>3-6</sup> The relatively frequent occurrence of this problem has led to the indiscriminate use of NSAIDs by medical practitioners, without arriving at a specific etiological diagnosis. The latter can be easily arrived at by using a fairly simple technique of percutaneous synovial aspiration and biopsy and specific treatment be instituted in cases like tuberculosis.

Synovial fluid analysis and biopsy have been found to be a valuable adjunct to conventional investigations and are routinely advised in most cases of joint diseases.<sup>7</sup>

## METHODS

Patients presenting with complaints of Joint pathologies visiting Outpatient department of Narayana medical college & Hospital, Nellore, of which 100 of them willing to undergo procedure were participated in the study, with proper informed written consent. The period of study was from August 2013 to September 2016. Detailed history taking and meticulous clinical examination was done in all cases with reference to various symptoms.

Close attention was paid to location, nature and course of joint involvement. In cases of polyarthritis the location of joint first involved and the pattern of progression to other joints was noted. Morning stiffness, frequency and periodicity of the episode with characteristic waxing and waning, barometer relationship were the other important considerations noted. Fever, fatigue, anorexia, asthenia, cough were important constitutional enquiries made in cases where systemic diseases were suspected. Complaints of 'red eye', dysentery, urethritis were other important points in history taking. A special effort was made to probe and find out any history suggestive of noninflammatory osteoarthritis, chronic infection and inflammation like tuberculosis, rheumatoid lesion and gout and severe inflammation like septic arthritis.

In conventional laboratory aid a special note was made for the level of erythrocyte sedimentation rate (ESR). Rheumatoid arthritis (RA) factor, serum uric acid level estimation, C – reactive protein (CRP) were done in suspicion of rheumatoid lesion and gouty arthritis. In suspected case of tuberculosis, sputum and 24 hour urine for AFB by concentration methods and Mantoux test were carried out. In suspected pyogenic arthritis, culture of throat swab, urine and blood were done. Beside routine Roentgenographic examination of affected joint in different planes AP, lateral and oblique, X- ray chest was done in suspected cases of tuberculosis.

All these patients after through clinical evaluation were subjected to synovial fluid study and synovial needle biopsy. Synovial fluid was aspirated before arthroscopy. Analysis was started as soon as the fluid was aspirated. The fluid was subjected to physical, biochemical, and cytological analysis. The parameters studied in physical examination included color, clarity, viscosity, mucin clot test, and wet preparation. The biochemical analysis included difference in fasting blood and synovial fluid glucose and estimation of protein in synovial fluid. Cytology entailed estimation of the total leukocyte count and study of the centrifuged deposit to see predominant white blood cells (WBCs). RA factor was estimated in synovial fluid. Bacteriological analysis includes Gram's

staining, acid fast (AFB) staining, culture and sensitivity and PCR to detect *Mycobacterium tuberculosis* DNA.

## Procedure of arthrocentesis of knee joint

The patient was admitted or detained in the ward for the needle biopsy and aspiration. The patient was kept starving for at least 6 hours prior to the procedure so that the fasting level of glucose could be determined. Arthrocentesis and synovial biopsy was carried out in operation theater as a minor surgical procedure.

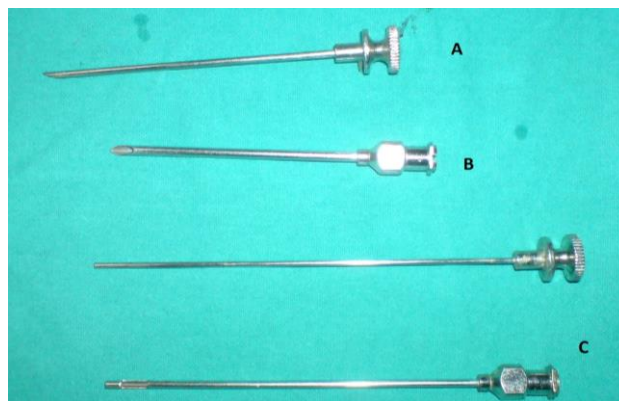


Figure 1: Parker Pearson needle.

Full aseptic surgical care was taken in the local preparation, draping of the patient and scrubbing by the surgeon. About 2 ml of 2% lignocaine was infiltrated into the skin, subcutaneous tissue and joint capsule. For children GA/dissociated anesthesia with ketamine used. The knee was kept in extension; the synovial fluid was displaced from suprapatellar pouch to medial or lateral aspect of patella. After infiltration of joint capsule the needle A as shown in Figure 2 was introduced through a point on lateral aspect 2 cm above and 2 cm lateral to midpoint of upper border of patella into the joint cavity and synovial fluid aspirated and collected in five empty test tubes as described later on.

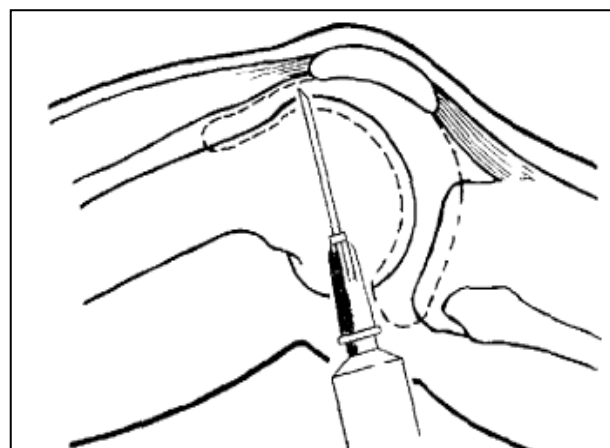
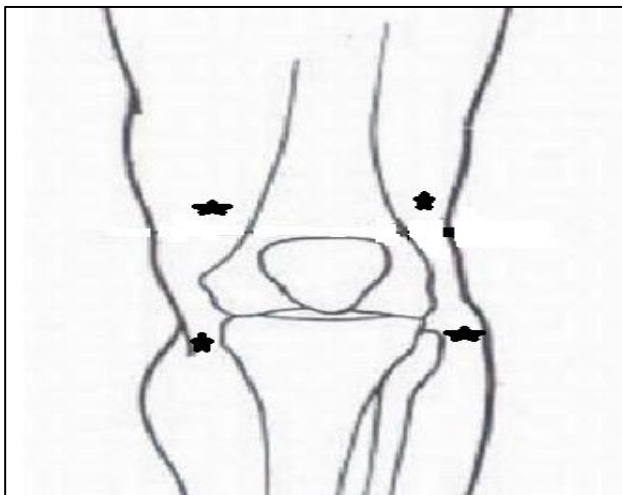


Figure 2: Showing the entry point into supra patella pouch.

The needle A was taken out leaving the cannula (B) in position. Now the notched needle C which had been previously fitted with a 20 ml syringe was inserted through the lumen of the cannula so that its blunt end saw tooth entered the synovial space. Strong suction was then applied to the barrel of the syringe and the toothed needle was slightly withdrawn after the aspiration of few ml of synovial fluid, when the notched orifice become occluded by synovial membrane and further aspiration become impossible. The suction was maintained to hold the synovial specimen within the notch. The syringe and the inner needle were held motionless in the right hand where left hand slowly advanced the outer cannula using a slight twisting and rotating motion for about 1 cm to ensure that specimen has been severed and held in the notch. The outer cannula was then left in situ and the inner needle with the attached syringe was removed. The piece of synovial tissue was removed from the notch with a needle point and the same process repeated several times in different direction and region of the joint. The specimens were collected in a vial containing formalin (10%) solution and sent for histopathological examination.



**Figure 3: Sites of tissue taken.**

In multiple joint affections, the knee joint was selected in the preference for the ease with which synovial fluid can be aspirated and synovial tissue can be taken for biopsy. Otherwise also the knee was seen as commonest joint involved. For arthrocentesis of the hip, lateral, anterior or posterior approaches are possible. For arthrocentesis of the wrist, the needle was inserted into the joint from dorsal aspect just medial to anatomical snuff box. For elbow joint, elbow was kept in acute flexion and the needle was inserted on the posterior aspect just lateral to the olecranon. In the ankle, the needle was inserted at the antero - lateral aspect of the joint about 2.5 cm proximal and 1.3 cm medial to lateral malleolus.

Open biopsy/arthroscopic biopsy were done where needle biopsy failed, and to confirm the histologic diagnosis obtained after needle biopsy, in some cases. Caution was necessary at operation not to mistake fibrinous exudates

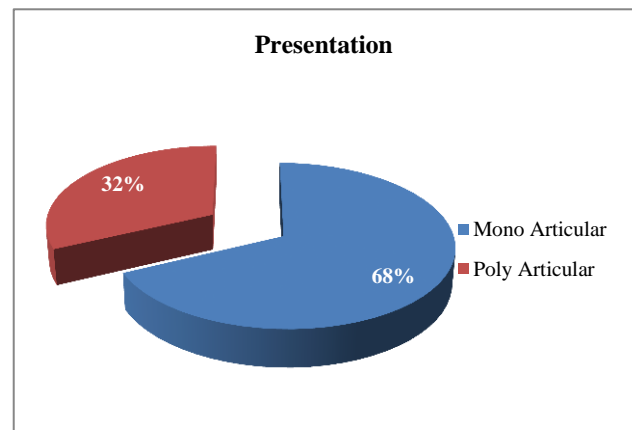
or necrotic material (yellow/white/pink) for synovial tissue.

After the procedure, one dose of intravenous Cefuroxime (as per weight and age) is given and compression bandage was applied over the joint and if needed the patient was observed in the ward for 48-72 hours for any evidence of post aspiration infection like throbbing pain, high fever or any untoward effect otherwise patient is left to go home and advised for follow-up with reports.

## RESULTS

Evaluation of synovial fluid and synovial biopsy studies of 100 cases of joint disease during the study has been made and following are observations.

Mono articular pathologies were 68% and poly were 32% as shown in Figure 4. Various joints involved in poly and mono arthropathies are enumerated in Table 1. Knee joint was found to be affected more than other joints in both mono and poly arthritis.



**Figure 4: Affection of joint disease.**

Variety of joint pathologies diagnosed by synovial fluid analysis and biopsy are illustrated in Table 2.

\*2 =1 case of synovial chondromatosis+1 case of osteochondritis dissecans

The Figure 5 shows the incidence of trauma in various joint diseases. History of trauma was predominant in 6 cases of traumatic arthritis and chronic nonspecific synovitis followed by 5 cases in tubercular arthritis.

Table 3 presents the age pattern in different joint diseases. Rheumatoid arthritis was found between age group of 31-50 and above 50 dominantly and tubercular arthritis was found mainly in the younger age group between 11-30 years in most of the cases. Males predominated over females in this study (n =61, 61%) as given in Figure 6. In osteoarthritis of course it was observed that above 45 years, both sexes were almost equally affected.

Table 4 presents the ESR in synovial fluid. It was observed that rise of ESR above 30 was found in total 66 cases (66%). The raised ESR level found in patients of tuberculous arthritis, rheumatoid lesion and pyogenic arthritis. In chronic nonspecific synovitis, osteoarthritis and traumatic arthritis ESR was found at normal range.

Rheumatoid factor was found to be present in synovial fluid in all cases of rheumatoid arthritis, where as it found to be positive in 10 serum samples of the same patients as shown in Table 5.

**Table 1: Showing number of monoarticular/polyarticular affection of different joints.**

S. No.	Joints	Monoarticular involvement (no. of cases and % involvement among mono articular)	Polyarticular involvement (no. of cases and % involvement among poly articular)
1.	Knee	43 (63.23%)	17 (53.12%)
2.	Hip	11 (16.17%)	2 (6.25%)
3.	Wrist	7 (10.29%)	3 (9.38%)
4.	Hand	-	5 (15.63%)
5.	Elbow	-	3 (9.38%)
6.	Foot	3 (4.41%)	-
7.	Ankle	2 (2.94%)	1 (3.12%)
8.	Shoulder	-	1 (3.12%)
9.	S.I. joints	2 (2.94%)	-

**Table 2: Showing variety of joint diseases.**

S. No.	Name of disease	Number of cases		
		Monoarticular (A)	Polyarticular (B)	Total (A+B)
1.	Rheumatoid arthritis	5 (5%)	28 (28%)	33 (33%)
2.	Tubercular arthritis	21 (21%)	1 (1%)	22 (22%)
3.	Chr. nonspecific synovitis	16 + 2*		18 (18%)
4.	Osteoarthritis	11 (11%)		11 (11%)
5.	Traumatic arthritis	6 (6%)		6 (6%)
6.	Gouty arthritis	3 (3%)	3 (3%)	6 (6%)
7.	Septic arthritis	4 (4%)		4 (4%)
<b>Total</b>				<b>100 (100%)</b>

**Table 3: Showing age distribution pattern in different joint diseases.**

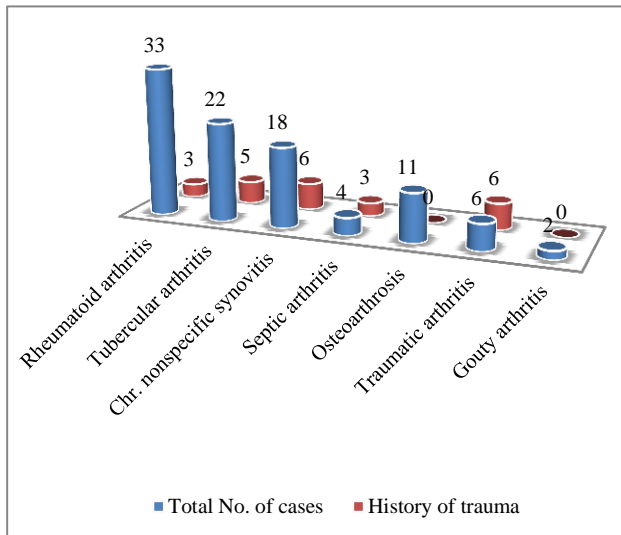
S. No.	Joint disease	No. of cases	Age in years range			
			0 – 10	11 – 30	31 – 50	Above 50
1.	Rheumatoid arthritis	33	-	5	17	11
2.	Tubercular arthritis	22	1	15	6	-
3.	Chr. Nonspecific synovitis	18	1	12	5	-
4.	Septic arthritis	4	2	2	-	-
5.	Traumatic arthritis	6	-	3	3	-
6.	Osteoarthritis	11	-	-	1	10
7.	Gouty arthritis	6	-	-	6	-

**Table 4: Level of erythrocyte sedimentation rate (ESR).**

Mm in 1 <sup>st</sup> hr (Wintrobe)	No. of cases	Percentage
0 - 10	20	20
11 – 20	6	6
21 – 30	8	8
31 – 49	36	36
50 and above	30	30

**Table 5: RA factor in 33 cases of rheumatoid arthritis.**

Specimen	Positive	Negative
Serum	26	7
Synovial fluid	33	0



**Figure 5: Incidence of trauma in various joint diseases.**

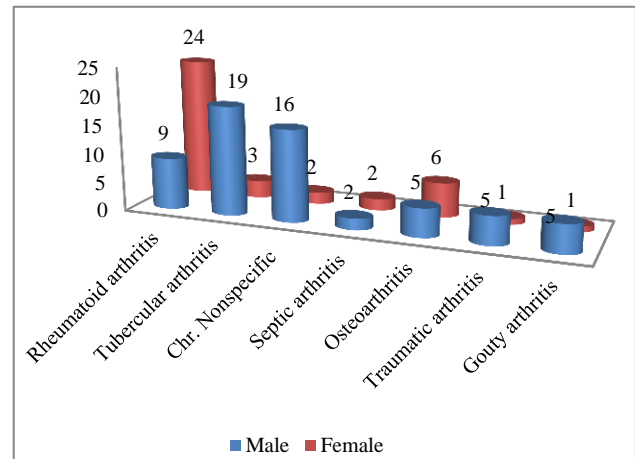
In all 100 cases with joint diseases, arthrocentesis and closed synovial biopsy using Parker Pearson needle was done commonly in knee joint (n =60; 60%).

Physical properties, biochemical nature (specific gravity, synovial fluid protein in gm% and blood – synovial fluid sugar difference in mg/100 ml) and cytological picture (total WBC/mm<sup>3</sup> and predominant cells) of synovial fluid in joint diseases of different pathology have been shown in Table 6, 7 and 8 respectively. On bacteriological examination of synovial fluid, pyogenic arthritis was observed in two cases in which staphylococcus had shown its presence in the culture medium.

**Table 6: Showing physical properties of synovial fluid in normal and diseased joints.**

No.	Disease	Volume in ml	Appearance color/clarity	Viscosity	Mucin clot test	Fibrin clot	Specific gravity
1	Normal	3.5 ml	Straw/ clear	High	Good	-	1014-1020
2	Rheumatoid arthritis	Variable	Yellowish to greenish/ cloudy	Low	Fair to Poor	+	1019-1025
3	Tubercular	Moderate Increase	Yellow/ turbid	Low	Poor	+	1020-1026
4	Chronic nonspecific	Moderate Increase	Yellowish/ clear	Low	Fair to Good	+/-	1014-1018
5	Septic arthritis	Abundant	Yellow, grey/ turbid	Low	Very Poor	+	1025-1028
6	Osteoarthritis	Scanty	Pale/ clear	High	Good	-	1014-1016
7	Traumatic arthritis	Variable	Hemorrhagic or xanthochromic	High	Good	-	1015-1018
8	Gouty arthritis	Variable	Yellowish/ cloudy	Low	Fair	+	1018-1022
9	Alkaptonuria	Variable	Turns to black on standing			-	
10	Pseudogout	Variable	Yellow, milky		Firm-friable		

The findings of Table 6-8 determines the type of joint disease in the study participants as tabulated in Table 9 and they were graded as given below.



**Figure 6: Sex distribution of the disease.**

**Histopathology**

With Parker-Pearson needle technique adequate representative synovial tissue for histopathology was obtained in 90 cases (90%) out of 100 and their break down in different joint disease was given in Table 10 and number of failure cases was given in Table 11.

The clinical findings of synovial fluid were matched with the histopathological studies in 74 out of 100 cases. In rest of 13 cases (26%) the histopathological diagnosis differs from the clinical diagnosis as given in Table 12.



**Table 7: Showing cytological appearance of normal and diseased joints.**

No.	Condition	Total WBC count/mm	Predominant cell%
1.	Normal synovial fluid	<200	Mixed cell with poly, Lympho mono poly less 12 (25%)
2.	Rheumatoid arthritis	7000 – 15000	Polymorphs 65 to 80%
3.	Tubercular arthritis	4000 – 11500	Lymphocytes 60 to 80% with monocytes
4.	Chronic nonspecific arthritis	400 – 10000	Variable from polymorphs to lymphocytes
5.	Osteoarthrosis	200 – 500	Variable from polymorphs to lymphocytes
6.	Gouty arthritis	7000 – 13500	Polymorphs 60 to 80%
7.	Septic arthritis	>10000	Polymorphs 80 to 95%

**Table 8: Showing protein content of synovial fluid and blood – synovial fluid glucose difference in various joint diseases**

S. No.	Condition	No.	Protein gm%	Blood – synovial fluid glucose level difference mg%
1.	Normal synovial fluid		1.5 – 2.5	< 10
2.	Rheumatoid arthritis	33	3.5 – 6.4	>20 - <30
3.	Tuberculous arthritis	22	4 – 6.8	>20 - <35
4.	Chronic nonspecific synovitis	18	2 – 3	>10 - <16
5.	Osteoarthrosis	11	1.5 - 2	<20
6.	Traumatic arthritis	6	1.5 – 2	<20
7.	Gouty arthritis	6	3	<25
8.	Septic arthritis	4	5 – 7	>50

**Table 9: Gradings of joint diseases as per clinical findings.**

Grade	Disease
<b>Grade I: Non inflammatory e.g.</b>	Traumatic arthritis (6 cases)
	Osteoarthrosis (11 cases)
	Synovial chondromatosis (1 case)
	Osteochondritis dissecans (1 case)
<b>Grade II: inflammatory (mild to moderate)</b>	Chronic nonspecific synovitis (16 cases)
	Rheumatoid arthritis (33 cases)
	Gouty arthritis (6 cases)
	Tubercular arthritis (22 cases)
<b>Grade III: Sever inflammation</b>	Septic arthritis (4 cases)

**Table 10: Showing breakdown of 90 successful closed needle synovial biopsy in joint diseases.**

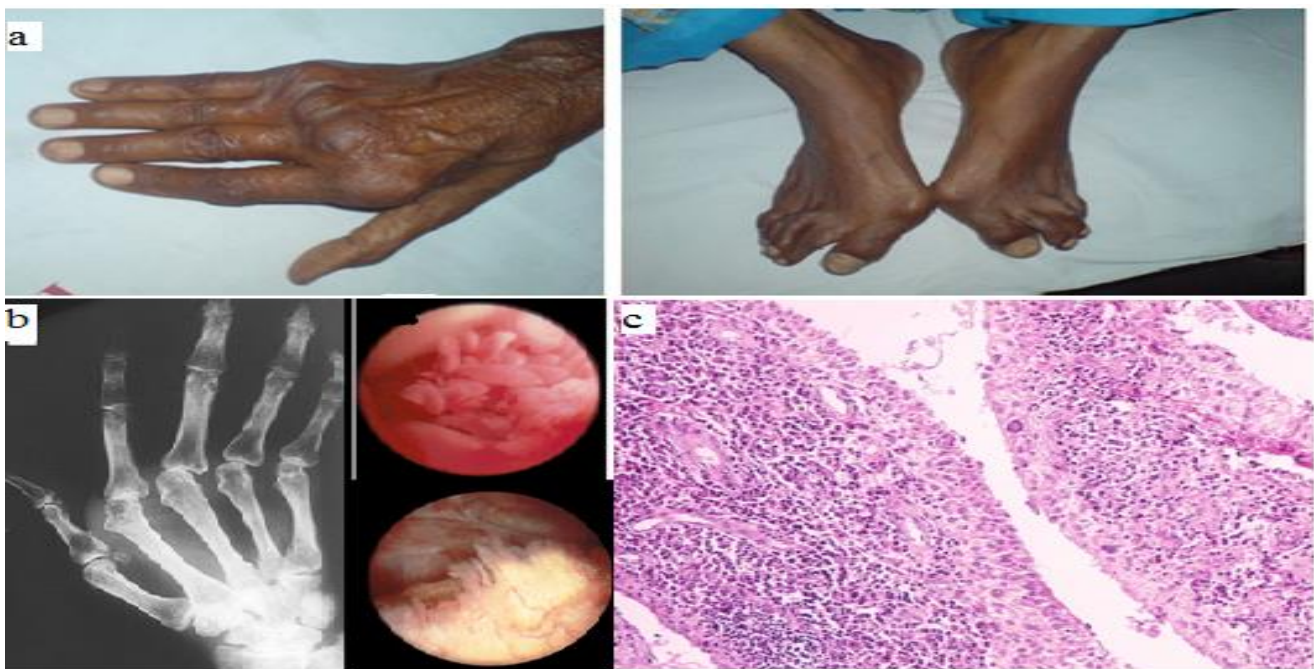
S. No.	Joint diseases	Total no. of cases	Percentage (%)
1.	Rheumatoid arthritis	31	27.9
2.	Tuberculous arthritis	21	18.9
3.	Chronic nonspecific synovitis	15	16.66
4.	Osteoarthrosis	9	10
5.	Traumatic arthritis	5	5.55
6.	Gouty arthritis	5	5.55
7.	Septic arthritis	4	4.44

**Table 11: Showing location of 5 cases of failure.**

Location	Number cases
<b>Hip joint diseases</b>	6
<b>Foot</b>	2
<b>Knee joint</b>	2

**Table 12: Showing the cases where histological diagnosis differed from clinical diagnosis.**

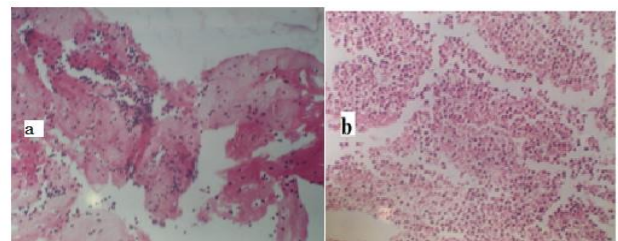
S. No.	Clinical diagnosis	Histopathological diagnosis
1.	Tuberculous arthritis, left hip (case 7)	Chronic nonspecific synovitis
2.	Tuberculous arthritis, right hip (case 12)	Chronic nonspecific synovitis
3.	Nonspecific synovitis, right knee (case 13)	Tuberculous arthritis
4.	Osteoarthritis both knee (case 16)	Rheumatoid arthritis
5.	Tuberculous arthritis, left ankle (case 20)	Rheumatoid arthritis
6.	Tuberculous arthritis, right knee (case 21)	Chronic nonspecific synovitis
7.	Rheumatoid arthritis, right knee (case 27)	Chronic nonspecific synovitis
8.	Tuberculous arthritis, right hip (case 74)	Rheumatoid arthritis
9.	Rheumatoid arthritis, right knee (case 34)	Tuberculous arthritis
10.	Tuberculous arthritis, right wrist (case 62)	Rheumatoid arthritis
11.	Tuberculous arthritis, right hip (case 31)	Rheumatoid arthritis
12.	Rheumatoid arthritis, right knee (case 5)	Chronic nonspecific synovitis
13.	Rheumatoid arthritis, right knee (case 92)	Tuberculous arthritis



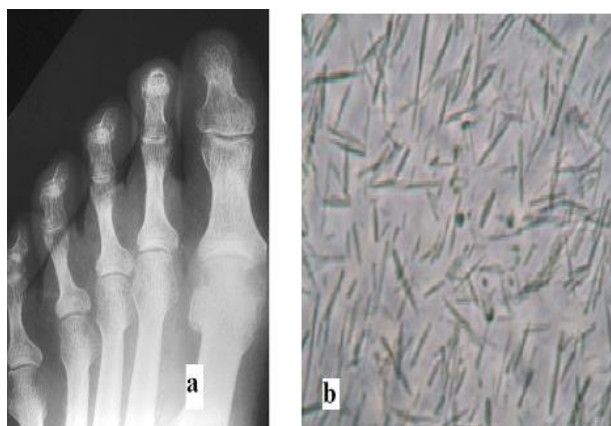
**Figure 7: Characteristic features of rheumatoid arthritis (a =showing deformities of hand and feet in a patient of rheumatoid arthritis; b =X- ray hand and wrist demonstrating metacarpophalangeal joints demonstrate marked narrowing, subluxation, and ulnar deviation and arthroscopic view of the knee joint showing edematous hypertrophied synovial villi; c =histology of RA synovitis).**



**Figure 8: Characteristic features of tuberculous arthritis (a =X- ray hand and wrist demonstrating soft-tissue swelling and severe osteopenia of the carpal bones; b =histology of tuberculous synovitis).**



**Figure 9: a =Histology of chronic nonspecific synovitis revealing collagenous tissue with acute and chronic inflammatory cells; b =histology of septic arthritis revealing large number of neutrophils in fibrin background.**



**Figure 10: a =X-ray shows soft-tissue swelling medial to the first metatarsophalangeal joint and bilateral erosions of the head of the proximal phalanx; b =polarised microscopy showing negatively birefringent needle-shaped urate crystals.**

## DISCUSSION

Affection of the joints, monoarticular or polyarticular by various diseases is a common orthopedic problem. On the basis of clinical examination with conventional radiological and laboratory aids, the diagnosis often can be reasonably made. These findings are sometimes equivocal and therefore necessity of tissue diagnosis arises. Closed needle biopsy is a simple outpatient procedure without complications that aids in establishing the diagnosis after clinical and radiological correlation. Careful review of literature would reveal that the importance of this simple procedure as an aid to diagnosis of joint diseases has been stressed by various authors from time to time.<sup>8-11</sup> Further, it has been mentioned in the literature that the macroscopic features of inflammation seen at arthroscopy do not predict the microscopic features. Thus, the use of closed needle biopsy technique is justified.<sup>12</sup>

Involvement of knee has been found commonest in joint disease both by present study and also by previous workers.<sup>13-15</sup> Monoarticular involvement of knee has been found more common than polyarticular affection both in present study 60 (65.78%) and by previous workers Bhatia et al (68%).<sup>9</sup>

Tubercular and rheumatoid were seen in maximum numbers and next common group chronic nonspecific synovitis. Septic arthritis, osteo arthritis and traumatic arthritis formed the third common group. Rheumatoid lesion and osteoarthritis were seen largely a polyarticular affection, while tubercular arthritis, chronic nonspecific synovitis, septic arthritis, gout and traumatic arthritis were predominantly single joint involvement. This observation noticed by present study almost tallied with study of previous workers.<sup>14,15</sup>

On the basis of synovial fluid evaluation (physical, biochemical and cytological examination) and according to severity of inflammation, the various types of arthritis are grouped. The results of all categories are in accordance with the findings of Venkataraman et al and Singhal et al.<sup>14,15</sup>

From the present study comparing with that of previous workers, it is proposed that a fairly reasonable interpretation can be made after synovial fluid evaluation as outlined earlier, correlating with clinical and radiological findings in rheumatoid arthritis, septic arthritis, gouty arthritis, traumatic arthritis, osteo arthrosis and also tubercular arthritis.<sup>8,16</sup> In some cases clinical, radiological and synovial findings are equivocal or inconclusive. In these cases, it is only the synovial biopsy that solves the diagnostic dispute.

Comparing the present study with that of Naib and Broderick et al, it is evident that both Naib and Broderick et al have shown good correlation.<sup>17,18</sup> It may be due to better facility like viscometry for measuring viscosity, large number of cases included in their series and they have got more experience in the subject.

From the present study comparing with previous study synovial biopsy has been found to be of important diagnostic value in correlating the diagnosis after clinicoradiological and synovial fluid evaluation. Closed needle synovial biopsy as merited against open synovial biopsy through arthrotomy has been found quite satisfactory (90%) in obtaining the adequate synovial tissue for histologic examination both in the present study as well as in the study of previous workers and their success rate was 100%.<sup>8</sup>

The difficulty in negotiating the needle into the joint, particularly hip, being deeper with accompanying contracture were principal causes of failure in getting the adequate synovial tissue for histologic study, as experienced in the present study and also in the series of Schumaker.<sup>16</sup>

In the present study of 100 cases of arthritis, histologic examination of closed needle synovial biopsy proved to be of diagnostic value in correlating and confirming the diagnosis of definite pathology after clinic radiological and synovial fluid evaluation in 68 (68%). Out of the rest 32 (32%) cases, in 16 (16%) cases no histopathologic diagnosis of any definite disease could be obtained and were labeled as chronic nonspecific synovitis. In 16 cases (16%) where the clinico-radiological and synovial analyses were equivocal and inconclusive, synovial biopsy only gave conclusive diagnosis of definite pathology. In another 16 cases (16%) the clinical radiological, synovial fluid findings and even the histologic study by closed needle biopsy were inconclusive for any definite disease and were labeled as chronic nonspecific synovitis. These cases were proved chronic nonspecific synovitis also by open biopsy.



## CONCLUSION

The evaluation of synovial fluid and synovial biopsy should be an important part of investigative procedure in patients presenting with joint effusion. The nature of underlying synovial tissue reaction is often reflected in synovial fluid and synovial tissue histologic study which may give conclusive diagnosis where clinical diagnosis is equivocal.

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