A STUDY OF HEMI-BODY IRRADIATION IN AIDS-RELATED KAPOSI SARCOMA

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by

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DECLARATION

I, James Sospater Msirikale, hereby declare that this dissertation is my original work and has not been presented for a degree in any other university,

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SUMMARY

Treatment of advanced AIDS-related Kaposi sarcoma is essentially palliative. Various modalities of treatment have been used in the literature but have not improved the survival of these patients. Hemi-body irradiation has been found to be safe and effective in palliation of haemopoietic and lymphoproliferative disorders in non-immunosuppressed patients.

Advanced AIDS-related Kaposi sarcoma patients have a poor prognosis therefore palliative therapy when indicated should be simple and convenient. A study of the role of hemi-body irradiation was thus initiated. The treatment consist of a single treatment to one half of the body. This may be followed by another single treatment to the other half.

The main objectives were to study the response, clinical side effects, haematological side effects, duration of response and survival after hemi-body irradiation so as to make recommendations on its use.

From 10/4/1991 to 15/2/1992, 25 patients with stage 3 and 4 AIDS-related Kaposi sarcoma were studied at Mpilo Radiotherapy Centre.

A checklist of patients' particulars was made and a descriptive study performed on the effects of hemi-body irradiation.

The main findings were that the overall response for skin lesions and lymphadenopathy was 94%. The clinical side effects were generally mild, being predominantly alopecia and vomiting in upper hemi-body irradiated patients. Overall median survival was 100 days from the day of first hemi-body irradiation. Poor prognostic factors were the presence of pleuro-pulmonary lesions, short duration of symptoms, unemployment, female gender and poor performance status. Patients with these factors had a median survival of 45 - 60 days. Recurrence occurred in 5 patients within 10 - 13 weeks. It was concluded that hemi-body irradiation is safe and effective but has a tendency to short duration of remission. Further studies with larger sample size are required to provide statistically significant data.

It is recommended that studies of better anti emetics be made for use during hemi-body irradiation, close monitoring of haematological indices after upper hemi-body irradiation, and studies on quality of life be made to further clarify the role of this modality.

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LIST OF ABBREVIATIONS

AIDS	-	Acquired Immunodeficiency Syndrome
EKS	-	Epidemic Kaposi Sarcoma
HIV	-	Human Immunodeficiency Virus
HBI	-	Hemi-body Irradiation
UHBI	-	Upper Hemi-body Irradiation
LHBI	-	Lower Hemi-body Irradiation
CO-60	-	Cobalt-60
K	-	Karnofsky Performance Status
AFB	-	Acid Fast Bacilli
TAR	-	Tissue Air Ratio
cGy	-	Centi-Gray
SSD	-	Source Skin Distance
FBC	-	Full Blood Count
WBC	-	White Blood Cells
n-r/n-r+1	-	Proportion of patients surviving through each time interval n = sample size, r = uncensored rank
s (t)	-	Product limit estimate of the cumulative proportion surviving

1. INTRODUCTION

Kaposi sarcoma is usually treated at the Radiotherapy Centre for patients referred to Mpilo Hospital in Bulawayo. On reviewing the hospital records, the number of Kaposi sarcoma patients treated at the centre has been increasing from less than 10 cases per year in the 1980's to more than 30 cases per year in the 1990's. The increase has been attributed to AIDS-related or epidemic Kaposi sarcoma (EKS).

Endemic Kaposi sarcoma has traditionally been treated with localized fractionated radiotherapy or with systemic chemotherapy. EKS tends to present as widespread lesions. This may manifest with disfiguring skin lesions and other sites such as the oral cavity, the viscera and lymph nodes. The treatment of EKS would therefore require systemic chemotherapy or if radiotherapy is used then extended fields to encompass all the sites of disease.

The duration of survival in EKS patients tends to be short. In a study of 187 patients by Berson et al in the United States of America, the median survival from the time of diagnosis of AIDS was 15 months, and median survival from time of radiotherapy was 6 months.[1] Various other treatments for EKS include interferons[2], photodynamic therapy[3] and various combinations of chemotherapy. No

significant impact of available treatments on survival among patients with AIDS-related KS has been demonstrated therefore antitumour therapy should be considered palliative. Krigel[4] points out that the overall prognosis for survival in patients with EKS appears to depend on the severity of immune suppression and HIV infection rather than on the neoplastic proliferation and tumour load. He goes on to suggest that the ultimate ideal treatment for these patients would be a combination of anti retroviral therapy to suppress further effects of HIV, biological therapy to reverse the immunologic defects, chemotherapy to control tumour development, and haemopoietic growth factors to ameliorate treatment toxicities.

Symptoms and signs in EKS patients that need palliation include cosmetically displeasing lesions, pain, bulky lesions, bleeding, surrounding edema, lesions interfering with swallowing, limited mobility, shortness of breath or cough. In Berson's study local control by single radiotherapy fraction of 800 cGy was just as effective as multiple fraction regimens, and severe complications were significantly lower in the single fraction regimens. That study was however non randomized and the single large fractions rarely covered half the body. Some previous reports had showed that EKS patients were unusually sensitive to generally well tolerated radiation doses [5,6].

But rather paradoxically, Berson's results showed that large single fraction doses had less severe side effects on normal tissue than fractionated doses.

Total body irradiation has been used to treat radiosensitive diseases of the haematopoietic and reticuloendothelial systems. Fitzpatrick and Rider[7] irradiated the upper half body (UHBI) and lower half body (LHBI) sequentially with an interval of 5 weeks between treatments to allow sufficient time for haematopoietic stem cells from the unirradiated half of the body to repopulate the irradiated marrow spaces. They used 800 cGy in a single fraction to the lower hemi-body (4th lumbar vertebra to the knees) and 600 cGy to the upper half body without unacceptable toxicity.

Side effects of hemi-body irradiation (HBI) were reviewed by Salazar in 2 papers. Incidence of radiation pneumonitis for doses uncorrected for lung transmission of less than 600, 600, 800 and 1100 cGy was respectively reported as 2, 12, 19 and 52%[8]. With the dose at 600 cGy corrected for lung transmission, the incidence was only 4%[9]. Other side effects of sequential HBI that have been reported in the literature in non immuno suppressed cases by Aziz[10] include acute radiation syndrome which is more common in UHBI. This occurs soon after the radiotherapy and subsides within 8 - 10 hours. It manifests as nausea, vomiting, increases in

body temperature, increased heart rate, and a fall in blood pressure. Subacute toxicity occurs between 3 weeks and 3 months from treatment and is also more common with UHBI. This manifests as

(i) Haematologic depletion (with platelet fall greater than white cell count depletion and haemoglobin being least affected). Counts return to near normal in 6 - 8 weeks.

(ii) Temporary alopecia in 70% of patients.

(iii) Dry mouth and loss of appetite in 22%. Dry mouth can be prevented to some extent by parotid shielding.

(iv) Radiation pneumonitis peaks at 2 - 3 months.

Chronic toxicities are seen between 4 months and 2 years post treatment.

For UHBI these include pulmonary fibrosis, cataracts, and hypothyroidism. For LHBI they consist of minimal gastrointestinal and lower urinary tract damage, and infertility.

In Zimbabwe no studies on the role of radiotherapy in EKS has been reported. The findings and experience gained from this study may show the potential benefit of this relatively cheap method of treatment for palliation of prognostically poor EKS patients.

2. OBJECTIVES

2.1 The general objective was to determine the effect of hemi-body irradiation on disseminated EKS.

2.2 The specific objectives were:

a) determination of response to HBI by site of disease;

b) determination of clinical side effects and haematological toxicity to HBI;

c) determination of duration of response;

d) determination of disease (KS) free survival;

e) determination of overall survival;

f) determination of survival by duration of symptoms and signs of EKS, Karnofsky performance status, sex, employment status and site distribution of EKS as possible prognostic factors.

3. MATERIALS AND METHODS

3.1 Study type: Descriptive.

3.2 Setting: The study was done at Mpilo Radiotherapy Centre which is one of the two radiotherapy centres in Zimbabwe. It receives referred patients from most of the southern half of the country.

3.3 Patients selection: From 10/4/1991 to 15/2/92 a sequential sample of 25 patients was enrolled in the study. The criteria for inclusion were histological proof, Stage III (disseminated cutaneous involvement and or lymph node involvement) or Stage IV (visceral involvement based on clinical, chest X-ray, bronchoscopy, biopsy), serologic evidence of HIV infection, patients willing to participate in the study as evidenced by signed informed consent, WBC > 3 x 10^{9}/L, platelets > 100 x 10^{9}/L, Hgb > 8 g/dL, Lymphocytes > 30%, Lymphocyte count > 1.5 x 10^{9}/L, and

patients amenable to follow up. Patients previously treated with chemotherapy (3), or localized radiotherapy (1) more than 4 weeks prior were included.

3.4 **Exclusion criteria:** 7 cases were excluded from response and side effect evaluation because of death (2) or loss to follow up (5) within 4 weeks of HBI.

3.5 **Pre-treatment studies** included

(i) history on duration of earliest signs of EKS, employment and marital status, age and symptoms;

(ii) physical examination for performance status, site and size of lesions,presence or absence of lymph nodes and or oedema;

(iii) full blood count, U&E, LFT

(iv) chest X-ray;

(v) HIV serology;

(vi) sputum for AFB and culture.

3.6 Patient characteristics

3.6.1 Demographic particulars

There were 16 males and 9 females (ratio 1:8:1). The median age was 31 years (range 21 - 42). For females the median age was 26 years while for males it was 34 years. The number of unemployed patients was 12 and 13 had some employment. 15 patients were married, 9 were single and 1 was divorced.

3.6.2 **Karnofsky performance status (K)** 19 patients (76%) had K > 50% while 6 (24%) had K < 50%.

3.6.3 **Duration of symptoms of EKS.** The median duration was 5 months (range 2 - 24). 10 patients presented with symptom duration of < 3 months while 15 patients presented with > 3 months duration.

3.6.4 **Previous treatment for KS.** 3 patients had chemotherapy and 1 patient had fractionated radiotherapy more than 4 weeks prior to entering the study.

3.6.5 **Clinical presentation.** At presentation patients could be categorized into 4 main groups:

Group 1: cutaneous lesions, leg oedema and lymphadenopathy (5 patients);

Group 2: oropharyngeal lesions and lymphadenopathy (5 patients);

Group 3: cutaneous lesions, oropharyngeal lesions and lymphadenopathy (2 patients); and

Group 4: presence of pleuro-pulmonary lesions (13 patients).

Miscellaneous lesions in the 25 patients included facial edema (4 patients), scrotal edema (2 patients) and eyelid lesion (1 patient).

3.6.6 **Earliest sign noticed by the patient.** Skin lesions (plaques, nodules) was first noticed in 17 patients (68%), lymph node swelling in 4 patients, and 1 patient each for leg edema, cough, facial edema, and eyelid lesion.

3.7 Treatment protocol

3.7.1 Anti-emetics: Stemetil injection 12.5 mg was given about 1 hour before HBI, then orally 5 mg tds for 2 days.

3.7.2 **Radiotherapy.** This was given by external beam using the cobalt 60. The patient was treated lying on the floor for the extended SSD of 140 cm. The UHBI field size covered the level of the umbilicus to the top of the head including the upper limbs. The LHBI covered a field from the level of the umbilicus to the soles of the feet. Bolus was not routinely used for skin lesions. The dose of UHBI was 650 cGy to the mid-plane (uncorrected for lung). The LHBI mid-plane dose was 800 cGy. The fields were parallel opposed. The dose calculations made use of TAR tables and correction factors for distance and field size. Treatment took 30 - 40 minutes per session. The time interval between UHBI and LHBI when both were indicated was 4 - 6 weeks. 8 patients had UHBI only, 8 LHBI only, and 9 had both.

3.7.3 **Additional irradiation.** During subsequent visits additional irradiation was given to one patient who received 2000 cGy in 10 fractions for a persistent tonsillar lesion 4 weeks after UHBI. One patient received localized radiotherapy, 800 cGy for relapse of nodules in upper thigh and ipsilateral inguinal nodes. One patient who had disease mainly in the lower hemi-body received

localized radiotherapy to a palm lesion which was not included in the LHBI field.

3.8 **Monitoring Evaluation** after UHBI involved weekly monitoring of FBC and acute side effects in the first 4 weeks, and response assessment at the end of 4 weeks. Further visits were then scheduled every 2 - 3 weeks to monitor side effects and relapse.

3.9 **Assessment of tumour response.** Measures of response was according to the AIDS cooperative Trials Group[7]. Complete response (CR) was defined as the absence of any detectable residual disease, including tumour associated oedema for at least 4 weeks. For those with EKS lesions detected by chest X-ray a repeat film was done. Partial response (PR) was defined as 50% or greater decrease in the number or size of previously existing lesions as determined clinically and or radiologically. For cutaneous lesions it meant a complete flattening of at least 50% of the lesions. Stable disease was defined as not meeting the criteria for partial or progressive disease. Progressive disease meant an increase of 25% or more in the size, or new lesions, new

sites, increase in tumour associated edema or pleural effusion.

3.10 **Clinical side effects** were graded into 3 categories. Grade 1 was defined as mild, grade 2 or moderate, requiring medical intervention, and grade 3 as severe, requiring hospitalization. The side effects involved the skin, hair, oral mucosa, gastrointestinal system (nausea, vomiting, diarrhoea) and lungs. Acute side effects was considered to occur within 90 days and late side effects thereafter.

3.11 **Haematologic toxicity** was also measured in 3 grades: Grade 1 (WBC 2,000 - 3,000/ml^3 , platelets 60,000 - 100,000/ml^3 , lymphocyte 20 - 30%, lymphocyte count 1,000 - 1,500/ml^3 , haemoglobin 5 - 8 g/dL), Grade 2 (WBC 1,000 - 1,999/ml^3 , platelets 20,000 - 59,999/ml^3 , lymphocyte 10 - 19%, lymphocyte count 500 - 999/ml^3 , haemoglobin 3 - 4.9 g/dL, Grade 3 (WBC < 1,000/ml^3 , platelets < 20,000 per/ml^3 , lymphocyte < 10%, lymphocyte count < 500/ml^3).

3.12 **Follow up**. All patients on the study were directed to me for follow up at the radiotherapy centre. Patients who failed to turn up for their follow up appointments were reminded by letters or telephone. 4 of the patients responded after reminders. In one case the employer reported death of the patient as the reason of not attending.

3.13 **Relapse**. Relapse was defined as the development or reappearance of disease at the treated sites following initial response. Additional radiotherapy was given using small localized fields for localized relapse.

3.14 **Potential sources of bias**. Early deaths (before 4 weeks) could be due to treatment failure or complications of treatment. This reduced the number of evaluable cases. Similarly some cases were lost to follow up before the initial evaluation. Opportunistic infections like Pneumocystis carinii (PCP) could not be assessed due to lack of proper diagnostic investigations for them. The impact of this on response results or prognosis of the patients could not be accurately assessed. Drugs like bactrim could

also cause haematological toxicity in AIDS patients and bactrim drug history was not systematically asked for.

3.15 Data analysis

3.15.1 Response by site. A table showing the percentage CR, PR and no response (NR) was drawn for the various sites. Evaluable cases for pleuro-pulmonary, leg edema, facial edema and eyelid sites were less than 10 in each case limiting the usefulness of the analysis by site.

3.15.2 Clinical side effects and haemotological toxicity. A table was constructed for UHBI showing the number of cases and percentage of the various observed side effects. A table was also constructed for haemotological toxicity showing the frequency distribution of the various grades of toxicity under UHBI, LHBI both types and overall. Due to the small number of cases in each category statistical analysis was not applicable.

3.15.3 **Duration of response.** This was defined as the time from the first day of HBI to the first day of relapse within the treated sites. The median duration was calculated for the 5 cases who reported back with recurrence.

3.15.4 **Disease free survival**. This could not be analyzed in the current study as the cause of death could not be ascertained in most patients.

3.16 **Survival**

Kaplan-Meier Product Limit (PL) method was used to estimate survival times. This technique incorporates the survival times contributed by all study subjects regardless of the length of time each patient is followed, i.e. censored as well as uncensored observations. This has the advantage of including individuals with short term as well as long-term follow-up. The probability of surviving any length of time, t, from the beginning of the study is the product of the cumulative proportion surviving up to the previous time period multiplied by the proportion surviving at time, t. Using this method graphs were plotted for cumulative proportion surviving since HBI

against time in days since the HBI. The survival time at the 50th percentile was taken as the estimated median survival. Comparison among the various possible prognostic factors was made. Using the computer programme SPSS, comparison of survival was done using the Lee-Desu statistic test for significance. In constructing the life tables the variables were survival interval (days), number of patients entering that interval, number withdrawn during that interval, number exposed to risk of dying during the various time intervals, number of terminal events (dying, loss to follow up), proportion terminating, proportion surviving, cumulative proportion surviving at end of each time interval, and probability of surviving.

4. RESULTS

4.1 Response by site

This is illustrated in Table 1 which suggests an overall response rate of 80 - 94% at sites with a larger sample size (skin, lymph nodes and oropharynx). Sites with sample sizes less than 10 also showed overall response rates of 80 - 100%

except for the only eyelid lesion which remained stable.

TABLE 1 Response by site

	Number of cases				Percentage			
	CR	PR	NR	Evaluable	CR	PR	NR	Overall
Skin	11	5	1	17	65	29	6	94
Lymph nodes	12	4	1	17	71	23	6	94
Oropharynx	8	4	3	15	53	27	20	80
Pleuro-pulmonary	0	4	1	5	0	80	20	80
Facial edema	1	3	0	4	25	75	0	100
Eye lid	0	0	1	1	0	0	100	0
Leg edema	4	3	0	7	57	43	0	100

4.2 Side effects

4.2.1 Clinical

These were mostly associated with UHBI as illustrated in Table 2. Only one patient developed diarrhoea thought to be associated with LHBI Mild skin desquamation and hyperpigmentation also occurred in the LHBI patients but it was difficult to quantify this because of other confounding factors like the dry weather and not taking bath.

TABLE 2 Clinical side effects after UHBI in 13 evaluable cases

	Number of cases	Percentage
Grade 1 vomiting	8	62
Grade 3 vomiting	1	8
Acute radiation syndrome	2	15
Grade 1 oral mucositis	5	38
Grade 1 dry mouth	3	23
Herpes labialis	2	15
Oral candidiasis	2	15
Alopecia	13	100

4.2.2 **Haematological**

Table 3 illustrates the pattern of haematological side effects. The overall incidence was 82% but grade 3 accounted for only 6%. The side effects were predominantly in the UHBI group which showed that every one had at least grade 1 toxicity. The differences were not statistically significant.

TABLE 3 Haematological side effects after HBI

	Number of cases				Percentage			
	Gr.1	Gr.2	Gr.3	Evalu-able	Gr.1	Gr.2	Gr.3	Total
LHBI	1	1	0	5	20	20	0	40
UHBI	2	3	1	6	33	50	17	100
Both	3	2	0	5	60	40	0	100
Total	6	6	1	16	38	38	6	82

4.3 Duration of Response

During follow up 5 patients presented with relapse at periods ranging from 10 weeks to 13 weeks. The relapse sites were skin (2 patients), oropharynx (1 patient), lung (2 patients) and leg edema (2 patients). The follow up period ranged from 27 days to 174 days with a median of 65 days.

4.4 Disease Free Survival

Data for this objective was not obtained. Relapse was recorded for only those cases which came back for follow up while information on death was recorded from all reliable sources like relatives and employers.

4.5 Overall Survival

Using the Kaplan-Meier (PL) method the median survival was 100 days from the day of first HBI

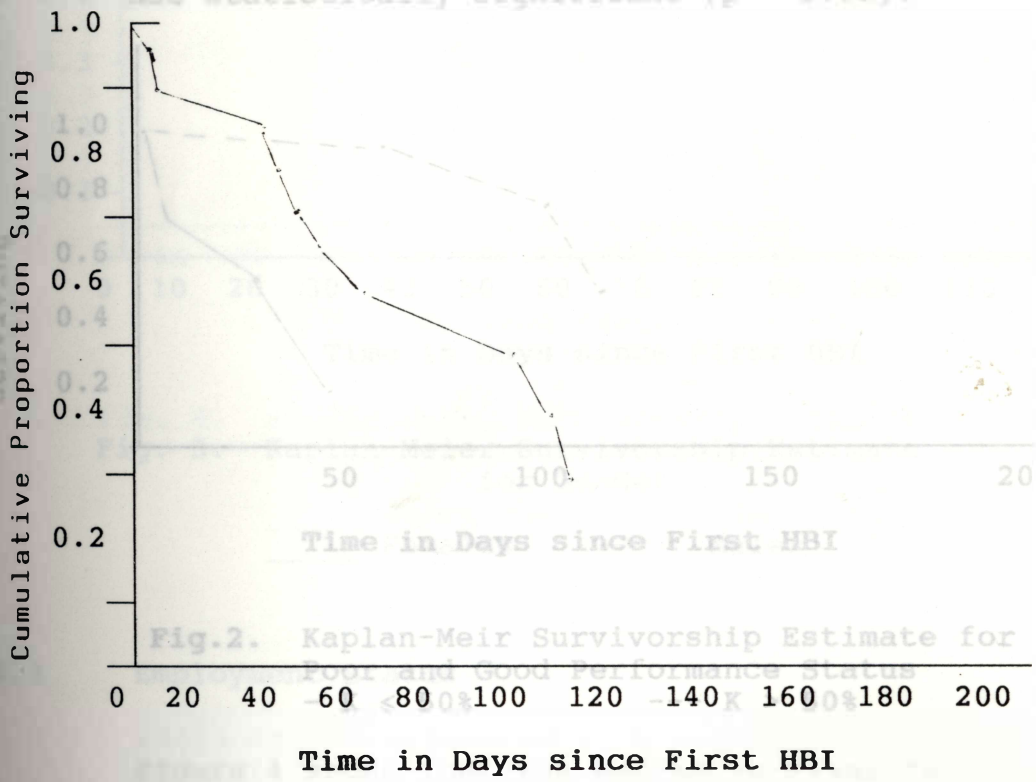

Fig. 1. Overall survival distribution from day of first HBI.

4.6 Survival by possible prognostic factors

4.6.1 Karnofsky Performance status (K) Figure 2 shows that the median survival for patients with poor K (≤ 50%) was 45 days while those with K > 50% had a median survival of 115 days. The difference was not statistically significant (p = 0.77).

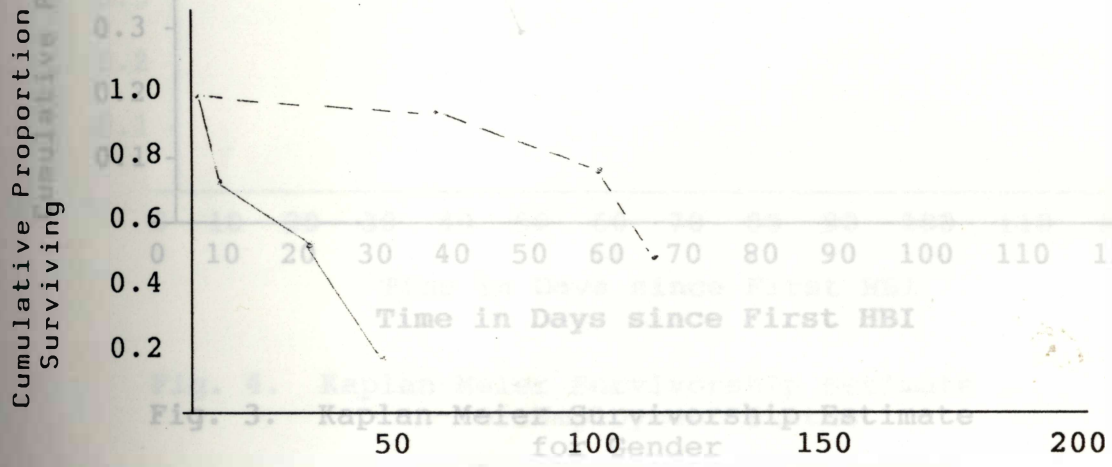

Fig.2. Kaplan-Meir Survivorship Estimate for Poor and Good Performance Status
- K ≤ 50% --- K > 50%

4.6.2 **Gender**

The median survival for female patients was 45 days and for male patients, 105 days. This is illustrated in Figure 3. The difference was not statistically significant (p = 0.56).

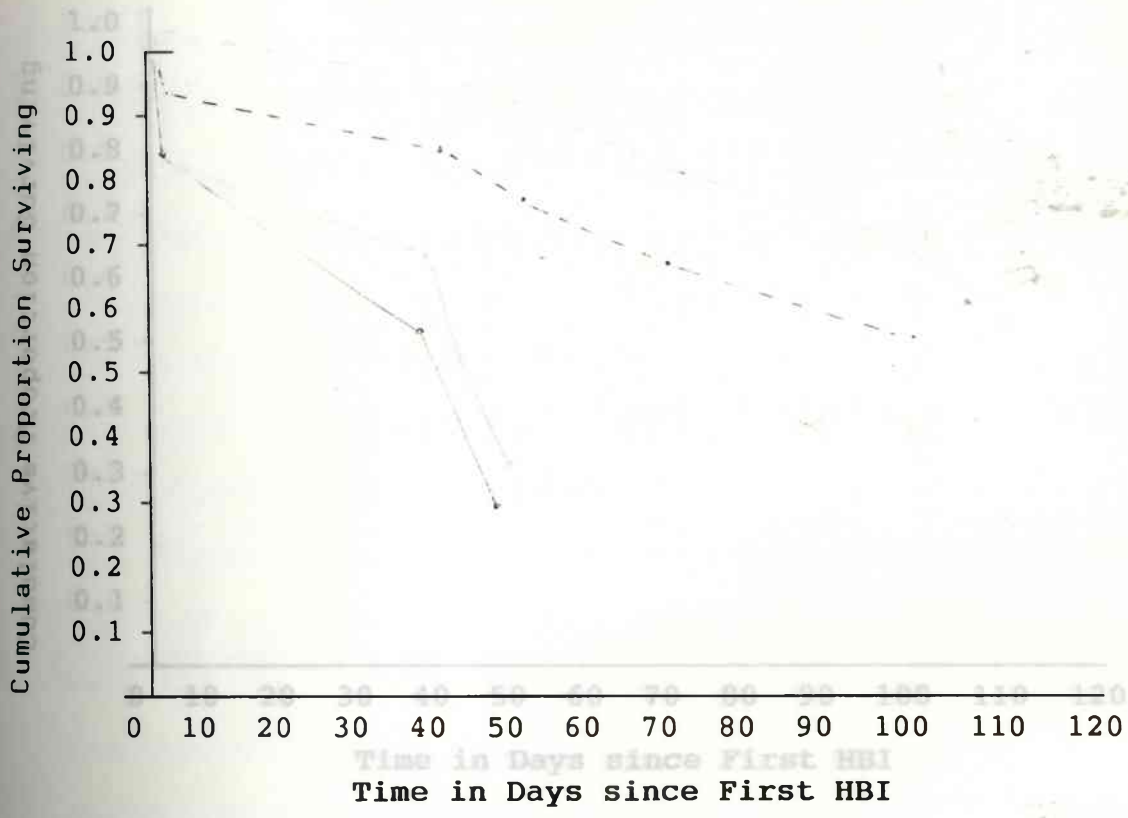

Fig. 3. Kaplan-Meier Survivorship Estimate for Gender

_____ Females ----- Males

4.6.3 Employment Status

Figure 4 shows that the median survival for unemployed patients was 42 days while for employed patients it was 110 days. This difference was however not statistically significant (p = 0.52).

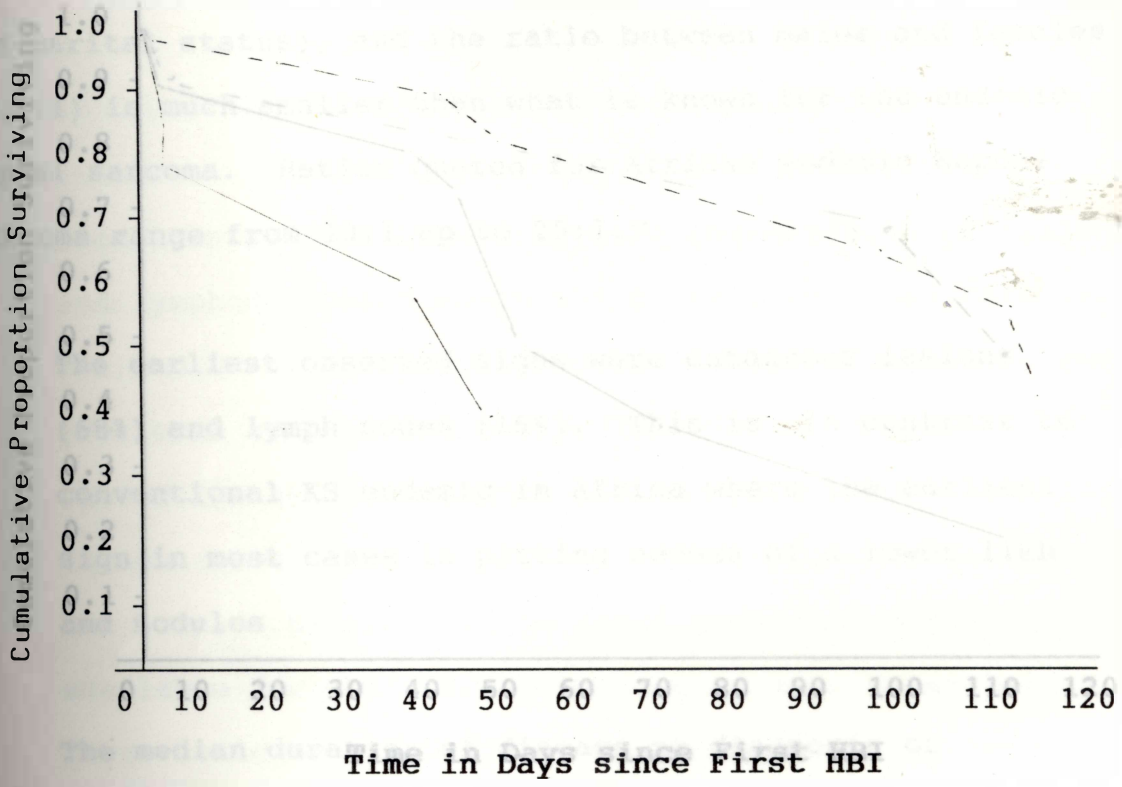

Fig. 5. Kaplan-Meier Survivorship Estimate for Duration of Symptoms

_____ ≤ 3 months ----- > 3 months

4.6.5 Site Distribution

Figure 6 showed that the median survival for patients presenting with pleuro-pulmonary lesions (Group 4) was 60 days while those without pleuro-pulmonary lesions (Group 1-3) had a median survival of 110 days. The difference was not statistically significant (p = 0.48).

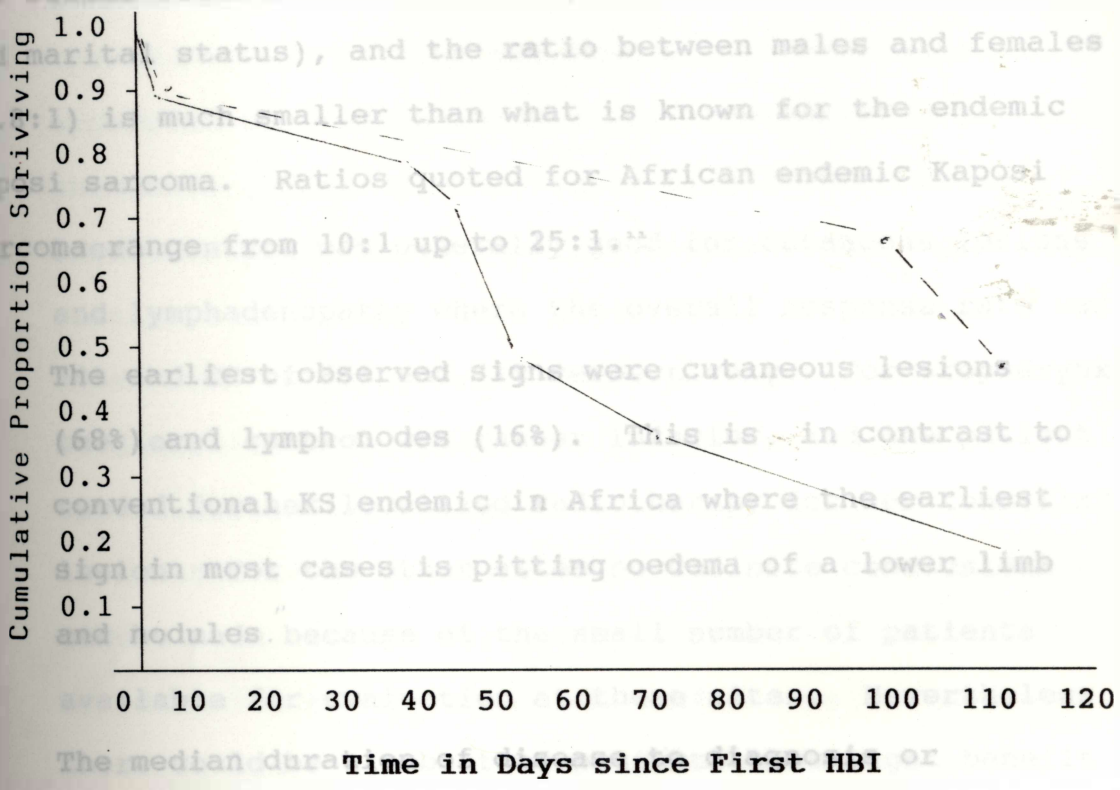

Fig. 6. Kaplan-Meier Survivorship Estimate Estimate for Site Distribution

_____ Group 4 ----- Group 1-3

5. DISCUSSION

The demographic particulars are consistent with what others have found in relation to AIDs-related Kaposi sarcoma. The disease is more common in the sexually active age group.

All social classes are affected (unemployed and employed, and marital status), and the ratio between males and females (1.8:1) is much smaller than what is known for the endemic Kaposi sarcoma. Ratios quoted for African endemic Kaposi sarcoma range from 10:1 up to 25:1.[11]

The earliest observed signs were cutaneous lesions (68%) and lymph nodes (16%). This is in contrast to conventional KS endemic in Africa where the earliest sign in most cases is pitting oedema of a lower limb and nodules.[11]

The median duration of disease to diagnosis or presentation to hospital was much lower in this study (5 months) than in the conventional endemic KS which is about 31 months.

Other differences from endemic KS are the predominance of pleuro-pulmonary lesions and lymphadenopathy in EKS as seen in this study. These clinical features are rare in endemic KS. Such differences influence the choice of treatment modality.

Six patients in the study presented with poor performance status. This however could be due to a selection bias, with most patients in poor performance

status dying at home.

Local control was generally good for cutaneous lesions and lymphadenopathy where the overall response rate was 94% and CR of 65% and 71% respectively. For oropharynx the local control was rather inferior, and one patient needed further localized radiotherapy for her tonsillar lesion. For the other sites no definite conclusions can be made because of the small number of patients available for evaluation at these sites. Nevertheless there could be a subset of patients that might benefit from individualized treatment apart from hemi-body irradiation. The ultimate palliative benefit may not be clearing all KS lesions in the patient's body but local control of the most distressing sites. In a study on ophthalmic lesions, Shuler[12] found that out of 100 homosexuals with AIDS-related KS, 20 had ophthalmic lesions. Sixteen of these had eye lid lesions and 4 conjunctival. In 12 patients treated by local radiotherapy 10 had CR with mild side effects like skin erythema.

Side effects depend on the treatment modality. In one study, Shields[13] noted that treatment of advanced HIV

related KS with combination chemotherapy yields a high tumour regression rate but also a high incidence of opportunistic infections, notably Pneumocystis carinii pneumonia (PCP). His attempts to use lower doses of chemotherapy resulted in lower response rates and only partial remissions. In a phase II trial of Beta interferon therapy, Miles[2] reported a preliminary evidence of antiviral activity and low incidence of opportunistic infections, i.e. 6 opportunistic infections in 39 patients in 285 patient observation months. In the current study of using HBI the incidence of PCP opportunistic infections was not assessed since its routine diagnostic investigation is not performed at Mpilo hospital. There were however 2 cases of herpes labialis and 3 cases of oral candidiasis that appeared within a few days of UHBI.

Clinical side effects were generally mild. Alopecia which predominated in the UHBI was not permanent and hair regrew after about 3 months. Vomiting was generally not controlled on stemetil medication possibly due to inadequate dose. The view that AIDS patients react unfavourably to radiotherapy than non-AIDS patients may not be true for HBI patients. Late side effects were however not assessed in this study

because of the limitations in follow up and short life span of the patients. Haematological side effects were comparable in incidence to non-AIDS patients treated with HBI in other studies. The recovery of the depressed haematological indices also followed the normal pattern.

In these immuno-suppressed patients however, the depression of white cells and platelets need to be carefully monitored. Prophylactic drugs against infections might be indicated, i.e. antibacterial, antifungal and antiviral.

No trend was significantly observed for patients with previous history of chemotherapy. There were only 3 cases. One of them was still alive and well 6 months after LHBI. No haematological or clinical side effects were detected in the patient. The second patient had grade 2 toxicity for white cell count after UHBI. The third patient could not be evaluated for haematological toxicity because he died 5 days after UHBI.

The few patients who returned with relapse indicate tendency to short duration of remission (10-13 weeks). In Berson's series[1] patients treated with a single fraction of 8 Gy were about 3 times more likely to be

retreated due to relapse than those who had fractionated regimens. In another study[11], 23 out of 36 radiation treatment fields using single fraction with a follow up of at least 4 months, showed progression of the tumour and or new lesions in the field of radiation, and/or recurrence of lymphoedema within that period.

Lung involvement as a poor prognostic factor in EKS has been studied by others. In one study in which the lung KS was treated with daily 1.5 Gy to the lungs only, to a total of 10.5 Gy t o 15 Gy, the median survival was 2.5 months. Our lung KS cases were diagnosed clinically and radiologically without histological confirmation. Obrien[13] reported 21 out of 105 AIDS related KS to have pleuro-pulmonary involvement. Thirteen of them had pleural effusions. Chest X-ray findings were usually in the form of non-loculated bilateral pleural effusions, parenchymal infiltrates or both. Cytologic examination of pleural fluid or needle biopsy of the parietal pleura failed to establish the diagnosis although most effusions were serosanguineous, mononuclear cell predominant exudates. In our study, out of the 13 cases with pleuro-pulmonary involvement, 2 had pleural effusions, 1 had both pleural effusion and parenchymal infiltrates, and 10 had only

parenchymal infiltrates. Objective response was seen in those with parenchymal infiltrates. In a case report, Lai, of the University of Massachusetts medical centre described a case of an AIDS patient with cutaneous and pulmonary KS with the unusual radiological findings of multiple cavitary lesions in addition to diffuse reticular nodular infiltrates[15]. This case serves to emphasize the protean radiological manifestations of pulmonary KS. PCP infection is the most likely differential on X-ray. But this is said to occur much less commonly in African AIDS patients than in North American patients, the reasons of which are not clear.[17-20]

Unemployment and female sex as apparent poor prognostic factors could be attributed to other confounding variables like lack of nutritional and supportive care. Patients presenting with a short duration of symptoms could represent a subset of patients with rapidly progressive disease.

Age did not appear to be an independent prognostic factor in this study possibly because all of them could be considered young. A study on survival in San Francisco on 1015 male patients between July 1981 to 31/12/1987 showed that older age and year of diagnosis

were significant independent predictors of survival.[18]

This small pilot study suggests that HBI offers good palliation of symptoms and is well tolerated. The relapse free survival appears short. The best treatment should be able to provide palliation of symptoms and signs that outlast the survival of the patient.

6 CONCLUSIONS

6.1 The overall response or local control rates is 80-94% for skin,lymphnodes and oropharynx. Other sites (pleuropulmonary, facial oedema and leg oedema also showed good response but the number of patients were too few to make a solid conclusion.

6.2 Clinically the treatment was well tolerated. Most of the acute clinical side effects were mild (grade 1) and reversible.

6.3 Haematological complications were mostly mild or moderate and were predominantly associated with UHBI.

6.4 The duration of remission appeared to be short (10-13 weeks).

6.5 The causes of death in the study patients could not be accurately established, and it is unknown whether the treatment had any influence on survival. The median survival of 100 days indicates that the life span of these patients is very short.

6.6 Analysis of prognostic factors suggested that poor performance status, female sex, unemployment, duration of symptoms less than 3 months, and presence of pleuropulmonary lesions were poor prognostic factors. The trend was however not statistically significant in all of them except for the short duration of symptoms. This could be due to the small number of patients.

7. RECOMMENDATIONS

7.1 Further studies should be performed to establish the role of boosting or additional radiotherapy to selected sites in order to improve local control.

7.2 The role of HBI in survival of these patients is not known. It would seem reasonable to avoid HBI in patients with poor performance status to spare them the clinical and haematologic side effects which could further worsen their condition. Radiotherapy localized to sites of most distress could be recommended. The best approach would be a randomized trial comparing HBI

and localized radiotherapy to compare quality of life.

Regarding survival, some studies have pointed out that p24 antigenaemia and CD4 levels provide the main influence on survival rather than the amount of neoplastic transformation.[19] These levels were not recorded in the present study. It would be interesting to study how these values vary with therapy. The routine measurements of these tests is expected to start in 1994 in the ongoing EKS study at Harare.

7.3 The role of HBI on quality of life should be studied as a pre-requisite for recommending this modality as treatment of choice. The ongoing randomized study in Harare under the sponsorship of WHO is addressing the issue of quality of life in various treatment options for EKS.

7.4 Studies on various antiemetics for use during UHBI need to be done to find better drugs for the relief of nausea and vomiting which appeared quite commonly. To lessen the effect of haematological toxicity future studies could incorporate the use of haematopoietic growth factors. From a practical point of view doctors should monitor the haematological indices closely after UHBI and consider the use of prophylaxis against

infections if indicated.

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Annex 1

CHECKLIST FOR PATIENT PARTICULARS

NAME

DATE OF BIRTH SEX MARITAL STATUS:

S/M/D

OCCUPATION

LOCAL ADDRESS

HISTORY

Complaints

SPECIFIC SYMPTOMS/DURATION

1. Skin plaques Y/N
2. Skin nodules Y/N
3. Orpharyngeal lesions Y/N
4. Enlarged lymph nodes Y/N
5. Cough/shortness of breadth Y/N
6. Diarrhoea Y/N

Earliest sign of KS: ------- Duration -------

PAST MEDICAL HISTORY

1. Past chemotherapy Y/N
2. Past radiotherapy Y/N
3. Tuberculosis Y/N
4. Herpes zoster Y/N
5. Pneumonia Y/N

EXAMINATION

1. Karnofsky Performance Status
2. Disease Distribution: skin: plaques/nodules
   lymph nodes
   oedema
   oral
3. Size of lesions
4. Chest X-ray: O - None
   I - hilar lymph nodes
   II - pulmonary infiltrates
   III - pleural effusion

5. FBC: WBC PLT Hgb Lymphocyte %
Lymphocyte count

STAGE **III**
IV

RESPONSE 1 2 3 4 5 6 month visit

CR
PR
SD
PD
Death

Date of Death

Opportunistic infections - specify

Clinical side effects 1 2 3 4 5 6 months

Specify

Grade 1
2
3

Assessment and Plan

KARNOFSKY PERFORMANCE SCALE

100%	Normal
90%	Minor symptoms
80%	Normal activity with effort
70%	Cares for self; unable to carry on normal activity
60%	Requires occasional assistance, but is able to care for most personal needs.
50%	Disabled; requires special care and assistance
40%	Requires considerable assistance and medical care
30%	Severely disabled; hospitalization indicated
20%	Very sick; hospitalization necessary; active support treatment is necessary.
10%	Moribund
0%	Dead

METHOD USED IN CONSTRUCTING KAPLAN MEIER PL METHOD

1. A life table based upon the deaths of all patients since the first hemi-body irradiation.

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
2	2	-	-	-
7	3	3	0.95	0.95
7	4	4	0.95	0.90
8+	5	-	-	-
27+	6	-	-	-
33+	7	-	-	-
36+	8	-	-	-
41	9	9	0.93	0.84
44	10	10	0.93	0.78
48+	11	-	-	-
50	12	12	0.92	0.72
51	13	13	0.91	0.66
59+	14	-	-	-
71	15	15	0.89	0.58
72+	16	-	-	-
73+	17	-	-	-
101	18	18	0.83	0.48
111	19	19	0.80	0.39
113	20	20	0.75	0.29
136+	21	-	-	-
141+	22	-	-	-
174+	23	-	-	-

2. A life table based upon the deaths of patients with poor performance status (K< 50%).

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
7	2	2	0.86	0.86
7	3	3	0.83	0.71
8+	4	-	-	-
41	5	5	0.75	0.54
44	6	6	0.67	0.36
50	7	7	0.50	0.18
51	8	8	0	0

3. A life table based upon the deaths of patients with better performance status (K > 50%)

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
27+	2	-	-	-
33+	3	-	-	-
36+	4	-	-	-
48+	5	-	-	-
59+	6	-	-	-
71	7	7	0.89	0.89
72+	8	-	-	-
73+	9	-	-	-
101	10	10	0.83	0.74
111	11	11	0.80	0.59
113	12	12	0.75	0.45
136+	13	-	-	-
141+	14	-	-	-
174+	15	-	-	-

4. A life table based upon the deaths of female patients

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
7	2	2	0.83	0.83
33+	3	-	-	-
36+	4	-	-	-
41	5	5	0.67	0.56
50	6	6	0.50	0.28
72+	7	-	-	-

5. A life table based upon the deaths of male patients

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
7	2	2	0.93	0.93
8+	3	-	-	-
27+	4	-	-	-
44	5	-	0.92	0.86
48+	6	-	-	-
51	7	7	0.90	0.77
59+	8	-	-	-
71	9	9	0.88	0.68
73+	10	-	-	-
101	11	11	0.83	0.56
111	12	12	0.80	0.45
113	13	13	0.75	0.34
136+	14	-	-	-
141+	15	-	-	-
174+	16	-	-	-

6. **A life table based upon the deaths of unemployed patients**

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
7	2	2	0.89	0.89
7	3	3	0.88	0.78
33+	4	-	-	-
36+	5	-	-	-
41	6	6	0.80	0.63
44	7	7	0.75	0.47
50	8	8	0.67	0.31
72+	9	-	-	-
73+	10	-	-	-

7. **A life table based upon the deaths of employed patients**

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
8+	2	-	-	-
27+	3	-	-	-
48+	4	-	-	-
51	5	5	0.89	0.89
59+	6	-	-	-
71	7	7	0.86	0.77
101	8	8	0.83	0.64
111	9	9	0.80	0.51
113	10	10	0.75	0.38
136+	11	-	-	-
141+	12	-	-	-
174+	13	-	-	-

8. **A life table based upon the deaths of patients presenting with < 3 months duration of symptoms**

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
7	2	2	0.89	0.89
7	3	3	0.88	0.78
8+	4	-	-	-
33+	5	-	-	-
36+	6	-	-	-
41	7	7	0.75	0.58
50	8	8	0.67	0.39
59+	9	-	-	-
71	10	10	0	0

9. **A life table based upon the deaths of patients presenting with > 3 months duration of symptoms**

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
2+	1	-	-	-
9	2	-	-	-
15+	3	-	-	-
27+	4	-	-	-
44	5	5	0.91	0.91
48+	6	-	-	-
51	7	7	0.89	0.81
72+	8	-	-	-
73+	9	-	-	-
101	10	10	0.83	0.67
111	11	11	0.80	0.54
113	12	12	0.75	0.40
136+	13	-	-	-
141+	14	-	-	-
174+	15	-	-	-

10. A life table based upon the deaths of patients in Group 1 -3

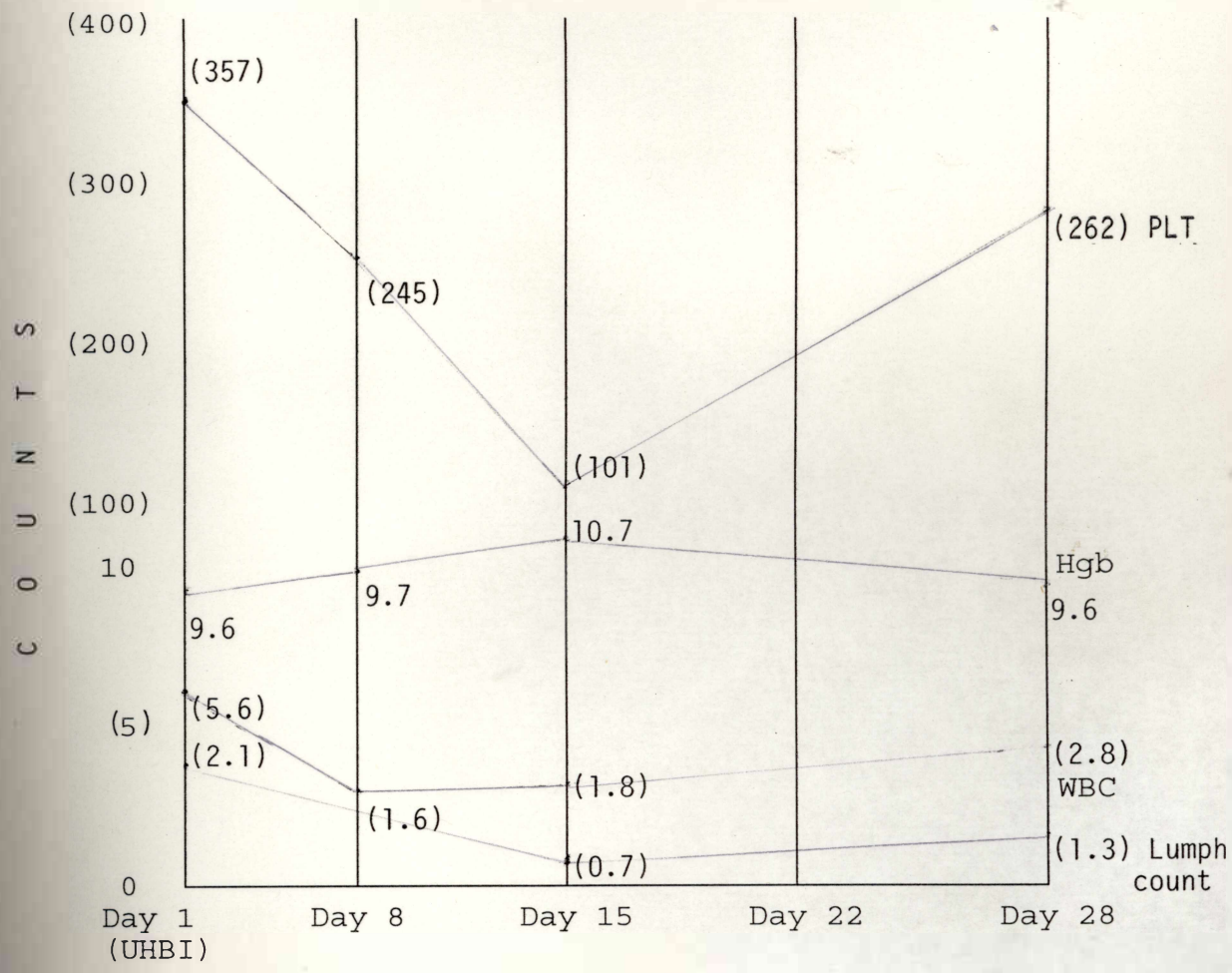
(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
2+	1	-	-	-
7	2	2	0.91	0.91
9+	3	-	-	-
15+	4	-	-	-
27+	5	-	-	-
33+	6	-	-	-
59+	7	-	-	-
72+	8	-	-	-
101	9	9	0.75	0.68
111	10	10	0.67	0.46
136+	11	-	-	-
174+	12	-	-	-

11. A life table based upon the deaths of patients in Group 4

(1) Survival time (ti) Days	(2) Rank	(3) Uncensored rank (ri)	(4) n-r/n-r+1	(5) s(t)
1+	1	-	-	-
7	2	2	0.92	0.92
8+	3	-	-	-
36+	4	-	-	-
41	5	5	0.89	0.82
44	6	6	0.88	0.72
48+	7	-	-	-
50	8	8	0.83	0.60
51	9	9	0.80	0.48
71	10	10	0.75	0.36
73+	11	-	-	-
113	12	12	0.5	0.18
141+	13	-	-	-
136+	14	-	-	-
141+	15	-	-	-
174+	16	-	-	-

Annex 4

PATTERN OF HAEMATOLOGICAL INDICES FOLLOWING UHBI FOR PATIENT S.D. (No.22)



( ) means count in thousands.