Case fatality due to cryptococcal meningitis in a retrospective cohort in Kenya

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Introduction

- Cryptococcal meningitis (CM) usually occurs in patients with a CD4<100
- CM is the 2nd leading cause of death in African cohorts [1,2]
- CM has a case fatality rate of up to 81-100% in inpatient cohorts in sub-Saharan Africa [3,4] in contrast to a case fatality of 9% in the developed countries[5]

Objectives

- To determine case fatality due to cryptococcal meningitis among HIV infected individuals receiving out-patient HIV care and treatment in Kenya
- To determine key predictors of case fatality due to cryptococcal meningitis among HIV infected individuals

Methods

Study Site:

- Family Aids Care and Education Services (FACES)
- PEPFAR funded family-centred HIV prevention, care and treatment outpatient services at 62 health facilities in Western Kenya; 79,250 patients in care, of whom 27,046 are on HAART
- Retrospective cohort of HIV infected adults and children drawn from all 62 FACES clinical sites from across Nyanza province
- All HIV infected outpatients with positive serum Cryptococcal Antigen (sCrAg) tests identified from laboratory database between Jan 2006-Oct 2009
- Chart review of all positive sCrAg cases
- Exclusion: inpatient samples

Case Definitions:

1. Positive sCrAg
2. Positive sCrAg plus any symptom **including** headache
3. Positive sCrAg plus any other symptom **excluding** headache

- Lumbar puncture and cerebrospinal fluid (CSF) cultures not available in our care settings

Analysis

- Bivariate comparisons of key clinical characteristics between fatal and non-fatal CM cases was performed using Fishers exact test for proportions and t tests for continuous variables
- Logistic regression models used for multivariate analysis
- Sensitivity analysis to compare case fatality rates and relationships with key clinical predictors using 3 case definitions

Results

- 90 positive sCrAg tests identified from laboratory database
- 72(80%) of charts were found and reviewed
- Sensitivity analysis using more stringent clinical definitions of CM did not demonstrate significant difference in overall case fatality or bivariate relations (data not shown)
- No significant differences were observed between individuals with fatal and non fatal CM except for BMI
- No differences were observed between case fatality, current CD4 count, type of antifungal treatment, being on ARVs or any signs and symptoms of CM
- Higher BMI was significantly associated with lower case fatality in both multivariate and bivariate models

Table 1: Case fatality using different case definitions

Case Definitions for Cryptococcal Meningitis	N	Case fatality N (%)	Fishers exact P- value
1. Positive sCrAg	68	26 (38.2%)	0.96
2. Positive sCrAg plus any symptom including headache	63	23 (36.5%)	
3. Positive sCrAg plus any other symptom excluding headache	43	17 (39.5%)	

Table 2: Descriptive statistics and comparison of key clinical characteristics between fatal and non fatal CM cases using Definition 1

Characteristics	Overall (n=68)	Fatal CM cases (n=26)	Non-fatal CM cases (n=42)	P value
Age [mean (SD)]	38.3(9.2)	35.6 (8.3)	39.9 (9.4)	0.06
Female [n (%)]	33(48.5%)	13 (50.0)	20 (47.6)	1.00
CD4 Count [mean (SD)]	66.5(79.4)	49.2 (42.1)	76.4 (93.3)	0.06
CD4 Count median	39.5			
CD4 Count range	1-392			
BMI [mean (SD)]	18.7(4.06)	16.6 (2.8)	19.8 (4.2)	0.01
On ARVs for at least 2 wks prior to sCrAg [n (%)]	20(36.4%)	5 (35.7%)	15 (36.6)	1.00
Treatment type [n (%)] Fluconazole Amphotericin +/- Fluconazole	55(80.9%) 4(5.9%)	20(90.9%) 2 (9.1%)	35(94.6%) 2 (5.4%)	0.62

Symptoms	Overall (n=68)	Fatal CM cases (n=26)	Non-fatal CM cases (n=42)	P value
Fever	10(17.2%)	4(19%)	6(16%)	0.12
Headache	58(89.2%)	20 (80%)	38(95%)	0.097
Altered mental Status	8(12.3%)	5(20%)	3 (8%)	0.243
Stiff Neck	18(27.7%)	8 (32%)	10(25%)	0.578
Photophobia	11(16.9%)	4(16%)	7(18%)	1.00
Seizures	7(10.8%)	3(12%)	4(10%)	1.00
Focal Neurological Deficit	6(9.2%)	1(4.0%)	5(12.5%)	0.39

Table 3 (a): Bivariate analysis of key clinical predictors and case fatality using Definition 1

Clinical Predictors (continuous)		Odds Ratio	P value
Age in years		0.95	0.06
CD4 Count		1.00	0.19
BMI		0.75	0.01
Clinical Predictors (categorical)		**Case fatality**	**P value**
Gender	Female	39% (13/33)	1.00
	Male	37% (13/35)	
On ARVs for at least 2 wks prior to sCrAg	Yes	25% (5/20)	1.00
	No	26% (9/35)	
Treatment type [n (%)] Fluconazole		36% (20/55)	0.62

Table 3 (b): Bivariate analysis of key clinical predictors and case fatality using Definition 1

Symptoms	Case Fatality % (# dead/total)	P value
Fever	40% (4/10)	0.12
Headache	34% (20/58)	0.097
Altered mental Status	63% (5/8)	0.243
Stiff Neck	44% (8/18)	0.578
Photophobia	36% (4/11)	1.00
Seizures	43% (3/7)	1.00
Focal Neurological Deficit	17% (1/6)	0.39

Table 4: Multivariate logistic regression model of key clinical predictors and case fatality

Covariate	OR	95% CI	P VALUE
BMI	0.78	0.61,0.99	0.04
Current CD4 count	1.00	0.99,1.01	0.87
On ARVs for at least 2 wks prior to sCrAg	1.11	0.28,4.39	0.88

Limitations

- Small sample size
- Cryptococcal meningitis diagnosis based on sCrAg, not culture proven
- Missing charts

Conclusions

- CM has high case fatality rate of 38% in this out-patient cohort
- Higher BMI was associated with lower case fatality
- CD4 count was not a predictor of case fatality
- Type of anti fungal treatment was not associated with lower case fatality

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