

**SAINT PAUL HOSPITAL MILLENNIUM MEDICAL COLLEGE
DEPARTMENT OF SURGERY**



**RESEARCH PAPER ON:
CD4 LEVEL AND POSTOPERATIVE OUTCOME OF RVI
PATIENTS; A THREE YEAR CASE CONTROL STUDY.**

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**CD4 LEVEL AND POSTOPERATIVE OUTCOME OF RVI
PATIENTS; A THREE YEAR CASE CONTROL STUDY.**

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Contents

Abstract	5
<i>1. INTRODUCTION.....</i>	<i>7</i>
<i>1.1 BACKGROUND</i>	<i>7</i>
<i>1.2 STATEMENT OF THE PROBLEM.....</i>	<i>7</i>
1.3 OBJECTIVE OF THE STUDY.....	9
<i>1.3.1 GENERAL OBJECTIVE.....</i>	<i>9</i>
<i>1.3.2 SPECIFIC OBJECTIVES.....</i>	<i>9</i>
<i>1.4 DEFINITION OF TERMS.....</i>	<i>9</i>
2. LITRATURE REVIEW.....	10
3 METHEDOLOGY.....	12
3.1 STUDY AREA.....	12
3.2 Source population.....	12
3.3 STUDY POPULATION.....	12
3.4 INCLUSION CRITERIA.....	12
3.5. EXCLUSION CRITERIA.....	13
3.6 SAMPLE SIZE.....	13
3.6 SAMPLING TECHNIQUE.....	14
3.7 DATA COLLECTION.....	14
3.8 DATA COLLECTION PERSONELS.....	14
3.9 DATA QUALITY.....	14
3.10 VARIABLES.....	14
Independent variables.....	14
Dependent variables.....	14
3.11 DATA ANALYSIS.....	15
3.12 ETHICA CONSIDERATIONS.....	15
3.13 LIMITATIONS OF THE STUDY.....	15
4. Results.....	17

5. discussion.....	Error! Bookmark not defined.
6. Conclusion.....	19
7. Recommendations.....	20
8.Reference.....	23
9 Questioner	24

Abstract

INTRODUCTION

HIV/AIDS continued to be global public health burden. The WHO 2016 report indicates worldwide prevalence of the disease is 36.7 million of which 19.4 million are found in eastern and southern Africa. It was a major challenge for surgeons for years with significant post-operative morbidity and mortality.

OBJECTIVE

The objective of this study is to determine the association between CD4 level of RVI patients and post-operative outcome following surgeries in St. Paul hospital millennium medical college.

METHODOLOGY

A retrospective case control study of all RVI patients who were operated in the past three years in SPHMMC.

RESULTS

47 HIV positive patients and 60 HIV negative patients of comparable age, sex and procedure were involved in the study. Overall postoperative complications and hospital stay were significantly increased in patients with low CD4 and operated on emergency bases. Complications were also increased in patients whose HIV status is known recently. No significant association found based on age and sex of the patients. There is no significant change in mortality.

CONCLUSION

There is statistically significant association found between CD4 level and postoperative complications and hospital stay of RVI patients.

1. INTRODUCTION

1.1 BACKGROUND

HIV continues to be global public health issue. In 2016, an estimated 36.7 million people were living with HIV, with global HIV prevalence of 0.8% among adults¹. The vast majority of people living with HIV are located in low and middle income countries, with an estimated 25.5 million living in sub-Saharan Africa¹. Among this 19.4 million are living in east and southern Africa¹. Ethiopia, as one of the sub-Saharan country is one of high burden areas. There are 1.2 million people living with HIV in Ethiopia with the prevalence of 2.4% in the adult population². In the earlier times, surgery for HIV patients was beyond considerations because of the high morbidity and mortality associated and also the fear and stigma among professionals. Early surgical complications in RVI patients were as high as 85%. Despite the prevalence and incurability of the disease, the introduction of anti-retroviral drugs has increased the survival years and quality of life of people with HIV. Currently, people living with HIV are developing different surgical conditions which need surgical intervention as the rest of HIV negative populations.

1.2 STATEMENT OF THE PROBLEM

Of the 36.7 million people living with HIV worldwide, 25.5 million are found in sub-Saharan Africa¹. The earliest experiences regarding surgical procedures in HIV patients reported complication rates as high as 85% and mortality rates

ranging from 55% to 70%³. This information however has mainly been derived from previous retrospective studies and has mainly been carried out in the western world where the presentation of HIV is not exactly the same as that in sub-Saharan Africa. As a low income country, in Ethiopia there is no access for determination of viral load in HIV patients except in tertiary hospitals, which may also be a better tool to assess patients' immune status. But CD4 count can be done almost in all hospitals for free and can be used in majority of the setups. Although sub-Saharan Africa is a high burden area of the world with HIV, the studies done in this area are very few. Unlike the previous times, where the presentation of HIV patients are mainly HIV related illness and mostly non-surgical; after the introduction of HAART, RVI patients are living longer and showing variety of non RVI related surgical conditions as the rest of the non RVI patients⁴. Therefore it is important to have cost effective accessible prognostic indicator in this group of patients.

SIGNIFICANCE OF THE STUDY

The research from other countries shows that postoperative morbidity and hospital stay of HIV patients are significantly high, especially prior to the era of HAART. But as to the best of my knowledge there is no study in Ethiopia which shows the outcome of HIV patients in our country.

CD4 level was found to be good prognostic indicator of out-come in HIV patients in research done in other countries. Since it's routinely done in our country for follow-up, it will be of great importance in predicting patient outcome if the study shows significant relation.

1.3 OBJECTIVE OF THE STUDY

1.3.1 GENERAL OBJECTIVE

To determine post-operative outcome of HIV positive patients based on the level of CD4.

1.3.2 SPECIFIC OBJECTIVES

To determine common post-operative complications

To determine the type of surgeries with increased rate of complications

To determine the relation of complications with the patients CD4 count

1.4 DEFINITION OF TERMS

- HIV positive patients are those whose sero status is confirmed either by rapid antibody test or antigen tests in the health facility
- HAP – pneumonia acquired after 72 hours of hospital admission
- HAART- Highly active anti Retroviral Therapy

2. LITRATURE REVIEW

In the early years of HIV pandemic, reports on outcome of surgery in HIV infected Patients indicated a dramatic mortality and complication rates⁵. These reports specifically pointed septic complications and poor wound healing amongst other adverse events⁶. It was also suggested that the rate of infective complications was worse for surgery performed for a condition considered to be contaminated⁷. Over the past two decades, the operative mortality in HIV-infected patients has dropped drastically from above 85 % to less than 15 %, especially in those requiring urgent laparotomy⁸. This is mainly due to the introduction of HAART and also surgeons understanding of the special care for this patients and indicators of poor prognostic factors.

In a study done in Cameroon by (Alain Chichom Mefire et al)⁹, 112 cases of HIV-infected patients undergoing major abdominal surgery are studied. They categorized the patients into three group (HIV negative, HIV positive with CD4 >200, and HIV positive with CD4 <200) and compared perioperative morbidity and mortality. Accordingly, among HIV negative patients the overall post-operative complication was 10%; where as in those with HIV positive with CD4>200 it was found to be 18% and 52 % in HIV positive with CD4<200. The

study also showed that there is significant association between hospital stay and level of CD4 in HIV positive patients. 14% of patients with CD4 > 200 had hospital stay greater than 20 days as compared to 38% of patients with CD4 < 200. In this study they adjusted the patients in terms of age, co-morbidity and other poor prognostic factors such as low albumin and anaemia. This study also showed that the complications are more common for septic procedures and also more in emergency surgeries than elective surgeries.

There is also study done by (Isichei M.W et al)¹⁰ which showed comparable results. The study involved 282 HIV patients who undergone major surgeries. The study population had a mean CD4 count 168 +/- 140.cell/ml, One hundred and ten patients (39%) healed normally and were discharged without complications, while 114(40.3%) had delayed wound healing and were discharged home after two weeks. There was 20.7% mortality in this study (58 patients). Patients that had delayed wound healing had a mean CD4 count of 160, while mortality was seen in patients with a mean CD4 count of 150. Again implicating low CD4 is a risk factor for post-operative morbidity and mortality.

Study done in USA by (George N.Guild et al)¹¹ involving 64 HIV positive patients showed significant post-operative morbidity in HIV patients with low CD4 count. The infection rate was found to be 23 % (15 of 64 patients) compared to the 3.9% overall infection rate in the control group

3 METHEDOLOGY

3.1 STUDY AREA

The study will be conducted at St. Paul hospital Millennium Medical College (SPHMMC) .St Paul hospital is the second largest hospitals located in Addis Ababa, Ethiopia. It is established by the late emperor Hailesilassie in 1969 with the help of German Evangelical church. The hospital became medical college in 2007 under the Ethiopian ministry of health. The hospital has 350 beds and a catchment population of more than 5 million. It has 1200 clinical and non-clinical staff. Currently there are over 13 departments which includes; surgery, internal medicine neurology, ENT, psychiatry, ophthalmology, dentistry, radiology, dermatology, gynaecology and obstetrics, paediatrics, emergency medicine.

3.2 Source population

All patients operated in St Paul Hospital millennium medical college in the past three years(Jan 2015- Dec 2017)

3.3 STUDY POPULATION

All HIV positive patients who undergo surgeries in st.paul hospital millennium medical college in the past three years.

3.4 INCLUSION CRITERIA

All HIV patients whose status is confirmed in health facility with recently known CD4 level.

3.5. EXCLUSION CRITERIA

- Newly diagnosed patients with unknown CD4 level
- Children under 18 months of age
- Patients with other known immunocompromizing illness such as DM and malignancies
- Patients with anaemia and hypoalbumenemia.

3.6 SAMPLE SIZE

4.1 Sample size

The minimum sample size required is:

$$n = Z^2 p (1-p) / d^2$$

Where: n = minimum required sample size

P= population proportion in problem (estimated prevalence) = 0.024

d = degree of accuracy (estimated error) = 5% or 0.05

Z = the standard normal value at confidence interval of 95% = 1.96

$$\begin{aligned} n &= (1.96)^2 * .024 * (1-0.024) / (.05)^2 \\ &= (3.84) * (0.976) * (0.024) / 0.05^2 \\ &= 32 \end{aligned}$$

3.7 SAMPLING TECHNIQUE

No sampling technique is used due to small sample size. All HIV positive patients operated in SPHMMC in the past three years fulfilling the inclusion criteria will be involved and compared to matched non RVI patients.

3.8 DATA COLLECTION

Data is collected from patients chart based on the questioners formulated for the study.

3.9 DATA COLLECTION PERSONELS

At list two data collecting personnel (interns) will be recruited and briefed on the questioners and the objectives of the study.

3.10 DATA QUALITY.

During data collection, there will be daily supervision and update for data collectors to obtain quality and consistent information.

3.11 VARIABLES

Independent variables

Age, sex, Duration of HIV infection, type of procedures and CD4 levels are independent variables.

Dependent variables

- Post-operative morbidity
- post-operative mortality
- Hospital stay

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3.12 DATA ANALYSIS

Data collected based on the questioners will be analysed using SPSS statistical software version 23.

3.13 ETHICA CONSIDERATIONS

Ethical permission was obtained from college's ethical review board before collecting information from patients chart. Information from the patients chart will be kept confidential and patients name was not used in this research.

3.14 LIMITATIONS OF THE STUDY

Since the study is a retrospective study, retrieving patient's charts and obtaining all information from the chart was a major challenge. Also, majority of the patients have their HIV follow up in other facility and the retrieval of the level of CD4 was mainly dependent on patient's information or referral papers.

4. Results

There were a total 89 HIV positive patients operated over the past three years of which 47 patients are found to fulfil the criteria of this study and 60 HIV

negative matched patients also included making total of 107 patients. The HIV positive patients are categorized in to four groups based on their recent known CD4 level (Group one CD4 <100, group two CD4 100-300, group three CD4 > 300-500, and group four CD4 > 500). Majority of patients has CD4 level greater than 300 cells and only two patients have CD4 level < 100. Of the 47 Positive patients 21 are male and 26 are female.

Age , sex and Serostatus of patients.

Count

Serostatus			sex		Total
			male	femal	
Positive	Age	21-40	9	19	28
		>40	12	7	19
	Total		21	26	47
Negative	Age	0-20	4	1	5
		21-40	10	18	28
		>40	11	16	27
	Total		25	35	60
Total	Age	0-20	4	1	5
		21-40	19	37	56
		>40	23	23	46
	Total		46	61	107

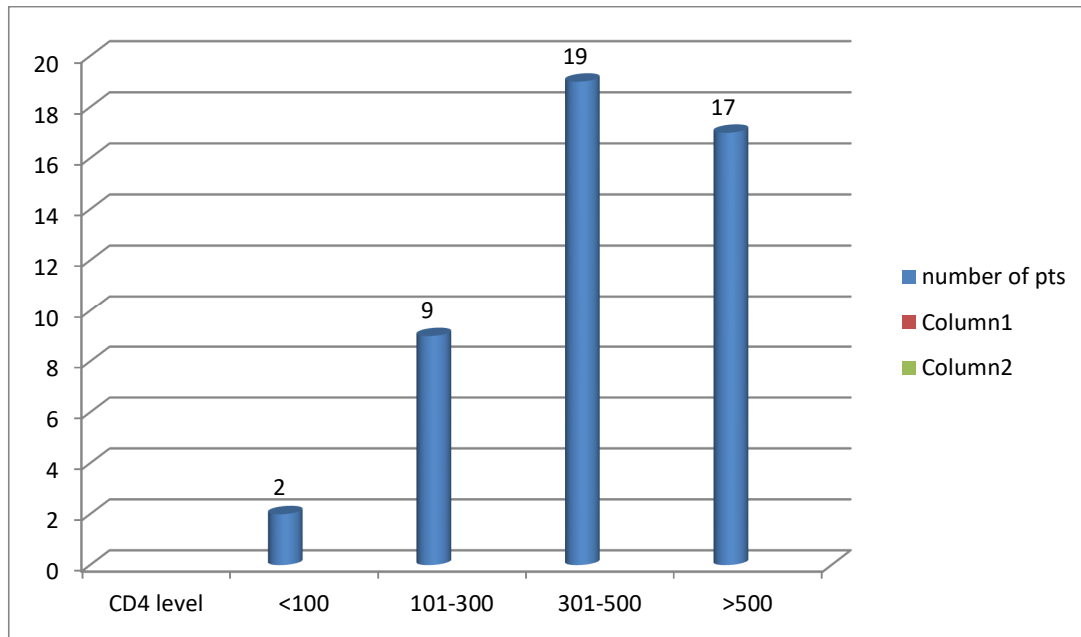


Fig.1 Number of patients based on their CD4 count

Of the 47 HIV positive, 35 patients (74.4%) undergone elective procedures and 12 patients (25.6%) undergone emergency procedures (table). 43 of the seropositive patients are on HAART at the time of surgery and 4 patients were not on HAART. The indications for emergency procedures were different abdominal complaints which includes gangrenous large bowel obstruction, peritonitis secondary to perforated viscus and appendicitis and its complications. Elective procedures for both seropositive and seronegative patients involve thyroid pathologies, biliary pathologies, Breast pathologies and hernias.

Of the 47 seropositive patients 14 were complicated which makes complication rate of 29.78%. Surgical site infection was seen in 7 patients (14.89%), dehiscence in 2 patients (4.25%), hospital acquired pneumonia in 3 patients (6.3%) and there were 2 deaths (4.25%). The overall complications in seronegative patients are 4 (6.66%) of which 3 are SSI and one wound dehiscence.

Out of the twelve seropositive patients undergone emergency procedures seven patients (58.3%) were complicated. Five of the seven complications among emergency procedure have CD4 count of < 300 cells. There were two patients with CD4 count less than 100 cells and both were complicated.

Among the 35 patients operated on elective bases 7 (20%) were complicated and five of them have CD4 count < 500 cells. There is no patient with CD4 < 100 found among the elective procedures. Seropositive and post-operative complication is significantly associated ($P < 0.001$)

Table 2.1 Type of surgery and complications of patients

Serostatus			Type of complications				Total
			SSI	dehiscence	HAP	dead	
Positive	Type of surgery	elective	5	1	1	0	7
		emergency	2	1	2	2	7
	Total		7	2	3	2	14
Negative	Type of surgery	elective	1	0			1
		emergency	2	1			3
	Total		3	1			4
Total	Type of surgery	elective	6	1	1	0	8
		emergency	4	2	2	2	10
	Total		10	3	3	2	18

Table 2.2 Type of surgery , level of CD4 and complications

Out come			level of CD4				Total
			<100	101-300	301 -500	>500	
smooth	Type of surgery	elective		4	12	12	28
		emergency		0	2	3	5
	Total			4	14	15	33
complicated	Type of surgery	elective	0	2	3	2	7
		emergency	2	3	2	0	7
	Total		2	5	5	2	14
Total	Type of surgery	elective	0	6	15	14	35
		emergency	2	3	4	3	12
	Total		2	9	19	17	47

Postoperative hospital stay was found to be significantly prolonged in seropositive patients when compared to the seronegative patients. Of the 47 seropositive patients 12(25.5%) has stayed for more than 10 days in the hospital postoperatively. Among this 6(50%) are operated on emergency bases. 18 seropositive patients(38.2%) has stayed for more than five days postoperatively as compared to 5% of the seronegative patients. The post-operative hospital stay is also significantly associated CD4 level of the patients ($P < 0.007$). 63.5 of patients with $CD4 < 300$ has stayed for more than 10 days. Table 3 below shows postoperative hospital stay of patients.

Table 3 Serostatus , Post-operative hospital stay and Type of surgery

Count

Type os surgery			Post operative hospital stay			Total
			<5days	5-10days	>10days	
elective	Serostatus	Positive	22	7	6	35
		Negative	26	5	0	31
	Total		48	12	6	66
emerngency	Serostatus	Positive	4	1	6	11
		Negative	24	5	0	29
	Total		28	6	6	40
Total	Serostatus	Positive	26	8	12	46
		Negative	50	10	0	60
	Total		76	18	12	106

The duration since HIV diagnosis and outcome of the surgery is also analysed in this study and the number of complications were found to be more in patients who are diagnosed with HIV recently($P=0.49$).Table 4 below shows duration of HIV diagnosis and post-operative outcome of patients.

Table 4. years since known and Out come

Count

		Out come		Total
		smooth	complicated	
years since known	0-5	11	7	18
	5-10	15	4	19
	>10	6	3	9
	33.00	1	0	1
Total		33	14	47

There was no significant difference in postoperative complications observed based on the sex of the patients ($P > 0.63$). There were four patients, who were not on started on HAART at the time of surgery. Two of them were operated on elective bases and two were operated on emergency bases. Both patients operated on emergency bases were complicated($P = 0.19$), one patient developed hospital acquired pneumonia and the other developed surgical site infection.

Table 5.On HAART * Outcome of surgery

Count

Type os surgery			Out come		Total
			smooth	complicated	
elective	On HAART	yes	26	7	33
		No	2	0	2
	Total		28	7	35
emerngency	On HAART	yes	5	5	10
		No	0	2	2
	Total		5	7	12
Total	On HAART	yes	31	12	43
		No	2	2	4
	Total		33	14	47

6. Discussion

The main finding in this research is that HIV patients are associated with increased risk of post-operative complications as compared to the matched seronegative patients of same age, sex and procedures. This complication rate was found to be significant in emergency surgeries.

In a study done in Cameroon, among HIV negative patients the overall post-operative complication was 10%; where as in those with HIV positive with CD4>200 it was found to be 18% and 52 % in HIV positive with CD4<200.

The overall complication rate in seropositive patients in our study is 29.78%, and 6.6% in seronegative patients.

Post-operative hospital stay is also significantly increased in seropositive patients as compared to seronegatives and has significant association with the CD4 level. 63.3% of patients with CD4 <300 has hospital stay greater than ten days in this study. The study in Cameroon also showed significant association between CD4 level and hospital stay (38% of patients with CD4<200 had hospital stay > 20days).

Complications like surgical site infection, dehiscence and pneumonia are also increased in seropositive patients and are significant in emergency procedures and patients with CD4 <300 (57%). In the study in the Cameroon it is also found to be 62% in those with CD4<200.

There is no difference noted in overall postoperative mortality in patients with seropositive and the control group.

Serostatus , Type of complications and level of CD4

Count

level od CD4			Type of complications				Total
			SSI	dehiscence	HAP	dead	
<100	Serostatus	Positive	1			1	2
	Total		1			1	2
101-300	Serostatus	Positive	3	1	2		6
	Total		3	1	2		6
301 -500	Serostatus	Positive	2	1	1	1	5
	Total		2	1	1	1	5
>500	Serostatus	Positive	1				1
	Total		1				1
Total	Serostatus	Positive	7	2	3	2	14
	Total		7	2	3	2	14

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7. Conclusion

HIV patients undergoing surgeries has increased risk of postoperative morbidity and prolonged hospital stay as compared to non HIV infected patients. The rate of complication and hospital stay was found to be significant in patients with low CD4 and those operated on emergency bases. There is no change in mortality rate observed.

8. Limitation

Due to limited sample size its difficult to generalize the result.

WHO staging of the patients were not analysed due to lack of documentation

The exact cause of death is not known and difficult to associate with HIV status.

9. RECOMMENDATION

HIV positive patients are at increased risk of septic complications and strict postoperative follow-up is needed, especially following emergency surgeries and in patients with low CD4.

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5.3 QUESTIONER

1. Age_____
2. Sex a. M b. F
3. HIV Sero-status 1.Reactive 2.nonreactive
4. Years since known a. < 5yrs b. 5-10 yrs. c. > 10 yrs.
5. Last CD4 count level
6. WHO stage a. I b. II c. III d. IV
7. Patient on HAART a. Yes b. No
8. Duration on treatment _____
9. Other comorbid illness? 1.yes 2.no
- 10.Disease1.Specify_____
- 11.Type of Surgery a. Emergency b. Elective
- 12.Site of surgery a. Abdominal b. Others_____
- 13.Outcome of Surgery a. smooth course b. complicated c. Dead
- 14.Type of complications a. SSI b. HAP wound dehiscence
d. others_____