THE EFFECT OF HIV INFECTION ON MORTALITY AND LENGTH OF HOSPITAL STAY IN THE ADULT BURN UNIT, CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

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Declaration:

I, Claire Joy Sanders, declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Medicine in the branch of General Surgery at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.

………………C.J Sanders……………

Signed at …Johannesburg..on the ……24th day of……May……2019.

Abstract:

Background:

Human Immunodeficiency Virus (HIV) infection and burn injuries both represent significant public health concerns in South Africa. Studies showing the effect of HIV on the outcome of burns in Africa have been limited by small sample sizes with conflicting results.

Objectives:

To compare mortality and length of stay in HIV positive *versus* HIV negative burns patients admitted to the Adult Burn Unit, Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa.

To compare the mortality in HIV positive burn patients with high and low viral loads.

Methods:

Retrospective review of 204 patients admitted to the Adult Burn Unit, Chris Hani Baragwanath Academic Hospital from January 2012 until July 2015.

Results:

Of the 204 patients included in the study, 60 were HIV positive (29%) and 146 HIV negative (21%). Twelve HIV positive patients died (21.7%), compared with 22 of the HIV negative patients (15.3%). There was no statistical significance between the two groups (p=0.270). Length of stay was not statistically significant between the groups of patients (p=0.241) either. No significant conclusion could be drawn comparing mortality in patients with high *versus* low viral loads as very few patients had their viral loads tested.

Conclusions:

Although HIV positive patients showed a higher mortality rate, this difference was not statistically significant. Length of hospital stay was similar between the two groups.

Acknowledgements:

I would like to thank my supervisors for their advice and support in completing this report.

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Abbreviations:

ABU	Adult Burn Unit
AIDS	Acquired Immunodeficiency Syndrome
ARVT	Antiretroviral drug therapy
BEAMS	Burns Evaluation and Mortality Study
CEO	Chief Executive Officer
CD4	Cluster of differentiation 4
CHBAH	Chris Hani Baragwanath Academic Hospital
GBD	Global Burden of Disease report
HIC	High income countries
HIV	Human Immunodeficiency Virus
HIV-VL	Human immunodeficiency viral load
ICU	Intensive Care Unit
NHLS	National Health Laboratory Services
NK	Natural killer
LOS	Length of hospital stay
LIC	Low income countries
MIC	Middle income countries
SASOS	South African Surgical Outcomes Study
TBSA	Total body surface area
USA	United States of America
WHO	World Health Organisation
Wits HREC	Human Research Ethics Committee (Medical), University of the Witwatersrand

CHAPTER ONE: Literature review:

1.1 Background

In South Africa, both Human Immunodeficiency Virus (HIV) infection and burn injuries represent significant public health concerns. The impact of HIV on patient outcomes has been examined across various groups of surgical patients, as well as those with traumatic injuries, including burns. The Human Sciences Research Council estimated that 12.2% of South Africans were infected with HIV in 2012 [1]. Statistics South Africa estimated the prevalence of HIV in people aged 15-49 years at 15.9% in 2013 [2]. The World Health Organisation (WHO) Global Health Observatory Data Repository estimated the 2010 prevalence of HIV infection in peopled aged 15-49 years to be 18.1%, with the prevalence in 2017 at 18.8% [3]. The antenatal prevalence in Gauteng in 2015 was 30.2% [4]. In 2017, an estimated 7.2 million South Africans were living with HIV infection [3].

Globally, the average prevalence of HIV infection in adults between the ages of 15 and 49 years (as reported by the WHO in 2017) was 0.8%, with an average of 0.4% in Europe, 0.5% in the Americas and 4.1% in Africa [3]. This contrasts sharply with the HIV prevalence in South Africans of the same age group. When compared with the countries sharing borders with South Africa, the HIV prevalence in South Africa becomes the median value, with three countries that have a higher prevalence and three countries a lower prevalence.

This data is summarised in Table 1.1:

Table 1.1 Prevalence of HIV infection amongst adults aged 15-49years in 2017

REGION / COUNTRY	HIV Prevalence among adults aged 15-49years (%)
Global	0.8
Europe	0.4
Americas	0.5
Africa	4.1
South Africa	18.8
Eswatini (Swaziland)	27.4
Lesotho	23.8
Botswana	22.8
Zimbabwe	13.3
Mozambique	12.5
Namibia	12.1

This emphasises the fact that HIV does indeed represent a significant burden of disease in South Africa. The Global Burden of Disease [5] (GBD) Report from 2015 placed HIV as the highest cause of disability for all countries in the southern Sub-Saharan region. The global mortality from HIV fell by 33.4% from 2005 to 2015, likely reflecting the increased use of antiretroviral therapy (ARVT) and improved prevention of mother to child transmission. With the use of ARVT, HIV can be seen as a chronic disease rather than a fatal illness, and thus its effects on patients require further investigation.

There are a number of published studies on the prevalence of HIV infection amongst hospital inpatient populations. Included in these are patients suffering from traumatic injuries and those undergoing surgery. A Canadian trauma population surveyed in 2003 had no patients testing positive for HIV infection in that year [6]. In the United States of America (USA), between the years 1994 to 2004, a prevalence of 26% among trauma patients and 24% in surgical patients was noted. In this particular group of patients, intravenous drug use was noted to be a significant risk factor for

HIV infection. Testing was also less likely in trauma patients, with only 21% of these patients being tested while in hospital [7]. An Indian study on HIV prevalence in a trauma centre from 2007 until 2013 showed that 0.28% of their patients were infected with HIV [8]. This was found to be higher than the reported prevalence in the general population. In Nigeria, a prevalence of HIV infection of 4.5% was found in trauma patients with open wounds [9]. This was reported as similar to the national prevalence rate of 5%. In Soweto, South Africa, 32.8% of patients admitted to surgical units were HIV infected with a median CD4 cell count of 219 and an HIV viral load (HIV-VL) of 102 000 copies/ml [10]. Similarly, in the province of Kwa-Zulu Natal, South Africa, data published in 2006 showed a 39% prevalence among surgery and trauma patients, in comparison with the provincial antenatal HIV infection prevalence rate of 35%. In this study, a quarter of participants had Acquired Immunodeficiency Syndrome (AIDS) defining CD4 counts [11]. These rates are higher than the 13.2% prevalence reported in 2015 in the South African Surgical Outcomes Study (SASOS). Notably, SASOS also reported HIV infection to be the most common co-morbidity in the study population of surgical patients [12]. The African Surgical Outcomes Study (2016) reported on surgical patients from 25 countries across Africa, and showed an HIV prevalence of 11% [13]. This is significantly higher than the overall prevalence of 4.1% reported by the GBD report in 2015 [6].

The GBD report documented mortality from fires, heat and hot substances at 3.3/100 000 in 2005, with a decline of 23.5% to 1.9/100 000 in 2015. However, in South Africa, 3.2% of people suffer thermal injuries every year, [14] with estimates from Cape Town placing mortality due to burn injuries at 7.9/100 000 person years between 2001 and 2004 [15]. An analysis from the province of Mpumalanga, South Africa, estimated mortality from burn injury in 2007 and 2008 at 3.8/100 000 population [16]. In 2000, fire ranked fourth in cause of death due to injuries across South Africa [17]. This discrepancy between high income countries (HIC) and middle and low income countries (LMIC) is not unique to South Africa. In reviewing epidemiological data, Peck noted in 2011 that 90% of burn mortalities occurred in LMIC's [18].

Burn injuries have significant economic implications. In 2011, Allorto *et al.,* (2011) assessed the total cost of care for patients at a burn centre in South Africa as ZAR29 549 750 [19]. The average cost of care for patients admitted to the Tygerberg burn intensive care unit (ICU) was estimated at ZAR59 500 per patient [20]. In a

Malawian burn unit, the cost per day in the unit was calculated at US$387.42 [21]. In Australia in 2008, the average cost per day for burn injured patients was US$73.53 [22]. The primary determinant of cost in this particular study was TBSA percentage burn. In assessing the components of this cost, length of hospital stay (LOS) accounted for the highest proportion. The economic implications of burns extend beyond the cost of treating the individual burn patient. On average, only 66% of burn injured patients return to work, with the time taken to return ranging from 4.7 to 24 months [23]. Burn injuries also contribute to loss of quality of life, with a long term loss averaging 11% in a USA burn cohort [24].

The epidemiology of burn injuries also varies among geographic and economic regions. Peck (2011) noted the difference in gender distribution among burn victims between HIC's and LMIC's [18]. In the US, non-fatal burns rates were noted to be higher in men than women, with the exception of scald injuries in elderly women. In the 20 - 44 year age group, mortality from fire in men was nearly double of that in women. This differs from LMIC's where female deaths from burns are higher than in males. This is particularly more common in Asian countries. Nthumba (2014) reviewed publications from Sub-Saharan Africa, noting a male to female ratio of burn injuries of 1.2:1. The majority of patients studied, however, were under the age of 10 years [25]. In Mpumalanga, South Africa, mortality was also noted to be higher in males compared with females [17]. This trend is similar to that seen in the USA.

Immunosuppression occurs with acute illness and trauma. Suppressed CD4 counts and blunted neutrophil response have been shown to occur with acute infectious illness [26]. In addition, viral load (VL) has been shown to increase 7.8 fold in patients with acute infectious illnesses [27]. Burn injury is known to cause immunosuppression of both the cellular and humoral immune systems. Natural killer (NK) cell function is depressed, with the extent of this correlating with the percentage of total body surface area (TBSA) involved in the burn injury [28]. Both T- and B-cell populations are suppressed in burn patients, which are exacerbated in part by increased suppressor T-cell activity [29]. Neither the effect of HIV infection on these processes, nor the impact on the reliability of using the CD4 cell count as a marker of immunosuppression in HIV infected patients with concomitant burn injuries, are known.

The effects of HIV infection on peri-operative complications, including wound healing have been examined over decades. The reported outcomes, however, differ somewhat. In general surgical patients, HIV infection and AIDS have been shown to be associated with a higher rate of wound infection and mortality in patients undergoing laparotomies [30] and appendicectomies, [31] with no difference in patients with asymptomatic HIV infection who underwent emergency caesarean sections [32]. In HIV infected patients, a higher risk of post-operative infective complications in gastrointestinal, trauma and orthopaedic surgery has been shown in patients with contaminated wounds and CD4 cell counts below 200cells/mm^3 [33]. Infective complications following abdominal surgery have been shown to be higher than those of the general population, with clean-contaminated wounds being the highest risk [34]. This risk was higher in patients with a lower CD4 cell count [35]. Conversely, in another study looking at a wide range of surgical procedures undertaken in HIV positive patients, a VL of 30 000copies/ml or greater was identified as a risk factor for complications, whilst the CD4 cell count was not identified as a risk factor. In this group of patients, the only complication that was higher in HIV infected patients was pneumonia [36].

Again, HIV infection with CD4 cell counts of less than 300copies/ml in orthopaedic trauma patients has been associated with a higher risk of postoperative infection [37] while in 1996, a review of HIV infected trauma patients showed that CD4 cell counts could not be associated with an increased risk of bacterial infectious complications. In fact, the only risk factor for infectious complications identified in this group of patient was the Injury Severity Score [38]. Research on outcomes for skin grafts showed similar conflicting trends. HIV-associated delayed skin autograft loss was reported as early as 1990 [39]. Furthermore, HIV infection was shown to impair skin graft survival and to prolong hospital stay [40]. However, James *et al.,* (2003) found no difference in graft take, need for skin graft or overall length of hospital stay [41].

The effect of HIV infection on trauma outcomes as well as outcomes in general surgery patients has also been examined. Stawicki *et al.,* (2005) compared a cohort of HIV infected trauma patients from Pennsylvania, USA, with controls [42]. No difference in mortality was noted amongst the groups, but the length of hospital stay (LOS) was noted to be higher in the group who were HIV infected. Pre-existing medical conditions were also noted to be higher in this group of patients.

Furthermore, another study from USA that reviewed patients from 2000-2005 also found no difference in both mortality and LOS between HIV infected *versus* non-infected patients. However, patients who were HIV infected did have a higher rate of complications [43]. These outcomes were unrelated to the CD4 cell counts. More recently, a review of the National Trauma Data Bank from the USA also showed no difference in mortality, but an increased LOS in HIV infected patients. Although ICU stay was similar in both groups, HIV infected patients had higher rates of pneumonia, wound infection and bacteraemia [44].

In assessing patients presenting for surgery (elective and emergency, including trauma) SASOS found no statistically significant difference in mortality between patients who were HIV infected and those who were not [13]. In Soweto, Johannesburg, from May 2003 until January 2004, HIV infected surgical patients assessed had no difference in LOS and wound sepsis compared with controls. However, hospital-acquired pneumonia was higher [11]. In Kwa-Zulu Natal, South Africa, HIV infection was not associated with higher mortality or with longer LOS. In this group of patients, CD4 cell counts did not influence outcomes [12].

A study analysing data of over 33 000 patients from the National Burn Repository in the USA, showed symptomatic HIV/AIDS to be a significant predictor of mortality (odds ratio 10.2), although the proportion of such patients in the study group was very small (comprising only 0.2% of the total study population) [45]. In agreement with this, a Malawian study showed that HIV positive burn injured patients have higher mortality rates. However, it should be noted that in this particular study group patients with greater than 30% TBSA burns had a mortality rate approaching 100% [46].

In contrast to the study from Malawi, other smaller studies in Sub-Saharan Africa did not show significant differences in mortality between HIV positive and negative patients. Most of these studies were however limited by small sample sizes. Edge *et al.,* (2001) from Stellenbosch, South Africa, included 33 HIV positive patients, of which only 2 had stigmata of AIDS. The study suggested AIDS rather than HIV to be a predictor of mortality [47]. Sjoberg *et al.*, (2004) from Zimbabwe showed a similar mortality to Edge *et al.*,, (2001), but only had 6 HIV positive patients in the study group [48]. Data from a study at Kalafong Hospital (Pretoria, South Africa), [47] presented at the South African Burn Society Congress in 2011, also suggested that AIDS rather than HIV infection alone may be a predictor of mortality. Sheyo (2012) from Zambia, found similar results with regards to mortality, but the majority of patients included in this study were paediatric patients under five years of age [50]. Recently in 2017, a retrospective analysis of patients at Tygerberg Burns Unit, Western Cape, South Africa, demonstrated a higher mortality rate as well as higher complication rates in HIV positive patients compared with HIV negative patients [48]. These results however, were not statistically significant.

The following two tables show mortality rates for burn centres in high income countries (HICs) (Table1.2), and in published studies as described above (Table 1.3).

Table 1.2 Mortality rate: high income countries

Centre	**Mortality rate (%)**
Birmingham [49] **(UK)**	5.96/6.45
Sweden [50]	3
Rotterdam Burn Centre [51] **(Netherlands)**	6.9
American burn repository [46] **(USA)**	5.6
Calgary [52] **(Canada)**	1
New York [53] **(USA)**	3.2
Burns Evaluation and Mortality Study (BEAMS) (Intensive care patients only) (Australia & New Zealand) [54]	10.9

Table 1.3 Mortality rates: published studies involving patients with burn injuries and HIV infection

Centre	Mortality HIV – (%)	Mortality HIV + (%)
US Cohort [46]	9 overall	Not calculated
Malawi [47]	18	33
Stellenbosch [48] **(South Africa)**	24	27
Zimbabwe [49]	50	50
Kalafong [50] **(South Africa)**	10.2	6.4
Zambia [51]	15	9.5
Tygerberg [52] **(South Africa)**	5	13.3

As demonstrated in Tables 1.2 and 1.3, studies demonstrating equivalent outcomes irrespective of HIV status also showed higher mortality rates than those for the majority of burn centres in HIC's reported above. The study from Tygerberg Hospital, South Africa, is the exception. Thus HIV infection may not be reported as significant in causing mortality because the true effect is potentially masked by the overall higher mortality rates generally shown in these studies. The exception to this is the study from Malawi which in contrast showed the effect of HIV on mortality to be significant in a study population that had very high mortality rates for larger burns. A review of burn injuries in Sub-Saharan Africa placed the overall burn mortality at 17%, [26] highlighting this disparity in mortality rates between high *versus* low income countries.

The interpretation and comparison of these studies with each other is further limited by the heterogeneity of the populations studied. Study populations include differing age groups amongst participants. Study populations also differ from each other in mean TBSA burn injury in the particular study. Some studies distinguished patients with HIV infection from those with AIDS whilst others did not. Currently, no data has been published on the mortality within the Adult Burn Unit (ABU) at Chris Hani Baragwanath Academic Hospital (CHBAH).

Length of hospital stay has implications for cost of healthcare [53]. Increased length of stay may represent higher prevalence of complications or be a reflection of constraints within the social support system. Length of hospital stay has been associated with inhalation injury, age and TBSA percentage burn [55]. The US Burn repository study found HIV/AIDS to be a significant predictor of increased length of stay [46], whilst the studies from Malawi, [47] Stellenbosch (South Africa) [48], Zimbabwe [49] and Tygerberg [52] (South Africa) showed no difference in the length of hospital stay related to HIV status. These studies may represent an overall increased LOS in the study population groups, thus masking the effects of HIV.

This study aims to evaluate the difference in mortality and length of hospital stay between HIV positive and HIV negative burn injury patients within the ABU, CHBAH.

1.2 Aims and objectives

This is a retrospective study of adult patients admitted to the ABU, CHBAH from January 2012 until July 2015. The aims were:

1. To compare mortality in HIV positive *versus* HIV negative burn patients.
2. In patients who are HIV positive, to compare mortality in those with high *versus* low VLs.
3. To compare length of hospital stay in HIV positive and HIV negative burn patients.

CHAPTER TWO: Methods

2.1 Study design

This study was undertaken at the Chris Hani Baragwanath Academic Hospital Adult Burn Unit, in Soweto. The Burn Unit serves the population of Soweto (approximately 1.2 million people) [56] and the greater Johannesburg area. However, due to the fact that it is the only specialist burns unit in a large geographical area, patients are transferred to the unit from across Gauteng (approximately 13.4 million people) [57] as well as neighbouring provinces.

Records of patients admitted to the ABU from January 2012 until July 2015 were reviewed. Records of patients younger than 18 years, those with a burnt TBSA % above 60, and those who were readmissions or late (more than 24 hours from time of burn) presentations to the ABU were excluded. Patients who presented late after the initial burn injury were excluded from the study due to the potential for a complicated recovery which may have biased comparisons with other patients. Files not obtainable from the Records Department were excluded from the analysis. Only files with admission and discharge or death dates, burn percentage documentation and traceable documentation of HIV test results were included. Records with missing ARVT status, viral load or CD4 cell counts were however included in the study.

Currently, the ABU offers HIV testing and counselling to all newly admitted patients able to give consent and who are not already on antiretroviral therapy. The patients who test positive subsequently have both their CD4 cell count and HIV-VL tested as part of their work-up.

Patients were further subdivided based on CD4 cell count, where this data was available. A CD4 cell count of 350 was used to stratify patients, as this corresponded with the national guideline recommendation for starting ARVT at the time of the study. It should be noted that this is not necessarily an accurate indicator of immune status in these patients. Patients with CD4 cell counts of less than 350 qualified for this treatment [58]. In addition, HIV-VLs were recorded for patients with HIV and these values correlated with mortality. HIV-VL levels were categorised based on risk categories as defined by Mellors *et al*., (1997): < 500copies/ml, 501 – 3000, 3001-10 000, 10 001-30 000 and >30 000copies/ml [62]. Co-morbidities, age and TBSA were also recorded due to the potential of these variables to affect patient outcome.

Clinical criteria defining AIDS was not used to characterise these patients, due to the concern that this information would most likely not be well documented in the clinical records, leading to bias in the results.

2.2 Data collection

Details of patients admitted for the study period were obtained from the admission registry of the ABU. These details were used to obtain the available patient files from the Records Department. Relevant data was extracted from the files and recorded in a Microsoft ® Excel spreadsheet. HIV serology results were obtained from the National Health Laboratory Services (NHLS) online laboratory system when these were not recorded in the patients files. Patients whose HIV results were not known and were not tested during the course of admission were subsequently excluded from the study.

Patients were allocated a study number once data was collected to ensure anonymity. Ethics approval for the study was granted by the Human Research Ethics Committee (Medical), University of the Witwatersrand (Wits HREC) and permission to conduct the study at CHBAH was obtained from the Chief Executive Officer (CEO) of the hospital. Informed patient consent was not required due to the retrospective nature of the study.

2.3 Statistical methods

Data was captured on a Microsoft ® Excel spreadsheet. Data was analysed using the chi-squared test for categorical variables and t-test for continuous variables. Assistance was obtained from a statistician in analysing the results.

CHAPTER THREE: Results

3.1 Overview of data

Of 901 patients identified who were eligible for the study, 204 were included. The remainder were excluded due to either:

1) missing or incomplete clinical records, or
2) no HIV serology results available.

Although not specifically assessed, a trend was noted that the rate of HIV testing in patients seemed to be related to the junior doctor who was working in the unit at the time.

3.2 Demographics

3.2.1 Gender

The majority of patients were male (69%) compared to female (31%).

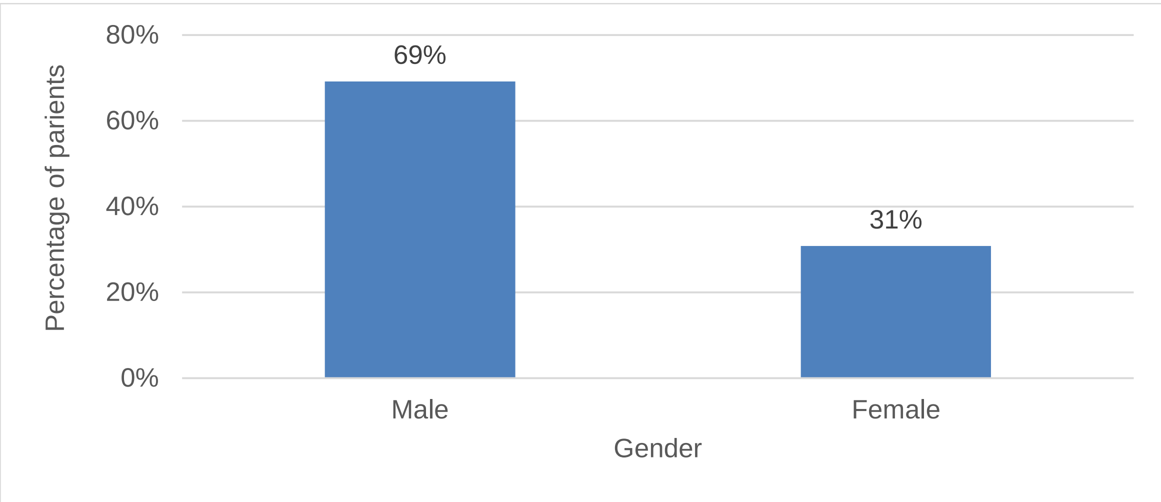

Figure 3.1: Patient gender.

This result is in keeping with findings from both South Africa[19] and sub-Saharan Africa[20].

3.2.2 Age

The ages of patients in this study ranged from 18 to 77 years. The patients were on average 35.45 ± 12.57 years old, as depicted in Figure 3.2:

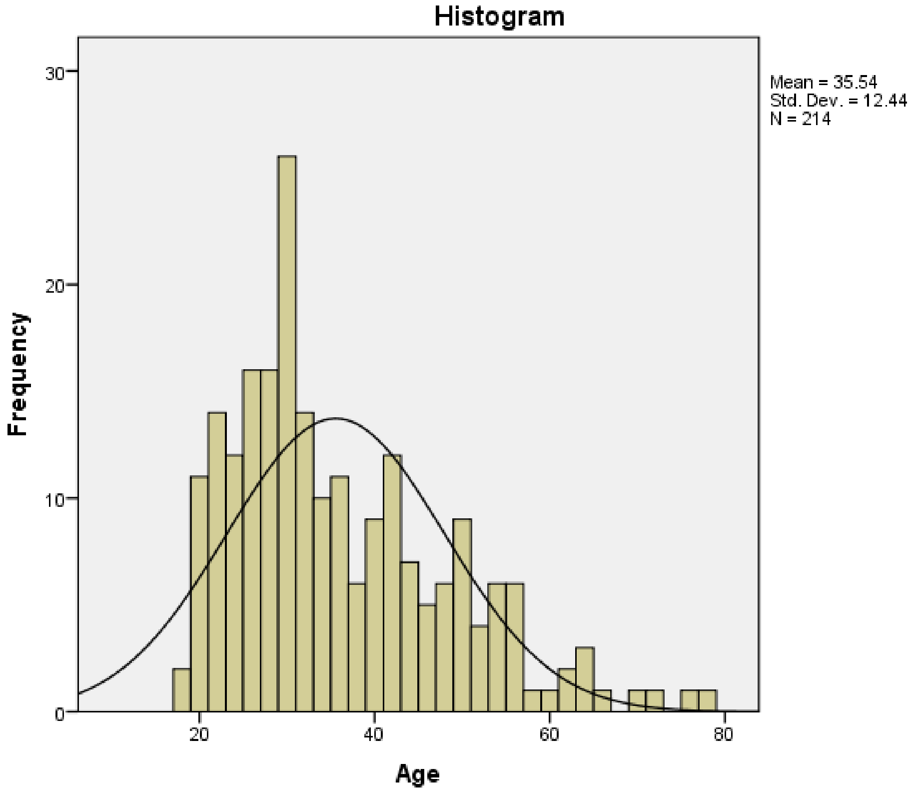

Figure 3.2: Age distribution

3.3 HIV status, CD4 cell counts, viral loads and anti-retroviral treatment (ARVT)

Of the 204 patients included in the study sample, 60 were HIV positive (29%) and 146 were HIV negative (71%). Only 17 of these patients had serological testing for VL, and 32 CD4 cell count results were found. Of the 17 patients who had VL recorded, the VL for 29.4% of these patients was < 500 copies/ml, for 5.9% of the patients it was 500 – 10 000 copies/ml, none had VL between 10 001-30 000 and for the remaining 64.7% of patients it was >30 000 copies/ml.

Table 3.1 below shows the VLs:

Table 3.1: Viral Load grouped

VL grouped					
Copies/ml		**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	< 500	5	8.3	29.4	29.4
	500-10 000	1	1.7	5.9	35.3
	10 001-30 000	0	0.0	0.0	35.3
	> 30 000	11	18.3	64.7	100.0
	Total	17	28.3	100.0	
Missing	Unknown	45	71.7		
Total		62	100.0		

Of the 32 patients who had their CD4 counts recorded, 65.6% had a CD4 cell count of less than or equal to 350 cell/µL while the other 34.4% had a CD4 count greater than 350 cells/µL.

Table 3.2 below shows the CD4 counts:

Table 3.2: CD4 cell count grouped

CD4 Count					
CD 4 cell count (cells/µL)		**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	≤ 350	21	35.0	65.6	35.0
	>350	11	18.3	34.4	53.3
	Total	32	53.3	100.0	100
Missing	Unknown	28	46.6		
Total		62	100.0		

Of the 32 patients with clinical information on ARVT use, 60% had been initiated on and were compliant with ARVT, 37.1% had not been initiated on ARVT, and the remaining 2.8% had been initiated on ARVT but defaulted. The remaining 41.7% of HIV infected patients had no clinical information available on their ARVT usage.

Table 3.3 shows those HIV positive patients taking ARV's:

Table 3.3: Anti-retroviral (ARVT) use

ARVT					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	On ARVs	21	35.0	60.0	35.0
	Not on ARVs	13	21.7	37.1	56.67
	ARV defaulter	1	1.7	2.8	58.3
	Total	35	58.6	100.0	100
Missing	Unknown	25	41.7		
Total		60	100.0		

3.4 HIV status and mortality

The mortality in HIV positive patients was higher (21.7%) than that in HIV negative patients (15.2%). However using the chi-squared test this difference was not statistically significant (p-value = 0.270).

The relationship between HIV status and mortality is shown below in Table 3.4:

Table 3.4: Relationship between HIV status and mortality

		HIV Status			**p-value**
Variable	**Category**	**Positive**	**Negative**	**Total**	
Mortality	Yes	13 (21.7%)	22 (15.2%)	35 (17.1%)	0.270
	No	47 (78.3%)	122 (84.7%)	169 (82.8%)	

3.5 HIV viral load and mortality

The mortality in patients with a VL of < 500 copies/ml was 38.3%, while in patients with VLs > 30 000 it was 66.7%. There were no mortalities in the group who had VLs of between 500 and 10 000 copies/ml. These differences were not statistically significant (p-value = 0.589). The association of other potential confounding factors such as % TBSA, co-morbidities and age were not examined due to the small number of patients who had VLs recorded.

Table 3.5: Viral Load (VL) and mortality

		Mortality			p-value
	copies/ml	**Yes**	**No**	**Total**	
VL	< 500	3 (33.3%)	2 (22.2%)	5 (29.4%)	0.589
	500-10 000	0 (0%)	1(11.1%)	1 (5.8%)	
	10 001-30 000	0 (0%)	0 (12.5%)	0 (0%)	
	> 30 000	6 (66.7%)	5 (62.5%)	11 (64.7%)	

3.6 HIV status and length of hospital stay (LOS)

The patients in this study had an average length of hospital stay (LOS) of 23.15 ± 21.67 days with the shortest LOS being one day and the longest being 130 days. Cox regression was fitted with LOS as the dependent variable, death as the event of interest and age and gender (female) as covariates. There was no statistically significant difference in LOS between HIV positive and negative patients (p-value = 0.241).

These results are shown in Tables 3.6 and 3.7 below:

Table 3.6: Patient LOS

Descriptive Statistics					
	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
LOS	201	1	130	23.154	21.671

Table 3.7: Length of hospital stay: age and gender

Stratum status[a]

Stratum	Strata label	Event	Censored	Censored Percent
1,00	Positive	13	41	75.9%
2,00	Negative	21	117	84.8%
Total		34	158	82.3%

a. The strata variable is : HIV Status

Omnibus tests of model coefficients[a]

-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig	Chi-square	df	Sig	Chi-square	df	Sig
259.487	2.849	2	.241	2.694	2	.260	2.694	2	.260

a. Beginning Block Number 1. Method = Enter

Variables in the equation

	B	SE	Wald	df	Sig.	Exp (B)	95,0% CI for Exp(B)	
							Lower	Upper
Age	-.005	.014	.153	1	.696	.995	.968	1.022
Female	.603	.362	2.778	1	.096	1.827	.899	3.713

3.7 HIV and co-morbidities

There was no association between the co-morbidities recorded and the study patient mortality. All patients with multiple co-morbidities had hypertension and either a co-morbid neurological or psychiatric condition.

Table 3.8 shows comorbidities recorded for all patients:

Table 3.8: Co-morbidities in study patients

Co-morbidities		Mortality		P-value
	N	No. patients mortality	No. patients survived to discharge	
Respiratory	4	1(25%)	3 (75%)	0.482
Multiple	4	2 (50%)	2 (50%)	0.114
Trauma	3	3 (100%)	0 (0%)	0.004
Metabolic Syndrome	1	0 (0%)	1 (100%)	0.729
Hypertension	16	5 (31.3%)	11 (58.7%)	0.076
Pregnancy	3	0 (0%)	3 (100%)	0.623
Neurological disorders	7	1 (14.2%)	6 (85.7%)	0.725
Psychiatric disorders	17	1 (5.8%)	16 (94.1%)	0.280
None	149	22 (14.7%)	127 (85.2%)	0.102
All	55	13 (23.6%)	42 (76.3%)	0.102

In patients who were HIV infected with a concurrent co-morbidity, no increased risk of mortality could be demonstrated.

This is shown in Table 3.9:

Table 3.9: Co-morbidities and mortality

		Mortality		P-value
	N	No. patients mortality	No. patients survived to discharge	
Respiratory	2	1 (50%)	1 (0%)	0.399
Multiple	1	0 (0%)	1 (0%)	1.000
Trauma	0	0 (0%)	0 (0%)	-
Metabolic syndrome	0	0 (0%)	0 (0%)	-
Hypertension	6	3 (50%)	3 (50%)	0.241
Pregnancy	2	0 (0%)	2 (100%)	0.636
Neurological	2	0 (0%)	2 (100%)	0.636
Psych	4	0 (0%)	4 (100%)	0.765
None	42	9 (21.4%)	34 (80.9%)	0.137

3.8 %Total Body Surface Area (TBSA), mortality and length of hospital stay (LOS)

Mortality in both patient groups was higher in patients with a TBSA burn of more than 40%. This relationship was statistically significant (p-value = 0.000 and p-value = 0.004). Mortality for HIV infected patients in this category was 80%, with a mortality of 78.5% in HIV uninfected patients. This is significantly higher than the mortality rate of 10.9% found in BEAMS ICU burn patients [57].

In patients with a TBSA burn of between 20 and 39%, the mortality in HIV infected patients was 25% *versus* 14.3% in the uninfected group. In burns of less than 20%, the mortality in HIV infected patients was 12.8% *versus* 2.4% for uninfected patients.

In HIV infected patients, the LOS showed no relationship.

In the HIV negative group, higher percentage burns had the shortest LOS (p-value = 0.006). This can be explained by the increased mortality in the higher % TBSA burns groups.

These findings are shown in Table 3.10:

Table 3.10: Mortality and Total Body Surface Area (TBSA) in HIV and non-HIV infected patients

TBSA	HIV Positive Patients		HIV Negative Patients	
	Length of stay	mortality	Length of stay	Mortality
< 20	14 (6;26)	5 (12.8%)	19 (9;32)	2 (2.4%)
20-39	20 (17;36)	4 (26.7%)	23 (10;31)	8 (17.8%)
≥ 40	11 (9;12)	4 (80%)	6 (4;7)	12 (78.5%)
p-value	0.326	0.004	0.006	0.000

CHAPTER FOUR: Discussion and conclusions

This retrospective analysis covers the timeframe from January 2012 until July 2015 and includes 204 patients that were admitted to CHBAH ABU. The majority of patients admitted during this time were not eligible to be included in the study due to incomplete clinical records. None of the patients included in this study had estimated TBSA burns above 60%.

4.1 Demographics

The age range of patients was from 18 to 77 years, with an average age of 35.54 years. The majority (69%) of patients were male. This differs from other LMIC's, where the majority of burn victims were female [18], but however concurs with findings from Mpumalanga [19], South Africa and sub-Saharan Africa [26].

4.2 HIV status, CD4 cell counts, viral loads (VL) and anti-retroviral therapy (ARVT)

HIV positive patients account for 29% of the study population. This is above both the estimated national average of 12.2% of all South Africans and the averages of 16.9%[2], 18.1% and 18.8% reported in those aged 15-49 years [4]. It is similar to the prevalence rate of 32.2% found in surgical patients admitted to CHBAH, Soweto between 2003 – 2004 [11] as well as the Gauteng antenatal prevalence of 30.2% in 2015 [3].

As only 17 patients had an HIV-VL recorded and 32 a CD4 cell count recorded, unfortunately no significant statistical analysis of this data could be performed due to the low numbers and thus no conclusions could be drawn.

For 41.7% of the study patients, no clinical information was available on their ARVT usage. Of the remaining patients, 60% were initiated on ARVT during their admission or were already on ARVT prior to their admission in the ABU at CHBAH.

4.3 HIV status and mortality

The mortality rate for HIV positive patients was 21.7% compared with 15.3% in those who were HIV negative. However, statistical significance could not be demonstrated.

These figures are higher than those of burn centres in high income countries (see Table 1.2), but are in keeping with studies of other African countries (see Table 1.3).

4.4 Mortality and HIV viral load (VL)

Very few (17 out of 60 HIV positive) patients had serological testing for VLs. No statistically significant difference in mortality could be demonstrated in those with higher *versus* lower VLs.

4.5 HIV status and length of hospital stay (LOS)

Length of stay was not statistically different between the two groups of patients. This is similar to findings of studies from Malawi [47], South Africa (Stellenbosch) [48] and Zimbabwe [49].

4.6 Co-morbidities, mortality and HIV status

No correlation could be found between mortality and documented co-morbidity. In patients who were HIV infected and had an additional co-morbidity, no increase in the risk of mortality was observed.

4.7 %Total Body Surface Area (TBSA), mortality and length of hospital stay (LOS)

A relationship between HIV and mortality as well as LOS was not observed when assessing burns of different % TBSA. However, the risk of mortality was related to increased % TBSA burn, and was significant in burns of over 40% TBSA ($p = 0.000$). This suggests that % TBSA burn, rather than HIV status is a more significant predictor of patient outcome.

In HIV uninfected patients, the LOS was higher for lower % TBSA burns, most likely reflecting the increasing mortality with increasing % TBSA burns. Of note, in patients with burns of 40% TBSA or higher, the mortality rates were 78.5% and 80%. This very high mortality rates can be compared with the BEAMS ICU study, which showed a mortality rate of 10.9% in patients requiring ICU admission [57]. However, the mean % TBSA for patients included in the BEAMS study was 17%.

4.8 Limitations

Due to the retrospective nature of the study, clinical information was not obtainable in the majority of patients admitted during the time period of the study, thus limiting the sample size. As few patients had HIV-VL and CD4 cell counts done, no conclusions could be drawn from the collected data.

As the majority of patients did not undergo HIV serological testing, it is possible that those patients who had a complicated in-hospital course were more likely to be tested. This is a potential source of bias and may compromise the usefulness of the results.

4.7 Conclusions

Although there was a trend toward increased mortality in HIV positive patients, statistical significance could not be demonstrated. However, mortality rates were similar to those reported in studies from other African countries. Mortality in patients with burns of more than 40% TBSA was particularly high. There was no difference in LOS between the HIV positive and the HIV negative groups of patients included in this study.

4.8 Recommendations

In view of the high prevalence of HIV (29%), voluntary counselling and testing (VCT) as part of the ABU admission protocol should be considered in the unit. The high mortality rates in patients with a burn injury of more than 40% TBSA need further investigation.

Prospective studies involving routine VCT for HIV for all patients admitted to the ABU will allow for accurate documentation and follow-up of clinical information. This is more likely to definitively address the question regarding mortality and LOS in HIV positive *versus* HIV negative burns patients. Testing the HIV-VL would potentially enable a better understanding of the impact of the severity of the HIV infection on the burn patient's progress to recover, as well as the prognosis.

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APPENDICES:

R14/49 Dr Claire Sanders

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150911

NAME: **(Principal Investigator)**	Dr Claire Sanders
DEPARTMENT:	Surgery Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	The Effect of HIV on Mortality and Length of Hospital stay at the Adult Burn Unit, Chris Hani Baragwanath Academic Hospital
DATE CONSIDERED:	02/10/2015
DECISION:	Approved unconditionaly
CONDITIONS:	
SUPERVISOR:	Dr R Moore and Dr Marietha Nel
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	08/04/2016

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 in Room 10004, 10th floor, Senate House/2nd Floor, Phillip Tobias Building, Parktown, 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 September and will therefore be due in the month of September each year.

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