Comparison of platelet count in tuberculosis spine to other spine pathology

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Abstract

Purpose Haematological markers currently used to investigate TB spine vary from WCC, Anaemia, ESR and CRP. Platelet count in TB spine as a marker has been inadequately investigated.

Method In this retrospective review, Platelet count in TB spondylitis on admission was compared to patients undergoing other elective spinal surgery (control) preoperatively. Comparisons of the platelets with ESR and the effect of HIV on platelet count in TB spine were also evaluated.

Results 160 TB spine patients showed statistically significant higher platelet count when compared to 210 patients in the control group ($p < 0.001$). 52.5 % patients had a raised platelet count in the TB spondylitis group. Raised Platelet count had a sensitivity and specificity of 52.5 % and 86.2 %, respectively in TB spondylitis. ESR and platelet count had a Pearson correlation $r = 0.31$ ($p < 0.001$). HIV however did not statistically show any difference in the platelet count ($p = 0.12$).

Conclusion A raised platelet count in spinal pathology may be used as an inflammatory marker of TB spondylitis.

Keywords Tuberculosis · Spondylitis · Platelets · ESR · HIV

Introduction

Tuberculosis (TB) has plagued the world for centuries. Words like *Phthisis* [1] (mid-16th century Greek word to ‘decay’) and white plague [2] were used to describe the course of the disease.

Mankind’s unrelenting warfare following identification of the mycobacterium tuberculosis and the era of antibiotics has set the scene for generations to come. In 2012 report, according to the World Health Organisation [3], the global burden of this disease amounts to almost 7 billion people. Nine million new cases of TB were diagnosed in 2011 of which 13 % co-infected with Human Immunodeficiency Virus (HIV). The mortality following TB is 1.4 million people, of which 30 % were HIV positive. TB has second highest mortality rate from a single most infectious agent, following HIV [3].

The prevalence of HIV in the South Africa’s population is approximately 10.6 %. [4]. The overall prevalence of TB spine in South Africa is 948 in 100,000 [5]. According to the World Health Organisation report in 2011, HIV cases co-infected with TB accounted for 82 % in Africa [6]. In our HIV prevalent population, atypical presentations and lack of access to adequate resources makes TB a diagnostic challenge.

Various haematological markers have been used to raise suspicion of TB spondylitis. These markers have also been used prognosticate the efficacy of its treatment. Haematological findings from lymphocytosis, anaemia, a raised ESR and CRP are found in active tuberculosis [7, 8]. Baynes et al. [9] noted reactive thrombocytosis in pulmonary TB. While HIV has been shown to cause thrombocytopenia [10]. The only study done to the best of our knowledge on TB spondylitis and thrombocytosis is by Muzaffar TM et al. Their cohort of 17 patients with TB

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spine had thrombocytosis in 52.9 % [11]. The platelet count at diagnosis of TB spondylitis has not been adequately researched.

The study has two aims. The primary aim is to evaluate the diagnostic role of platelet count and its significance in TB spondylitis when compared spinal conditions other than TB. Secondly to evaluate the effect HIV has on platelet count in the TB spondylitis group.

Materials and method

This is a retrospective review of laboratory results comparing the platelet count in TB spondylitis patients (TB group) on admission and patients with non-TB spinal pathology (Control group) treated at the Groote Schuur Hospital spinal unit and Constantiaberg Hospital from 2003 to 2012.

Approval from the Departmental Research council and Ethics council of University of Cape Town was obtained for this study.

Data collection

In the TB spondylitis group, data of patients were obtained from surgical record database collected by the senior author. These patients had undergone spinal biopsies and/or decompression with or without instrument fusion for TB spondylitis. The South African National Health Laboratory (NHLS) and PathCare Laboratory database were used to accumulate microbiological, histological, haematological markers (Platelets and ESR) and HIV status on admission for the procedure.

Elective surgical patients were used as a control group. Patients who had undergone surgery for non-infective spinal conditions were identified from the senior author's database. These included surgery degenerative spinal pathology, scoliosis, coccydynia, tumour, etc. The NHLS and PathCare lab database were utilised to assemble the admission platelet count.

Inclusion and exclusion criteria

Patients were included in this TB spondylitis group if one or more of the following findings were present, viz. positive Acid Fast Bacilli (AFB) on *Ziehl–Neelsen* stain (ZN), positive TB culture or TB PCR or necrotising granuloma on histology were found. Patients were excluded if the diagnosis of TB was made other than histological or microbiological means. The patients were also excluded if platelet count were not available on the labs database and notes.

In the control group, patients were included in this review if they underwent surgery other than for TB spondylitis. Patients were excluded from the control group if platelet count was not available from the database and notes. In the control group conditions like tumours were not excluded as there is enough evidence from literature showing tumours are more likely to induce thrombocytosis [12]. Hence a statistically significant result will be significant.

Patients were excluded from the review if they were younger than 13 years of age in the TB spondylitis group and the control group. The reason is patients younger than 13 were treated at the Red Cross Hospital, a specialized paediatric unit. At the same time, the diagnosis of TB spondylitis in this cohort was not made on biopsy.

The student *t* test was used as a statistical analysis marker to compare platelet count in both groups and the also in the HIV positive versus negative group. A linear correlation was done between ESR and Platelet count.

Platelet count greater than 400×10^9 per litre in our lab is considered as the upper limit of normal. This value is in keeping with international limits [13, 14]. Using that value as a cut off when comparing TB spondylitis group and the control group the positive predictive value, sensitivity and specificity of platelet count as a diagnostic tool was determined. The Fisher's Exact test was used as an statistical comparison of platelet count of $>400 \times 10^9$ per litre in the TB spondylitis and control group.

Results

160 TB patient's data was included in the review and each one having their platelet count recorded on admission. Of these, 124 patients had documented ESR results. 78 of the 160 patients had known HIV status. The control group included 210 patient's pre-operative platelet count prior to elective surgery.

The breakdown of how the confirmed diagnosis of TB spondylitis was ascertained is represented in Table 1 and Fig. 1.

The average age of TB spondylitis group was 40.5 years (13–79 years, SD 16.2 years) with 69 males (43.1 %) and 91 females (56.9 %). The mean platelet count in the TB

Table 1 Number of patient with TB spine and their respective microbiological and histological results following biopsy

	Positive result	Negative result	Sensitivity (%)
ZN	35	124	22.01258
Histology	126	23	84.56376
Culture	126	32	79.74684
PCR	122	21	85.31469

Fig. 1 Graphics representation of the culture and microbiological results in TB spondylitis

Fig. 2 Control group (age distribution)

spondylitis group was 410×10^9 per litre ($88\text{--}853 \times 10^9$ per litre, SD 138.68). The platelet count was $>400 \times 10^9$ per litre in 84 (52.5 %) patients with TB spondylitis.

The control group average age group was 54.5 years (13–86 years, SD 19.2). Of which 125 were females (59.5 %) and 85 males (40.5 %). The graphic representation comparing both groups age and gender distribution is shown in Figs. 2, 3 4. While the platelet count of the control group has a mean of 294×10^9 per litre ($125\text{--}546 \times 10^9$ per litre, SD 83.0). The student *t* test comparing platelets count in TB spondylitis and with control group was statically significant ($P < 0.001$).

The positive predictive value is 74.3 % with a sensitivity and specificity of 52.5 and 86.2 %, respectively when comparing the TB spondylitis and control group with

Fig. 3 TB spondylitis group (age distribution)

Fig. 4 Gender distribution

platelet count $>400 \times 10^9$ per litre. Table 2 shows the represented data from the comparison between both groups with platelets $>400 \times 10^9$ per litre. The Fisher's Exact of the latter comparison has a *p* value < 0.001 .

In the TB spondylitis group, HIV data was available in 78 cases with 57 HIV negative and 21 HIV positive. In the remaining patients the HIV status was not tested or not available. The average platelets in the TB spondylitis group that was HIV negative is 443×10^9 per litre (SD = 140) and the HIV positive group is 389×10^9 per litre

Table 2 Comparison of the TB spondylitis group and control group with platelets (Plt) greater or less and equal to 400×10^9 per litre

	TB	Control	Total
Plt > 400	84	29	113
Plt ≤ 400	76	181	257
Total	160	210	370

Fig. 5 Representation of pearson correlation of ESR and platelet count in TB spondylitis

(SD = 121). Comparison of the platelets of these groups using a two tailed *t* test shows a *p* value of 0.12.

The ESR results of the TB spondylitis were also obtained from 123 patients who had a mean ESR of 76.2 (SD 36.3). When the ESR was compared to platelets count in the TB spondylitis group the Pearson correlation showed a *r* value of 0.31 (*p* < 0.001) depicted in Fig. 5.

Discussion

Various conditions causes thrombocytosis and some of these are mentioned in Table 3. These conditions should be included of the differential diagnosis of thrombocytosis. Systemic inflammation in response to infectious and inflammatory conditions is the common cause of thrombocytosis. IL6 release has been shown to produce an acute inflammatory cascade in pulmonary TB causing megakaryocytopoiesis [15, 16].

Although thrombocytosis and pulmonary tuberculosis has been described in literature its diagnostic significance in TB spondylitis is not well researched [9]. In fact current literature reviews do not even mention platelets count in TB spondylitis as a consideration [5, 7, 17]. The fact that TB of the spine has a delayed presentation compared to pulmonary TB makes the diagnosis even more challenging.

Table 3 Causes of thrombocytosis

Primary

Essential thrombocytosis
Myeloproliferative disorders

Secondary (reactive)

Inflammatory: infective, rheumatoid arthritis, Inflammatory bowel disease

Surgery

Tumour: osteosarcoma, soft tissue sarcoma

Drugs

Nephritic and nephrotic disease

52.5 % of patients on admission had raised platelets and which was statistically significant when compared to control. Our study suggests that thrombocytosis is common in TB spondylitis. This is supported by Muzaffar et al. [11]. Other consideration in our study may be the use of anti-pyretic agent, anti-tuberculosis medication and thromboprophylactic agents such as heparin are known agents to cause a decrease in platelet count. These have not been accounted for. Thus further suggesting that in TB spondylitis thrombocytosis may be a more common occurrence.

Compared to patients who underwent elective spinal surgery (control group) the TB spondylitis showed a statistically significant raise in platelet count (*p* < 0.001). This suggests that when looking at spinal conditions in general, TB spondylitis is most likely to have a higher platelet count. Unfortunately its sensitivity is as low as a diagnostic marker. Despite this a 73.8 % positive predictive value, 82.6 % specificity and statically significant Fisher's Exact *p* value suggests its use as a high index of suspicion for tuberculosis in spinal pathology, especially in a population with high prevalence of TB.

In the TB spondylitis patients, HIV negative group did not show a statistically significant difference in platelet count than the HIV positive group. There are no similar papers comparing these groups in a TB spondylitis cohort at the time of publication. However Sloand et al. [10] findings in 1004 HIV patients had a 30 % thrombocytopenic prevalence. That paper showed the higher the CD4 count, the higher the platelet count raises. This reflects greater immune response by the HIV negative group when compared to the HIV positive group. Unfortunately our cohort did not differentiate with CD4 counts, anti-retroviral therapy and viral load in the HIV positive group.

On the other hand ESR is known inflammatory marker of active tuberculosis and its prognosticating the response of treatment is well known [5, 18, 7, 11, 19]. Govender et al. [20] 's average ESR value in their 39 HIV positive patients was 91 mm/h. While Guo et al. [21] shows an average ESR of 79.4 mm/h of their 67 TB spondylitis patients. In this study ESR averaged 77.1 mm/h which is

similar to Guo et al. Once again ESR can be used as a valuable indicator of inflammatory process in TB spondylitis.

There was a statically significant linear correlation with ESR and platelets of $r = 0.31$ ($p < 0.01$). This value when compared to Muzaffar et al. $r = 0.6$ has a lower gradient and $p < 0.01$. The Pearson correlation shows platelet counts do increase as the ESR increases and therefore suggesting its significance as an inflammatory marker.

T-Helper Cell 1 (TH-1) and T-Helper Cell 2 (TH-2) activity in active TB has been investigated. TH1 is essential for the attack against intracellular mycobacterium tuberculosis while TH2 has been associated with a poor clinical outcome [20] Cytokine CCL7 is released by platelets causing an increase in TH-2 activity as illustrated by Feng et al. [22]. Platelet count may therefore have prognostic value in the long term and further research needs to be implemented.

Conclusion

Platelets count and ESR may be used as inflammatory markers in TB spondylitis. However, a raised platelets count is non-specific and other causes must be excluded. In TB spondylitis patients, HIV status may not influence platelet count. Despite these investigations a biopsy is mandatory to confirm the diagnosis of TB spondylitis.

The prognostic effect of platelet count has yet to be fully established and further work needs to be done.

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Conflict of interest None.

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