The Effect of HIV on the Microbiology of Adult Patients Presenting with Septic Arthritis at Chris Hani Baragwanath Academic Hospital

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Dr. Loyiso Gqamana

In partial fulfilment for the degree of Master of Medicine. A research report is submitted to the University of the Witwatersrand, Faculty of Health Science.

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DECLARATION

I, Dr. Loyiso Gqamana declare that this research report is my own work. It is submitted for the degree of Master of Medicine in the division of Orthopaedics Surgery, Faculty of Heath Science, University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.

……

Signature of candidate.

Signed on 30/04/2024 in Johannesburg

DEDICATION

This study is dedicated to my wife Stephanie, son Caleb and my mother Nosipho, who have been an immense support system through the many years of preparing and finalising this research report. Their encouragement, prayers and patience never wavered. To the rest of my family and those that have walked with me to prepare me for this time, I am grateful for the motivation and hope that this will motivate others to pursue their goals.

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And last but not least, my sincere gratitude to both my supervisors Dr. M.P. Kgagudi and Dr. M. Jingo. Thank you for the assistance and guidance during the preparations for this research report, it would not have been possible without you.

ABSTRACT

Background: Septic arthritis is an orthopaedic emergency that can result in severe morbidity and mortality if not managed timeously. Risk factor assessment of these patients is crucial in early diagnosis of the disease. Inflammatory septic markers (White cell count, C-reactive protein, and Erythrocyte sedimentary rate) have been found to assist in the process of making an early diagnosis. Human Immunodeficiency Virus (HIV) infection is known as a risk factor for septic arthritis. Immunosuppression that is observed with the HIV infection may lead to low septic marker values, resulting in a delay in confirming the diagnosis of septic arthritis. The markers of HIV infection such as Cluster of Differentiation 4 (CD4+) count and the viral load can be used to assist in the prediction of infection.

Method: We conducted a retrospective study of patients who presented to the orthopaedic department at Chris Hani Baragwanath Academic Hospital (CHBAH) from 01 January 2015 to 30 June 2019 with septic arthritis. The clinical presentation; serological inflammatory marker; retroviral status with CD4+ count and viral load count; and post arthrotomy microbiology, culture and sensitivity were analysed. The sensitivity, specificity and likelihood ratios (LLR) for the inflammatory markers were calculated and compared to data published in the literature. The impact or association of the retroviral status with some of the categorical and continuous variables were assessed, to study if there were any differences in those variables when comparing the HIV-infected and HIV-non-infected patients. Finally, the microbiological growth results were compared between the HIV-negative, HIV-unknown and HIV-positive groups.

Results: The prevalence of HIV-infected patients presenting with an osteoarticular infection was found to be 31.7% in our study population. A median CD4+ count of 281 cells per cubic millimeter with a median Viral Load (VLL) value of 2350 copies per millilitre was observed in our study sample. As a diagnostic test C-reactive protein, was found to have the best sensitivity (95%) and specificity (4.1%) out of all the inflammatory markers studied. However, the Likelihood ratio (LLR) for the diagnosis of septic arthritis by all inflammatory markers studied was low, making them poor diagnostic measures for the diagnosis of septic arthritis.

Across the three groups of retroviral status in our study, i.e. HIV-negative, HIV-positive, and HIV-unknown; a finding of similar microbiological culture and sensitivity was observed. Gram-positive bacteria were cultured in 50% of the cases, with *Staphylococcus aureus* being the commonest bacteria grown. Despite having not occurred commonly pathogens such as Mycobacterium Tuberculosis (MTB), *Acinetobacter Baumani*, and *Haemophilus influenza* were also observed; and they were associated with patients who cultured polymicrobial organisms. Polymicrobial cultures with Gram-negative and atypical micro-organisms were observed to increase the likelihood for morbidity and mortality.

The white cell counts, and erythrocyte sedimentary rate results were tested to be statistically significant with p-value = 0.025 ($p < 0.05$) and p-value 0.034 ($p < 0.05$), respectively. However, HIV status was not shown to have an impact on producing a positive or negative culture post arthrotomy.

Conclusion: There was no difference in the overall cultured microbiology between HIV positive and HIV negative groups presenting with acute septic arthritis. However, it was noted that polymicrobial cultures were usually a combination of gram-negative and atypical bacteria. The latter was associated with HIV co-infection with CD4+ count of less than 200 cells per millimeter. The predictive power of inflammatory markers in making a diagnosis of septic arthritis was statistically significant in the HIV negative than the HIV positive group. All the studied inflammatory markers were seen to have low likelihood ratios.

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NOMENCLATURE

ART Antiretroviral Therapy

AVN Avascular Necrosis

CD4+ Cluster of Differentiation 4+ cell

CHBAH Chris Hani Baragwanath Academic Hospital

CRP C-Reactive Protein

CT Computer Tomographic

ELISA Enzyme-linked Immunosorbent Essay

ESR Erythrocyte Sedimentary Rate

HIV Human immunodeficiency Virus

HREC Human Research and Ethics Committee

IL-10 Interleukin-10

IQR Interquartile Ratio

LDL Lower than detectible level

LLR Likelihood Ratio

MRI Magnetic Resonance Image

MRSA Methicillin Resistant Staphylococcus Aureus

MTB Mycobacterium Tuberculosis

NHLS National Health Laboratory Service

PCR Polymerase Chain Reaction

PCT Procalcitonin

RA Rheumatoid Arthritis

RNA Ribonucleic Acid

SA Septic Arthritis

WCC White Cell Count

1. INTRODUCTION

1.1 Introduction

Septic Arthritis (SA), is an infectious process occurring within the joint, most commonly caused by bacteria (1, 2, 3). However, mycobacteria tuberculosis (MTB), viruses and fungi may also be implicated. All age groups of patients can be affected by this disease from neonates to the elderly. Some of the common risk factors of SA are extremes of age; co-morbidities such as Diabetes Mellitus, Rheumatoid Arthritis (RA), Human Immunodeficiency Virus (HIV); intravenous drug usage; and previous joint surgery (4, 5). Gavet *et al.* found that with advanced age there was an association with worse outcomes, especially in the patients aged above 80 years being treated for septic arthritis (5). In that study mortality rate increased by 9.5% for those aged 80 years and older. The joint infections associated with the increased use of prosthetic joint replacement devices have also presented different challenges for septic arthritis management (5, 6).

In our South African population there is a large number of patients who get admitted with medical conditions that are caused/related to HIV (7, 8). South Africa boasts the largest burden of the HIV epidemic in the world with 7.1 million people living with the virus. HIV infection prevalence is high at 18.9% with only 56% of the adult population being on antiretroviral treatment (8).

South Africa HIV statistics in the year 2021 (8):

1. Adults aged above 15 years living with HIV infection – 7 300 000.
2. Women aged 15 years and above – 4 800 000.
3. Men aged 15 years and above – 2 400 000.
4. New infections 210 000 (2021) declined as compared to 510 000 (2001).
5. Acquired Immunodeficiency Syndrome (AIDS) related deaths for all ages also declined – 66 000 (2018) compared to 280 000 (2006).
6. People receiving Anti-retroviral Therapy (ART) for all ages improved significantly – 74% (2021) compared to 26% (2010).

HIV infection results in progressive depletion and dysfunction of the CD4+ cells coupled with defects in macrophages and monocytes predisposing to infections (9, 10). Modes of transmission include unprotected sexual intercourse; blood transfusions; intravenous drug use; and prenatal and perinatal transmission (10, 11, 12). The laboratory diagnostic tests for HIV include: a serum test, Enzyme-linked Immunosorbent Essay (ELISA) which is a screening test and a confirmatory test with HIV Ribonucleic Acid (RNA) detection with Polymerase Chain Reaction (PCR) test (11, 12). Clinical manifestations of HIV are variable and dependent on the stage of the disease at presentation. With weakening of the immune system, manifestation of opportunistic infections is the norm. The manifestations seen in orthopaedics includes myositis, septic arthritis, osteomyelitis and Avascular necrosis (AVN) (12).

In the literature, a number of studies have sought to describe the burden of SA and the impact it has on the healthcare system. To date, many studies have focused on the pattern of presentation, diagnostic evaluation and treatment in order to decrease the morbidity and mortality associated with SA. However, there is a lack of studies looking at the impact of HIV co-infection and assessing whether there is a change in the natural history of SA in this specific population group (13, 14).

The purpose of our study was to assess the impact of HIV on patients presenting with SA, and to evaluate whether the microbiology and treatments were adequate. With the improvements noted in the access to retroviral drug treatment, the benefits of improved immunity can also be studies to see how CD4+ count and Viral Load (VLL) can play a role in stratifying those patients that may require a different or accelerated treatment protocol to minimise the complications associated with SA.

1.2 Literature Review

1.2.1 Pathophysiology

The pathophysiological process of the joint infection may occur by haematogenous dissemination, spread from a contiguous infection, or by direct inoculation into the native joint (14). The normal joint has protective mechanisms, such as the synovial cell phagocytic activity and the bactericidal activity of the synovial fluid. Diseases that hamper the activity of the synovium may result in poor immune defence system activation in eliminating the causative infection (13, 14). To the latter, joints that have been previously damaged are much more susceptible to micro-organism invasion (13). Damage to synovial membranes of joints leads to neo-vascularisation and an increase in adhesion factors, which all promote an increase in bacterial colonisation and joint infection (13, 14). Bacteria such as *Staphylococcus aureus* (*S. Aureus*) possess properties such as chondrocyte protease which stimulates the host polymorphonuclear leukocyte response. Cytokines and other inflammatory products are then activated resulting in the weakening and destruction of the articular cartilage. Continuation of the destructive process leads to pannus formation and a large joint effusion ensues, which further impairs the blood supply resulting in necrosis of the bone (see Figure 1.1).

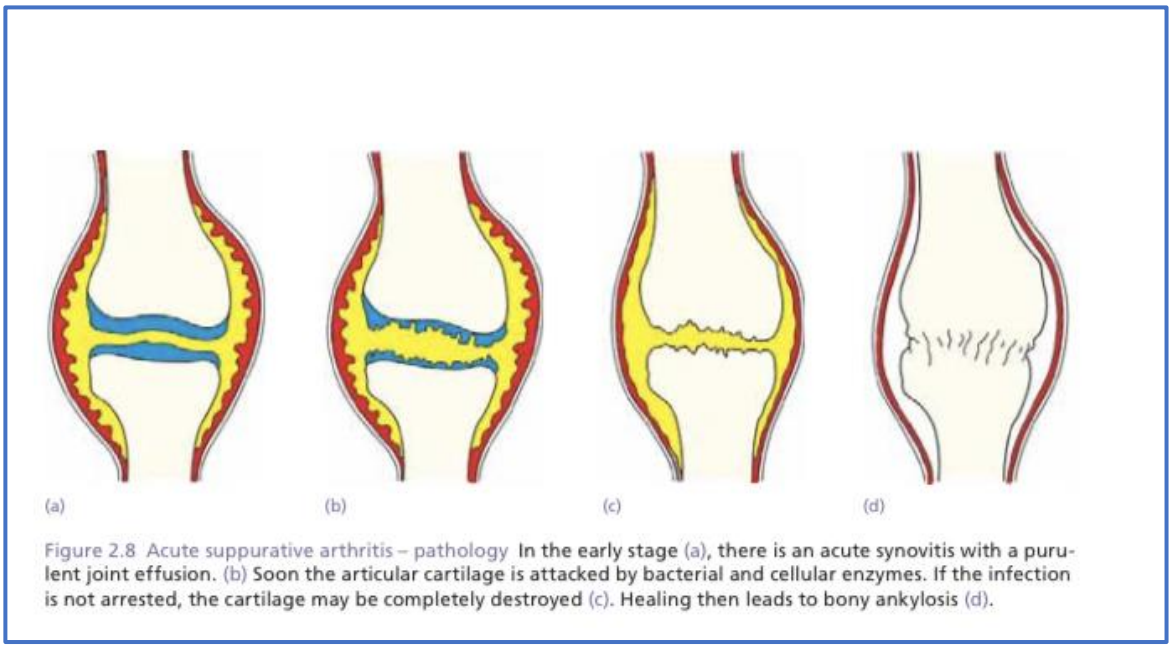

Figure 2.8 Acute suppurative arthritis – pathology In the early stage (a), there is an acute synovitis with a purulent joint effusion. (b) Soon the articular cartilage is attacked by bacterial and cellular enzymes. If the infection is not arrested, the cartilage may be completely destroyed (c). Healing then leads to bony ankylosis (d).

Figure 1.1: Acute suppurative arthritis – pathology (adapted from Apley and Solomons) (15) where:

(a) Acute synovitis with purulent joint effusion.

(b) Articular cartilage is attacked by bacterial and cellular enzymes.

(c) Ongoing infection results in cartilage completely destroyed.

(d) Healing then leads to bony ankylosis.

1.2.2 Diagnosis

The diagnosis of SA is confirmed by joint aspiration and fluid and tissue analysis. It has been noted that it is important to take the microbiological samples prior to the administration of any antibiotics (16, 17, 18, 19). A rapid and accurate diagnosis is crucial in order to isolate a true joint infection from other similarly presenting pathologies such as rheumatoid arthritis, gout, chondrocalcinosis, to avoid delays in management (20, 21, 22, 23, 24). On presentation the patient can have the following symptoms: a painful swollen joint, the inability to weight bear, and/or pyrexia. Nel *et al.* showed that SA as a cause of a swollen joint was significantly high at 48% in South Africa when compared to the rate of 8% in the Israel and 33% in the United Kingdom (25). Laboratory examinations such as elevated White Cell Count (WCC), Erythrocyte Sedimentary Rate (ESR), or C-reactive Protein (CRP) may further suggest the presence of joint infection, although these tests have a low specificity (26, 27, 28) With regards to radiological investigations, X-rays will show some degree of soft tissue swelling, joint space widening and most often no bony changes, especially early stages. However, a normal plain

radiograph does not rule out SA. Ultrasonography is useful in assessing and quantifying the joint effusion and in aiding in arthrocentesis of suspicious joints (27). Computer Tomographic (CT) scan with contrast and Magnetic Resonance Imaging (MRI) have more sensitivity suggesting the diagnosis of septic arthritis; they show early synovial enhancement and presence of a joint effusion. Joint aspirations are used to make a definitive diagnosis and to isolate the causative micro-organism for the initiation of targeted antimicrobial therapy. Joint aspiration is performed under sterile conditions, either as an open incisional arthrotomy or arthroscopically (28, 29, 30, 31, 32). Johns *et al.*, showed that arthroscopically treated patients had early post-operative mobilisation, fewer wound complications and shorter admission duration as compared as to those who had an open procedure (28).

Definition of SA by Kocher *et al.* was made based on presence of the following parameters. Although described for use in the paediatric population, it has been commonly used to infer the diagnosis SA in adult patients (29):

- Positive micro-organism culture growth from arthrocentesis
- Positive micro-organism culture growth from arthrotomy sample
- Synovial WCC of more than 50 000 cells/mm^3
- Positive blood cultures

Newman described a diagnostic criterion for SA, where cases diagnosed with SA fell into the following categories (33):

Group A: Positive synovial fluid cultures.

Group B: Positive blood cultures with negative synovial cultures.

Group C: Negative cultures due to process of antibiotic but purulent drainage of the knee joint.

Group D: Definitive radiological or post mortem diagnosis of septic arthritis.

Staphylococcus aureus is widely recognised as the single commonest cause of SA. It is responsible for 50% to 60% of these infections (33,34). The second most common cause of SA is *Streptococci,* accounting for up to 20% of all cases, with gram-negative bacilli accounting the least for 5 – 10% of bacteria cultured. SA is more common in patients with HIV co-infection compared to HIV non-infected individuals (34). However, the microbiology organisms cultured were similar between the HIV negative and HIV positive groups, with *S. Aureus*

infection being the commonest micro-organism isolated followed *Streptococcal* infection (34, 35). In HIV-positive patients with SA, Pretell-Mazzini *et al*., found that in 68% of the cases the causative organism was *S. Aureus* or *Streptococcus* species (9). Gram negative aerobic bacteria are mostly seen in the very young, the elderly, diabetics, immuno-suppressed and intravenous drugs abusers. Polymicrobial joint infections with anaerobic microbes are usually as a consequence of trauma or abdominal infections (35, 36, 37). Although the rate was not quantified, literature also showed that the HIV-positive group had a higher rate of atypical micro-organisms such as gram-negative bacilli, and Mycobacterium tuberculosis (36, 37).

1.2.2.1 Diagnostic serological markers – WCC, CRP, AND ESR

There are similarities in clinical presentations SA and crystal arthropathies, with an increase in ESR and CRP seen in both the former and the latter. The value of WCC and ESR in the diagnosing SA are important enough that it has been added to the Kocher diagnostic criteria along with fever and inability to weight bear. Although having no validated utility in adult diagnosis of SA, it is widely used for the paediatric group diagnosis for patients with suspected for SA (37, 38).

Laboratory tests with a sensitivity and specificity of more than 90% serve as rapid suggestive tests while waiting for the definitive culture results. WCC, ESR and CRP although valuable as biomarkers have been shown to have a low sensitivity and specificity for SA. Longs *et al*., showed that WCC had a sensitivity of 42 – 90%, a sensitivity of 66% for ESR (ESR > 15 mm/hr) and 90% (ESR > 30 mm/hr), while CRP had a sensitivity of 90% for CRP values above 10 mg/L. Novel markers that may aid in the diagnosis of SA are on the rise, namely Procalcitonin (PCT) levels, calprotectin levels, lactate and glucose ratio, delta neutrophil index and Interleukin 10 (IL-10) (38). Weston *et al.*, showed that the former laboratory marker (WCC, ESR, CRP) were usually lower to normal in HIV positive patients and that IL-10 (a marker of immunodeficiency) was seen to be much higher in the HIV positive group (38).

1.2.3 Treatment

Early targeted antimicrobial therapy is paramount in order to reduce the morbidity and mortality associated with SA (38, 39). There is usually a delay in isolating the causative micro-organism after arthrocentesis and or blood culture samples, therefore empiric treatment is usually initiated based on the commonest micro-organism in that clinical context. Negative cultures may be due to initiation of antibiotics prior to synovial fluid sampling and/or inadequate laboratory plating and growth requirements (39). Cloxacillin is the empiric antibiotic of choice as it provides cover for the common *Staphylococcus* species. However, Nel *et al.* showed that Cloxacillin empirically only covered 32% of isolated micro-organisms. A study with 125 patients at Steve Biko Academic Hospital, found gram-positive cultures in 53% - *S. Aureus* was found in only 25% of cases. Multi-drug resistant gram-positive cultures were isolated in 38% of those cases, with those bacteria requiring Vancomycin treatment. Gram-negative cultures made up to 36% of total isolates and the remainder were anaerobic micro-organisms (25).

Cho *et al.*, described targeted antimicrobial therapy for different microbials cultures. *Staph. Aureus* isolates were sensitive to Cloxacillin or Cefazolin; *Methicillin Resistant Staphylococcus Aureus* (MRSA) to Vancomycin, Streptococcal species to Penicillin G, gonococcal diplococci (N. gonorrhoea or N. meningitis) to Ceftriaxone and gram-negative bacillus to Ceftriaxone or Ceftazidime (40). Treatment of patients with negative cultures included the combination of vancomycin and a third-generation cephalosporin. The treatment duration described in literature is that of targeted intravenous targeted antimicrobial treatment for two weeks followed by oral targeted antimicrobial treatment for a further 4 weeks; total treatment duration of six weeks. Patient's treatment responsiveness being determine by clinical improvement and decreasing septic markers (42).

A paucity of data describing the influence of HIV on the micro-organism spectrum of SA in the adult populations exists to date. Robertson *et al*. reported that HIV played a role in the prevalence of SA and osteomyelitis in the paediatric population (40). In their study 21.6% of the total number of patients were found to have HIV co-infection. *Streptococcal pneumonia*, requiring broad-spectrum antibiotics, were isolated in 66.7% of the HIV infected group *versus* 9.7% in the non-HIV group (40).

1.2.4 Prognosis

Mortality rate despite antibiotic usage in SA is between 7% and 15%, and a third of patients presenting with SA develop a morbidity secondarily. This morbidity and mortality increases with age, co-morbid conditions and a pre-existing joint disease of the affected joint (41, 42). *Neisseria* is rarely associated with mortality, whereas infections with *Staphylococcus* carry a mortality rate that is concerning. Complications of SA include osteomyelitis, osteonecrosis, systemic sepsis, leg length discrepancies and death.

1.3 Study Aim and Objectives

The aim of the study is to review and analyse the effect of HIV on the microbiology of adult patients presenting with SA.

The objectives of this study were to:

- To identify and document the commonest micro-organism cultured in SA.
- To compare the cultured micro-organisms between the HIV-infected and the non-HIV infected individuals.
- To compare the negative culture rates in HIV-negative *versus* HIV-positive patients.

1.4 Study Relevance.

HIV places a massive burden on the South African health system. Stringent HIV treatment campaigns were created in order to prevent new cases of infection as well as improving the initiation, rollout and compliance to the treatment. There is a need to assess the evolution of diseases such as SA, within the HIV-infected individual in relation to clinical outcome. The study aims to look at whether the treatment guidelines need to be tailored differently in patients with HIV infection; assessing whether this patient group is at risk of atypical features of SA. Whether the demographics, presentation, investigation results – septic marker, nature of cultured micro-organism and their respective antibiotic drug resistance profiles.

CHAPTER 2

2. METHODOLOGY

2.1 Research question

What is the microbiology profile of patients diagnosed with HIV presenting with SA at Chris Hani Baragwanath Academic Hospital (CHBAH)?

2.2 Null hypothesis

There is no difference in microbiology between HIV-negative and HIV-positive presenting with SA at CHBAH.

2.3 Research design

This retrospective study examined the microbiology of the arthrotomy specimens taken from patients presenting at CHBAH with acute SA. A review of patients admitted from the 01 January 2015 to 30 June 2019 was carried out, included was the clinical presentation and serological biomarkers that assisted in making the diagnosis of SA. Ethics clearance was obtained from the Human Research Ethics Committee (HREC), Medical, University of the Witwatersrand (Clearance Number: **M230274**).

2.4 Materials and Methods

Patients presenting at the Acute and Emergency unit at CHBAH with a suspected presentation of SA, are triaged and referred to the Orthopaedics unit. Here patients are assessed, and relevant investigations are done in order to prove the suspected diagnosis. The investigations performed on admission include: bloods (WCC, CRP, ESR plus minus a blood culture), and X-rays for the affected regions and a chest X-ray. Admitted and consented patients after diagnosis underwent surgical management and microbiological tests were ran for confirmation of the diagnosis and causative agents. For the determined study period, a data sheet (see Appendix A) was designed in to assist in retrospectively collecting the necessary demographic; serological; radiological; and the outcome microbiological results.

2.5 Sample size and selection criteria

The study sample consisted of all patients presented at CHBAH with SA during the study period, those that met the inclusion criteria were captured after collating various sources for authenticity. Using the National Health Laboratory Service (NHLS) system, at the end a total of 183 patients were included in the final sample size for our study.

The inclusion criteria for the study:

- Adult patients of both sexes that presented with a suspected diagnosis of SA to the CHBAH Acute and Emergency unit.
- Patients with new or recurrent history of SA.
- Patients with known and unknown retroviral disease status.
- Patients with a positive and negative microbiological culture results post arthrotomy sampling.

The exclusion criteria for the study:

- Patients with previous arthroplasty surgery
- Patients post arthrotomy with confirmed diagnosis of gout and or pseudogout.

2.6 Data Collection

Particularly for our study, the results of interest were the WCC, CRP and ESR values on admission; HIV status; and the culture results post arthrotomies of all joints. The HIV status of patients that had been previously tested and the results reflecting on the NHLS system as positive or negative, and those without results were categorised.

The arthrotomy results captured were documented as specimens that either had a positive or negative culture result. For positive culture specimen, the microbiology was identified, and drug sensitivity were documented. The negative culture specimens were also used, to compare the rate of negative specimen culture in SA and in comparing the difference between the HIV-positive and HIV-negative groups. A study specific data sheet was created for statistical analysis (see Appendix A). Data from admission books and theatres notes were also extracted to improve data quality.

2.7 Data Analysis

The data collected was entered onto the Microsoft Excel spread sheet and was analysed using the Stata version 17.0. The description of the demographics and presentation of the participants was the first objective of the study – frequency, proportions and percentages were reported for all the categorical variables. Variables included: gender, joint involved, HIV status, and arthrotomy culture results. The numerical variables (i.e. age, WCC, CRP, ESR, CD4+ and VLL) median, mean and standard deviation were reported. The next objective was to the analyse the differences between the HIV positive and the HIV negative group with regards to the presentation of SA, and this was done by comparing the following parameters:

Continuous variables both groups: age distribution, WCC, CRP, ESR, CD4+ count and VLL were assessed for their influence on diagnosis of SA. Emphasise was on the microbiological culture and antibiotic sensitivity rates. The serological diagnostic markers sensitivity, specificity and likelihood ratio were calculated.

Categorical variables were used to compare for any difference in the following categories:

- If HIV status had an effect on the culture rates?
- The HIV status effect with regards to the microbial cultures, to assess the demographics of the cultures seen and frequency of atypical cultures that were present?

2.8 Limitations

The sample size is more influenced by the methods of data capturing than the frequency of patients presenting with SA. This will require the need to use of multiple sources including admission notes, theatre notes and laboratory results *via* NHLS system etc. As this was a retrospective study, some patients could not be used as part of the study as they were missing important variable that were required.

CHAPTER 3

3. RESULTS

Patients' demographic data was collected and analysed. The serological and arthrotomy sampling results were analysed to assess the accuracy rates of diagnostic tests for SA and the impact of HIV status on the disease and therefore the latter tests.

3.1 DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS

A total of 183 patients were included in the study as they were diagnosed with SA at CHBAH between 01 January 2015 and 30 June 2019 were included in the study. Of this cohort, 22 (12.1%) were initially diagnosed by the internal medicine department prior to orthopaedic referral. All patients had a definitive arthrotomy that was performed under sterile theatre conditions. Of these patients 18 (9.8%) required a relook arthrotomy, for re-accumulation of joint fluid.

Tables 3.1 and 3.2 as well as Figure 3.1 below show the demographic characteristics of the patients that were collected for the study. The following characteristics were included: age, sex, anatomical joint involvement.

3.1.1 Age and sex of patients

Table 3.1: Summary of the gender characteristics of the study.

Sex	**Frequency**	**Percentage (%)**
Male	123	67.21%
Female	60	32.79%
TOTAL	**183**	**100.00%**

Table 3.2: Characteristics of the patient's age in the study.

Number *(n)*	**Mean (years)**	**Standard deviation (years)**	**Minimum age (years)**	**Median age (years)**	**IQR**	**Maximum age (years)**
183	42.28	15.85	18	41	30 – 50	88

IQR = interquartile range, and *n* = sample size

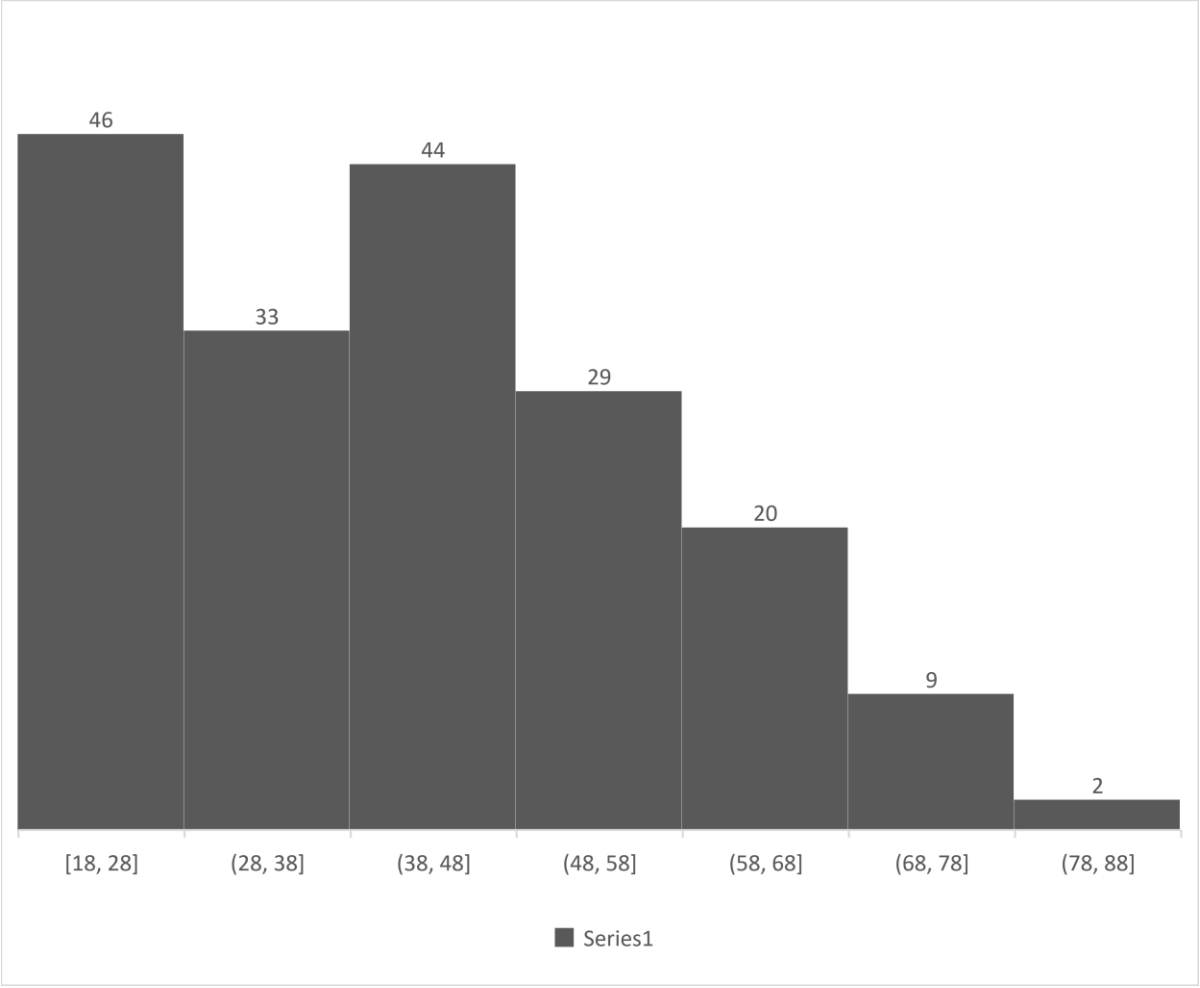

Figure 3.1: Frequency of the age distribution.

Male patients accounted for 67.21% patients making up the male-to-female ratio of 2:1. The median age of study patients was 41 years with the IQR of (30 – 50). The mean age of all patients was 42.28 years, with peak age at presentation being age group (18 – 28) years and followed by another peak in age group (39 – 48) years. The number of cases presenting with SA tapered down from the age group (49 – 58) years onwards with the least case presentations seen in the (79 – 88) age group, with only three patients documented in the latter group.

3.1.2. Anatomical site of joint involvement

Table 3.3 shows that the most commonly affected joint at presentation was the knee joint, with, the right and left knee involved in 36.52% and 35.39% of all joints, respectively.

Table 3.3: Further breakdown of isolated joint involvement.

Anatomical site	**Numbers per joint *(n)***	**Percentage (%)**
Right knee	65	36.52%
Left knee	63	35.39%
Right ankle	7	3.93%
Left ankle	6	3.37%
Right elbow	6	3.37%
Left elbow	6	3.37%
Left wrist	5	2.81%
Polyarticular	5	2.81%
Left hip	4	2.25%
Right hip	3	1.69%
Right wrist	3	1.69%
Right shoulder	3	1.69%
Left shoulder	2	1.23%
TOTAL	**178**	**100%**

Collectively, the knee joint was involved in 71.90% in our study as seen in Figure 3.2. The right ankle joint was the second commonest site to be affected accounting for 3.93% of cases. The least affected anatomical site was the shoulder joint, with less than 2% involvement. Of all cases 2.81% were polyarticular.

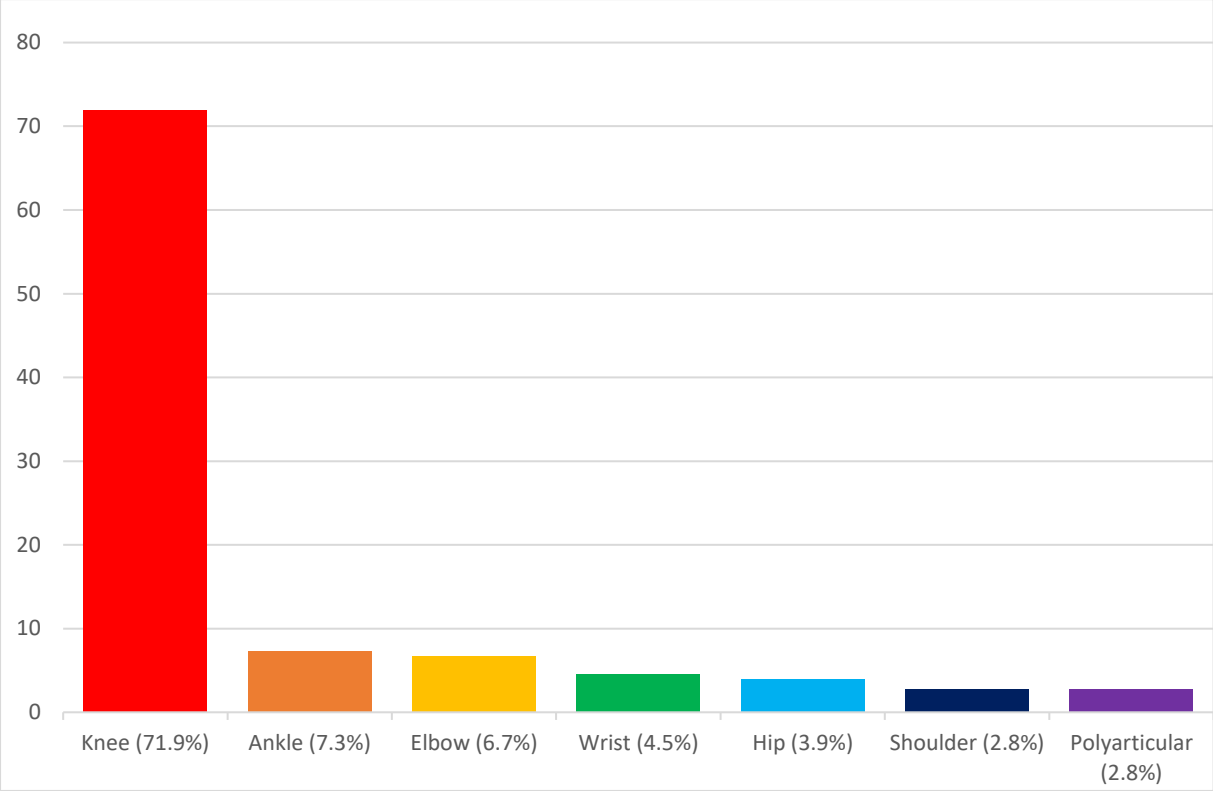

Figure 3.2: Joints involvement in percentages.

3.2 PATIENTS' SEROLOGICAL BIOMARKERS ON PRESENTATION

The Tables and Figures below show the serological markers that were used to aid in making the diagnosis of SA. These included the retroviral status, CD4+ count, VLL, WCC, CRP and ESR.

3.2.1 The retroviral (HIV) status of patients in the study

Table 3.4 shows that from the study of 183 patients that presented with SA, 58 (32%) of patients were confirmed to be HIV-positive; 45 (25%) of patients were HIV-negative and remaining 80 (43%) had an unknown HIV status. The prevalence of HIV-positive patients with septic arthritis was 31.7% in our sample population. We also found that 13 (22%) of the 60 female patients in the study were HIV-positive, a figure lower than in our male patient population as 36.5% of the male cohort was HIV-positive. Table 3.4 and Figure 3.3 below, show the relationship of the HIV status and the average age amongst the different HIV groups in the study.

Table 3.4: HIV status by gender.

HIV status	**Males**	**Females**	**Total**
HIV negative	22	23	**45**
HIV positive	45	13	**58**
HIV unknown	56	24	**80**
Total	**123**	**60**	**183**

Figure 3.3 below, shows the relationship of the HIV status and the average age amongst the different HIV groups in the study.

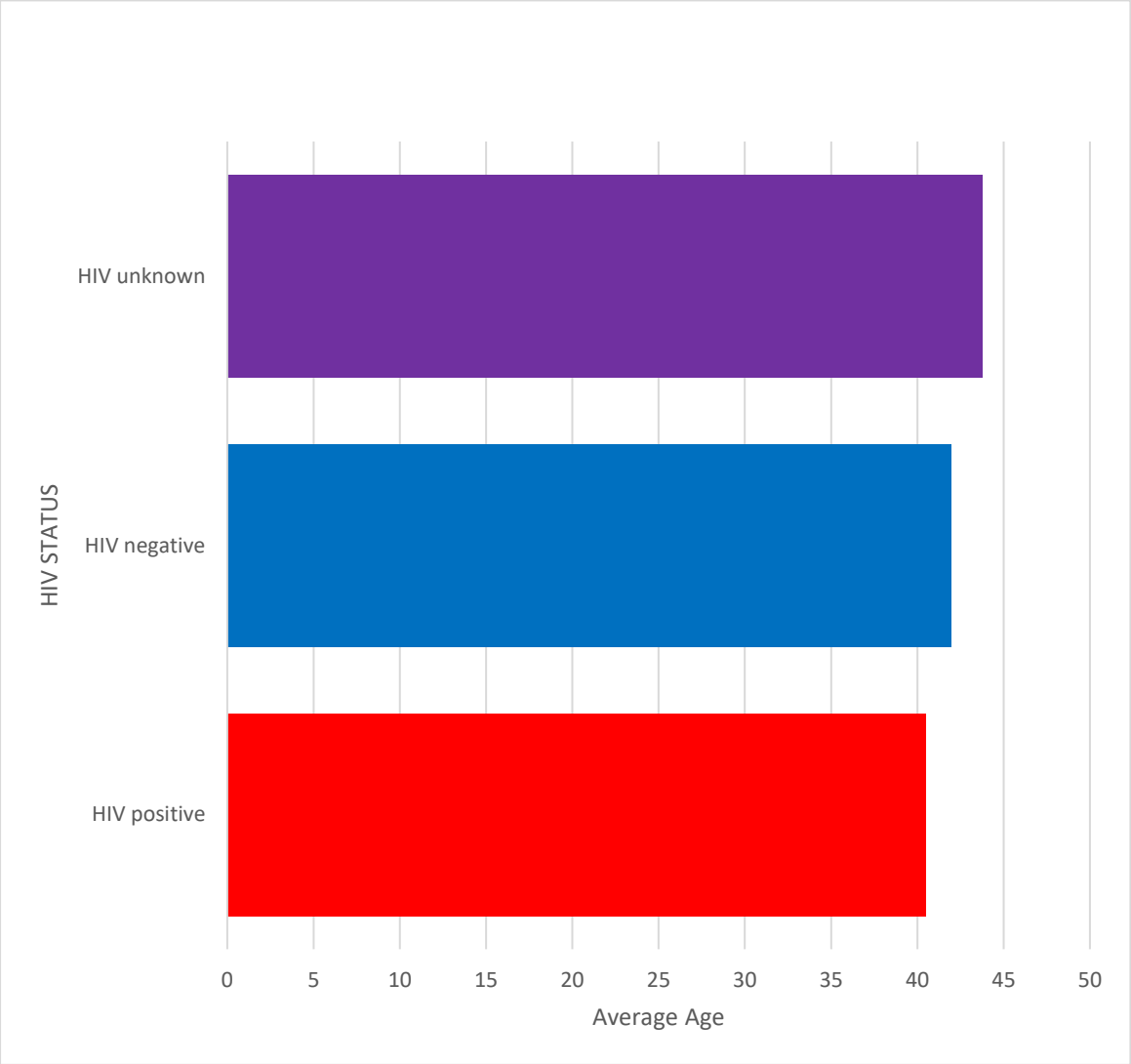

Figure 3.3: Distribution of HIV status with the average age.

3.2.2 CD4+ count and VLL values

The analysed CD4+ count and VLL values in the study, are summarised in the Table 3.5 below.

Table 3.5: Absolute CD4+ and VLL values.

Number *(n)*	**Mean**	**Standard deviation**	**Minimum**	**Median**	**IQR**	**Maximum**
CD4+ (33)	329.4	269.8	15	281	158 – 432.5	1198
VLL (33)	49453.8	101663	LDL	2350	69.5 – 48810	495000

LDL = Lower than detectible level

Of the total cohort of 183 patients, only 33 had documented absolute CD4+ count and VLL results. The absolute CD4+ counts of those patients were above 200 cells per cubic millimetre, with counts below 200 cells per cubic millimetre signalling advanced HIV infection. Only 3 (9%) out of 33 patients had a lower than detectible VLL result. Overall, our HIV-positive group had a median absolute CD4+ count and a VLL of 281 and 2350, respectively.

3.2.3 Inflammatory markers associated with SA – WCC, CRP, and ESR

3.2.3.1 WCC

Tables 3.6 and 3.7 below show the findings and interpretation of the WCC count in our study sample.

Table 3.6: Summary of the WCC results.

Numbers (n)	Mean	Standard deviation	Minimum	Median	IQR	Maximum
171	10.2	5.9	2.2	8.8	6.4 – 11.9	41.5

Table 3.7: Summary of the analysis of the WCC values.

Statistics	Values	95% Confidence Interval
Sensitivity	44%	29.9% – 58.8%
Specificity	52.5%	43.2% – 61.6%
Positive LLR	0.93	0.64 – 1.33
Negative LLR	1.07	0.79 – 1.44

3.2.3.2 CRP

Tables 3.8 and 3.9 below show the findings and interpretation of the CRP results in the patient sample used in our study.

Table 3.8: Summary of the CRP results.

Numbers (n)	Mean	Standard deviation	Minimum	Median	IQR	Maximum
169	120.7	99.4	1	371	39.5 – 170.5	371

Table 3.9: Summary of the analysis of the CRP values.

Statistics	**Values**	**95% Confidence Interval**
Sensitivity	95.7%	85.5% – 99.5%
Specificity	4.1%	1.3% – 9.3%
Positive LLR	1.00	0.93 – 1.07
Negative LLR	1.04	0.21 – 5.17

3.2.3.3 ESR

Table 3.10 and 3.11 show the findings and interpretation of the ESR results in the patient sample used in our study.

Table 3.10: Summary of the ESR results.

Number (*n*)	**Mean**	**Standard deviation**	**Minimum**	**Median**	**IQR**	**Maximum**
123	72.3	69.9	1	65	28 – 108	666

Table 3.11: Summary of the analysis of the ESR values.

Statistics	**Values**	**95% Confidence Interval**
Sensitivity	86.7%	73.2% – 94.9%
Specificity	9.4%	4.8% – 16.2%
Positive LLR	0.96	0.84 – 1.09
Negative LLR	1.42	0.56 – 3.61

3.3. MICROBIOLOGICAL CULTURES AND SENSITIVITY

Table 3.12 shows that the post arthrotomy microbiological results in the group of 183 patients revealed that 65 of those patients had a positive culture result, leaving a large number 118 patients (65%) of patients within the study as a having a negative arthrotomy culture result. The negative culture rate for HIV-positive *versus* HIV-negative patient groups are calculated as shown in the Table 3.12 below. Polymicrobial cultures were also identified: one patient in the HIV-unknown group, two patients in the HIV-negative group and three patients in the HIV-positive group. Only 9.8% of cases from the original study sample required a relook arthrotomy post initial joint surgery.

Table 3.12: Summary of the microbiological cultures and negative culture rate.

HIV GROUPS	**NEGATIVE CULTURES**	**Negative culture rate**	**POSITIVE CULTURES**	**TOTAL**
HIV-negative	24	59.4%	21	**45**
HIV-unknown	60	75%	20	**80**
HIV-positive	34	63.7%	24	**58**
TOTAL	**118**		**65**	**183**

Table 3.13 shows the distribution of the microbiological gram stains in the retroviral categories. Included are the gram positive *versus* gram negative and/or *Mycobacterium tuberculosis* cultures analysed.

Table 3.13: Distribution of Gram stain when compared amongst the retroviral categories.

Retroviral status	**Gram positive culture (%)**	**Gram negative ± Mycobacterium (%)**
HIV-negative	61.9%	38.1%
HIV-unknown	68%	32%
HIV-positive	76%	24%

3.3.1 Microbiological culture and sensitivity in the HIV-negative group

Table 3.14 shows the distribution of the microbiology cultured bacteria in the HIV negative group as total numbers and percentages.

Table 3.14: Summary of the bacteria and antibiotic sensitivity in the HIV-negative group.

Bacteria species	**Antibiotic sensitivity**	**Numbers *(n)***	**Percentage (%)**
Staphylococcus aureus	Cloxacillin	11	52.3%
Streptococcus pyogenes	Penicillin G	1	4.8%
Streptococcus pneumoniae	Cefazolin	1	4.8%
Acinetobacter Baumanni	Colistin	1	4.8%
Escherichia coli	Imipenem	1	4.8%
Enterococcus faecalis	Ampicillin, Vancomycin	2	9.5%
Salmonella species	Ceftriaxone	1	4.8%
Proteus vulgaris	Imipenem	1	4.8%
Morganella morganii	Imipenem	1	4.8%
Mycobacterium tuberculosis	Rifampicin sensitive	1	4.8%
Total		**21**	**100%**

3.3.2 Microbiological cultures and sensitivity in the HIV-unknown group

Table 3.15 shows the distribution of the microbiology cultured bacteria in the HIV-unknown group as total numbers and percentages.

Table 3.15: Summary of the bacteria and antibiotic sensitivity in the HIV-unknown group.

Bacteria species	**Antibiotic sensitivity**	**Number (*n*)**	**Percentage (%)**
Staphylococcus aureus	Cloxacillin	11	50%
Streptococcus pyogenes	Penicillin G	4	18%
Pseudomonous aeruginosa	Tazocin, Ceftazidime	2	9%
Acinetobacter baumanni	Colistin	1	4.5%
Haemophilus influenzae	Ampicillin	1	4.5%
Serratia marcescens	Ertapenem	1	4.5%
Salmonella species	Ceftriaxone	1	4.5%
Mycobacterium tuberculosis	Rifampicin sensitive	1	4.5%
Total		**22**	**100%**

3.3.3 Microbiological cultures and sensitivity in the HIV-positive group

Table 3.16 shows the distribution of the microbiology cultured bacteria in the HIV-positive group as total numbers and percentages.

Table 3.16: Summary of the bacteria and antibiotic sensitivity in the HIV-positive group.

Bacteria species	**Antibiotic sensitivity**	**Number (*n*)**	**Percentage (%)**
Staphylococcus aureus	Cloxacillin	15	60%
Streptococcus pyogenes	Penicillin G	4	16%
Klebsiella Pneumonia	Amoxicillin-clavulanic acid	2	8%
Escherichia coli	Trimethoprim-Sulfamethaxone	1	4%
Enterobacter faecalis	Ampicillin	1	4%
Serratia marcescens	Ertapenem	1	4%
Mycobacterium tuberculosis	Rifampicin sensitive	1	4%
Total		**25**	**100%**

3.4. THE ASSOCIATION BETWEEN THE DEMOGRAPHICS AND SEROLOGICAL BIOMARKERS TO RETROVIRAL STATUS

3.4.1 The association of the age and retroviral status

The association between the age and retroviral status is shown in the Table 3.17. The median age in each group was used.

Table 3.17: Association between the median age and retroviral status.

Total number of patients	103
HIV-negative	41.9
HIV-positive	40.5
Z score	-0.79
***p*-value**	0.429 ($p < 0.05$)

No statistically significant differences found in the median age between the HIV-negative and HIV-positive patients.

3.4.2 The association of the WCC values and retroviral status

Table 3.18 shows the association of the median WCC against the retroviral status in each group.

Table 3.18: Association between the median WCC and retroviral status.

Number of patients	97
HIV-negative	8.7 (4.5 – 10.3)
HIV-positive	10.9 (6.88 – 12.2)
Z score	2.28
***p*-value**	0.025 (p-value < 0.05)

There was a statistically significant association in WCC values with retroviral status in our study population. The WCC values were found to be different in the HIV-negative and HIV-positive patients.

3.4.3 The association of the CRP values and retroviral status

Table 3.19 shows the association of the median CRP against the retroviral status in each group.

Table 3.19: Association between the median CRP and retroviral status.

Number of patients	97
HIV-negative	117.8 (32.3 – 169)
HIV-positive	121.2 (30.5 – 213)
Z score	0.025
***p*-value**	0.98 (*p*-value < 0.05)

No statistically significant differences found in the median CRP values between the HIV negative and HIV positive patients.

3.4.4 The association of the median ESR values and retroviral status

Table 3.20 shows the association of the median ESR against the retroviral status in each group.

Table 3.20: Association between the median ESR and retroviral status.

Number of patients	68
HIV-negative	83.8 (27.8 – 119)
HIV-positive	72.8 (26.8 – 90)
Z score	-2.11
***p*-value**	0.034 (*p*-value < 0.05)

There was a statistically significant association in ESR values and retroviral status in our study population. The ESR values were found to be different in the HIV negative and HIV positive patients.

3.4.5 The association between retroviral status and the overall culture results post aspiration.

Table 3.21 shows whether there is an association with retroviral status and likelihood of having a positive or negative culture result.

Table 3.21: Chi-squared calculation of association between retroviral status and culture result outcome.

Chi-squared (X^2)	0.372
***p*-value**	0.54 (*p*-value < 0.05)

No statistical significant association between HIV status and in having a positive or negative culture results, as *p*-value = 0.54.

CHAPTER 4

4. DISCUSSION

This chapter explains the results and findings of this study in references to other published relevant studies. The inferences from the study will be discussed and the relevant new findings gathered from the study highlighted. Furthermore, the study limitations and recommendations will be elaborated.

4.1 DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF PATIENTS

The demographic characteristics of the patients that presented with SA are discussed below.

4.1.1 Age and sex of patients

The findings of this study confirmed that SA occurred more commonly in the male population with male to female 2:1 ratio, 67.21% males and 32.79% females documented (see Table 3.1). A finding similar to that of Helito *et al.* which showed a male population of 63.8% and that of females to be 36.2% (1, 4). Ferrand *et al.* whose article showed a 67.9% male population in their study (41). However, Weston *et al.* found an equal distribution across both genders (38).

The mean age distribution in our study was 42.28 years and a median of 41 years (IQR of 30 – 50) (see Figure 3.1 and Table 3.2). Helito *et al*. showed a similar mean age of 42.5 years (4), Munoz-Egea *et al*. in their study showed a mean age of 61 years (1) and Ferrand *et al.* had a median age of 62 years (range 16 – 96) (41); both showing a higher mean and median age of presentation when compared to our study.

4.1.2 Anatomical site of joint involvement

There were noted similarities in the number when comparing the joint affected, the laterality did not show a significant difference, and the numbers when assessing laterality were close for most joints. The commonest joint of involvement in our study was the knee joint with 71.90% of the total cases at CHBAH affecting this joint. Further isolated breakdown of the joint involvement results showed the least affected joints in our study to be the right hip (1.69%), the right wrist (1.69%), the right shoulder (1.69%) and with the left shoulder (1.27%) being the lowest (see Table 3.3). Monoarticular joint involvement, was by far the most prevalent with polyarticular presentation occurring in only 2.81% of the total cases (see Figure 3.2). Long *et al.* reported 20% polyarticular involvement (43), Cho *et al.* had a 15% polyarticular joint involvement (42) which was similar to the results by Weston et al. With 14.8% poly articulate involvement (38). In our study after the knee joint, the ankle and elbow joints were the second and third most frequently affected joints, respectively. Long *et al.* showed that the next frequent joint involved after the knee joint was the hip, then the shoulder (43). On the other hand, Weston *et al.* showed the hip joint then polyarticular involvement to follow the knee joint in that order of frequency (38). The knee joint being the commendation joint involved in all the above studies is certainly due to the anatomical variation in the joint as compared to others. From our sample the polyarticular joint involvement when compared to cited literature was seen to be lower and this might be due to our low sample size, a prospective study may allow for a better yield in the sample size.

4.2 PATIENT'S SEROLOGICAL BIOMARKERS ON PRESENTATION

4.2.1 The retroviral (HIV) status of patients in the study

A total of 103 out of a total 183 patients in the study had a confirmed serological retroviral status, with 58% patients confirmed to be HIV-positive. In terms of the male to female distribution, 45% males and 23% females were found to HIV-positive, respectively, in our study (see Table 3.4). The average age when comparing the three HIV groups was found to be similar, with the average of 41 to 44 years (see Figure 3.3). The prevalence of HIV-positive patients who presented with SA in our study was found to be 31.7%. Casado *et al.* in their study had 23% prevalence of HIV-positive patients presenting with SA (35) and Robertson *et al*. in the paediatric population showed a prevalence of 21% (40). Guilio *et al.* found that intravenous drug use rather than HIV status was the main risk factor when reviewing HIV-positive patients presenting with osteoarticular infections (13). Pretell-

Mazzini *et al.* observed that with the advancement in ART leading to the increase in life expectancy there was an observed increase in the number of osteoarticular presentations, including SA (9). This finding was also true in our study, the increasing number of HIV positive patients were seen presenting with SA, due to the improvement in compliance and treatment of HIV positive patients resulting in an increase in overall survival.

4.2.2 CD4+ count and VLL values

A total of 33 patients of HIV-positive retroviral status had a documented CD4+ count and VLL results. The median absolute CD4+ count was found to be 281 cells per cubic millimeter and the median of VLL was 2350 copies per millilitre (see Table 3.5). Casado *et al.* in their study found a mean CD4+ count in SA to be 164.7 cells per cubic millimeter and found that the SA infection appeared when the CD4+ count was below 200 cells per cubic millimetre (35). Surprisingly, most of our study patients had a CD4+ count above 200 cells per cubic millimetre which is the opposite of what Casado *et al.* reported testament to our ART rollout success. Vassilopoulos *et al.* documented a similar CD4+ counts value to those in our study, with a median value of 249 cells per cubic millimeter in that study (49).

4.2.3 Inflammatory markers associated with SA – WCC, CRP and ESR

The inflammatory markers results are summarised in the sequence of WCC, CRP and ESR values, were documented as median (mean) as follows: WCC 8.8 (10.2); CRP 371 (120.7); ESR 65 (72.3) (see Tables 3.6, 3.8 and 3.10). Ferrand *et al.* found that WCC was elevated in 50% of his study population and that the CRP had a median of 120 mg/dL (41). Helito *et al.* described the mean values of WCC to be 11.52, CRP of 117.8, and ESR of 53.3 (4). Comparative to the above two reference studies our results showed a low WCC value but similarly high CRP and ESR values.

The diagnosis accuracy was assessed by calculating the sensitivity, specificity and LLR. When calculated that WCC had a sensitivity of 44%, a specificity of 52.5%, a positive LLR of 0.93 and a negative LLR of 1.07 (see Table 3.7). Long *et al.* described similar values to our study on WCC; a sensitivity of 41% – 90 % with a positive LLR of only 1.4 (43) in their study. Our CRP calculated values were as follows; a sensitivity of 95.7% and a specificity

of 4.1%, with a low positive LLR of 1 and negative LLR of 1.42 (see Table 3.9). When compared with findings from Long *et al.*, which showed a sensitivity of approximately 90% (43) making CRP an excellent diagnostic test. Lastly, our ESR values were assessed as follows; a sensitivity of 86.7% and a specificity of 9.4%, a positive LLR 0.96 and a negative LLR of 1.42 (see Table 3.11). For our study group a ESR value was considered to be raised when it was found to be above 20 mm/hr. Carpenter *et al.* found that the ESR sensitivity changes when the raised value definition was assessed to be above 20 mm/hr or when adjusted to above 30mm/hr. The sensitivity was found to be 75% when ESR was assessed at 20 mm/hr, with an improved sensitivity of 96% when 30 mm/hr was upper limit of a normal value (3). Long *et al.* reported a sensitivity for ESR to be 66% when considered to be raised at ESR values above 15 mm/hr *versus* a sensitivity of more 90% when ESR was considered to be raised above 30 mm/hr (43).

4.3 MICROBIOLOGICAL CULTURES AND SENSITIVITY

The microbiological culture and sensitivity found in our study were reviewed in three groups; HIV-negative, HIV-unknown and HIV-positive in order to be able to compare each group. Sixty-five out of a total of 183 (35%) post arthrotomy samples had a positive culture result (see Table 3.12). This study had a much higher negative culture rate, 65% when compared with the findings from Mue *et al.* where they had only 22.9% no growth rate. The negative culture rate was similar between the HIV-positive (63.7%) and the HIV-negative groups (59.4%) (30). Across all groups gram-positive bacterium were cultured significantly more than the gram-negative bacterium or atypical *(Mycobacterium tuberculosis)* (see Table 3.13). The commonest bacteria in all groups were *Staphylococcus aureus* sensitive to Cloxacillin, making up more than 50% of total cultures in group, followed by *Streptococcus pyogenes* sensitive to Penicillin G (see Tables 3.14, 3.15 and 3.16).

Acinetobacter baumanni was diagnosed once in both the HIV-negative and HIV-unknown groups, with one case of *Haemophilus influenzae* in the HIV-unknown group and each of the above groups had a single case of *Mycobacterium tuberculosis*. *Staphylococcus aureus* was seen in 60% of the HIV-positive cases and in 52.3% of the HIV-negative cases as the leading causative bacteria. Similar to our study results, Zalavras *et al*. found that *Staphylococcus aureus* remained the commonest bacteria despite of the HIV status in patients with SA. *Mycobacterium tuberculosis* was cultured in 16% of our study sample (29). Similarly, studies by Munoz-Egea *et al.*, Helito *et al.*, Mue *et al.*, Weston *et al.*, and

Ferrand *et al.*, had comparable results with Staphylococci as the commonest pathogen in 50% of cases (1, 4, 30, 38, 41).

With regards to *Mycobacterium tuberculosis*, Moreira *et al*. found that HIV-positive status increased mycobacterium and fungal SA infection (37). Weston *et al.* in their review found a low 0.5% of cases of *Mycobacterium tuberculosis* (38), may be due to TB not being endemic in that region of the world as opposed to our South African context.

The presence of polymicrobial species in the microbiological culture results although significant was low. Polymicrobial cultures were seen more in the HIV-positive group, with only three cases showing a mixed gram-negative and gram-positive culture. Zalavras *et al*. found polymicrobial cultures were associated with an HIV-positive status especially in patients presenting with polyarticular SA (29).

4.4 THE ASSOCIATION BETWEEN THE DEMOGRAPHIC AND SEROLOGICAL BIOMARKERS TO THE RETROVIRAL STATUS

The following parameters were assessed for their association with that of the patient's retroviral status:

4.4.1 The association of the age and retroviral status

In our study there was no association found, p-value = 0.429 ($p < 0.05$) when assessing the median age and retroviral status (see Table 3.17). Guilio *et al.* similarly concluded that age and sex were not statistically significant as an association or risk factor of osteoarticular infection in HIV infected patients (13).

4.4.2 The association of the serum inflammatory markers to the retroviral status

The serum inflammatory markers as previously discussed as important in helping make a diagnosis of SA and they are altered in the presence of immune suppression. Evaluating the impact and differences in the influence retroviral status has on these markers is key to recognising their usefulness as a diagnostic tool. The calculated p-value of 0.98 ($p < 0.05$) found that the median CRP value between the two groups was not statistically significant (see Table 3.19). Whereas the calculated p-values for both the WCC, $p = 0.025$ ($p < 0.05$) and ESR, $p = 0.034$ ($p < 0.05$) were found to be statistically significant (see Tables 3.18 and

3.20). Both values were found to be different in each confirmed retroviral status group. In comparison to Moreira *et al.* whom found that both WCC and CRP were generally lower in HIV positive patients presenting with SA (37).

4.4.3 The association between the retroviral status and the overall culture results post arthrotomy

With a value of $p = 0.54$ ($p < 0.05$) there was no statistical significance in the association of the retroviral status and in having a positive or negative culture result (see Table 3.21). Many factors may be associated with a negative culture result, some were described by Turner *et al*. that may be linked but not limited to the initiation of antibiotics prior to synovial fluid aspiration and to inadequate microbiological plating and growth conditions (12).

4.5 STUDY LIMITATION

The sample size consisted of a majority of patients with unknown retroviral status. Testing of all patients on admission could aid in getting a larger sample and may have potentially given different results.

4.6 RECOMMENDATIONS

- A multicentre and prospective study is recommended, in order to make sure that all diagnostic measures are met, including evaluating the association of VLL values on SA and assess the morbidity and mortality rates over time.
- With patients that have been confirmed to be immuno-suppressed, it is encouraged to consider adding a gram-negative antibiotic cover during the empiric stage of treatment.

CHAPTER 5

5 CONCLUSION

The studied population at CHBAH showed a male (67.21%) predominance, with a mean age of 42.28 years. The knee joint was the most common joint involved with polyarticular joint involvement occurring in 2.81% of cases in our study, which was less than rates described in literature, 15 – 20% being coined by studies reviewed. As a diagnostic marker, CRP was found to have the best sensitivity (95%) and specificity (4.1%). Although, the LLR across all the inflammatory markers studied, showed a low value, making them poor diagnostic tests for SA. The evaluation of other inflammatory markers such as PCT and IL-10 have shown to have better prediction scores.

The prevalence of SA with HIV co-infection was found to be 31.7% in our study population. The reason for this relatively high percentage to the data found in literature may be due to the increase in the life expectancy secondary to improved distribution and compliance to the ART programme in South Africa. A median CD4+ count of 281 cell per cubic millimetre was observed in our study sample. With those with CD4+ count < 200 cells per cubic millilitre to have an increased likelihood for polymicrobial cultures.

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APPENDICES

APPENDIX A: DATA COLLECTION SHEET

Patient Demographics:

Study Number

Age

Sex

Date of admission

Joint involvement

Serological biomarkers:

WCC

CRP

ESR

Retrovial status

CD4+ count

VLL

Microbiology culture and sensitivity:

Culture

Sensitivity

APPENDIX B: HUMAN RESEARCH ETHICS CLEARANCE CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Loyiso Gqamana

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M230274 MED23-02-054

NAME: (Principal Investigator)	Dr Loyiso Gqamana
DEPARTMENT:	Orthopaedic Surgery Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	*The effect of HIV on the microbiology of adult patients presenting with septic arthritis at Chris Hani Baragwanath Academic Hospital*
DATE CONSIDERED:	24/02/2023
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - Nicoleen.Potgieter@wits.ac.za
SUPERVISOR:	Dr M. Jingo and Dr P. Kgagudi
APPROVED BY:	Professor Paul Ruff, Chairperson, HREC (Medical)
DATE OF APPROVAL:	22/09/2023 **EXPIRY DATE:** 22/09/2028

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. I **agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **February** and will therefore be due in the month of **February** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

23/09/2023
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX C: NHLS APPROVAL LETTER TO ACCESS RESOURCES FOR RESEARCH PURPOSES

NATIONAL HEALTH LABORATORY SERVICE

Academic Affairs and Research
1 Modderfontein Road, Sandringham, 2031
Tel: +27 (0)11 555 0367/0406
Email: babatyi.kgokong@nhls.ac.za
academic.research@nhls.ac.za
Web: www.nhls.ac.za

10 August 2023

Applicant: Loyiso Gqamana
Institution: University of the Witwatersrand
E-mail Address: loygqa@gmail.com
Tel: 011 933 8211 **Cell:** 072 898 4451

Project Title: THE EFFECT OF HIV ON THE MICROBIOLOGY OF ADULT PATIENTS PRESENTING WITH SEPTIC ARTHRITIS AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL
Reference Number: PR2345362

Research Application Type(s):
1. Permission to use NHLS Facilities
2. Request for Data

RE: APPROVAL LETTER: REQUEST TO ACCESS NHLS RESOURCES FOR RESEARCH PURPOSES

This letter serves to advise that the application requesting permission to conduct the above-mentioned research using the listed NHLS resources has been reviewed and **"Approved"**. Please note that the approval is granted on the condition that you comply with the NHLS Research Material and Data Access Policy and requirements stated below.

1. All material and data requested shall be used as per the research protocol submitted to the NHLS and as approved by the relevant Health Research Ethics Committee (HREC) in South Africa.
2. Access to the NHLS material and/or data shall be limited to the minimum required for successful completion of the approved study and shall be made available ***without patient names and other patient identifiers (including, but not limited to, national identity numbers, hospital/clinic file numbers, addresses and telephone numbers)***.
3. Confidentiality shall be maintained at the participant and institutional level and there shall be no disclosure of personal information or confidential information.
4. Data and/or material shall not be shared with other parties unless approved by the NHLS
5. The material and/or data obtained from the NHLS shall be anonymised and not, for any reason, be used to track or recruit patients as no pre-approval/consent is obtained from patients.
6. Processes shall be discussed with the relevant NHLS departments (i.e. Corporate Data Warehouse (CDW), NHLS Laboratory Management, Operations Office, etc.) and agreed upon.
7. Any amendments to the study requirements, including the use of the material and/or data for purposes not initially disclosed to the NHLS) shall be cleared by an approved HREC and submitted to the NHLS for approval via the AARMS system – https://aarms.nhls.ac.za.
8. The NHLS shall be acknowledged as a source of material and/or data in any output, such as abstracts and journal articles, emanating from the project.
9. A final report of the research study and any published output resulting from this study shall be submitted to the NHLS via AARMS

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. The NHLS entities tasked with providing the material and/data may have additional requirements for access. Data related queries may be directed to NHLS CDW, email: zarina.sabat@nhls.ac.za; contact number: 011 386 6074 and sample related queries (if applicable) shall be directed to the relevant business manager.

Dr Babatyi Malope-Kgokong
National Manager: Academic Affairs and Research