Evaluation of Clinical Management of Cryptococcal Meningitis among Health Care Providers in Selected Hospitals, Kisumu, Kenya

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Abstract
Background: Prevalence of CM has risen and remained high over the last several decades in line with the HIV/ADS pandemic which has consequently led to the increase of CM associated mortality rates ranging from 17% to 100% in Africa.Effective outcome of CM depends majorly on early diagnosis of the infection, prompt initiation of appropriate antifungal therapy, monitoring and prevention of amphotericin (AmpB) toxicity, raised intracranial pressure (ICP) monitoring and management, institution of antiretroviral therapy, prevention of inflammatory syndrome caused by immune reconstitution and treatment response monitoring. Objective. The aim of the present study was to asses clinical management of cryptococcal meningitis in adults among health care providers in Kisumu County, Kenya. Design. The study was a cross-sectional analytical study. Setting. The study was carried out in Kisumu County SampleProportionate random sampling method was applied in the selection of the sample. In this study, the sample size was obtained using Yamane (1967) formula. This sampling method was suitable because the sample population was homogeneous and was less than 10,000. The sample size calculation yielded a sample of 116 respondents. Analysis. Bivariate analysis was done using and logistic regression from which the chi square, odds ratios and the p- values were drawn. Main outcome measures. Clinical management strategies and adherence to WHO guidelines Results. Findings from demographics showed that many were females (n=64, 55.2 %). This implied that majority of health workers in public hospital in the study area are female as opposed to males. Distribution of age bracket showed that many (n=74, 64.3%) were aged 30 years or below.From the results, many of the health care providers had good management strategies (n=65, 55.7%), while 44.3 %(n=51) had poor management strategies. Specifically, 76%(n=88) reported using lumbar puncture with rapid CrAg assay while very few reported using lumbar puncture with rapid CSF India ink test (3%, n=4). When asked which antifungal drugs they commonly used in cryptococcal meningitis during the induction phase, majority (90.5%, n=105) reported using amphotericin B deoxycholate + fluconazole.With regards to methods of diagnosis of cryptococcal meningitis, it was observed that 100 % (n=60) did history taking of the patient and physical examination. In management of hypokalemia, majority (93%, n=56) did not monitor potassium daily but all (100%, n=60) administered 1 liter of normal saline infused with 20 mEq of potassium chloride beyond two hours prior to each infusion of amphotericin B. 93%(n=56) did not administer two of 250-mg tablets of magnesium trisilicate, or magnesium chloride 4 mEq twice/ day for supplementation of magnesium. Bivariate analysis on demographic factors that are associated with clinical management strategies for cryptococcal meningitis shows that there was a borderline significant correlation between age and management strategies in the study area (OR: 0.7; 95% CI: 0.7 – 1.5; p=0.06) as portrayed in Table 4. The respondents aged 30 years and below were 80% less likely to have poor management strategies compared to respondents aged 31 years and above. Conclusion. The study concludes that only a satisfactory number of health care providers (55.7%) had good clinical management strategies and recommends that the policy makers should lay down strategies and mechanisms to scale up the resources, supplies and facilities in the study area which will streamline, promote and sustain optimal adherence to WHO endorsed guidelines on the management of patients suffering from cryptococcal meningitis
Keywords: cryptococcal meningitis, Kisumu county, Kenya, health care providers

I. Background

Meningitis is an inflammatory disorder of the meninges, which are structures that cushion the spinal cord and brain to provide protection. Most patients with this infection at least develop fever, severe headache, and neck rigidity and associated altered level of consciousness (Ganiem, 2013).Although recommended CM control guidelines by WHO are in place, cryptococcal meningitis disease is the major reason for reported deaths

amongst HIV infected patients in under developed areas though it is reducing in the developed countries with ART access (WHO, 2011).Prevalence of CM has risen and remained high over the last several decades in line with the HIV/ADS pandemic which has consequently led to the increase of CM associated mortality rates ranging from 17% to 100% in Africa (Muendo&Mutinda, 2012). There is expanded mortality noted from this infection of cryptococcal meningitis in economically developing countries. The estimated Loss life in people infected and living with HIV and associated cryptococcal meningitis is at 70% in underdeveloped countries in contrast with 20–30% for high-income countries (WHO, 2011).CM treatment with potent antifungal drug combination results in effective cure but unavailability of these drugs remain an obstacle in Sub-Saharan Africa (Adeyemi, 2014).Management of CM effectively, involves prompt diagnosis and initiation of recommended fungicidal drugs, institution of priority interventions to prevent and combat elevated intracranial pressure (ICP), management of inflammatory syndrome related to immune reconstitution and prevention, monitoring and management of hypokalemia and nephrotoxicity (Sogbanmu et al.,2014).

Oyella et al., (2012) advocates for screening for CM in all patients newly diagnosed, living with HIV infection and have associated low CD4 counts of less than 50cells/mm3 for appropriate plan of action. In addition, those individual patients with compromised immunity secondary to HIV infection and are malnourished with a very low body mass index (BMI) accompanied with clinical presentations of meningitis should equally be screened for CM for prompt management to promote desirable patient outcome.Abbas, et al., (2016) points out a common diagnostic tool CM to be India ink staining and culture of the yeast as the definitive test for diagnosis of cryptococcal meningitis. In addition, CSF, serum, or plasma CrAg should be offered for all patients thought to suffer from meningitis. On the other hand, the CrAg lateral flow assay remains a convenient diagnostic test in the point of care.

According to Cox & Perfect et al., (2018), the most effective therapeutic intervention for the patient with cryptococcal meningoencephalitis in the induction phase consists of amphotericin B plus flucytosine, in consolidation phase, fluconazole is administered and continued throughout the maintenance phase. In addition, throughout therapy, monitoring of patients for recurrence of clinical symptoms suggestive of increased intracranial pressure, relapse of infection as a result of non- adherence or drug resistance, adverse events following antifungal therapy, and IRIS secondary to antiretroviral therapy. The WHO (2011) advices administration of a combination of Fluconazole and Flucytocine or high dose of stand-alone Fluconazole during the induction phase in the absence of Amphotericin B, then continue with 8 weeks of consolidation phase of oral Fluconazole and finally provide a maintenance phase of oral fluconazole.

Sloan&Parris, (2014) states that patients infected and living with human immunodeficiency with asymptomatic cryptococcal must be initiated on ART promptly antigenemia. According to John & Pradeep, (2017) the fungicidal therapy goal in HIV co-infected patients with CM is to eradicate and control the infection in acute phase then continue with a longstanding fluconazole regimen to suppress the cryptococcal organism. In patients with cryptococcal infection without HIV comorbidity, the therapeutic goal may differ.Mdodo et al., (2010), emphasizes on the recommended clinical standards for treatment of AIDS associated CM for sub-Saharan Africa as; induction phase of 1 mg/kg/day AmpB for two weeks, consolidation period of Fluconazole 800 mg for four weeks, Fluconazole 400mg or 200mg orally for eight weeks, followed by a maintenance phase Fluconazole 200 mg until CD4 counts were >200 cell/μL.

Rothe et al., (2013) noted significant baseline CNS complications and poor clinical outcomes with associated increased deaths and failure of drug efficiency from cryptococcal meningitis in HIV infected adults related to fluconazole monotherapy.

With early diagnosis of CM, consistence adherence to the basic principles of clinical guidelines by health care providers, and control of the underlying disease, this infection can successfully be managed in majority of patients (Perfect, et al., 2010). Failure to adhere to clinical standards results into overtreatment or under treatment leading to a reduction of potential benefits with increased risks. On the other hand, adherence to standards, assures provision of recommended care and also minimizes health care costs. In addition, there is a realization of quality of care when recommendations are followed than when they are not (Sidorenkov, et al., 2011). According to Austad et al., (2015), to improve quality, minimize variations in provision of health care and assist in setting priorities among HCP, clinical practice guidelines are developed. However, in patients with co- morbidities, simultaneous application of several standards for single diseases may result into pill burden and overtreatment. The aim of the present study was toasses clinical management of cryptococcal meningitis in adults among health care providers in Kisumu County, Kenya

II. Methods

The study was conducted in Kisumu county and ethics approval was obtained from Masinde Muliro University of Science and Technology ethics board, National commission for science and technology. No further approval was needed since the project didnot require access to patients or personal data.

Research Design

The study designs adopted for this study was cross-sectionalanalytical and applied both quantitative and qualitative approaches. This particular design was ideal since the research entailed collecting and comparing data from the phenomena at the same time of study(Basavanthappa, 2011). Polit & Hungler (2010) observed that a cross sectional research design was used when data was collected to describe persons, organizations, settings or phenomena. The purpose of the design was to gather data at a particular point in time with the intention of describing the nature of the existing conditions (Burns and Grove, 2011).Cross sectional analytical study design was also ideal as the study was carried out in a limited geographical scope and hence it was logistically easier and simpler to conduct considering the limitations of this study (Mugenda& Mugenda, 2008). Therefore, the cross-sectional analytical design was deemed the best strategy to fulfill the objectives of this study.

Study setting

The research was performed in the medical wards, outpatient departments and the patient support center (PSC) of JOOTRH and KCRH in July – September, 2019.JOOTRH is located in Kisumu county, Kisumu East constituency, Kondele ward. It is now the largest referral hospital in Western Kenya and serves more than 100 county and sub-county hospitals in the region. Its main mandate is to provide curative, preventive, promotive, diagnostic and rehabilitative services. It serves a catchment population of 83642 (JOOTRH Hospital Strategic Plan, 2016-2021). Its medical units have a bed capacity of 110 with a total number of 100 health care providers including those working in the out -patient clinics and patient support center. The mortality rate in the female medical ward is 25% while that of the male medical ward is at 27 % (JOOTRH Health Records, 2018). Kisumu County Referral Hospital is the second largest public hospital in Kisumu County located in Kisumu city center, Kisumu East constituency, Railways ward. Its medical units have a bed capacity of 61 with a total number of 40 health care providers. The bed occupancy for the medical wards is 100%. It serves the peripheral facilities and offers diagnostic curative, preventive, promotive, and rehabilitative services. The hospital refers its complicated cases to JOOTRH for further management.

Participants

Mugenda and Mugenda (2008) defined population as all elements (individuals, objects and events) that meet the sample criteria for inclusion in a study. The target population were the qualified health care providers offering care to adult patients suffering from CM in the medical wards, patient support center (PSC) and outpatient clinics in the two hospitals. There is a total of 140 health care providers in the aforementioned units in the two hospitals, 40 from KCRH and 100 from JOOTRH.Proportionate random sampling method was applied in the selection of the sample. This sampling method produces approximations of total population parameters with high accuracy, thereby guaranteeing a more representative sample is obtained from a fairly homogeneous population. In addition, proportionate methods goal is to decrease standard error by affording slight control over variance (Barbie, 2004). In this study, the sample size was obtained using Yamane (1967) formula. This sampling method was suitable because the sample population was homogeneous and was less than 10,000. The sample size calculation yielded a sample of 116 respondents. The inclusion criteria were all qualified health care providers employed in the medical units, outpatient clinics/casualty and the patient support center for at least three months, were involved in the research. The exclusion criteria were all the qualified health care providers in the target population who did not consent to participate in the study were excluded.

Questionnaire

Questionnaires were selected as data collection instruments. A questionnaire is a printed self-report from designed to elicit information that can be obtained through the written responses of subjects. The information obtained through a questionnaire is similar to that obtained by an interview, but questions to have less depth (Denzin, 1970).Kothari, (2007), clarifies that self-administered questionnaires are the only way to prompt peoples' attitudes, beliefs, opinions and values. The researcher applied questionnaires in the collection of primary data to examine the clinical management strategies of CM and assessment of the factors influencing adherence to WHO standards on management of CM among health care providers. In addition, an observational check list was used to evaluate the adherence to WHO guidelines among HCP.The research instrument for obtaining data in the study had three parts. Part A obtained demographic features of the respondents, part B solicited for data on clinical management strategies of cryptococcal meningitis and part C probed for factors influencing adherence to WHO standards on cryptococcal meningitis. An instruction for selecting the responses was provided in all the sections. The questionnaire consisted of closed ended questions. The observation check list was scored according to individual HCP's performance during observation.To increase the validity and reliability of the instruments, the questionnaire was evaluated by experts. Then based on the feedback the final questionnaire was prepared for pre-test. The pretest study was conducted in one sub-county hospital.The

reliability of the scale of the questinnaire was found to be: Internal consistency = (Cronbach's α = 0.701). Deleting selected items would not increase the alpha.

Data Analysis

Data analysis was done using the statistical program for social sciences (SPSS) version 25. Inferential and descriptive statistics were used to analyze data. Descriptive analysis of data was done using the mean, frequencies and percentages. In this study association between the study variables was assessed by a two-tailed probability value of $p<0.05$ for significance. Visual inspection of the data illustrated that missing data appeared to be missing at random. Univariate analysis was used to describe the distribution of each of the variables in the study objective, appropriate descriptive analysis was used to generate frequency distributions, tables and other illustrations used to analyze community knowledge. Bivariate analysis was done using and logistic regression from which the chi square, odds ratios and the p- values were drawn. Qualitative data collected from FGDs was analyzed by thematic content analysis. Hours of recording were integrally and literally transcribed into verbatim transcripts which wereanalyzed using NVivo 9 – QSR International software to identify patterns and themes for thematic content analysis then recorded, translated and transcribed.

III. Results

The research targeted a sample size of 119 respondents out of which 116 completed and returned the questionnaires, making a total response rate of 97%. According to Mugenda and Mugenda (2003) a response rate of 50 percent is adequate, a response rate of 60 percent is good, and a response rate of 70 percent is very good. Therefore, the 87 percent response rate reported for this study formed an acceptable basis for drawing conclusions. While we should not expect full response in studies where responding is voluntary, scholars utilizing questionnaires should aim for a high response rate (Baruch&Holtom, 2008). The study sought to obtain information on the respondents' background characteristics based on the gender, job title, experience, age bracket and unit currently working.The summary of their responses is given in Table 1.

Table 1. Demographic background characteristics of respondents

		n	%
Gender	Male	52	44.8%
	Female	64	**55.2%**
Age groups	30 years and below	74	**64.3%**
	31-40 years	24	20.9%
	41-50 years	9	7.8%
	51 years and above	8	7.0%
Job title	medical consultant	5	4.3%
	medical officer	14	12.1%
	nursing officer	78	**67.2%**
	clinical officer	19	16.4%
Experience categories	5 years and below	75	**64.7%**
	6-10 years	17	14.7%
	11-20 years	12	10.3%
	20 years and above	12	10.3%
Unit of work	male medical ward	52	44.8%
	female medical ward	37	31.9%
	patient support center	15	13.0%
	outpatient clinics	12	10.3%

With regard to their gender profiles, many were females (n=64, 55.2 %). This implied that majority of health workers in public hospital in the study area are female as opposed to males. Distribution of age bracket showed that many (n=74, 64.3%) were aged 30 years or below. Results on their job titles revealed that majority (n=78, 67.2%) were nursing officers while only a few (n=5, 4.3%) were medical consultants. A Greater part of the respondents had experience of 5 years or below (n=75, 64.7%).

Clinical management strategies of cryptococcal meningitis

The first question of the research was to obtain the clinical management strategies of cryptococcal meningitis in Kisumu county public hospitals. Firstly, the respondents were asked which method they commonly used to diagnose cryptococcal meningitis. Results showed that 76%(n=88) reported using lumbar puncture with rapid CrAg assay while very few reported using lumbar puncture with rapid CSF India ink test (3%, n=4). When asked which antifungal drugs they commonly used in cryptococcal meningitis during the induction phase, majority (90.5%, n=105) reported using amphotericin B deoxycholate + fluconazole. Their responses are illustrated in Table 2

Table 2. Clinical management strategies of cryptococcal meningitis among health care providers

		n	%
Method commonly used to diagnose cryptococcal meningitis	lumber puncture with rapid CrAg assay	88	**75.9%**
	lumber puncture with rapid CSF India ink test	4	3.4%
	lumber puncture with CSF culture	22	19.0%
	serum CrAg	2	1.7%
Antifungal drugs commonly used in the treatment of cryptococcal meningitis during the induction phase	amphotericin B deoxycholate + flucytosine + fluconazole	8	6.9%
	Fluconazole + flucytosine	3	2.6%
	amphotericin B deoxycholate + fluconazole	105	**90.5%**

When asked if they perform monitoring, management and prevention of amphotericin B deoxychlolate toxicity, 95.7% (n=111) accepted, 83%(n=96) reported to be doing monitoring and management of raised intracranial pressure, 90%(n=104) reported to be timing ART initiation in HIV infected patients, 62%(n=72) reported not using adjunctive corticosteroids in the management of cryptococcal meningitis in HIV infected patients, 94%(n=109) reported to use monitoring of treatment response, 85%(n=98) reported to do monitoring and management of immune inflammatory reconstitution syndrome while 86%(n=100) reported to be doing management of relapse for cryptococcal meningitis. Table 3 below portrays an evaluation of the responses

Table 3.Clinical management strategies provided for the patient suffering from cryptococcal meningitis

	YES		NO	
	n	%	n	%
Prevention, monitoring and management of amphotericin B deoxycholate toxicity	111	**95.7%**	5	4.3%
Monitoring for and management of raised intracranial pressure	96	82.8%	20	17.2%
Timing of ART initiation in HIV infected patients	104	89.7%	12	10.3%
Use of adjunctive corticosteroids in the management of cryptococcal meningitis in HIV infected patients	44	37.9%	72	62.1%
Monitoring of treatment response	109	**94.0%**	7	6.0%
Monitoring and management of immune reconstitution inflammatory syndrome	98	84.5%	18	15.5%
Management of relapse for cryptococcal meningitis	100	86.2%	16	13.8%

Respondents answered a total of seven closed ended questions. Each response was given a mark based on the level on the dichotomous scale with the anchors being No=0 to Yes=1 and vice versa for questions that were reverse coded. Scale scores were computed by adding responses to the seven questions leading to a minimum possible score of 0 and a maximum of 7. Respondents who scored below the mean score of 3.8 were classified as having poor management strategies and those that scored above the mean score were classified as having good management strategies.

- Good management strategies (above mean score of 3.8)
- Poor management strategies (Below mean score of 3.8)

From the results, many of the health care providers had good management strategies (n=65, 55.7%), while 44.3 %(n=51) had poor management strategies (figure 1)
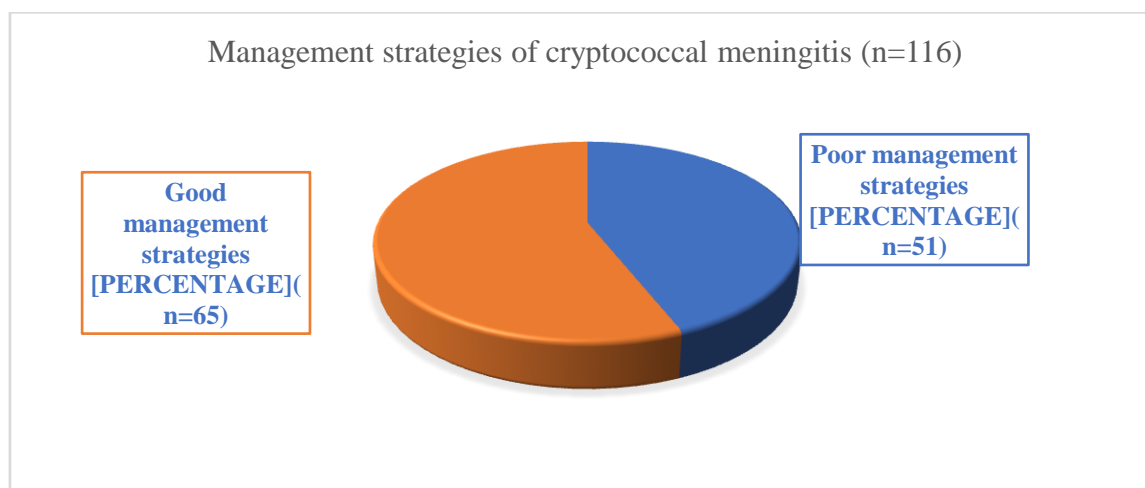
Figure 1. Management strategies of cryptococcal meningitis

Bivariate analysis of demographic characteristics associated with management strategies of cryptococcal meningitis

Bivariate analysis on demographic factors that are associated with clinical management strategies for cryptococcal meningitis shows that there was a borderline significant correlation between age and management strategies in the study area (OR: 0.7; 95% CI: 0.7 – 1.5; p=0.06) as portrayed in Table 4. The respondents aged 30 years and below were 80% less likely to have poor management strategies compared to respondents aged 31 years and above. Males were 1.3 times more likely to have poor management strategies compared to women (OR: 1.3; 95% CI: 0.7 – 2.3; p=0.97). Job titles was not statistically significant with management strategies with the results showing that respondents who were medical consultants/medical officers being 1.7 times more likely to have poor management strategies compared with their counterparts nursing officers/clinical officers (OR: 1.7; 95% CI: 1.5 – 3.0; p=0.14). Similarly, respondents who had an experience of five years or less were 80% more likely to have poor management strategies in contrast to those with an experience of six years or more (OR: 1.8; 95%CI: 0.6 – 2.2; p=0.008).

Table 4 Demographic characteristics associated with clinical management strategies

	n	Management strategies		Overall OR	95% CI	p-value
		Poor	Good			
Age						
<=30	74	85.3(157)	14.7(29)	0.2	0.7 – 1.5	**0.06**
>31	42	93.2(111)	6.8(8)			
Gender						
Male	52	61.7(66)	38.2 (41)	1.3	0.7 – 2.3	0.97
Female	64	61.2 (121)	38.8(77)			
Job titles						
Medical consultant/Medical officer	19	73.5(193)	26.5 (69)	1.7	1.5 – 3.0	0.14
Nursing officer/clinical officer	97	54.4 (23)	45.6(20)			
Experience						
<=5	75	58.8(62)	41.2 (44)	1.8	0.6 – 2.2	**0.008**
>6	41	33 (66)	67(43)			

Adherence to WHO guidelines on clinical management of cryptococcal meningitis

The second research question of the study was to find out adherence to WHO standards on clinical management of cryptococcal meningitis. The information was obtained via observation checklists. Firstly, with regards to methods of diagnosis of cryptococcal meningitis, it was observed that 100 %(n=60) did history taking of the patient and physical examination. An analysis of feedback is shown on Table 5 below.

Table 5 Adherence to WHO guidelines on clinical management of cryptococcal meningitis

	Yes		No	
	n	%	n	%
History taking	60	100.0	0	0.0
Physical examination	60	100.0	0	0.0
Diagnostic tests;				
Lumber puncture with measurements of CSF fluid opening pressure	0	0.0	60	**100.0**
Lumber puncture with rapid CSF CrAg assay	60	100.0	0	0.0
Lumber puncture with CSF India ink test	40	66.7	20	33.3
Rapid serum/whole blood CrAg assay	60	100.0	0	0.0
Induction phase of treatment				
Two weeks amphotericin B 1mg/kg/day + fluconazole 1200mg/day	60	100.0	0	0.0
Fluconazole 800mg daily for 8 weeks following induction phase	44	73.3	16	26.7
Preventing, monitoring and managing of amphotericin B toxicity				
Serum potassium:				
Initial Serum potassium	60	100.0	0	0.0
Serum potassium 2-3 times/week in the second week of amphotericin B administration	20	33.3	40	66.7
Hypokalemia				
Daily serum potassium measurement	4	6.7	56	**93.3**
20 mEq of potassium chloride infused in 1 liter of normal saline over two hours before each dose of amphotericin B	60	100.0	0	0.0
8-mEq potassium chloride 1-2 tablets orally twice daily	0	0.0	60	**100.0**
8-mEq tablet may be added twice/ day during the second week	4	6.7	56	**93.3**
Supplement magnesium 2 of 250-mg tablets of magnesium	4	6.7	56	**93.3**

trisilicate twice / day, or magnesium chloride 4 mEq twice/ day				
Serum creatinine				
Initial serum creatine measurement	60	100.0	0	0.0
Serum creatine 2-3 times weekly in the second week of amphotericin B therapy	16	26.7	44	**73.3**
Timing of ART in HIV positive patients				
Withhold ART 4-6 weeks from the initiation of antifungal drugs	56	93.3	4	6.7
Give blood transfusion in severe Amphotericin B related anemia	32	53.3	28	46.7
Monitoring for raised intracranial pressure				
Have an initial lumbar puncture	60	100.0	0	0.0
Measurement of CSF opening pressure	0	0.0	60	**100.**
Perform repeat lumbar puncture with measurement of CSF opening pressure	0	0.0	60	**100.0**
Management of raised intracranial pressure				
Therapeutic lumbar puncture	16	26.7	44	**73.3**
Persistent raised intracranial pressure				
Perform lumbar puncture if possible, every day with measurements of CSF opening to evaluate progress	0	0.0	60	**100.0**
Monitoring treatment response				
Performed every day in the period of induction therapy	60	100.0	0	0.0

With regards to diagnostic tests, none (0%, n=0) did LP with measurement of CSF fluid opening pressure, all (100%, n=60) did the rapid serum/whole blood CrAg assay and LP with rapid CSF CrAg assay, majority (67%, n=40) did lumbar puncture with CSF India ink test while did the rapid serum. In the induction phase of treatment all (100%, n=60) gave two weeks amphotericin B 1mg/kg/day + fluconazole 1200mg/day while a majority (73%, n=44) of them gave Fluconazole 800mg daily for 8 weeks following induction phase.With regards to monitoring, preventingand managing of amphotericin B toxicity, all (100%, n=60) did serum potassium baseline, majority (67%, n=40) did not perform serum potassium 2-3 times every week in the second week of amphotericin B drug therapy.

In management of hypokalemia, majority (93%, n=56) did not monitor potassium daily but all (100%, n=60) administered 1 liter of normal saline infused with 20 mEq of potassium chloridebeyond two hours prior to each infusion of amphotericin B. 93%(n=56) did not administertwo of 250-mg tablets of magnesium trisilicate, or magnesium chloride 4 mEq twice/ day for supplementation of magnesium. In monitoring of serum creatine, all (100%, n=60) measured initial serum creatine levels but 73% (n=44) did not measure 2-3 times/ week during the second week of amphotericin B drug therapy. In timing of ART, in HIV co- infected patients, 93% (n=56) withheld HAART for 4-6 weeks following the initiation of antifungal regimen. In monitoring for raised intracranial pressure, all (100%, n=60) did not measure CSF opening pressure and also did not carry out a repeat lumbar puncture with measurement of CSF opening pressure to for monitoring of patient progress.

In management of raised intracranial pressure all (100%, n=60) did not do repeat daily therapeutic lumbar puncture (with measurements of CSF opening pressure where available. With regards to monitoring treatment response, all (100%, n=60) assessed patient response to treatment every day during the first two weeks of induction treatment.The observation checklist had a total of twenty-five items. Each response was given a mark based on the level on the dichotomous scale with the anchors being No=0 to Yes=1 and vice versa for items that were reverse coded. Scale scores were computed by adding responses to the seven items causing a minimum possible score of 0 and a maximum of 25.

Respondents who scored below the mean score of 20.6 were classified as not adhering to WHO guidelines and those that scored above the mean score were classified as adhering to WHO guidelines.
- Adhering to WHO guidelines (above mean score of 20.6)
- Not adhering to WHO guidelines (Below mean score of 20.6)

From the results, many of the health care workers were adhering to WHO guidelines (n=37, 61%), while 39% (n=23) did not adhere to WHO guidelines (Figure 2)
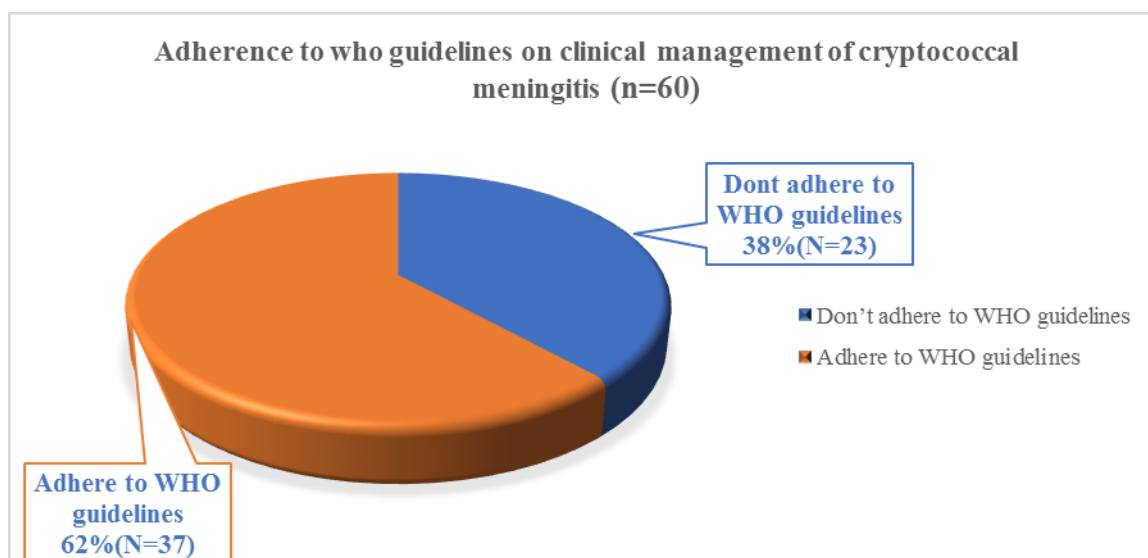
Figure 1. Adherence to who guidelines on clinical management of cryptococcal meningitis

Bivariate analysis of socio-demographic characteristics associated with adherence to WHO guidelines

A Bivariate logistic regression was done to evaluate the relationship amongst adherence and socio demographic characteristics. Nurses were 40% less likely to adhere compared to clinical officers (OR: 0.6; 95% CI: 0.4 – 0.9; p=0.01). Males were 1.2 times more likely to adhere compared to females (OR: 1.2; 95% CI: 0.8 – 1.9; p=0.3). This is shown in the Table 6 below

Table 6 Socio demographic characteristics associated with adherence to WHO guidelines

		Adhere		Don't Adhere		Overall OR	95% CI	p value
		n	%	n	%			
Job Titles	Nurses	14	45.1	18	54.9	0.6	0.4 – 0.9	**0.01**
	Medical officers	3	33.3	7	66.7	0.7	0.2 – 2.7	0.7
	Clinical officers	7	40.9	11	59.1	*	*	*
Gender	Females	18	46.4	21	53.6	1.2	0.8 – 1.9	0.3
	Males	4	16.7	17	83.3			
* Reference category								

IV. Discussion

The objective of the present study was to asses clinical management of cryptococcal meningitis in adults among health care providers in Kisumu County. This study findings show that only 55.7%, n=65 of the health care providers had good clinical management strategies with a mean score of above 3.8. Although the WHO standards, 2018 does not recommend steroid use among HIV infected CM patient during the period of induction phase, this study identified that 37.9% (n=44) carried out this outdated strategy indicating an urgent need for prompt updates for the HCP on the most current WHO guidelines. Majority of the HCP (95.5%, n=111) monitored and managed amphotericin B deoxycholate toxicity which is in line with the WHO guidelines. This finding differs with a research carried out in South Africa on cryptococcal management in adults by Sogbanmu et al., (2014) which identified that while managing patients with cryptococcal meningitis, effective measures such as renal toxicity monitoring and documentation of fluid administration were not done. Respondents who had an experience of five years or less were 80% more likely to have poor management strategies in contrast to those with an experience of six years or more (OR: 1.8; 95%CI: 0.6 – 2.2; p=0.008).These findings tally along a study done by Barth et al., 2015, which revealed that there is a difference in practice over the generations and clinicians who are in their second half of their career, practice as individuals according to their knowledge and experience.The study identified that males were 1.3 times more likely to have poor management strategies compared to women (OR: 1.3; 95% CI: 0.7 – 2.3; p=0.97). Majority of health care providers were females (55.2%, n=64) and this possibly explains why there was fairly good clinical management strategies in the study area.

This study results show that, 61% (n=37) of the health care providers were adhering to WHO guidelines, the results further reveals that nurses were 40% less likely to adhere to the WHO recommended guidelines on management of CM compared to clinical officers (OR: 0.6; 95% CI: 0.4 – 0.9; p=0.01),in addition, males were 1.2 times more likely to adhere compared to females (OR: 1.2; 95% CI: 0.8 – 1.9; p=0.3). .

The study also realized 100% (n=60) history taking and physical examination of patients by the clinicians, this is consistent with the WHO 2018 guidelines which recommends that earlier diagnosis, and prompt treatment of cryptococcal malaise and its complications, is required to lessen the incidence and related high death rate in resource limited settings. All the HCP (100%,n=60) performed rapid serum/whole blood assay and lumbar puncture with rapid CSF CrAG assay while 67%,(n=40) of HCP performed lumbar puncture with CSF India ink test to diagnose CM .This is in line with the WHO 2018 guidelines and a study done by Oyella et al., 2012 which encourages clinicians to be cautious in diagnosis of cryptococcal disease in vulnerable patients who present with meningeal irritation, neck pain, a low BMI, and a recent HIV diagnosis before ART initiation for suitable intervention. It is established from this study that all the health care providers (100%, n=60) gave two weeks amphotericin B 1mg/kg/day + fluconazole 1200mg/day in the induction phase of treatment while a majority (73%, n=44) of them gave Fluconazole 800mg daily for 8 weeks following induction phase. This finding indicates that the HCP in the study area instituted appropriate therapy in the induction phase according to the WHO guidelines 2018 on clinical management of cryptococcal meningitis and a study done by Govender et al, 2013.

Although this study realizes that all the HCP (100%, n=60) did administer 20 mEq of potassium chloride infused in 1 liter of normal saline over two hours before each infusion of amphotericin B, all HCP (n=60) never monitored potassium daily and only 67% (n=40) checked the serum potassium levels 2-3 times weekly. This practice contradicts the recommended WHO guidelines, 2018. This finding proves that the monitoring of AMP B toxicity was not sufficiently performed in the study area hence increasing the risk for mortality from preventable AMP B toxicity. In addition, 93% (n=56) did not administer Magnesium to counteract AMP B complications. This outcome is commensurate to those of a comparable research done in South Africa by Sogbanmu et al., 2014 which revealed that preload and potassium supplementation were not done during the management of patients with CM. It is noted from the study that all the health care providers (100%, n=60) measured serum creatine at baseline but a large number of the HCP (73% n=44) did not measure 2-3 times weekly as stipulated in the WHO recommended guidelines. Majority of the HCP (93% n=56) of HCP did timing of ART, in HIV patients, through withholding it 4-6 weeks following antifungal treatment hence prevention of IRIS as a result of ART. This latter finding is in line with a study carried out by Cox & Perfect, 2018 on clinical management of CM.All the HCP (100%, n=60) neither measured CSF opening pressure nor performed any subsequent lumbar puncture with measurement of CSF opening pressure as recommended by WHO 2018 to monitor patient progress in regard to raised ICP. In addition, all the HCP (100%, n=60) did not perform repeat daily therapeutic lumber puncture and CSF opening pressure measurement as a means of managing raised ICP. These results agree with a study carried out in 2014 by Adeyemi & Ross which noted that previous studies had shown critical disparities in clinicians' compliance to recommendations on management of CM. However, all the HCP (100%, n=60) assessed the patients for response to treatment on a daily basis during the induction phase of regimen, this practice is line with the WHO 2018 recommended guidelines.

V. Conclusion

The study concludes that only a satisfactory number of health care providers (55.7%) had good clinical management strategies. Years of experience (p-value 0.008) greatly influenced the clinical management strategies of cryptococcal meningitis.Critical effective aspects in the WHO recommended guidelines in the management of CM such as measurement of CSF opening pressure, daily observation of serum potassium levels, monitoring of serum creatinine 2-3 times weekly and daily repeat of therapeutic lumber puncture in management of raised intracranial pressure, were not done in this study during the study period. This finding can be associated with the increased CM mortality rate in the study area. The study recommends that hospital management teams with the medicine departments in the two hospitals should consistently avail current recommended clinical guideline protocols in all the medical departments to ease reference, hence promote adherence. In addition, they should include the aspect of adherence to WHO guidelines on management of cryptococcal meningitis, as one of the yearly appraisal objectives and provide timely supportive supervision in order to promote and streamline optimal adherence. In addition, the policy makers at the county government of Kisumu should lay down strategies and mechanisms to scale up the resources, supplies and facilities in the study area which will streamline, promote and sustain optimal adherence to WHO endorsed guidelines on the management of patients suffering from CM. Further research is needed to determine patient related factors influencing adherence to WHO endorsed guidelines in the management of CM.

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