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PREVALENCE OF TUBERCULOSIS IN THE CHRONIC SYNOVITIS CASES BY CARTRIDGE BASED NUCLEIC ACID AMPLIFICATION TEST

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ABSTRACT

Aim: The aim of the present study was to assess the prevalence of tuberculosis among chronic synovitis cases by cartridge based nucleic acid amplification test

Material & methods: The study included specimens received between August 2022 to July 2024. from JLN Medical College & Hospital, Ajmer. The patients' socio-demographic characteristics from their test request form were collected, CBNAAT results from the CBNAAT register and PMDT culture and drug susceptibility testing (DST) register and validated the data by comparing the patient details and test results from the CBNAAT software.

Results: The maximum number of cases 27 (27%) belongs to the age group of 21-30 years followed by 41 - 50 years 21 (21%) and minimum 3 (3%) in the age group of 0-10 years. In the present study male contribute 62 % of the cases and female contribute 38% of the cases. Majority of cases belongs to married group i.e. 67 (67%) of the cases and the remaining 33% were unmarried. Out of 100 cases, most of the cases 68 (68%) belongs to the group of healthy weight. Out of 7 positive CBNAAT cases or 10 positive biopsy cases most of the cases of tubercular synovitis lie within the age group of 11-30 years (young). Out of total 7 CBNAAT positive cases, 3 were male (out of 62) which was 4.83% of the total male patients and 4 were female (out of 38) which was 10.52% of the female patients. The maximum number of patients 25 (25%) in this study were student, followed by housewife 15 (15%) after that agriculture worker and skilled worker 11 each (11%). The maximum number of cases 37 (37%) in this study belongs to lower middle class followed by upper middle 34 (34%) and then upper lower class 20 (20%).

Conclusion: CBNAAT or Gene Xpert assay has the advantage of less turn-around time (2 hours) for detecting tuberculosis and Rifampicin resistance with moderate sensitivity and high specificity in synovial sampling.

Keywords: Chronic Synovitis, Tuberculosis, Cartridge Based Nucleic Acid Amplification Test

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1. INTRODUCTION

Synovium is vascularized connective tissue which lines the space of diarthrodial joint, tendon sheath and bursae. It is the most metabolically active structure inside a joint and involved very early in most of the disorders involving the joints.[1]
Synovium secretes access of synovial fluid in response to any insult of joint leading to synovitis. Synovitis occurs because of various cause which includes Tuberculosis, gout, infection, local proliferative disorders, juvenile rheumatoid arthritis, systemic inflammatory arthritis, metabolic disorders, trauma, etc4. Chronic synovitis remains a diagnostic dilemma because of equivocal result in laboratory, radiological investigations and non-classical clinical presentation. Physical, biochemical, cytological and microbiological study of synovial fluid has proven to be useful adjunct for diagnosis but they have poor specificity so, synovial biopsy together with synovial fluid examination has a better role in diagnosis.[2]
As tuberculosis is very common in India, it is necessary to rule out tuberculosis in Indian scenario. It is caused by Mycobacterium tuberculosis that most often affects the lungs and is spread from person to person through air. Tuberculosis is an important health problem in developing countries like India and remains a key challenge to public health due to inadequate diagnostic assay. [3] Early detection is essential to interupt transmission and reduce death rate. About a quarter of global population is estimated to have been infected with tuberculosis bacteria but most people will not develop disease. In 2021, an estimated 10.6 million people fall ill with tuberculosis worldwide (6 million men, 3.4 million women and 1.2 million children)[4] in which 2.6 million cases reported in India with incidence rate of 188/lakh population with a total of 1.6 million people died worldwide.[5] Tuberculosis was 13 leading cause of death and second leading infectious killer after Covid-19 in 2021.[4]
Among all tuberculosis cases extra pulmonary tuberculosis range from 15-25% worldwide and 30-53% in India in which bone and joint tuberculosis accounts for approximately 10%. The diagnosis of extra pulmonary tuberculosis is challenging because of pauci bacillary in nature, lack of specific signs and symptoms and often negative acid-fast bacilli smear of biological specimens. Although the culture remain the gold standard for diagnosis of tuberculosis. Culture method and drug susceptibility testing is complex and take longer time which result in inappropriate or ineffective treatment and increase in morbidity. To overcome this issue there is need for a simple and rapid diagnostic tool. A newer diagnostic test CBNAAT was developed which was rapid, fully automated and based on PCR. CBNAAT (cartridge based nucleic acid amplification test) is an automated real time PCR (Polymerase Chain Reaction) assay designed for the rapid and simultaneous detection of Mycobacterium tuberculosis and Rifampicin resistance within 2 hours. Also, reagent use for processing is bactericidal and tubercular bacilli are inactivated in vitro. So biosafety risk is eliminated thus enabling its use as a rapid point of care diagnostic test.[6] Therefore, in this study all patients having synovitis are evaluated by mean of CBNAAT to assess the prevalence of tuberculosis in chronic synovitis cases.

2. MATERIAL & METHODS

A hospital based Prospective Study to study the prevalence of Tuberculosis in the chronic synovitis cases by Cartridge Based Nucleic Acid Amplification Test (CBNAAT) at JLN Medical College & Hospital, Ajmer in between the duration of August 2022 to July 2024.

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Informed consent of the patients was taken for this study. Approval from institutional ethical committee was taken for this study.

Inclusion Criteria

- Synovitis patient diagnosed clinically.
- Recurrent synovitis.
- History of previous pulmonary tuberculosis in patients presenting with synovitis.
- Synovitis associated with septicaemia
- Septic arthritis

Exclusion Criteria

- Traumatic synovitis
- Synovitis associated with Neoplastic atiology.
- Synovitis associated with neuropathy
- Patients not given consent

Method of collection of data:

1. Relevant history followed by patient or patient's attendant consent for synovial aspiration.
2. Synovial fluid aspiration for CBNAAT and other investigations.

The study requires investigations conducted on patients:

Routine Investigations such as CBC, PT-INR, Random blood sugar, Renal function test, Serum electrolyte, ECG, Chest X-ray, X-ray of the affected joint, Viral markers: HIV, HBsAg was done.

Special Investigations such as CBNAAT of synovial aspirate, Biopsy of synovium for histopathology, Synovial tissue for CBNAAT, Cytology and cell count of synovial fluid, Synovial fluid smear for Acid Fast Bacilli by ZN Staining, Mantoux Test and Biochemistry of synovial fluid: Sugar, chloride and protein were conducted.

STATISTICAL ANALYSIS

The socio-demographic characteristics of the study population were collected from the test request form sent from the referral sites. CBNAAT test results were collected from the CBNAAT register and PMDT culture and DST register and validated by comparing the patient details and test results from the CBNAAT software. All the data was entered in Excel 2010 (Microsoft Office, USA) for data analysis. The proportion of sputum and non-sputum samples from the public and private sectors was calculated, along with other demographic characteristics such as age and sex distribution.

3. RESULTS

Table 1: Baseline characteristics

Age Range (years)	Number of cases	Percent
0-10	3	3
11-20	13	13
21-30	27	27
31-40	14	14
41-50	21	21
51-60	9	9
61-70	13	13
Sex		
Male	62	62

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Female	38	38
Marital status		
Married	67	67
Unmarried	33	33
BMI		
Below 18.5 (Underweight)	21	21
18.5 – 24.9 (Healthy Weight)	68	68
25.0 – 29.9 (Overweight)	11	11
30.0 and Above (Obesity)	0	0
Habit of Addiction		
Alcohol	19	19
Smoking	11	11
Alcohol + smoking	13	13
Tabacco	3	3
Others	2	2

The maximum number of cases 27 (27%) belongs to the age group of 21-30 years followed by 41 - 50 years 21 (21%) and minimum 3 (3%) in the age group of 0-10 years. Most of cases are young having age less than 40 years. In the present study male contribute 62 % of the cases and female contribute 38% of the cases. Majority of cases belongs to married group i.e. 67 (67%) of the cases and the remaining 33% were unmarried. Out of 100 cases, most of the cases 68 (68%) belongs to the group of healthy weight i.e. BMI of 18.5-24.9 kg/m2 followed by the group of underweight (BMI<18.5 kg/m2) i.e. 21 (21%). Out of total cases having history of addiction, most of the cases [(19+13=32) (32%)] were having addiction of alcohol and then smoking [(11+13=24) (24%)].

Table 2: Positive TB cases as per age and sex distribution

Age Range (Years)	CBNAAT (Positive)	Biopsy (Positive)
0-10	0	1
11-20	3	3
21-30	2	2
31-40	0	0
41-50	1	2
51-60	0	1
61-70	1	1
Total	**7**	**10**
Sex Distribution Vs CBNAAT	**CBNAAT Negative**	**CBNAAT Positive**
Male	**59**	**3**
Female	**34**	**4**
Total	**93**	**7**

Out of 7 positive CBNAAT cases or 10 positive biopsy cases most of the cases of tubercular synovitis lie within the age group of 11-30 years (young). Out of total 7 CBNAAT positive cases, 3 were male (out of 62) which was 4.83% of the total male patients and 4 were female (out of 38) which was 10.52% of the female patients.

Table 3: Distribution of cases according to history of comorbidity

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History of Comorbidity	Number of cases	Percent
History of TB	4	4
Hepatitis Positive	2	2
COPD / Asthma	2	2
Hypertension	8	8
DM	7	7
HTN + DM	4	4
RA	4	4
HIV	3	3
Other	2	2

Most of the comorbid patients belongs to the group of hypertension 12 (12%) and diabetes mellitus 11 (11%). There were 4 cases who had history of TB and out of 100 cases 36 patients were having history of comorbidity.

Table 3: Distribution of cases according to occupation and socio-economic status

Occupation	Number of cases	Percent
Skilled Workers	11	11
Agricultural	11	11
House Wife	15	15
Govt. Job	10	10
Student	25	25
Other	28	28
Total	**100**	**100**
Socio Economic Status		
Upper	3	3
Upper Middle	34	34
Lower Middle	37	37
Upper Lower	20	20
Lower	6	6

The maximum number of patients 25 (25%) in this study were student, followed by housewife 15 (15%) after that agriculture worker and skilled worker 11 each (11%). The maximum number of cases 37 (37%) in this study belongs to lower middle class followed by upper middle 34 (34%) and then upper lower class 20 (20%).

Table 4: Montoux test

Montoux Test	Number of cases (n=8)	
	Positive	Negative
CBNAAT	3	5
Biopsy	4	4

Out of 8 Montoux positive cases, 5 were males and 3 were females. 3 were both CBNAAT and biopsy positive, 1 was only biopsy positive, and remaining 4 cases were neither CBNAAT nor biopsy positive. 2 patients were having history of previous TB treatment.

Table 5: Relationship of cases with BMI and socio-economic status

BMI		TB Positive

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	Number of cases	CBNAAT	Biopsy
Below 18.5 (Underweight)	21	5	5
18.5 – 24.9 (Healthy Weight)	68	2	4
25.0 – 29.9 (Overweight)	11	0	1
30.0 and Above (Obesity)	0	0	0
Total	**100**	**7**	**10**
Socioeconomic status			
Upper	3	0	0
Upper Middle	34	0	1
Lower Middle	37	3	4
Upper Lower	20	4	5
Lower	6	0	0

Out of 7 CBNAAT positive cases 5 belongs to underweight category and 2 was in healthy weight category. Out of 10 biopsy positive cases 5 belongs to underweight followed by healthy weight 4 and then by overweight 1. Out of 5 positive cases in underweight group, 4 were both CBNAAT and Biopsy positive and 2 patients were both CBNAAT and Biopsy positive in healthy weight category. Out of 7 CBNAAT positive cases, 4 belonged to upper lower class and 3 to lower middle class. Out of 10 biopsy positive cases, 5 belonged to upper lower class, 4 to lower middle and 1 to upper middle class. In both lower middle and upper lower income group, 3 - 3 patients were both CBNAAT and Biopsy positive in each group.

Table 6: Relationship of cases with comorbidity

History of Comorbidity	Number of cases	TB Positive	
		CBNAAT	Biopsy
History of TB	4	2	3
Hepatitis Positive	2	0	0
COPD / Asthma	2	0	0
Hypertesnion	8	0	0
DM	7	**0**	**1**
HTN + DM	4	0	0
RA	4	**0**	**0**
HIV	3	**0**	**0**
Other	2	1	0
No History	64	4	6

Out of 7 CBNAAT positive cases, 2 were having history of TB and 1 was having liver disease and 4 patients didn't have any history of comorbidity. And out of 10 biopsy positive cases, 3 were having history of TB and 1 was having DM and remaining 6 patients didn't have any history of comorbidity. The maximum number of TB positive cases belongs to the patients without any history of comorbidity.

Table 7: Relation of high CRP and ESR with TB

	Number of cases	TB Positive	
		CBNAAT	Biopsy
ESR	37	6	9
CRP	15	5	7

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Out of 37 increase ESR cases, CBNAAT were positive in 6 cases and biopsy positive in 9 cases. Out of 15 CRP reactive cases, CBNAAT were positive in 5 cases and biopsy were positive in 7 cases.

4. DISCUSSION

The etiological diagnosis of tuberculosis (TB) is made by demonstration of acid-fast bacilli (AFB) on smear in 30–50% cases[7], by mycobacterial culture in 10–30% instances[8] or by histology.[7,8] Mycobacterial culture, a gold standard for TB, is necessary for drug susceptibility testing (DST).[8] Epithelioid cell granulomas, granular necrotic background including caseous necrosis, lymphocytic infiltration, scattered multinucleated and Langhans' giant cells are observed on histology in TB. Histology report is consistent with tuberculosis (60%) if necrotizing granulomas with caseous necrosis are found while suggestive in the presence of non-necrotizing granulomas[9], with differential diagnosis of other chronic granulomatous diseases.

In our study, majority of patients were young which belongs to <50 years of age and were males with M:F ratio of 1.63 : 1 which is almost similar to many other studies like Alwani H et al (2022)[10] in which the male : female ratio was 1.19 : 1. Due to socio-economic and cultural factor leading to the barriers in excessive health care may cause under notification in women particularly in developing countries.[11] Most of the tubercular synovitis belongs to the age group of 11 - 30 years which is almost similar to the study of Connolly M et al (1996)[12] in which the greatest burden of disease occurs in 15-49 years age group. In the study of Gour SM et al (2017)[13] in which higher number of cases was in younger age group and maximum cases were in the age group of 21-30 years. In the present study, almost 2/3 of the cases 67 (67%) were married as compared to 33 (33%) unmarried.

The gold standard for diagnosis of tubercular synovitis remains synovial histopathology / biopsy (Karki P et al., 2022).[14] In this study, 7 cases were CBNAAT positive and 10 cases were histopathology positive. If we compare CBNAAT with the gold standard the histopathology, the sensitivity and specificity of CBNAAT comes to be 60.00% (95% CI 26.24 to 87.84) and 98.99% (95% CI 93.96 to 99.97) respectively, and PPV 99.9% (95% CI 99.28 to 99.99) and NPV 11.51% (95% CI 5.74 to 21.76). In the study of Hillemann D et al (2011)[15] they found the sensitivity of 69% for CBNAAT in case of biopsy specimen. In the study of Alwani H et al (2020)[10] the reported sensitivity and specificity was 50.0% and 85.7% respectively in biopsy specimen.

In the 7 positive CBNAAT positive cases 3 (4.83%) out of 62 cases were males and 4 (10.52%) out of 38 cases were females. In 10 positive biopsy or histopathology cases, 6 (9.67%) out of 62 were males and 4 (10.52%) out of 38 were females. This shows that female have higher incidence of synovial tuberculosis (extra pulmonary tuberculosis) as compared to males. Similarly, in the studies of Gaur P et al (2017)[13] and Denkinger C et al (2014)[16] which have higher reporting and incidence of extra pulmonary tuberculosis among females. And also in the study of Alwani H et al (2020)[10] in high prevalence countries, women of reproductive age have higher rate of progression to disease than men in this age group.

In the present study, majority of patients belongs to lower socio-economic status in which most of the cases lies within lower middle class (37%) followed by upper middle (34%), upper lower (20%) and remaining were at the extreme i.e. lower class (6%) and upper class (3%) and most of TB positive cases belongs to lower socio economic status which was similar to the results in the study of Gupta D et al (2004).[17] In the present study most of the case of tubercular

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synovitis belongs to underweight (BMI <18.5 kg/m2) followed by healthy weight group (BMI of 18.5-24.9 kg/m2) this conclude that tubercular synovitis are more common in malnourished population with low BMI which is similar to the study of Alwani H et al (2020)[10] observed that most of the patients of extra-pulmonary tuberculosis had evidence of malnutrition BMI 17.6 + 2.8 kg/m2

And in the study of Ockenga J. et al (2023)[18] noted that malnutrition is a risk factor for acquiring TB and TB- associated malutrition can render treatments less effective and worsen prognostic outcomes. In the present study out of 4 patients having history of TB, 3 patients became positive for Synovial tuberculosis in biopsy and 2 patients in CBNAAT (75% of the patients having history of contact developed TB according to biopsy, the gold standard test). Similar finding was observed by Alwani H. et al (2020)[10] they noted that 75% of the cases that had a history of contact in past developed disease. 1 patient of tubercular synovitis was having history of diabetes mellitus in the study of Srivastava AK et al. (2015)42 they mentioned that 10 cases (7.69%) out of 130 had history of DM which is highest among all the comorbid condition. In our study remaining patients do not have any history of comorbidity.

5. CONCLUSION

So, we conclude that the previous history of TB and DM could predispose patients to the development of EPTB. We also noted that most of the case of tubercular synovitis was having elevated levels of ESR, reactive CRP and increased level of protein and cell count in synovial fluid analysis with lymphocytic predominance. As histopathology reporting remains the mainstay for diagnosis of tubercular synovitis, CBNAAT can be a useful tool in diagnosis of synovial tuberculosis cases because of its simplicity, rapid turn-around time and ability to simultaneous detection of Rifampicin resistance. CBNAAT can help in timely initiation of effective treatment in synovial tubercular cases and Rifampicin resistant tuberculosis. The easy availability makes it ideal for the Indian health care setting. To sum up, CBNAAT or Gene Xpert assay has the advantage of less turn-around time (2 hours) for detecting tuberculosis and Rifampicin resistance with moderate sensitivity and high specificity in synovial sampling.

6. REFERENCES

1. Smith MD. The normal synovium. Open Rheumatol J, 2011; 5:100-6.
2. Goyal T, Paul S, Choudhury AK, Kalonia T. Monoarticular synovitis of knee: dealing with the dilemma. SICOT-J. 2020;6.
3. Sanjay MG, Radha PM, Babu NP, Sushant M, Jitesh A. Genotypic diagnosis of extrapulmonary tuberculosis-CBNAAT a novel tool. Med Pulse Int J Med. 2017;4(2):79-82.
4. World Health Organization : Tuberculosis, who.int, October 2022.
5. https://worldhealthorg.shinyapps.io/tb_profiles
6. Bairwa MC, Banera MK, Fatehpuria CM. Utility of cartridge based nucleic acid amplification test in the diagnosis of extra pulmonary tuberculosis. Int J Adv Med. 2019; 6(6):1801-1807.
7. Oommen S, Banaji N. Laboratory diagnosis of tuberculosis: Advances in technology and drug susceptibility testing. Indian Journal of Medical Microbiology. 2017;35(3):323.
8. Jain AK, Jena SK, Singh MP, Dhammi IK, Ramachadran VG, Dev G. Evaluation of clinico-radiological, bacteriological, serological, molecular and histological diagnosis of osteoarticular tuberculosis. Indian Journal of Orthopaedics. 2008;42(2):173–177.

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9. Garg RK, Somvanshi DS. Spinal tuberculosis: A review. Journal of Spinal Cord Medicine. 2011;34(5):440–454.
10. Alwani H, Subhankar S, Rao CM, Kar S, Kumar S, Bal HB, Das D, Dash DP. Role of CBNAAT in the diagnosis of extra-pulmonary tuberculosis: Experience from a tertiary care hospital in India. Indian J Chest Dis Allied Sci. 2022 Apr 8;64:9-14.
11. Bairwa MC, Banera MK, Fatehpuria CM. Utility of cartridge based nucleic acid amplification test in the diagnosis of extra pulmonary tuberculosis. Int J Adv Med. 2019; 6(6):1801-1807.
12. Connolly M, Nunn P. Women and tuberculosis. World health statistics quarterly. Rapport trimestriel de statistiques sanitaires mondiales. 1996 Jan 1;49(2):115-9.
13. Gour SM, Munje RP, Babu NP et al. Genotypic diagnosis of extra pulmonary tuberculosis – CBNAAT a novel tool MedPulse International Journal of Medicine November 2017; 4(2) : 79-82.
14. Karki P, Kodali R. Synovial Fluid Genexpert Quietus Diagnostic Jostle–A Case Report and Algorithmic Approach to Monoarthritis. Indian Journal of Rheumatology. 2022 Dec 1;17(4):412-5.
15. Hillemann D, Rüsch-Gerdes S, Boehme C, Richter E. Rapid molecular detection of extrapulmonary tuberculosis by the automated GeneXpert MTB/RIF system. Journal of clinical microbiology. 2011 Apr;49(4):1202-5.
16. Denkinger CM, Schumacher SG, Boehme CC, Dendukuri N, Pai M, Steingart KR. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis. European Respiratory Journal. 2014 Aug 1;44(2):435-46.
17. Gupta D, Das K, Balamughesh T, Aggarwal N, Jindal SK. Role of socio-economic factors in tuberculosis prevalence. Indian Journal of Tuberculosis. 2004;51(1):27-32.
18. Ockenga J, Fuhse K, Chatterjee S, Malykh R, Rippin H, Pirlich M, Yedilbayev A, Wickramasinghe K, Barazzoni R. Tuberculosis and malnutrition: the European perspective. Clinical Nutrition. 2023 Apr 1;42(4):486-92.
19. Shrivastava AK, Brahmachari S, Pathak P, Kumar R, Sainia T, Patel U, Mandil A. Clinico-epidemiological profile of extra-pulmonary tuberculosis in Central India. Int J Med Res Rev. 2015;3(2):223-30.