Journal of Medical and Biomedical Sciences (2012) 1(4): 13-20

ORIGINAL ARTICLE

HIV co-infection and mortality pattern of purulent meningitis: A 5 year retrospective autopsy study at the Korle-Bu Teaching Hospital

E.M. Der[1], R.K. Gyasi[1], M. Mutocheluh[2] and J.T. Anim[1]

[1]Department of Pathology, University of Ghana Medical School, Korle-Bu, Accra, Ghana; [2]Department of Clinical Microbiology, School of Medical Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

This study utilized retrospective autopsy data to examine the relationship between HIV co-infection and mortality pattern of purulent meningitis. All autopsy log books and available hospital files were reviewed for information on purulent meningitis for which autopsies were performed in 2005 through 2009 at the Pathology Department of the Korle-Bu Teaching Hospital, Accra, Ghana. The mean ± SD of the studied population was 34.6±19.5 years and the prevalence of HIV co-infection among this population was 4.3%. Female participants died at a significantly younger age (31.9±19.7 years; p=0.0103) compared to their male counterparts (36.1±19.2 years). Most of the cases in HIV negative purulent meningitis death had purulent meningitis as the primary cause (i.e. 87.9% *vs* 18.5%) whereas most of the death in HIV co-infection cases had purulent meningitis as the secondary cause of death to other conditions such as CVA, pneumonia, head injury due to road traffic accidents and various malignancies (i.e. 81.5% *vs* 12.1%). Purulent meningitis secondary to other conditions is more likely to be the cause of death in aged subject. The prevalence of purulent meningitis with HIV co infection was low in this study. The mortality pattern is related to the age and gender of the studied population and whether the purulent meningitis is primary or as a co infection with HIV.

Journal of Medical and Biomedical Sciences (2012) 1(4), 13-20

Keywords*:* Autopsy, Purulent meningitis, HIV, Co-infection, opportunistic infections

INTRODUCTION

Purulent meningitis is a life threatening acute bacterial inflammation of the meninges of the brain and spinal cord. It mostly affects children, the aged or the immune-compromised. Ghana lies within the meningitis belt in sub-Saharan Africa and as such outbreaks of bacterial meningitis are not uncommon (Molesworth *et al.*, 2002).

Human immune deficiency virus (HIV) infected patients have a defective immunity and so are susceptible to numerous opportunistic infections caused by both bacteria and fungi including purulent meningitis (Hakim *et al.*, 2000). The association of the meninges has the potential to worsen any opportunistic brain infections. Furthermore, primary infection of HIV is complicated by meningitis thus it is appropriate to expect co-infection of purulent meningitis and HIV especially in places where both conditions are endemic. A number of studies (Silber *et al.*, 1999; Gordon *et al.*, 2000; Hakim *et al.*, 2000) have examined various aspects of the relationship between HIV and purulent meningitis including the mortality pattern looking at the role played by the various opportunistic organisms. However, there is paucity of data on the relationship between these two conditions in Ghana. This study therefore aims to use retrospective autopsy data to examine the relationship between HIV co-infection and the mortality pattern of purulent meningitis.

Correspondence: *Dr. Der Muonir Edmund, Department of Pathology, University of Ghana Medical School, Korle-Bu, P.O Box 4236,* Accra, Ghana, E-mail,- maadelle@yahoo.com

MATERIAL AND METHODS

Study Site

All data were gathered from the Department of Pathology, Korle-Bu Teaching Hospital, Accra, Ghana. It is the nation's foremost teaching hospital and has the largest mortuary in the country. This mortuary performs 3,000 to 6,000 autopsies a year. Cases are received primarily from the Accra Metropolis, neighbouring towns and districts, and in some circumstances, from other regions across the country. However, autopsy was not done on all meningitis related deaths within the catchment area. This is because deaths that occurred in the communities and were not reported to the police did not have autopsy done on them.

Data Collection and Analysis

All autopsy log books and available hospital files of subjects who underwent autopsy were reviewed from the period of 2005 through 2009, and all cases of meningitis related deaths were recorded. Data were collected and cross-checked to prevent double entry. For each case of meningitis death, data were collected on age, gender, and category of death by location (Coroner's request or hospital). Coroner's cases are deaths that occurred in the community or within 24-hours of admission to a health facility, where no definitive diagnosis was arrived at before death. Hospital deaths, on the other hand, are deaths that occurred in a health facility while the subject was receiving care for a given diagnosis. The diagnosis of meningitis was based on the ante-mortem clinical and laboratory diagnosis as well as macroscopic autopsy findings. The HIV status was from ante-mortem testing. All cases of tuberculosis (TB) and Cryptococcus meningitis were excluded.

RESULTS

Gender distribution of the studied population

In 2005 through to 2009, a total of 24,787 autopsies were performed. Out of this number, purulent meningitis was recorded as the cause of death in 621 (2.5%) cases. As shown in Table 1, the mean age of the studied population (i.e. the 621 cases with purulent meningitis) was 34.6 ± 19.5 years. Majority of the deaths occurred within the communities with the primary cause of death in recorded. Coroner's cases (85.7%) being purulent meningitis (84.9%) and 95.7% of recorded cases without HIV co-infection. Death within the health facility was found in 14.3% of recorded cases and purulent meningitis was found to be the secondary cause of death to other conditions such as CVA, pneumonia, head injury due to road traffic accidents and various malignancies in about 15% of the studied population. The prevalence of HIV co-infection among this population was found to be 4.3% (Table 1).

When the studied population was classified based on gender, the females died at a significantly ($p = 0.0103$) younger age (31.9 ± 19.7 years) as compared to the male counterpart (36.1 ± 19.2 years). No significant differences were observed in the place of death, type of purulent meningitis as well as HIV co-infection among both sexes (Table 1). As noted in the total population, majority of deaths in both genders are Coroner's cases with purulent meningitis being the primary cause without HIV co-infection (Table 1).

Impact of HIV co-infection on the studied population

From Table 2, HIV related meningitis deaths occurred at a significantly ($p = 0.0432$) older age (41.6 ± 10.1 years) as compared to those without HIV co-infection (34.0 ± 19.3 years) among the total population. Significantly ($p < 0.0001$), HIV negative purulent meningitis death was more associated with Coroner's death (i.e. 87.5% *vs.* 44.4%) whereas HIV related meningitis deaths were more associated with death within the health facilities (i.e. 55.6%*vs.* 12.5%). Majority of the cases that occurred in HIV negative purulent meningitis deaths had purulent meningitis as the primary cause (i.e. 87.9% *vs.* 18.5%) whereas majority of the death that occurred in HIV co-infection cases had purulent meningitis as the secondary cause of death to other conditions such as CVA, pneumonia, head injury due to road traffic accidents and various malignancies (i.e. 81.5% *vs.* 12.1%) (Table 2). These same pattern of results were noted when the studied population

Table 1: General characteristic of the studied population stratified by gender

Variable	Total (n = 621)	Female (n = 220)	Male (n = 401)	P value
Age (yrs)	34.6 ± 19.5	31.9 ± 19.7	36.1 ± 19.2	0.0103
Place of death				
Coroner	532(85.7%)	183(83.2%)	349(87.0%)	0.1905
Permission	89(14.3%)	37(16.8%)	52(13.0%)	0.1905
Type of purulent meningitis				
Primary cause of death	527(84.9%)	187(85.0%)	340(84.8%)	1.0000
Secondary cause of death	94(15.1%)	33(15.0%)	61(15.2%)	1.0000
HIV co-infection				
Yes	27(4.3%)	10(4.5%)	17(4.2%)	0.8398
No	594(95.7%)	210(95.5%)	384(95.8%)	0.8398

Continuous data is presented as mean ± SD and analyzed using unpaired t-test whilst categorical data are presented as proportion and analyzed using Fischer's exact test

were stratified based on HIV co-infection and gender, except for the fact that age was not a significant factor among the male population (Table 2).

Impact of age on the studied population

When the total studied population was stratified based on age in Table 3, generally, fewer proportion of the female deaths occurred at older ages whereas higher proportion of male deaths occurred as subjects aged as indicated by the Chi-square test for trend. Coroner's death was negatively associated with age as opposed to the positive association between permission death and age (Table 3). Purulent meningitis was less likely to be the primary cause of death as the subjects aged whereas purulent meningitis secondary to other conditions was more likely to be the cause of death as the subjects aged (Table 3).

As the subjects aged, the prevalence of HIV co-infection assumed a "bell-shaped" curve whereas prevalence of HIV negative purulent meningitis assumed a "U-shape" curve. The highest prevalence of HIV co-infection of 8.8% was noted among the 35-44 years group, followed by 8.6% in 25-34 years group, 6.0% in 45-54 years group, 3.9% in 55-64 years group and 2.2% in 65 years and above group. No HIV co-infection was noted up to the age of 24 years (Table 3).

Stratification of the studied population based on age and gender in Table 4 indicated similar patterns of results as in the total population with regards to place of death and type of purulent meningitis. However, the highest prevalence of HIV co-infection of 11.1% was noted among the 55-64 years group followed by 10.0% in 25-34 years group, 8.3% in 35-44 years group, 6.7% in ≥ 65 years group and 3.2% in 45-54 years group among the female. No HIV co-infection was noted among females up to the age of 24 years (Table 4). Among the males, the highest prevalence of HIV co-infection of 9.0% was found among the 35-44 years group, followed by 7.5%, 7.2% and 2.4% among the 25-34 years group, 45-54 years group and 55-64 years group respectively. No male subject up to the age of 24 years and ≥ 65 years had HIV co-infection (Table 4).

DISCUSSION

Opportunistic infections including meningitis are common in HIV infection. This study sought to establish the relationship between HIV co-infection and the mortality pattern of purulent meningitis by examining retrospective autopsy data at the Korle-Bu Teaching Hospital (KBTH). The prevalence of purulent meningitis and HIV co-infection was 4.3% and factors such as age and gender affected the prevalence of purulent meningitis HIV co-infection

Table 2: Distribution of the type of purulent meningitis as well as the place of death of the studied population stratified by HIV co-infection and gender

Variables	HIV positive	HIV negative	P values
Total	***n = 27***	***n = 594***	
Age (yrs)	41.6 ± 10.1	34.0 ± 19.3	0.0432
Gender			
Female	10(37.0%)	210(35.4%)	0.8398
Male	17(63.0%)	384(64.6%)	0.8398
Place of death			
Coroner	12(44.4%)	520(87.5%)	< 0.0001
Permission	15(55.6%)	74(12.5%)	< 0.0001
Type of purulent meningitis			
Primary cause of death	5(18.5%)	522(87.9%)	< 0.0001
Secondary cause of death	22(81.5%)	72(12.1%)	< 0.0001
Female	***n = 10***	***n = 210***	
Age (yrs)	42.7 ± 14.3	30.0 ± 18.0	0.0294
Place of death			
Coroner	3(30.0%)	180(85.7%)	0.0002
Permission	7(70.0%)	30(14.3%)	0.0002
Type of purulent meningitis			
Primary cause of death	1(10.0%)	186(88.6%)	< 0.0001
Secondary cause of death	9(90.0%)	24(11.4%)	< 0.0001
Male	***n = 17***	***n = 384***	
Age (yrs)	40.9 ± 7.0	35.9 ± 19.6	0.2912
Place of death			
Coroner	9(52.9%)	340(88.5%)	0.0005
Permission	8(47.1%)	44(11.5%)	0.0005
Type of purulent meningitis			
Primary cause of death	4(23.5%)	336(87.5%)	< 0.0001
Secondary cause of death	13(76.5%)	48(12.5%)	< 0.0001

Continuous data is presented as mean ± SD and analyzed using unpaired t-test whilst categorical data are presented as proportion and analyzed using Fischer's exact test.

Table 3: The impact of age on purulent meningitis among the total studied population

Variables	≤ 18	19-24	25-34	35-44	45-54	55-64	≥ 65	P value
	n = 149	***n = 69***	***n = 93***	***n = 114***	***n = 100***	***n = 51***	***n = 45***	
Age (yrs)	10.6 ± 6.0	21.6 ± 1.7	30.1 ± 3.0	38.5 ± 2.9	48.9 ± 2.8	58.9 ± 8.1	74.4 ± 2.9	
Gender								
Female	62(41.6%)	27(39.1%)	40(43.0%)	36(31.6%)	31(31.0%)	9(17.6%)	15(33.3%)	0.0039
Male	87(58.4%)	42(60.9%)	53(57.0%)	78(68.4%)	69(69.0%)	42(82.4%)	30(66.7%)	0.0039
Place of death								
Coroner	135(90.6%)	66(95.7%)	84(90.3%)	98(86.0%)	78(78.0%)	40(78.4%)	31(68.9%)	< 0.0001
Permission	14(9.4%)	3(4.3%)	9(9.7%)	16(14.0%)	22(22.0%)	11(21.6%)	14(31.1%)	< 0.0001
Type of purulent meningitis								
Primary cause of death	137(91.9%)	68(98.6%)	83(89.2%)	90(78.9%)	79(79.0%)	40(78.4%)	30(66.7%)	< 0.0001
Secondary cause of death	12(8.1%)	1(1.4%)	10(10.8%)	24(21.1%)	21(21.0%)	11(21.6%)	15(33.3%)	< 0.0001
HIV co-infection								
Yes	0(0.0%)	0(0.0%)	8(8.6%)	10(8.8%)	6(6.0%)	2(3.9%)	1(2.2%)	0.0396
No	149 (100.0%)	69(100.0%)	85(91.4%)	104(91.2%)	94(94.0%)	49(96.1%)	44(97.8%)	0.0396

among the study population.

The 4.3% prevalence of purulent meningitis recorded in this study is compares closely to the 5% prevalence reported in the Western world (Currie and Casadevall, 1994) but contrary to the 20-30% reported in other sub-Saharan African countries and in Eastern Asia (Pinner *et al*., 1995). The low prevalence recorded among this population could be due to the fact that most HIV-infected patients die of other complications hence the low prevalence.

Palleres *et al.,* (1995) reported that there is no difference in relation to mortality rate between patients with only HIV infection and bacteria and HIV co-infection. This assertion however is inconsistent with observations made from this study. The inclusion of both HIV 1 and 2 patients in our study could account for differences in the age of mortality.

Several studies have examined the relationship between gender, prevalence and mortality rate of purulent meningitis. This study established a trend that fewer females died of purulent meningitis at an older age compared to males. This finding is in conformity to the study of Pfister *et al.,* (1993) who found purulent meningitis to be more prevalent in males. The longer life expectancy of females in Ghana could be the reason for the low mortality rate among the female participants.

Recent studies have reported higher mortality rates in meningitis without HIV co-infection compared to purulent meningitis HIV co-infection (Lynch and Kapila, 1996) which confirms the findings of this study. The low mortality rate among subjects with purulent meningitis HIV co-infection could partly be due to the reduced immunologic response that characterizes HIV infection. This phenomenon is known to reduce inflammatory responses produced in the brain in the initial stages of meningitis infection which is known to be linked directly to mortality (Almirante *et al*., 1998).

Various reports have established purulent meningitis due to various bacteria as the primary cause of

Table 4: Association between increase in age and place of death, type of purulent meningitis as well as HIV co-infection among the studied population stratified by gender

Variables	<19	19-24	25-34	35-44	45-54	55-64	>64	P value
Female	***n = 62***	***n = 27***	***n = 40***	***n = 36***	***n = 31***	***n = 9***	***n = 15***	
Age (yrs)	10.4 ± 5.8	20.8 ± 1.6	29.9 ± 3.0	38.4 ± 2.9	49.3 ± 3.4	60.8 ± 1.8	76.9 ± 8.2	
Place of death								
Coroner	57(91.9%)	26(96.3%)	34(85.0%)	29(80.6%)	23(74.2%)	5(55.6%)	9(60.0%)	< 0.0001
Permission	5(8.1%)	1(3.7%)	6(15.0%)	7(19.4%)	8(25.8%)	4(44.4%)	6(40.0%)	< 0.0001
Type of purulent meningitis								
Primary cause of death	58(93.5%)	27(100.0%)	33(82.5%)	29(80.6%)	24(77.4%)	6(66.7%)	10(66.7%)	0.0002
Secondary cause of death	4(6.5%)	0(0.0%)	7(17.5%)	7(19.4%)	7(22.6%)	3(33.3%)	5(33.3%)	0.0002
HIV co-infection								
Yes	0(0.0%)	0(0.0%)	4(10.0%)	3(8.3%)	1(3.2%)	1(11.1%)	1(6.7%)	0.067
No	62(100.0%)	27(100.0%)	36(90.0%)	33(91.7%)	30(96.8%)	8(88.9%)	14(93.3%)	0.067
Male	***n = 87***	***n = 42***	***n = 53***	***n = 78***	***n = 69***	***n = 42***	***n =30***	
Age (yrs)	10.5 ± 6.1	22.1 ± 1.6	30.3 ± 3.0	38.5 ± 2.9	48.7 ± 2.5	58.5 ± 3.0	73.2 ± 7.9	
Place of death								
Coroner	78(89.7%)	40(95.2%)	50(94.3%)	69(88.4%)	55(79.7%)	35(83.3%)	22(73.3%)	0.0029
Permission	9(10.3%)	2(4.8%)	3(5.7%)	9(11.5%)	14(20.3%)	7(16.7%)	8(26.7%)	0.0029
Type of purulent meningitis								
Primary cause of death	79(90.8%)	41(97.6%)	50(94.3%)	61(78.2%)	55(79.7%)	34(81.0%)	20(66.7%)	< 0.0001
Secondary cause of death	8(9.2%)	1(2.4%)	3(5.7%)	17(21.8%)	14(20.3%)	8(19.0%)	10(33.3%)	< 0.0001
HIV co-infection								
Yes	0(0.0%)	0(0.0%)	4(7.5%)	7(9.0%)	5(7.2%)	1(2.4%)	0(0.0%)	0.2124
No	87(100.0%)	42(100.0%)	49(92.5%)	71(91.0%)	64(92.8%)	41(97.6%)	30(100.0%)	0.2124

Continuous data are presented as mean ± SD and categorical data are presented as proportion. The association between age and other variables was access using Chi and analyzed using Chi-square test for trend.

death in the aged (Bruyn *et al.*, 1989; Durand *et al.*, 1993; McMillan *et al.*, 2001). Findings of from this study, however, contradict these observations as purulent meningitis secondary to other infections was the major cause of mortality amongst the aged subjects in this study.

As the participants advanced in age, the prevalence of HIV co-infection assumed a "bell-shape" with the total prevalence among the various age groups being far less than the 80% prevalence recorded among participants in a study in Malawi (Kelly *et al.*, 2012). The lower prevalence rate of HIV in Ghana coupled with the up scaling and wide provision of antiretroviral therapy (ART) to these patients which boosts their immunity could have accounted for reduced prevalence rate observed in this study.

CONCLUSION

The prevalence of purulent meningitis and HIV co-infection among studied population was 4.3%, with mortality rate being related to whether the purulent meningitis was primary or secondary to HIV infection. Primary infection with purulent meningitis was associated with a high mortality rate.

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

Almirante B., Saballs M., Ribera E., Pigrau C., Gavalda J., Gasser I. and Pahissa A. (1998) Favorable prognosis of purulent meningitis in patients infected with human immunodeficiency virus. *Clin Infect Dis* 27, 176-180.

Berhe T., Melkamu Y. and Amare A. (2012) The pattern and predictors of mortality of HIV/AIDS patients with neurologic manifestation in Ethiopia: a retrospective study. *AIDS Res Ther* 9, 11.

Bruyn G.A., Kremer H.P., de Marie S., Padberg G.W., Hermans J. and van Furth R. (1989) Clinical evaluation of pneumococcal meningitis in adults over a twelve-year period. *Eur J Clin Microbiol Infect Dis* 8, 695-700.

Currie B.P. and Casadevall A. (1994) Estimation of the prevalence of cryptococcal infection among patients infected with the human immunodeficiency virus in New York City. *Clin Infect Dis* 19, 1029-1033.

Durand M.L., Calderwood S.B., Weber D.J., Miller S.I., Southwick F.S., Caviness V.S., Jr. and Swartz M.N. (1993) Acute bacterial meningitis in adults. A review of 493 episodes. *N Engl J Med* 328, 21-28.

Gordon S.B., Walsh A.L., Chaponda M., Gordon M.A., Soko D., Mbwvinji M., Molyneux M.E. and Read R.C. (2000) Bacterial meningitis in Malawian adults: pneumococcal disease is common, severe, and seasonal. *Clin Infect Dis* 31, 53-57.

Hakim J.G., Gangaidzo I.T., Heyderman R.S., Mielke J., Mushangi E., Taziwa A., Robertson V.J., Musvaire P. and Mason P.R. (2000) Impact of HIV infection on meningitis in Harare, Zimbabwe: a prospective study of 406 predominantly adult patients. *AIDS* 14, 1401-1407.

Kelly M.J., Benjamin L.A., Cartwright K., Ajdukiewicz K.M., Cohen D.B., Menyere M., Galbraith S., Guiver M., Neuhann F., Solomon T., Lalloo D.G. and Heyderman R.S. (2012) Epstein-barr virus coinfection in cerebrospinal fluid is associated with increased mortality in Malawian adults with bacterial meningitis. *J Infect Dis* 205, 106-110.

Lynch A.M. and Kapila R. (1996) Overwhelming postsplenectomy infection. *Infect Dis Clin North Am* 10, 693-707.

McMillan D.A., Lin C.Y., Aronin S.I. and Quagliarello V.J. (2001) Community-acquired bacterial meningitis in adults: categorization of causes and timing of death. *Clin Infect Dis* 33, 969-975.

Molesworth A.M., Thomson M.C., Connor S.J., Cresswell M.P., Morse A.P., Shears P., Hart C.A. and Cuevas L.E. (2002) Where is the meningitis belt? Defining an area at risk of epidemic meningitis in Africa. *Trans R Soc Trop Med Hyg* 96, 242-249.

Pallares R., Linares J., Vadillo M., Cabellos C., Manresa F., Viladrich P.F., Martin R. and Gudiol F. (1995) Resistance to penicillin and cephalosporin and mortality from severe pneumococcal pneumonia in Barcelona, Spain. *N Engl J Med* 333, 474-480.

Pfister H.W., Feiden W. and Einhaupl K.M. (1993) Spectrum of complications during bacterial meningitis in adults. Results of a prospective clinical study. *Arch Neurol* 50, 575-581.

Pinner R.W., Hajjeh R.A. and Powderly W.G. (1995) Prospects for preventing cryptococcosis in persons infected with human immunodeficiency virus. *Clin Infect Dis* 21 Suppl 1, S103 -107.

Silber E., Sonnenberg P., Ho K.C., Koornhof H.J., Eintracht S., Morris L. and Saffer D. (1999) Meningitis in a community with a high prevalence of tuberculosis and HIV infection. *J Neurol Sci* 162, 20-26.

ISSN 2026-6294