

# TLC, ESR, CRP & Procalcitonin: Markers for prognosis in Musculoskeletal infections of Children

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DOI: 10.47750/pnr.2023.14.03.203

## Abstract

**BACKGROUND:** Musculoskeletal infections in pediatric age group account for 23% of the total infections. The most common musculoskeletal infections in children are Osteomyelitis and Septic Arthritis. Such children with underlying present with fever, inflammation, failure to thrive, refusal to feed, inability to bear weight, limp, Limb pain, swelling, restricted motion at joints. Total Leucocyte Count (TLC), Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are among the oldest laboratory tests used to detect inflammation in the body. Procalcitonin (PCT), a propeptide of calcitonin, is an important host response biomarker indicative of infection. In this context this study was done to evaluate change in severity of inflammation in patients of musculoskeletal infections.

**MATERIAL AND METHODS:** Patients who attended ortho OPD were included after they were diagnosed as a case of musculoskeletal infection. Treatment was started and baseline investigations were done. Medical/ Surgical treatment was given. TLC, ESR, CRP & PCT were checked at the time of admission and at 3 months, 6 months and 9 months for treatment outcomes.

**STATISTICAL ANALYSIS:** Both Descriptive and inferential statistics were applied to the data. Demographic characteristics were expressed as proportion. The values of TLC, ESR, CRP & PCT were compared using paired t test. All statistical analysis was done at 5% significance.

**RESULTS:** A total of 130 patients were evaluated over a period of 9 months of which 63% were male, 37% were female. Abscesses were in 37% cases, 28% were diagnosed as Septic Arthritis, 18% were Osteomyelitis, 9% were transient synovitis followed by 4% skeletal tuberculosis, 3% cellulitis and 1% tetanus. The overall decline in all the four inflammatory markers over 9 months was statistically significant ( $p < 0.00001$ ).

**CONCLUSIONS:** TLC, ESR, CRP & Procalcitonin are good indicators of musculoskeletal infections. Over a period of 9 months with medical/surgical treatment, these markers declined gradually indicating that the infection has subsided.

**Keywords:** Musculoskeletal infections, inflammation, ESR, CRP, Procalcitonin.

## INTRODUCTION

Musculoskeletal infections in pediatric age group account for approximately 23% of the total infections.[1] They are prone to infections because of naive immune system, umbilical sepsis, skin infections, circumcisions, eczematous lesions. Prematurity, caesarian section, neonatal jaundice and invasive procedures during hospitalization like venipunctures also predispose them to acquire infections. Nutritional deficiency of mother is also attributed in some of the infants acquiring infections.[2] In childhood the blood dyscrasias, hemoglobinopathies, intestinal infestations, exposure to unhygienic conditions, child abuse, viral and protozoal infections, trauma, chronic renal failure, patients treated in PICU, presence of any orthopaedic hardware (plates, screws, wires, anchors), nutritional deficiencies arising out of rapid growth, dietary prejudices and preferences are predisposing factors for infection (Lew DP et al, 2004). In addition to this in a smaller subset of patients lazy leucocyte syndrome, leucocyte adhesion disorders, chronic granulomatous disease, myeloperoxidase deficiency, chediak higashi syndrome, chemotactic disorders, job's syndrome are the responsible causes of infection. (Schuppen et al, 2012).

The most common musculoskeletal infections in children are Osteomyelitis and Septic Arthritis.

Total Leucocyte Count (TLC), Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are among the oldest laboratory tests still in use. Both bloods tests are used to detect inflammation in the body. Inflammation can present as either acute (ie, from injury or infection) or chronic. Multiple cells are involved in the release of inflammatory mediators, which combine to generate pain in joints, muscle, discs, ligaments, tendons, fascia, etc. Since pain and inflammation are often intertwined, these two tests can be indicators that pain and inflammation are present, as well as be markers of treatment effectiveness.

## MATERIAL & METHODS:

A total of 130 pediatric patients who attended ortho OPD in GMC Jammu were included after they were diagnosed as a case of musculoskeletal infection. The patients diagnosed with infection due to implant failure have been excluded. Treatment was started at our centre, inflammatory markers were checked which mainly included TLC, ESR, CRP and Procalcitonin. Medical/Surgical treatment was given. The above said markers were checked at the time of admission, 3 months, 6 months & 9 months for treatment outcomes.

Statistical Analysis:

Both descriptive and inferential statistics were applied to the data. Demographic characteristics such as gender and type/site of infection were expressed as proportion. The values of ESR, CRP, PCT and TLC were compared with the baseline using the repeated measures one way anova test. All statistical analysis was done at 5% significance on SPSS VERSION 25.

## RESULTS:

A total of 130 patients in pediatric age group were selected after applying the inclusion and exclusion criteria from the Orthopedics OPD, GMC Jammu and Pediatric OPD, SMGS Hospital, Jammu.

Of the total 130 patients 63% were males whereas 37% were female patients (Table 1, Fig 1).

Table 1: Overall Gender Distribution of patients

Sex	No. of Cases	Percentage (%)
MALE	82	63
FEMALE	48	37
<b>TOTAL (n)</b>	<b>130</b>	<b>100</b>

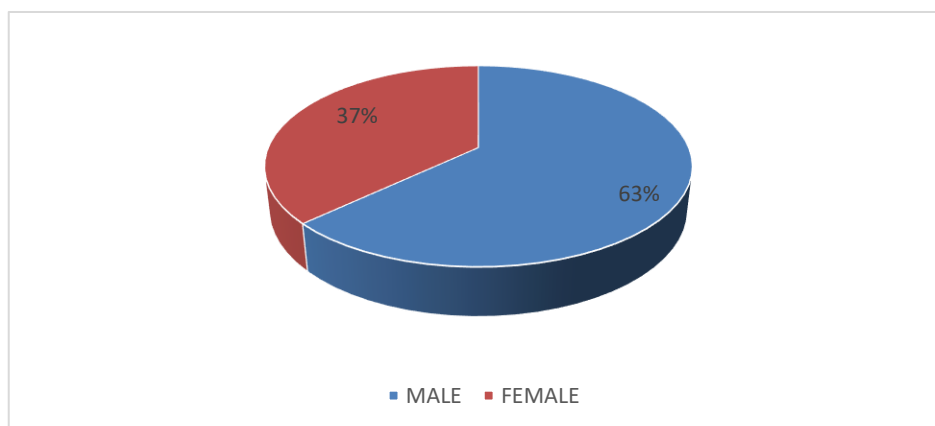


Figure 1 - Pie chart depicting gender distribution

The patients were diagnosed and classified on the basis of Signs, Symptoms and Radiography at presentation into the different types of musculoskeletal infections. We found abscesses in 37% cases, 28% were diagnosed as Septic Arthritis, 18% were Osteomyelitis, 9% were transient synovitis followed by 4% skeletal tuberculosis, 3% cellulitis and 1% tetanus (Table 2, Fig 2)

Table 2: Diagnosis at presentation of patients

Diagnosis		No. of Cases	Percentage (%)
Abscesses	Superficial	18	37
	Deep	30	
Septic Arthritis		36	28
Osteomyelitis	Acute	17	18
	Chronic	6	
Transient Synovitis		12	09
Skeletal Tuberculosis	Hip	2	04
	Spine	3	

Cellulitis	04	03
Tetanus	02	01
<b>TOTAL (n)</b>	<b>130</b>	<b>100</b>

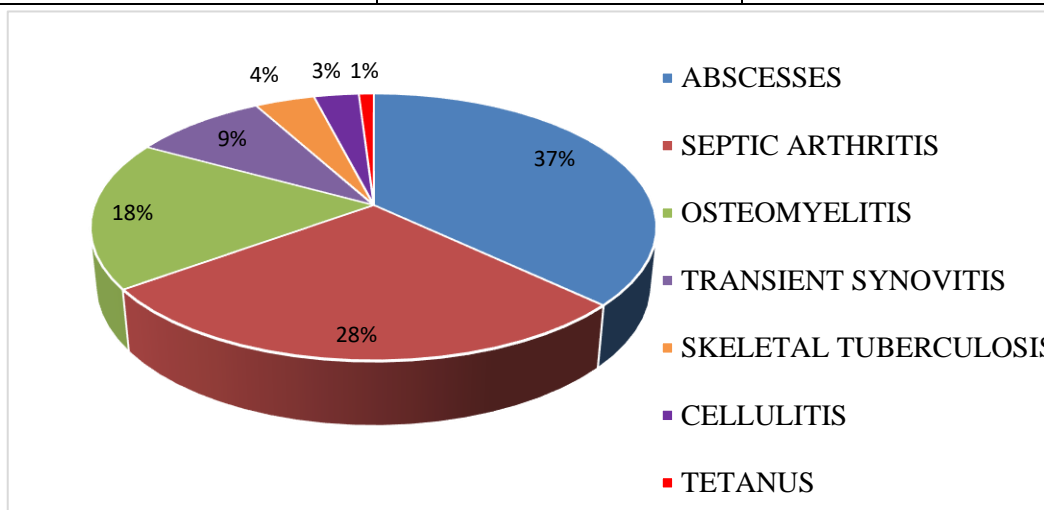


Figure 2 - Pie chart depicting diagnosis at presentation

Table 3- Cases with different ranges of inflammatory markers in Osteomyelitis on admission

Inflammatory Marker	No. of cases with normal values	No. of cases with high values	No. of cases with low values
TLC	11	12	0
ESR	01	22	0
CRP	0	23	0
PCT	08	15	0

Table 4- Cases with different ranges of inflammatory markers in septic arthritis on admission

Inflammatory Marker	No. of cases with normal values	No. of cases with high values	No. of cases with low values
TLC	28	08	0
ESR	10	26	0
CRP	21	15	0
PCT	26	10	0

Inflammatory Markers TLC, ESR, CRP, Procalcitonin were evaluated in all the patients to evaluate the severity of infections. They were recorded at baseline, 3 months, 6 months and 9 months after diagnosis of musculoskeletal infection.

Mean Total Leucocyte Count was  $10623.92 \pm 1966.95/\text{mm}^3$  at baseline,  $7768.46 \pm 1700.89/\text{mm}^3$  at 3 months,  $6732.29 \pm 1488.47/\text{mm}^3$  at 6 months and  $7018.46 \pm 1339.08/\text{mm}^3$  at 9 months whereas Erythrocyte Sedimentation Rate was calculated as  $112.36 \pm 5.0\text{mm/hr}$  at baseline,  $29.87 \pm 24.44\text{mm/hr}$  at 3 months,  $16.3 \pm 7.04\text{mm/hr}$  at 6 months and  $16.74 \pm 2.23\text{mm/hr}$  at 9 months respectively.

C Reactive Protein was  $41.86 \pm 25.94\text{mg/dl}$  at baseline,  $7.41 \pm 8.40\text{mg/dl}$  at 3 months,  $1.51 \pm 2.42\text{mg/dl}$  at 6 months and  $16.74 \pm 2.23\text{mg/dl}$  at 9 months respectively. Procalcitonin levels were evaluated as  $0.097 \pm 0.063\text{ng/dl}$  at baseline,  $0.079 \pm 0.007\text{ng/dl}$  at 3 months,  $0.075 \pm 0.007\text{ng/dl}$  at 6 months and  $0.075 \pm 0.006\text{ng/dl}$  at 9 months respectively.

The overall decline in all the four inflammatory markers over 9 months was statistically significant ( $p < 0.00001$ ) (Table 5).

Table 5: Progression of inflammatory markers over 9 months

Inflammatory Marker	Baseline	3 Months	6 Months	9 Months	p value
TLC	10623.92 ± 1966.95	7768.46 ± 1700.89	6732.29 ± 1488.47	7018.46 ± 1339.08	<0.00001*
ESR	112.36 ± 5.0	29.87 ± 24.44	16.3 ± 7.04	16.74 ± 2.23	<0.00001*
CRP	41.86 ± 25.94	7.41 ± 8.40	1.51 ± 2.42	0.80 ± 0.07	<0.00001*
PCT	0.97 ± 0.63	0.79 ± 0.07	0.75 ± 0.07	0.75 ± 0.06	<0.00001*

A post hoc analysis was done for all the four markers and line trends were drawn over 9 months (Fig 3a-3d).

The TLC levels dropped statistically significantly from baseline to 3 months and 6 months duration ( $p < 0.001$ ), whereas the decline from 6 months to 9 months was not statistically significant ( $p > 0.05$ ).

Similarly, for ESR & CRP levels the decline was statistically significantly from baseline to 3 months and 6 months duration ( $p < 0.001$ ), whereas the decline from 6 months to 9 months was not statistically significant ( $p > 0.05$ ).

The PCT levels declined significantly till 3 months ( $p < 0.001$ ), whereas the decline from 3 months to 6 months and 9 months was not statistically significant ( $p > 0.05$ ).

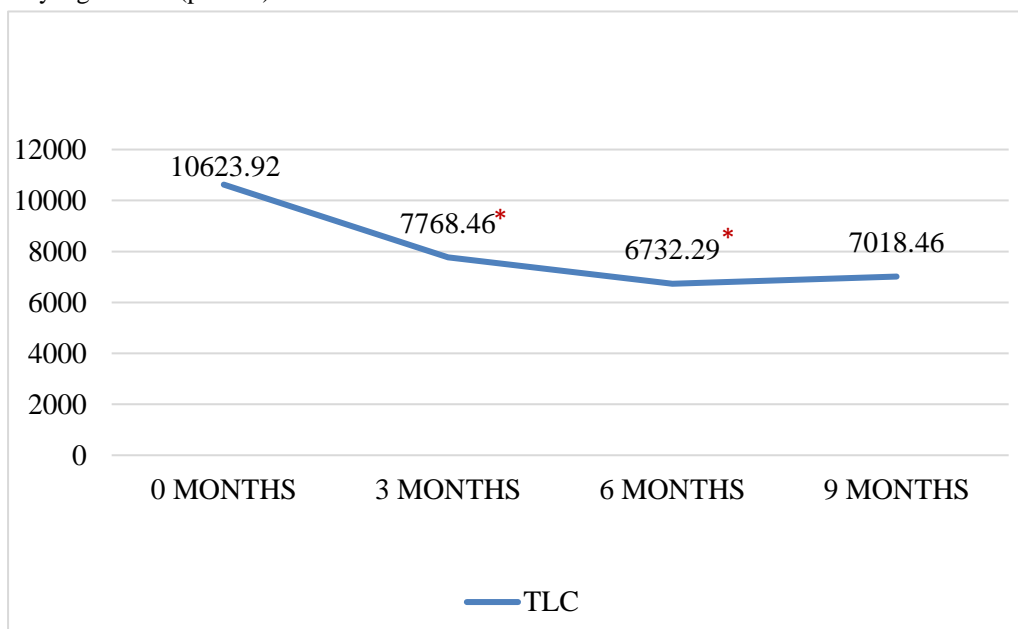


Figure 3a- Line diagram depicting variation in levels of TLC over 9 months



Figure 3b- Line diagram depicting variations in levels of ESR over 9 months

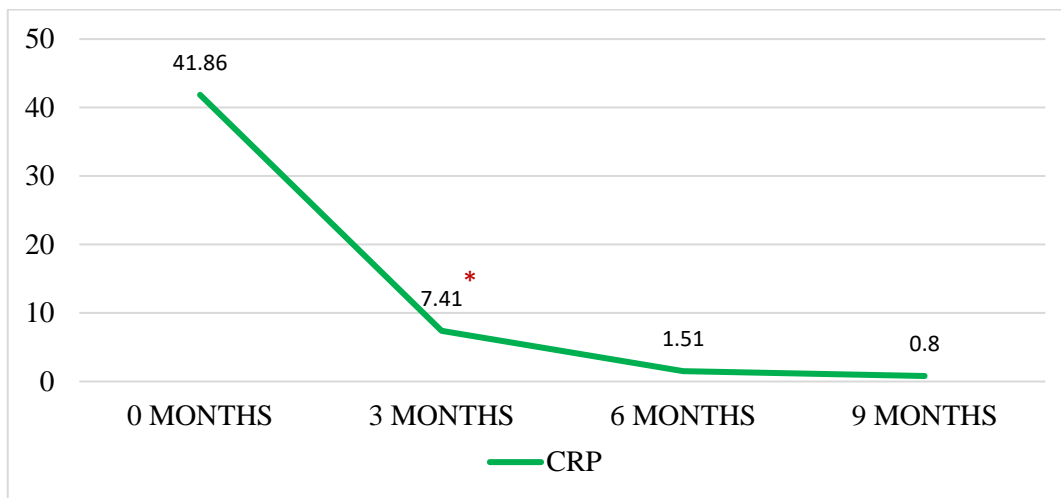


Figure 3c - Line diagram depicting variations in levels of CRP over 9 months

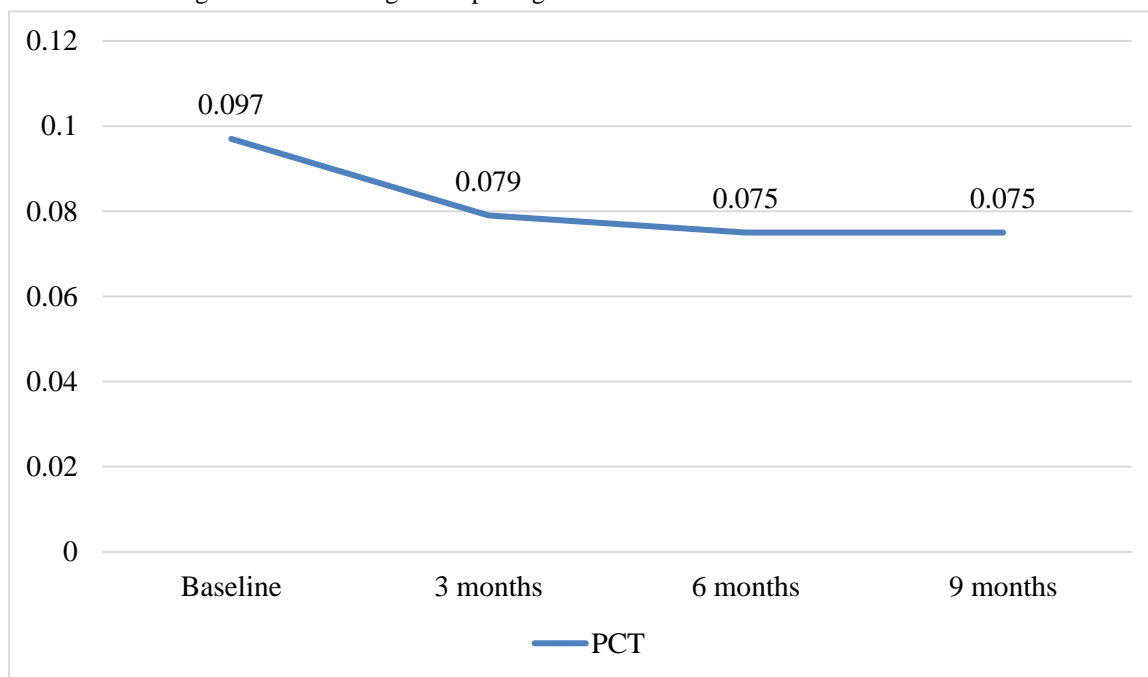


Figure 3d-Line diagram depicting variations in levels of procalcitonin over 9 months

## DISCUSSION:

A musculoskeletal infection is the invasion of an individual's muscles, bones, or joints by disease causing organisms, their multiplication, and the reaction of the individual's body tissues to these organisms and the toxins they produce. [Brinceton Phipps et al, 2021].

The population included in our evaluation included 63% males and 37% females which was similar to the study done by Godley et al, 2015. Muenchhoff M et al stated that strong sexual dimorphism can be observed for susceptibility and disease outcome in many childhood infections, long before sexual maturation and full expression of sexual traits. Sex biases in some infectious conditions vary with age, indicating the influence of differential levels of sex hormones throughout different stages of life. In the first years after birth, the increased risk of infection and the balance between immunotolerance and immunoreactivity is a delicate state of the immune system that might be even more susceptible to minor differences between the sexes than later in adult life. For many pathogens susceptibility is higher in males, which can be partially explained by the observation of stronger Th1 immune responses in females, but higher levels of proinflammatory immunity also predispose females to increased immunopathology in some infections. This simplified generalization, however, does not apply to all infectious conditions, reflecting a more complex interplay between sex and immunity, in addition to the differences in behavior between and toward boys and girls, which require further research.

Giordano M et al, 2019 in their study at a children hospital in Italy found that 52% of the musculoskeletal infection patients suffered from Osteomyelitis followed by 48% had Septic arthritis while only 33% of these had abscesses. This was in contrast

to our study, where 37% suffered from abscess, followed by 28% patients of Septic arthritis, 18% of Osteomyelitis, 9% of transient synovitis, 4% skeletal tuberculosis, 3% cellulitis, 1% tetanus.

In 23 cases of Osteomyelitis, 12 cases had higher than normal values of TLC with 11 cases having normal values. ESR was normal in 1 case only, rest had higher than normal values. CRP was raised in all the 23 cases. PCT was normal in 8 cases with 15 cases having higher than normal values (Table 3). Of the 36 cases of septic arthritis, 28 had normal values of TLC whereas 8 were above normal. ESR was raised in 26 cases, 10 cases had normal values. CRP was normal in 21 cases with 15 having higher values. 26 cases had PCT normal with 10 having raised values (Table 4).

Inflammatory Markers TLC, ESR, CRP, Procalcitonin were evaluated in all the patients to evaluate the severity of infections. They were recorded at baseline, 3 months, 6 months and 9 months after diagnosis of musculoskeletal infection.

There was significant decline in ESR levels from day 0 to post treatment at 3 months, 6 months and 9 months duration ( $p < 0.00001$ )

Similarly there was a significant decline in the CRP levels over 9 months from day of admission ( $p < 0.00001$ ).

Also, there was significant decline in levels of TLC and PCT over a period of 9 months ( $p < 0.00001$ ). Ajmera et al, 2019 stated that sensitivity of ESR in osteoarticular infections on admission was 93%. Using only CRP alone gave slightly better sensitivity of 96%. However, combining these markers gave a sensitivity of 100%.

## CONCLUSION:

In this study, 130 pediatric patients with musculoskeletal infections were evaluated in which 37% were abscesses, 28% septic arthritis, 18% osteomyelitis, 9% transient synovitis, 4% skeletal tuberculosis, 3% cellulitis & 1% Tetanus whereas, it included 63% males & 37% females. TLC, ESR, CRP & Procalcitonin are good indicators of musculoskeletal infections. Over a period of 9 months with medical/surgical treatment, these markers declined gradually indicating that the infection has subsided.

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