

Role of Arthroscopic Synovial Biopsy in Diagnosis and Management of Unilateral Synovitis Knee

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Abstract: *Background:* Monoarticular synovitis is relatively difficult to diagnose and delay in diagnosis leads to poor outcomes. Long-term occurrence of synovitis can result in degeneration of the joint due to the release of inflammatory cytokines which resulted in increased synthesis of matrix metalloproteinases and decreased expression levels of inhibitors. Tubercular synovitis and early arthritis are difficult to diagnose due to the atypical clinical presentation and lack of specificity in diagnosis. *Materials and Methods:* A prospective study was conducted on 55 patients and arthroscopic synovial biopsy was obtained and biopsy reports were evaluated. The paired t-test was used to compare serial changes in pain intensity using numeric pain rating scale. *Results:* Out of 55, 27 (49.09%) cases were diagnosed as inflammatory synovitis, 11 (20%) cases as tubercular synovitis, 3 (5.45%) cases of osteoarthritis, and 14 (25.45%) cases of non-specific chronic synovitis. The mean age of patients was 43.21 years. As a diagnostic aid, the role of synovial biopsy was found to be significant ($P < 0.05$). *Conclusion:* Monoarticular arthritis should be thoroughly investigated rule out infectious or metabolic diseases for their destructive potential to destroy cartilage rapidly. Arthroscopic-assisted synovial biopsy has added advantage as it permits macroscopic evaluation of the synovium, and cartilage inadequacy could also be noted along with serving as therapeutic purposes in some cases.

Keywords: Monoarticular, synovitis, synovial biopsy, numeric pain rating scale.

1. Introduction

Synovitis is the medical term for inflammation of the synovial membrane. The main purpose of this synovium is to provide smooth motion by preventing the bones of the leg from grinding together, when the knee is moved. Knee synovitis occurs when the synovial membrane which lines and lubricates the knee joint, becomes inflamed. This condition is usually painful, particularly when the joint is moved. Common causes of synovitis includes infection (septic arthritis), direct joint trauma, allergic reaction, gout, overuse syndromes, systemic autoimmune inflammatory diseases (Rheumatoid arthritis), osteoarthritis, pigmented villonodular synovitis and idiopathic. Synovitis may occur in association with other systemic diseases like lupus, psoriasis and other conditions. Early diagnosis and timely institution of anti-tubercular treatment (ATT) is crucial as delay leads to irreparable damage to the joint and restriction of joint mobility. Establishing the diagnosis of TB beyond doubt is very important when considering the cost and duration of treatment and the effects of delayed treatment including psychosocial implications¹. Even in disease endemic countries, only suspicion and imaging results are not accurate enough to diagnose and treat joint TB. Sensitivity of most tests is very low in joint tuberculosis, as there is dilution of tubercle bacilli in synovial fluid^{1, 2}. Conventional microbiological methods like smear and culture have low sensitivity and specificity, especially in synovial TB due to the paucibacillary nature of disease^{1, 3}. In addition, the culture of Mycobacterium tuberculosis is time consuming, taking 6–8 weeks for the growth to appear and much longer time for positive growth, especially in paucibacillary cases like joint TB⁴⁻⁶. Common conditions, such as rheumatoid arthritis, rarely cause diagnostic problems as they cause symmetrical joints involvement. Monoarticular synovitis is however difficult to diagnose and often times, routine x-ray and pathological investigations including synovial fluid analysis are unable to give conclusive result. Synovial biopsy is then helpful in distinguishing between various etiologies such as infective, traumatic or crystal induced^{7, 8}. Synovitis is usually a

secondary condition, which may also be caused by an injury to the knee joint or cancer (synovial sarcoma). For this reason it is important that suspected cases of synovitis are investigated thoroughly.

2. Materials and Methods

This prospective study was conducted on patients attending the orthopaedic OPD and emergency department from January 2017 to February 2017 presenting with pain and swelling of single knee, not responding to NSAIDs. All participants were recruited after taking written informed voluntary consent. A detailed history, examination (General systemic and local examination) along with investigation was knee pain and swelling not responding to NSAIDs for at least 6 weeks, patient of either sex aged 18-60 years. Exclusion criteria:- Age <18 year and >60year – Pregnant and Lactating women – Patient with multiple joint involvements – Patient with low platelet count (<70,000/cumm) – Advanced radiological osteoarthritic changes. All good clinical practice guidelines were followed and ethical clearance taken from hospital medical research committee, who approved the study. The initial aim of the evaluation of a patient with joint pain was to localize the source of the joint symptoms (bone or soft tissue) and to determine the type of pathophysiologic process responsible for their presence. Knee aspiration was done and fluid analysis sent for examination, which was found to be equivocal. Patient examined carefully to rule out involvement of any other joint and thorough history taken. Pain graded on scale of 0-10 (Numeric pain rating scale) and if restriction of movement present, then measured. Synovial biopsy results were studied and by interpreting histopathological findings diseases were diagnosed. Treatment is started as per standard measures against any causative condition diagnosed. Patients were kept in follow-up and closely monitored. For first two months patients came on every 15 days after which they were followed every month. Pain grading done at follow-up after 3 months to see improvement of patient and pain intensity compared to

before treatment. All 55 patients underwent arthroscopic synovial biopsy.

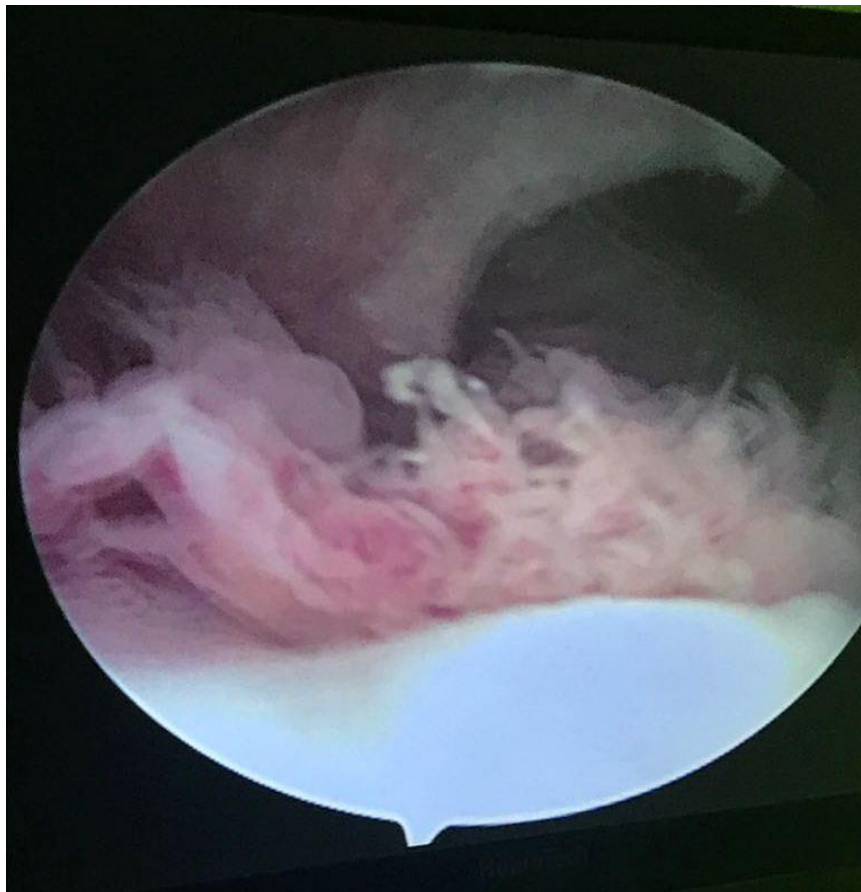


Figure 1 showing: synovitis arthroscopic image

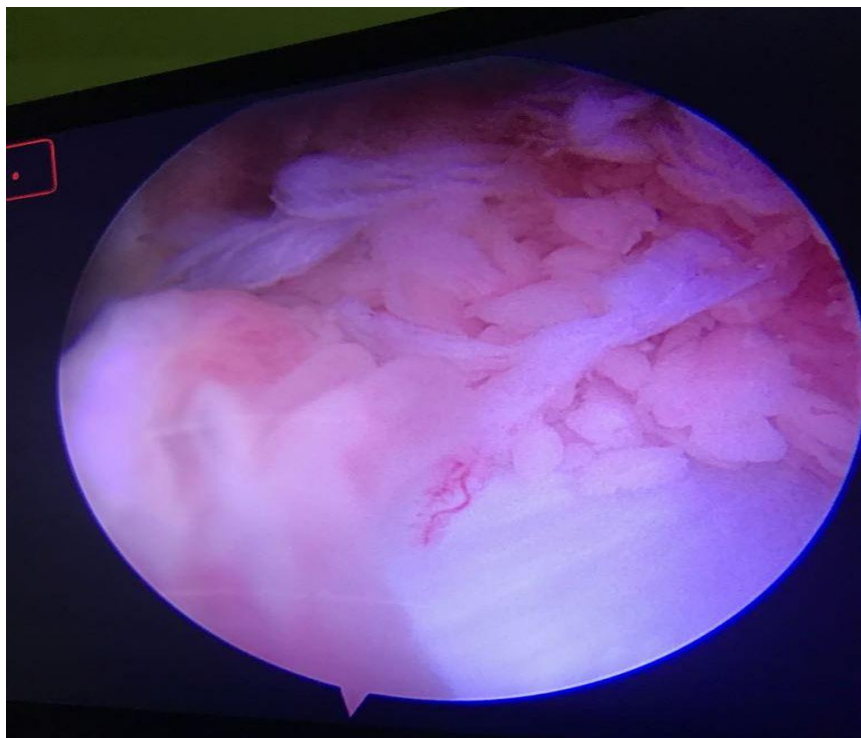


Figure 2 showing: Pigmented villonodular synovitis arthroscopic image

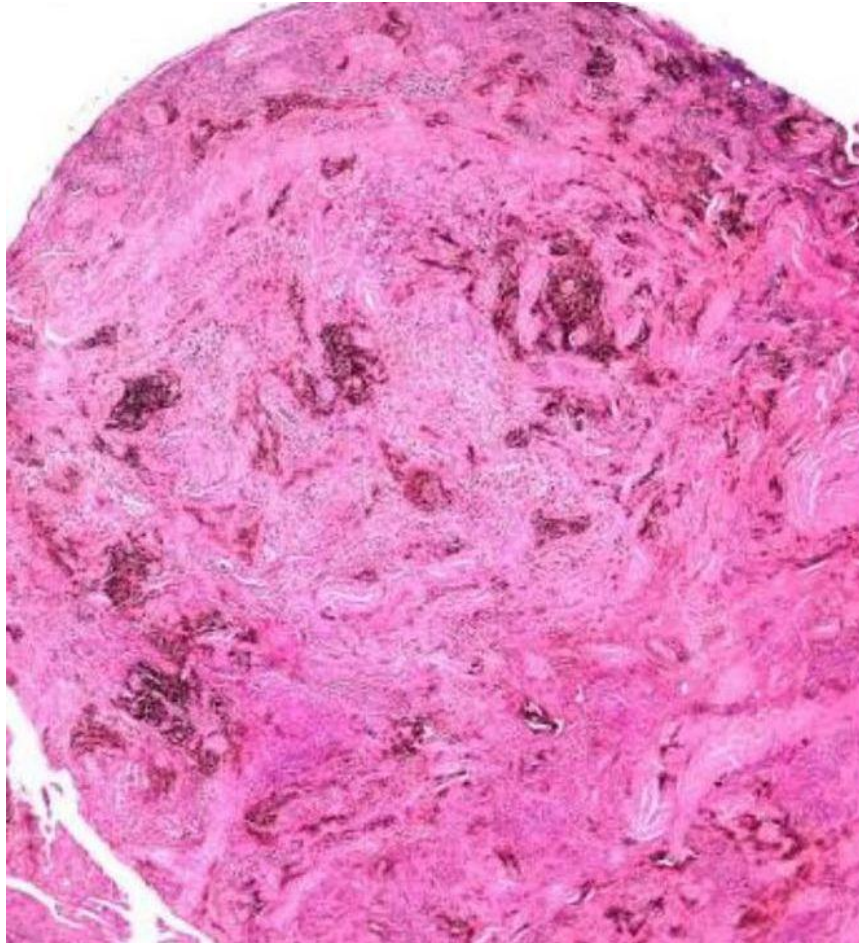


Figure 3: Histology slide of villonodular synovitis.

Arthroscopic synovial biopsy procedure: After general investigations procedure is planned and all surgeries were done under spinal anaesthesia. Arthroscopic evaluation was performed by a senior arthroscopic consultant of our institution. Patient was laid supine on OT table, after giving spinal anaesthesia and tourniquet applied over respective thigh. Part painted and draped as such, so knee can be flexed and extended during procedure. Standard anteromedial and anterolateral portals were used. Anterolateral portal made during the flexion of knee at 90o and 8mm skin incision made over the lateral joint line and another skin incision of 8mm made over medial joint line for anteromedial port. Arthroscope camera and arthroscope probe inserted through above made ports. Irrigation fluid switched on before switching on the light source to avoid thermal damage. On arthroscopic evaluation, joint was thoroughly inspected through standard portals. Sample for synovial biopsy was taken concentrating on suspected focal areas of pathology in synovium. Biopsy is obtained from different places like suprapatellar pouch, medial and lateral gutter and from patellar margins. After the final biopsy sample is taken, the skin is stitched if needed and covered with sterile wound dressing. Arthroscopic partial or subtotal synovectomy was done if needed. Synovial biopsy material is sent for histopathological examination, after packing it in formalin glass bottle. Patients were regularly followed up clinically, radiologically and with help of laboratory investigations like CRP and ESR. At the end of 3 months CRP levels were found to be nearly normal. Pain intensity was graded at 3 month follow-up using numeric pain rating scale. Pain

intensity scores at 3 months follow up were compared with pain intensity scores of pre-treatment.

3. Results

Out of the 55 cases we studied of monoarticular joint involvement of knee joint were subjected to synovial biopsy investigations and diagnosis was made on basis of histopathological picture (figure 1 showing typical tubercular histopathological picture: Necrotising granulomatous inflammation, comprising of caseous necrosis, surrounded by epithelioid cells, histiocytes and lymphocytes). Both rheumatoid (n=27, 49.09%) and tubercular (n=11, 20%) were found to be more common compared to other etiologies. Next common etiology observed in our study was chronic non-specific synovitis (n=14, 25.45%). There were 3 cases of osteoarthritis (n=3, 5.45%).- Rheumatoid was found to be most common etiology, with 27 patients (49.09%) out of 55 patients.- 3 patients (5.45%) were found to be suffering from osteoarthritis. - 11 patients (20%) were of tubercular arthritis.- The mean age of patient with synovitis knee, who underwent synovial biopsy was 43.21 years.- Maximum numbers of patients were from age group 36-50 years (n=33, 75%).- The period of hospitalization required ranged from 2-3 days and post-operatively, weight bearing and knee movement was allowed as tolerated by patient. No significant complications occurred in all 55 patients post synovial biopsy.- Pain intensity improved during follow up with time as graded according to numeric pain rating scale

compared to pre-treatment.- Paired t-test was applied for comparing pain intensity at pre-treatment and at 3 months follow-up which was found <0.05 which is significant.- Diagnosed cases were managed accordingly and responded well to treatment and were monitored during follow-up.

Age wise distribution: Age wise distribution: The youngest patient age was 19 years and oldest patient age was 66 years. 33 patients were in the age group of 36-50 years. The average age of patient was 43.21 years.

Incidence of different diseases as assessed by synovial biopsy: Among the 55 patients, 27 patients were diagnosed with rheumatoid arthritis, 11 patients with tubercular arthritis, 3 patients of osteoarthritis and 14 patients of non-specific chronic synovitis

4. Discussion

Inflammatory synovitis of the knee is one of the commonest clinical presentations in day to day orthopaedic clinical practice. The aetiology remains unclear in many cases. Routine laboratory and radiological investigations in monoarticular joint lesion are often equivocal. Diagnosis of arthritis is often made clinically and treatment is given empirically, due to which results are sometimes disappointing for both patients and doctors. In our study synovial biopsy was performed in 55 patients to obtain a sample of the tissue directly under vision from the suspected site of pathology. The average age of patients was 43.21 years. Youngest patient in this study was 19 years of age and oldest was 66. Maximum cases of unilateral synovitis were found in 4th and 5th decades. The maximum number of synovitis occurred in the age group of 36-50 years, 33 patients (75%). In G Raghunandan et al study there were 25 males and 15 females with male: female ratio of 5:3. Histological examination by synovial biopsy was found to be of significant diagnostic value. It was helpful in confirming the diagnosis of the underlying pathology after clinical evaluation in 44 cases including rheumatoid arthritis, tubercular arthritis and osteoarthritis. In remaining 14 cases, no specific pathology was found on histopathology and they were declared as chronic non-specific synovitis. In cases where clinical diagnosis was non-specific, histological examination of synovial biopsy helped in reaching the final diagnosis. In our study most common etiology was found to be rheumatoid followed by cases of non-specific chronic synovitis. Rheumatoid arthritis was found in 27 patients (49.09%) out of 55 patients. In Onisinghal et al study rheumatoid arthritis was found in 11 patients (22%) out of 50 patients. In Chen GQ et al study 39 (52.9%) cases of rheumatoid arthritis were found out of total 71 patients. In G Raghunandan et al study 5 (12.5%) cases were diagnosed with rheumatoid arthritis. In Sundararajan S R et al study 7 (20.58%) cases were diagnosed with rheumatoid arthritis out of total 34 patients. In Vijay P.M et al study rheumatoid arthritis was found in 4 patients (4.8%). Early diagnosis of rheumatoid arthritis with help of histopathology helps in improving prognosis of disease. There is evidence that the very early introduction of disease modifying therapy inhibit progressive structural damage maximally. Clinician exploiting this "window of opportunity" therefore requires very early indicators of the diagnosis and outcome in

patients who present with an undifferentiated inflammatory arthritis¹³. Serial synovial biopsies in open therapeutic studies and in randomized clinical trials showed that the immunohistological features of RA and other arthropathies changes after treatment with DMARDs (Disease modifying anti rheumatic drugs). It has been established that DMARDs therapy reduces the rate of progressive joint damage more effectively when introduced within 6 months of the onset of symptoms. It is now standard practice to introduce conventional DMARDs such as methotrexate, and even targeted biological therapies, as first line treatment in patient with RA. Although there is no diagnostic role in early RA, synovial biopsy and tissue analysis may provide important prognostic information. In our study 11 (20%) cases were diagnosed as tubercular arthritis. These were more commonly found in younger population. In OnisSinghal et al study tubercular arthritis was found in 13 patients (n=26%) out of 50 patients. In G Raghunandan et al study 6 cases (15%) were of tubercular arthritis out of 40 patients. In Chen GQ et al study 5 (6.5%) cases of tuberculosis arthritis were found out of total 71 patients¹⁴. In Sundararajan S R et al study 7 (20.58%) cases were diagnosed with tubercular arthritis out of total 34 patients. In Vijay P.M et al study 15 patients (18.07%) were found of tubercular arthritis. Another study was conducted on 70 cases of tuberculous synovitis by SantM et al¹⁵ and was published in 1992. In this study maximum number of cases were found in the age group of 11-30 years (58.58%) with a male preponderance. Knee joint was found to be most commonly (57.12%) affected. Diagnosis of tuberculous synovitis was possible clinically in 75.72% and radiologically in 67.14% of cases only. Such high percentage of tubercular arthritis patients were found, as our country is endemic for tuberculosis. As definitive treatment with anti-tubercular medication is available, diagnosis of early tubercular synovitis is very essential to prevent cartilage damage. Definitive tissue diagnosis and timely treatment helps in achieving excellent results in 3-4 months period¹⁶. In our study 14 cases were diagnosed as chronic non-specific synovitis. In Onis Singhal et al study chronic non-specific synovitis was found in 10 patients out of 50 patients (20%). In G Raghunandan et al study 25 cases (62.5%) were of chronic non-specific synovitis out of 40 patients. In Chen GQ et al study 3 (4.054%) cases of unknown causes were found out of total 71 patients. In Vijay P.M et al study 59 patients (83.099%) were found of chronic non-specific synovitis. In Sundararajan S R et al study 9 (26.47%) cases were diagnosed with chronic non-specific synovitis out of total 34 patients. Chronic non-specific synovitis is also known as monoarthritis of unknown origin. 80% of these can go into complete remission over a period of two years with just conservative treatment. This high occurrence of cases of chronic non-specific synovitis in our study may represent an early stage of rheumatoid arthritis, in which the disease is still in the stage of evolution without a fully developed picture of rheumatoid arthritis, some patients may be due to early osteoarthritis not fulfilling histopathological and radiological features for its diagnosis. If these patients are closely followed up and repeat biopsies are carried out in due course, they may help with specific diagnostic features or patients may have self-limited disease or may undergo complete therapeutic remission. In our study 3 cases were diagnosed as osteoarthritis. Apart from these four diseases diagnosed in our study, synovial biopsy also

helps in diagnosis of other diseases like Pigmented villonodular synovitis, septic arthritis, gouty arthritis, sarcoidosis, osteochondromatosis, haemochromatosis, amyloidosis, seronegativespodyloarthropathy and any synovial carcinoma. Arthroscopy is an excellent tool for visualizing and evaluating the condition of the synovium macroscopically and the suspected areas of increased activity were chosen for biopsy. In study by Latosiewicz et al 82 patients underwent arthroscopic synovial biopsy in the course of treatment for chronic knee synovitis. It concluded that arthroscopic synovial biopsy increases diagnostic potential in the synovitis of unclear etiology. In arthroscopic synovial biopsy gross examination gives added advantage in making a diagnosis, like visualizing subchondral bone defect. It has added advantage of performing therapeutic procedures along with biopsy at same time and knee joint lavage could be done during biopsy. Arthroscopic partial or subtotal synovectomy may be done if needed. Arthroscopic synovial biopsy was also better in terms of post biopsy recovery as incision was only made for port entry compared to open biopsy. Results of histopathology arrived in 15-18 days. Arthroscopic findings can alter or add to the treatment plan which includes surgical tissue resection or medical treatment like disease modifying anti-rheumatic drugs to the current treatment. In our study despite thorough arthroscopic and microscopic evaluation, we were not able to accurately diagnose in 25.45% of patients, which were finally diagnosed as chronic non-specific synovitis. In conclusion, the present case series demonstrates that synovial biopsy can be cost-effective diagnostic tools with therapeutic consequences. This is especially so when the differential diagnosis consists of a disease with characteristic histological hallmarks. Synovial biopsy is useful and cost-effective in mono-articular synovitis cases, especially where advanced radiological facilities like MRI are not available to general population. In terms of diagnostic accuracy, histopathology was found to be the most economical, accurate and time saving method.

References

- [1] Pandey V, Chawla K, Acharya K, Rao S, Rao S. The role of polymerase chain reaction in the management of osteoarticular tuberculosis. *IntOrthop* 2007;24:485-8.
- [2] Agashe V, Shenai S, Mohrir G, Deshmukh M, Bhaduri A, Deshpande R, et al. Osteoarticular tuberculosis—diagnostic solutions in a disease endemic region. *J Infect DevCtries*. 2009;3:511–6.
- [3] Negi SS, Gupta S, Khare S, Lal S. Comparison of various microbiological tests including polymerase chain reaction for the diagnosis of osteoarticular tuberculosis. *Indian J Med Microbiol* 2005;23:245-8.
- [4] Tuli SM. General principles of osteoarticular tuberculosis. *ClinOrthopRelat Res* 2002;398:11-9.
- [5] Watts HG, Lifeso RM. Current concepts review – tuberculosis of bones and joints. *J Bone Joint Surg* 1996;78-A:288-99.
- [6] Kerlequer A, Fabre M, Bernatas JJ, Gerome P, Herve V, Koeck JL. Clinical evaluation of the gen-probe amplified mycobacterium tuberculosis direct test for rapid diagnosis of tuberculosis lymphadenitis. *J ClinMicrobiol* 2004;42:5921-2.

- [7] Revell PA. The synovial biopsy in recent advances in histopathology. 1987;13: 79-89.
- [8] Jo CW, Edwards . The synovium in Rheumatoid arthritis, Edt. Harris Edward D., Philadelphia; Saunders B. Co. 1997.
- [9] G. Raghunandan, K. B. Vijayamohan Reddy, A. M. IliasBasha, G. Praneeth Kumar Reddy. "Selective Synovial Biopsy in Chronic Synovitis Knee – A Study". *Journal of Evidence based Medicine and Healthcare*; Volume 2, Issue 3, January 19, 2015; Page: 236-240.
- [10] OnisSinghal, VipleshKaur, ShivaniKalhan, Manish Kumar Singhal, Anshu Gupta, YV Machave. *Int J Appl Basic Med Res*. 2012 Jul-Dec; 2(2): 102–106.
- [11] Sundararajan SR, Jain SR, Rajasekaran S. Arthroscopic Biopsy and MRI Diagnosis in Monoarticular Joint Synovitis of Undifferentiated Origin – A retrospective study in 34 cases . *Asian Journal of Arthroscopy* Apr-June 2016;1(1):38-42.
- [12] Vijay PM, Doddikoppad MM. *Int J Biol Med Res*. 2011; 2(4): 88 –888.
- [13] Bresnihan B. Are synovial biopsies of diagnostic value? *Arthritis Res Ther*.2003;5(6):271-8. Epub 2003 Oct 2.
- [14] Scherer T, Kieser C, Gerber H. Assessment and course of 110 patients with monoarthritis. *TherUmsch*. 1989 Apr; 46(4):258-64.
- [15] Sant M, Bajaj H. Role of histopathology in the diagnosis of tuberculous synovitis. *J Indian Med Assoc*. 1992 Oct;90(10):263-4.
- [16] Cai D, Chen Y, Rong L. Arthroscopy in diagnosis and treatment of tuberculous synovitis. *ZhonghuaJie He He Hu Xi ZaZhi*. 1998 May; 21(5):276-7.
- [17] Chen GQ, Zhang HW, Li ZF, Guo DM, Yu YT. Significance of arthroscopy in the diagnosis of unilateral knee arthritis. *Zhonghua Yi XueZaZhi*. 2010 Jun15; 90(23):1615-7.