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## Synovial Fluid Analysis in Diagnosis of Joint Diseases.

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### ABSTRACT

Synovial fluid analysis is one of the most important diagnostic tests in Medicine. Yet it is not routinely practiced in most of the laboratories. Microscopic analysis for the number and type of cells, as well as presence or absence of crystals is equally important. The addition of bacteriological, chemical and immunological tests further enhances the ability to discriminate between vast number of disorders that affect the knee. The present study is taken to examine fresh synovial fluid aspirates with standard protocol of gross and microscopic examination with wet mount preparations to specify the cytomorphological features of abnormal synovial fluid. 100 samples of synovial fluid were analysed which included gross examination, wet mount preparation, total leukocyte count and permanent preparations. Biopsy correlation was available in 25 cases. Of the 100 synovial fluids analyzed, osteoarthritis was seen in 20 cases, rheumatoid arthritis in 15, traumatic arthritis in 9, septic arthritis in 5, tuberculous arthritis in 5, pigmented villonodular synovitis in 2, gout in 1, inflammatory arthritis - Not Otherwise Specified (NOS) in 22 and non-inflammatory arthritis – NOS in 14. Aspirate was non-diagnostic in 7 cases. Biopsy in 25 cases were Rheumatoid arthritis-07, Chronic nonspecific synovitis-07, Tuberculous arthritis-05, Septic arthritis-02, Pigmented Villonodular Synovitis -02 and Osteoarthritis -2 cases.

**Keywords:** Synovial fluid, Arthritis, Biopsy.

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## INTRODUCTION

Synovial fluid fills the spaces in the joint cavities. Its function is to moisturize and lubricate the joints [1]. Synovial fluid analysis has been widely recommended as an important aspect of diagnostic examination of patients with arthritis and joint effusions [2]. Synovial fluid analysis in joint diseases is akin to urinalysis in the study of renal disease. Rheumatologists fondly call synovial fluid analysis as the most important laboratory test in rheumatology so much so that it is considered as the 'liquid biopsy of the joint'. Synovial biopsies are usually done to diagnose joint diseases. However synovial fluid analysis may provide an easier noninvasive option [3]. Sampling synovial fluid is among the most useful test available to the clinician evaluating the patients [4]. Synovial fluid analysis forms a vital step in the diagnosis and management of arthritis [5]. It helps to distinguish between various inflammatory, non inflammatory, traumatic and crystal induced arthritis [6].

## MATERIALS AND METHODS

A prospective study was done on synovial fluid samples over a period of two years at the Department of Pathology. All patients with one or more joint effusions were included in this study.

After obtaining ethical committee clearance and informed consent from the patient, synovial fluid analysis was performed. Detailed clinical history was obtained and joint fluid was obtained by arthrocentesis. Patients with septicemia or cutaneous soft tissue infection mimicking acute arthritis were not be subjected to arthrocentesis to avoid direct introduction of the offending organisms into the joint space.

Processing of the synovial fluid specimens was done as soon as possible in the laboratory. But in cases where there was a delay, the specimens were stored in a refrigerator at 4<sup>0</sup>c. Gross examination for total volume, colour, clarity, viscosity and mucin clot test was done. Using WBC pipette synovial fluid was drawn up to 0.5 mark and diluted with RBC diluting fluid by drawing up to 11 mark. Total and differential leucocyte counts were performed using Neubauer's counting chamber.

## RESULTS

Table 1 shows the distribution of the cases of joint effusion in various diseases. Of the 100 synovial fluids analyzed, osteoarthritis was seen in 20 cases, rheumatoid arthritis in 15, traumatic arthritis in 9, septic arthritis in 5, tuberculous arthritis in 5, pigmented villonodular synovitis (PVNS) in 2, gout in 1, inflammatory arthritis - Not Otherwise Specified (NOS) in 22 and non-inflammatory arthritis – NOS in 14. Aspirate was non diagnostic in 7 cases due to delay in transportation of the sample to the laboratory without refrigeration which led to degeneration of the cells. Histopathological correlation was available in 25 cases of which rheumatoid arthritis was seen in 7 cases, chronic nonspecific synovitis in 7, tuberculous arthritis in 5, septic arthritis in 2, PVNS in 2 and osteoarthritis in 2 cases.

Joint effusion was seen in patients between 18- 76 years. Osteoarthritis and tuberculous arthritis was seen in the elderly with the age range between 40- 70 years. Rheumatoid arthritis was seen in the age group of 25-65 years. Post traumatic arthritis was seen all ages.

Joint effusion was seen in 51 female and 49 male patients. Osteo arthritis was more common in males and rheumatoid arthritis was more common in females.

Table 2 and 3 shows the viscosity and total leukocyte count in various joint diseases respectively.

Osteoarthritis was the most common cause of joint effusion seen in 20% of the cases. Synovial fluid was clear in 19 cases and opaque in 1. Viscosity was normal in 19 cases and low in 1. Mucin clot test showed firm clot in 19 cases and friable clot in 1. On wet mount examination cartilage fibrils were seen in all the cases. Total leukocyte cell count ranged from 150–1200 cells /cu mm with a mean of 385 cells/cumm. Differential leukocyte count showed predominance of lymphocytes (68%), neutrophils (24%) and macrophages (08%).

Rheumatoid arthritis was seen in 15% cases. Synovial fluid was clear in 2 cases and opaque in 13. Viscosity was normal in 1 and low in 14 cases. Mucin clot test showed firm clot in 1 and friable clot in 14 cases.

On wet mount examination ragocytes were seen in all cases. (figure 1) The total cell count range was from 3,500-18,500 cells/cumm with a mean of 16,000 cells/cumm. Differential leukocyte count was of polymorphs (85%), lymphocytes (12%) and macrophages (03%).

Traumatic arthritis was seen in 9% cases. Synovial fluid was hemorrhagic with normal viscosity and a firm clot all cases. On wet mount examination numerous red blood cells were seen with a total count ranging from 2000-4550 cells / cu mm and predominance of neutrophils.

Tuberculous Arthritis was seen in 5% cases. Synovial fluid was opaque with low viscosity and friable clot in all cases. The total cell count ranged from 8000-12000 cells/cumm and predominance of lymphocytes.

Septic arthritis was seen in 5% cases with a friable clot in all cases. The total cell count ranged from 50,000-62,000 cells/ cu mm. Differential leukocyte count showed predominance of polymorphs. Figure 2 shows the predominance of neutrophils in septic arthritis .

PVNS was in 2 cases. Synovial fluid was opaque with low viscosity and friable clot. Total leukocyte ranged from 3500-4000 cells/cu mm with predominance of macrophages.

Gout was seen in one case. On wet mount preparation, numerous intra and extracellular needle like crystals exhibiting yellow birefringence under polarizing microscopy were seen. (figure 3) Total count was 4500 cells/cumm with a predominance of neutrophils.

Inflammatory arthritis-NOS was seen in 22% cases. Synovial fluid was opaque with low viscosity and friable clot. Total count ranged from 2000-10500 cells/cumm with predominance of polymorphs.

Non-Inflammatory arthritis-NOS was seen in 14% cases. Synovial fluid was clear with normal viscosity and firm clot. Total count ranged from 100-800 cells/ cumm with predominance of lymphocytes.

**Table 1: Distribution of cases of joint effusion in various diseases**

Serial. No	Nature of Disease	No. of Synovial fluids
1	Osteoarthritis	22
2	Rheumatoid arthritis	15
3	Traumatic arthritis	09
4	Septic arthritis	05
5	Tuberculous arthritis	05
6	Gout	01
7	PVNS	02
8	IA –NOS	22
9	NIA –NOS	14
10	Non diagnostic aspirate	07
	Total	100

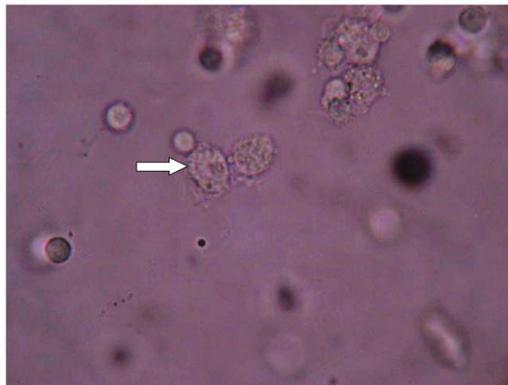
**Table 2: Viscosity of Synovial fluid in joint diseases**

Sl. No	Diseases	Normal	Low
1	Osteoarthritis	18	02
2	Rheumatoid arthritis	01	14
3	Traumatic arthritis	09	-
4	Septic arthritis	-	05
5	TB arthritis	-	05
6	Gout	-	01
7	PVNS	-	02
8	IA- NOS	02	20
9	NIA- NOS	08	06
10	Non diagnostic aspirate	-	-

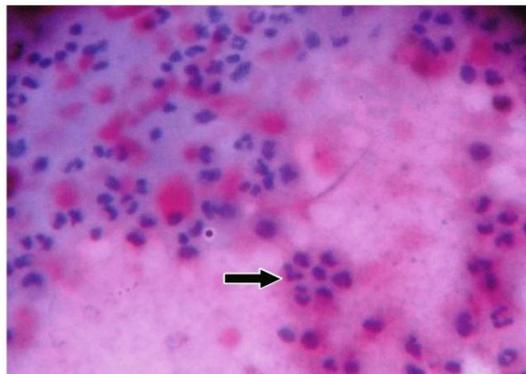
**Table 3: Total leucocyte count in joint diseases**

SL.No	Disease Category	TLC cells/cumm	Mean cells/cumm
1	Osteoarthritis	150 – 1200	385
2	Rheumatoid arthritis	3500 – 18,500	16,000
3	Septic arthritis	50,000– 62,000	56,000
4	TB arthritis	8000 – 12,000	5060
5	Gout	4500	-
6	Traumatic arthritis	2000 – 4550	5480
7	PVNS	3500 – 4000	3750
8	IA – NOS	2000 – 10,500	3670
9	NIA – NOS	100 – 800	321

**Figure 1: Wet mount examination of synovial fluid from rheumatoid arthritis showing ragocytes (arrow) (10x)**



**Figure 2 : Permanent stained smear showing predominance of neutrophils (arrow) from a case of septic arthritis (H&E, 10x)**



**Figure 3: Synovial fluid aspirate in a case of gout showing intracellular monosodium urate crystal under polarizing microscope.**



## DISCUSSION

Osteoarthritis (OA) is the leading cause of impaired mobility in elderly [7,8]. In the present study, mean age was 60 years which correlated with the study by Partik M et al where the mean age was 72 yrs [9]. In a study by Felson DT, total count was below 1000/cubic millimeter which correlated with our study.(8). Percy et al in his study showed that the synovial fluid in OA is clear yellow with high viscosity, good mucin clot test, total count less than 2000 cells/cumm and cartilage fibrils [10] which is similar to our study.

Ragocytes are found in rheumatoid arthritis, rheumatic fever, villonodular tenosynovitis and infrequently in septic arthritis [11]. In the present study ragocytes were present in all cases of rheumatoid arthritis on wet mount examination. Total cell count ranges from 1,200- 18,500 cells/cumm with a mean of 16,000 cells/cumm with predominance of neutrophils which correlates with the studies by other authors. [12,13].

In septic arthritis the knee joint is the most commonly involved joint but the other commonly involved joints include shoulder, wrist, hip, interphalangeal and elbow joints [14]. In majority of cases septic arthritis is monoarticular and occurs mostly commonly in the large peripheral joints such as knee [14]. In the present study patients presented with monoarticular arthritis affecting knee joint. Traditionally, the cut off value for synovial fluid count for diagnosis of septic arthritis has been greater than 50000/mm<sup>3</sup> however lower WBC counts can occur in early infectious arthritis or treated infection [15]. In present study , the total count was more than 50,000 cell/cumm which is consistent with the study by Kortenkongas et al [15].

In the study by Tauro et al, synovial fluid in traumatic arthritis was hemorrhagic, with normal viscosity and good mucin clot test. Hemosiderin containing histiocytes and foreign body giant cells may occasionally be seen in variable numbers [12]. These findings are consistent with the present study.

In a study by Foocharoen C. et al , chronic monoarthritis was the most common clinical manifestation in tubercular arthritis and knee joint was most commonly affected followed by ankle, wrist, forefoot, shoulder and elbow. Synovial fluid analysis revealed inflammation with neutrophil predominance [16]. This is similar to the present study in which knee joint was affected in all cases and total count was mean was 8000- 12,000 cells/ cumm with 77% neutrophils.

Naib et al found that the aspiration from PVNS produces variable amounts of serohemorrhagic, brown fluid with variable viscosity and mucin clot depending on the age of inflammation which is consistent with the present study. The presence of large number of foreign body giant cell, some containing large amount of coarsely granular yellow brown hemosiderin pigment is diagnostic [17]. In the present study, Synovial fluid was hemorrhagic with a mean Total leukocyte count of 3750 cells/ cumm and synovial biopsy showed the presence of hemosiderin containing histiocytes and foreign body giant cells.

Dai et al reported that the total count in gouty arthritis ranges from 4500-10,000 cells/cumm which correlates with our study where total count was 4500 cells/cumm [18]. Gordon et al found that the analysis of synovial fluid in cases of doubt reflects inflammatory type of change with leukocytosis and identification in the sediment particularly inflamed synovial fluid, intra cellular and extra cellular needle shaped crystals that have characteristic negative birefringence on polarized light microscopy which is similar to our study [19].

## CONCLUSION

Synovial fluid is a tool that helps in the diagnosis and treatment of arthropathies. It is necessary to define the macroscopic characteristics and cell count before proceeding with crystal screening and if necessary culture. Synovial fluid in disease states with alteration in mucin content reflects the degree of joint inflammation. Total and differential white cell counts provides a simple way of distinguishing non inflammatory arthritis, inflammatory arthritis and septic arthritis.

## REFERENCES

- [1] Tercic D, Bozic B. Clin chem lab Med 2001; 39: 1221-6.
- [2] Eisenberg M, Schumacher H, Davidson P, Kauffmann L. Arch Int Med 1984; 144:715-9.



- [3] Shmerling RH. Rheum Dis North Am 1994; 20(2): 503-12.
- [4] Sangeetha B, Vora IM, Abraham S, Srivastava S, Jignesh S, Chaturvedi R. BHJ Org J 2004.
- [5] Donge DR, Brouwer R, Smit M, Frankinjer M, Dulhain RJ, Toorenbergen V. Rheumatol 2004; 43: 170-3.
- [6] Revell PA. The synovial biopsy. In: Antony PP, Sween M, Lowe DG. editors. Recent Advances in Histopathology-13. New York : Churchill living stone; 1987. p. 79-83.
- [7] Ropes MW, Bennet GA, Bauer W. J Clin Invest 1939; 18: 351.
- [8] Felson DT. N Engl J Med 2006; 354: 841-8.
- [9] Patrik M, Hamiltone E, Wilson R, Austin R, Duherry M. Ann Rheum Dis 1993; 52: 97-103.
- [10] Percy JS, Russell AS. CMA J 1975 (112): 1320-8.
- [11] Kim SY, Chi JG. KJ Path 1987; 21(1): 54-6.
- [12] Tauro B. J Bone Joint Surg (Br) 1995; 77: 654-6.
- [13] Hollander JL, Reginato A, Torralba TP. Med Clin NA 1966; 50: 1281-93.
- [14] Davis MJ, Denton J, Freemont AJ, Holt PJL. Ann Rheum Dis 1998; 47: 559-62.
- [15] Kortenkangas P, Aro HT, Tuominen J. Scand J Rheumatol 1992; 21(6): 283.
- [16] Foocharoen C, Nanagera R, Foocharoen T, Mootsikpun P, Suwannroj S, Mahakkanukrach A. South east Asian J Trop Med Public Health 2010; 41(6):1438-1446.
- [17] Naib ZM. Acta cytol 1973; 17 (14): 299-309.
- [18] Dai , Pessler F, Chen LX, Glaybue , Schumacher HR. Rheumatol 2006; 45: 533-7.
- [19] Gordon TP, Bertouch JV, Waleb BR, Brooks PM. Arthritis Rheum 1991;34:141- 5.