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The Burden of HIV-Related Admissions and Mortality at Princess Marina Hospital, Botswana in 2000: A Pre-Combination Antiretroviral Therapy Era

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Abstract

Background: human immune virus and acquired immunodeficiency syndrome (HIV/AIDS) have been recognized in Botswana for the last three decades, however, combination anti-retroviral therapy (cART) was only introduced after 2000. Facility-based historical data of the burden of HIV/AIDS-related conditions pre-cART have so far not been analyzed. **Objective:** To analyze the burden of HIV-related admissions and HIV-related deaths, and identify the socio-demographic factors associated with HIV/AIDS deaths at Princess Marina Hospital (PMH) in the year 2000. **Methods:** A retrospective review of medical files was carried out between May and June 2014. Nine thousand seven hundred and forty-six (9746) records were analyzed for the year for 2000. Cases were identified as documented HIV/AIDS as per medical notes and/or documentation of any of the conditions listed in sections B20-B24 of the International Classification of Diseases (ICD 10 B20-B24). Outcomes were the percentages of HIV-related admissions and HIV-related deaths out of all admissions and deaths. The in-hospital case fatality rate (CFR) was also calculated. Log-binomial regression models were used to determine the most significant factors associated with HIV-related admission and death. **Results:** The percentages of HIV-related admissions and HIV-related deaths were 4.1% (403/9746) and 11.3% (80/707), respectively. The in-hospital HIV-CFR was 19.9% (80/403). Adjusted log-binomial models identified the most

significant protective factors for HIV-related admission were female sex and cART use while age >15 years old was the most significant risk factor. The se of cART was significant protective factor for HIV-associated death while age older than 15 years was the most significant risk factor. **Conclusion:** There was a significant burden of HIV-related admissions and deaths in PMH before wide-scale cART use in Botswana. This study highlights the increased risk of hospital admission for HIV-positive patients and underlines the need for cART to prevent deaths. Further studies evaluating the impact of wide-scale cART roll out are needed.

Keywords

Disease Burden, HIV-Related Admissions, HIV-Related Deaths, Princess Marina Hospital and Retrospective Analysis

1. Introduction

HIV/AIDS continues to be a significant contributor to hospital admission and mortality in the world [1] [2]. It is estimated that 2 million people die every year in sub-Saharan Africa alone due to HIV/AIDS [3] and that the incidence of HIV/AIDS continues to increase annually in some of the sub-Saharan Africa countries despite current global effort to the fight against HIV/AIDS [4].

Limitations in human and financial resources have been incriminated many times as reasons why developing countries were seriously burdened by the disease. This is because HIV/AIDS affects all sectors of communities including economically viable members of communities as well as family stability, structure and income [5].

In Botswana, before the advent of the government-funded free combination Antiretroviral Therapy (cART) program known as the "MASA" program, it was evident that HIV put existing resources under pressure as there was no corresponding growth in the infrastructural resources e.g. no increments in the number of hospital beds or staff in health care facilities, to be able to cope with the demand for HIV/AIDS care [6] [7]. This resulted in HIV/AIDS treatment and care being cascaded down to lower level facilities such as clinics so as to help deal with the demand [8].

Due to the nature of the disease, most patients in late stages of the disease required hospitalization for treatment of HIV associated complications as severely ill patients such as these were likely to spend more time in hospital [9] requiring extra medical tests, medications and investigations. In addition, given limited medical resources and treatment alternatives available then, it is worth documenting what HIV/AIDS-related admissions and mortality were before the full scale implementation of free cART delivery in 2001, so as to provide a base for monitoring and evaluating progress made towards reducing the burden of HIV/AIDS in Botswana. There is paucity in the data relating to levels of facility admissions and mortality associated with HIV/AIDS before 2001. This is re-

quired in order to gauge the contributions of various interventions introduced to minimize the impact of HIV/AIDS particularly on HIV/AIDS related morbidity and mortality.

In this study we aimed to: estimate proportions of HIV related admission and mortality and assess HIV/AIDS case fatality rate (CFR) for year 2000 and to identify socio demographic/economic and biomedical factors that were most associated with HIV hospital admission and mortality in 2000.

2. Methods

An exhaustive review of medical records was carried out at Princess Marina Hospital's records department, between May and June 2014. All medical records of patients ever admitted to Princess Marina Hospital in the year 2000, were reviewed. Records were matched with mortuary data to verify the outcome of the admission.

Operational case definitions for an HIV-related admission or death were developed. An HIV-related admission was defined as anyone documented on medical files as HIV-positive and stated to be admitted for any of the conditions listed in section B.20-B.24 of the International Classification of Diseases (ICD 10). Unknown HIV-status with any of the ICD B.20-24 conditions, and queried immunosuppression by the physician qualified as an HIV-related admission. An HIV-related mortality was a death that occurred to a known HIV-patient and the death was linked to any of the conditions listed in ICD 10 B.20-B.24 and the underlying cause of death was stated as HIV/AIDS as stated in the death certificate. Research assistants and data entry clerks were contracted for data collection and handling. A data capturing questionnaire was developed with inputs from the Ministry of Health of Botswana and the Department of Family Medicine and Public Health of the University of Botswana. The final version of the tool was not produced until the final edits from pre-testing were incorporated. The tool was pre-tested at Bamalete Lutheran Hospital, in the vicinity of Gaborone.

2.1. Data Collection

Each medical file pre-screened in the study was assigned a unique five-digit computer generated random number as a study code. We collected: (i) demographic data such as age, sex, residence, whether or not the patient was a citizen of Botswana as well as data related to patients' socio-economic status (SES); (ii) clinical data such as the date of admission, whether HIV positive/negative or unknown; final confirmed diagnosis and coding as appropriate date of discharge, whether the patient was discharged alive or dead, cause of death where applicable. The modes of discharge coded for the study were the following options: home, absconded, transfer-out and death. In terms of death, information on the stated cause of death was collected. We also collected data on whether the patient was or not on Anti-retroviral Therapy, the type of therapy based on the nucleotide reverse transcriptase inhibitor (NRTI)-base they were on. Whether cART was provided by the Government of Botswana, private sources, public-

private, out-of pocket, otherwise coded as not applicable were also recorded.

We excluded from the study all records of patients brought in the hospital for death certification purposes only and patients who died within 24 hours of admission. Records of patients admitted in other years were also excluded.

The ethical approvals to conduct the study were granted by the Botswana Ministry of Health Human Research Development Unit of the Ministry of Health, the University of Botswana Institutional Review Board and by the University of Pretoria. Further approval was granted by Princess Marina Hospital Ethical Review Board.

2.2. Data Analysis

Data were analyzed using STATA version 12 (College station, Texas). The burden of HIV-related admissions was estimated as a proportion (%) by dividing the number of HIV-related admissions over the total number of admissions multiplied by 100. The burden of HIV-related deaths was estimated as a proportion (%) by dividing the number of deaths attributable to HIV over all deaths that occurred in Princess Marina Hospital in year 2000 multiplied by 100. HIV CFR was computed as the number of deaths associated with HIV divided by the total number of inpatients whose cause of admissions was HIV/AIDS-related, multiplied by 100.

Associations of socio demographic/economic and biomedical factors with HIV hospital admission or mortality were investigated primarily through a series of bivariate analyses; unadjusted risk ratios (URR) and their 95% Confidence Intervals (CIs) were estimated. Potential exposure variables that achieved $P < 0.25$ in the bivariate analyses were further investigated using two log-binomial regression sub-models: sub-model A with HIV-related admissions as dependent variable and sub-model B with HIV related deaths as the dependent variable. The following variables were investigated as potential predictors in both sub-models to compute for ARR and their 95% CI as approximations of adjusted odd ratio (AOR): age, sex, SES, citizenship, CD4 cells and viral load. Sub models were investigated for effect modification and confounding. The level of significance was set at $P < 0.05$ in the final sub models. Model Goodness-of-fit was examined by performing the Hosmer-Lemeshow test.

3. Results

Of the 9793 medical records reviewed 17 were excluded as they were on hospital admission records for death certification purposes only while 30 were cases admitted on the ward for less than 24 hours, which brought the total study population to 9746. The median age was 28 IQR (21 - 40) years, the oldest patients was 103 years while the youngest was 1.5 years old ; 5596 (58%) were females compared to 4023 (41%) males, 127 records (1%) had missing data for gender; 9473 (96%) were citizens of Botswana compared to only 273 (3%) who were foreigners. Twenty nine patients or less than 1% were admitted to the private ward and thus classified as of high socio-economic status (HSES) against 9717 or >99%

admitted in the general ward were classified as of low socio-economic status (LSES). Four hundred and one (403) or 4% of the patients were diagnosed as HIV positive whereas 143 or 1.43% patients were documented as HIV negative. In other words, only 546 (5%) patients were tested for HIV, the rest 9203 or 94.3% had unknown HIV status. About a third (1/3) of the HIV-positive patients or 101 was on some form of anti-retroviral therapy.

In Table 1, The proportion of HIV related admission and mortality were 4.1% and 11.3%, respectively whilst the HIV case-fatality rate was 19.9%.

Table 2 shows sociodemographic and biomedical factors predicting HIV-related admission, both unadjusted and adjusted models. In the adjusted sub-model, Positive HIV status versus negative status and age-group above 15 years versus younger were statistically significant risk factors for HIV-related admission while use of cART versus not, and female sex versus male counterparts, were protective factors against HIV related admissions. The model had a goodness-of-fit of 0.57.

Table 1. Profiles of HIV-related admissions (%), deaths (%) and Case Fatality Rate (%) among patients admitted at referral hospital in Gaborone, Botswana.

Indicator	Numerator (n_1)	Denominator (n_2)	Percentage (n_1/n_2)
Proportion of HIV-related admission	HIV-related admissions (n = 403)	Total admissions (n = 9746)	4.1
Proportion of HIV-related deaths	HIV-related deaths (n = 80)	Total deaths (n = 707)	11.3
HIV-CFR	HIV-related deaths (n = 80)	HIV-related admissions (n = 403)	19.9

Legend: HIV-CFR (%) = HIV case fatality rate; n_1 = numerator; n_2 = denominator, n = number.

Table 2. Socio demographic/economic and biomedical factors independently associated with HIV admissions at referral hospital in Gaborone, Botswana; Sub-model A; Dependent variable: HIV-related admission (N = 546).

	Proportion	Unadjusted		Adjusted	
Independent variables	(%)	RR	95%CI	RR	95%CI
HIV status: Positive	403 (73.8)	27.56	11.01 - 68.97	25.4*	8.39 - 76.90
Negative	143 (26.2)	1	-	1	-
cART: No	445 (81.5)	1	-	1	-
Yes	101 (18.5)	0.59	0.35 - 0.99	0.34*	0.18 - 0.64
Sex: Male	176 (32.2)	1	-	1	-
Female	370 (67.8)	0.24	0.14 - 0.41	0.31*	0.16 - 0.60
Age: 1.5 - 14	39 (7.1)	1	-	1	-
15 - 49	443 (81.1)	1.36	1.14 - 1.64	1.39*	1.19 - 1.93
>50	64 (11.8)	1.67	1.36 - 2.04	1.68*	1.41 - 6.94

Sub model A Hosmer-Lemeshow test of goodness of fit P = 0.57; *P < 0.05.

Table 3 shows unadjusted and adjusted models associated with HIV-related death. Only data from 707 patients' files were suitable for this model and thus used. Furthermore, only two independent factors; cART and age, were suitable for use in this model. cART use had an RR of 0.21and 0.13 in the unadjusted and adjusted models, respectively showing a huge protective effect. Age older than 15 years was a significant risk factors for HIV-related death, at 5.62 CI (3.61 - 8.75) and 1.98 CI (1.26 - 3.11) for age-groups 15 - 49 years and older than 50 years, respectively. The adjusted model had a Hosmer-Lameshow goodness-of-fit p-value of 0.41.

4. Discussion

The Previous studies on infectious diseases have shown that when implementing prevention and control programs if for any reason, *i.e.*, bankruptcy, natural disasters etc, and it so happens that the control intervention ends before elimination or eradication of an illness, the infection level will bounce back to the pre control level or even to a level higher level where it may become even more difficult to control/contain than before [10]. In the Botswana case, it is almost a decade and half that Botswana introduced its HIV control program and the progress b made by this program is well documented [8] [11], however pre-control HIV data are lacking. In designing this study we aimed at filling this gap.

Indeed, data presented herein are self-explanatory, of the 9746 patients who were investigated only 546 were tested for HIV. This is not a surprise finding, as HIV testing in that era was uncommon, was on a voluntary basis, and even general awareness about HIV testing was low hence a large number, 9203 patients, were not tested for HIV or at the least had no documentation of their HIV status on the medical files and therefore their status remained unknown. This high number of people not tested for HIV describes the situation that persisted then, pre-ART for some of the reasons discussed above. From the sub sample of 546 that underwent HIV testing, 403 (73.8%) tested positive for HIV, an indication of possible similar HIV prevalence in the unknown HIV status group, at the worst. Therefore since we did not have any data to confirm this, we excluded this

Table 3. Socio demographic/economic and biomedical factors independently associated with HIV-death at referral hospital in Gaborone, Botswana; Sub-model B; Dependent variable: HIV-related death (N = 707).

	Proportion	Unadjusted		Adjusted	
Exposure Variables	**(%)**	**RR**	**95%CI**	**RR**	**95%CI**
cART: No	606 (85.7)	1	-	1	-
Yes	101 (14.3)	0.21	0.48 - 0.93	0.13*	0.03 - 0.64
Age: 1.5 - 14	207 (30.7)	1	-	1	-
15 - 49	295 (42.7)	5.06	3.33 - 7.68	5.62*	3.61 - 8.75
>50	205 (26.6)	1.75	1.14 - 2.70	1.98*	1.26 - 3.11

Sub model B Hosmer-Lemeshow test of goodness of fit (P = 0.41), *P < 0.05.

group from the analysis. Furthermore we would risk a high chance of differential misclassification by including them in the analysis. This is the first time that this level of morbidity and mortality information has been documented and it not only corroborate the high CFR of about 20% recorded in this work but at the same time affirms the highest level of mortality that Botswana has ever experience in its history [12]. HIV was already rampant in Botswana years 2000 as indicated by a high CFR of 20% and the high proportion of HIV-related deaths in excess of 10% but supportive data were lacking...

In determining sociodemographic, economic and biomedical factors possibly associated with HIV/AIDS-related facility admission and mortality, several factors were investigated however, some factors such as CD4, Viral load and SES lacked enough variability at pre-screening and thus were dropped out of the modelling process. However, we believe that these factors would be worth considering in subsequent studies related to this elsewhere. Our regression model exploring factors associated with HIV-related admission, showing that HIV positive had 25.4 time the risk of being admitted at PMH only support hypothesis that the majority of the 9203 with HIV unknown HIV status were likely admitted for HIV and the being among those age 50 years old. Although only a small number of patients were had documented HIV positive status, for those that had access to some form of cART, it was shown that being on cART was found to be significantly protective against HIV mortality, a reduction of 87% in mortality compared to those not on any form of cART.

In these estimates, we used the Log-binomial regression in our predictive models instead the most commonly used logistic regression because the former estimates the risk much better especially in common events such as HIV/AIDS in the patient community that we studied [13] [14].

Using medical records for research purposes is without limitations including but not limited to missing data. However, in countries like Botswana where health data are better kept, hospital data constitute a rich and an important source of information. In this study, unlike most studies reliant on electronic data, data were extracted from medical files. Since, we collected primary data and circumvented the issues associated with electronic data in our setting. e.g. availability, expertise and down-times, we would like to believe that outcomes presented herein cannot be explained by factors other than those investigated here.

5. Conclusion

In conclusion, the burden of HIV associated admission and mortality was significantly high as indicated by the high proportion of patients who were admitted with HIV-associated conditions or overt AIDS. Moreover, the mortality continued to be high from HIV-associated conditions. More studies evaluating the burden of HIV-associated admission and mortality post-cART period are needed to gauge the impact of cART.

Competing Interests

No competing interest declared by the authors.

Authors' Contributions

All authors contributed equally to the development of the manuscript. All authors read and approved the final manuscript.

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