

ORIGINAL ARTICLE

# Effects of malnutrition as a co-morbid factor on Neurocognitive functioning in HIV positive adults in Lusaka, Zambia

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## ABSTRACT

**Objectives:** To investigate the effects of malnutrition as a co-morbid factor on neurocognitive functioning in HIV positive adults in Lusaka.

**Design:** A cross-sectional study consisting of 263 participants. The sample comprised of 109 (40.2%) males and 162 (59.8%) females with an age range of between 20 and 65 years. Participants' educational level ranged from 5 to 20 years.

**Measures:** The International Neurobehavioural Test Battery was used to measure neurocognitive functioning. Body Mass Index (BMI), Glucose levels, Protein levels and Haemoglobin levels were used to determine nutritional status.

**Results:** Haemoglobin has the strongest relationship with global mean T-scores ( $\beta = 0.204$ ,  $p < 0.05$ ). It also accounted for a significant portion of the variance ( $\Delta R^2 = 0.040$ ,  $\Delta F = 9.252$ ,  $p < 0.05$ ). When ANOVA was run similar results were obtained. The results indicate that there is a statistically significant difference on neurocognitive test performance for the 3 levels of haemoglobin ( $F(2,255) = 5.588$ ,  $p = 0.004$ ). The results also show that significant effects of malnutrition as a co-morbid factor were observed on the following domains: BMI - learning ( $F(2,262) = 2.533$ ,  $p = 0.019$ ); Glucose - verbal fluency ( $F(2,255) = 2.501$ ,  $p = 0.029$ ); Hemoglobin - executive functioning ( $F(2,225) = 2.198$ ,  $p = 0.034$ , Recall ( $F(2,255) = 2.734$ ,  $p = 0.021$ ) and learning ( $F(2,255) = 4.668$ ,  $p = 0.036$ ).

**Conclusion:** Results obtained in the study seem to suggest that there is generally an effect of malnutrition as a co-morbid factor on neurocognitive functioning in HIV

positive adults in Lusaka particularly in low haemoglobin states. Malnutrition as a co-morbid factor affects a number of cognitive domains and these are learning, verbal fluency, recall, executive functioning.

## INTRODUCTION

Human Immunodeficiency Virus (HIV) is a virus that causes Acquired Immuno Deficiency Syndrome (AIDS), a disease of the immune system<sup>1,2</sup>. The infection is less prevalent in developed countries and more prevalent in developing countries like Zambia. In some developing countries like Swaziland, Botswana, Lesotho, rates of infections are as high as 20- 30 percent<sup>2</sup>. Sub-Saharan Africa is a region that is most affected by HIV. The region accounts for approximately 70% of people infected with HIV worldwide. The region also accounts for about 72% of the world's HIV death related cases<sup>4</sup>.

HIV affects the lives of all human beings in a number of ways. HIV crosses the blood brain barrier and enters the central nervous system (CNS)<sup>4</sup>. As endurance with HIV infection improves, the number of people harbouring the virus in their CNS increases. Thus the prevalence of HIV associated neurocognitive disorders (HAND) continues to increase<sup>5</sup>. Studies have demonstrated that despite effective general treatment and improved rates of survival, the high prevalence and adverse functional impact of HAND have endured in the era of Antiretroviral Therapy (ART) and continue to represent itself as a prominent public health issue<sup>6,7,8,9</sup>.

HIV not only affects neurocognitive functioning but it also affects nutrition of people infected with it. HIV infection

**Keywords:** cognitive functioning, malnutrition as a co-morbid factor, adults, Lusaka.

is a progressive disorder with major metabolic changes in nutrient utilization<sup>10</sup>.

States of normal and abnormal nutrition may affect the progression of HIV and response to ART treatment in different ways<sup>10,11,12,13</sup>.

Apart from playing an important role in survival, nutrition also plays an important role in cognitive functioning. Good nutrition brings about improvement in cognitive functioning. Malnutrition that is the lack of nutrients to sustain functioning of the brain may lead to cognitive impairment in individuals of various ages<sup>14</sup>. Other studies have also demonstrated that nutrition (normal and abnormal) affects cognitive functioning in both adults and children<sup>15,16,17</sup>.

The authors suggest that HIV, nutrition (either normal or abnormal) affect cognitive functioning separately. However there is little knowledge in literature on the effects of malnutrition as a co-morbid factor on cognitive functioning in HIV infected adults especially in Zambia. It is on these grounds that malnutrition as a co-morbid factor in HIV positive adults was the main focus of the study.

## METHODOLOGY

### *Sampling*

The sample of this study consisted of 263 HIV positive adults. It comprised of 107 males (40.7%) and 156 (59.3%) females. Their age range was from 20 to 65, with a mean of 40.78 and a standard deviation of 8.91. Their level of education ranged from 5 to 20 years of schooling, with mean of 10.02 and a standard deviation of 2.23. All participants were able to speak and understand English.

### *Testing*

Participants for the study were recruited from a number of Lusaka based health centres namely Kabwata, Kalingalinga, Chilenje, Matero Reference and Matero Main clinics. Recruitment of participants was done by the medical staff at the various study sites. The medical staff informed the prospective participants about the current study. Participants' informed consent was obtained by the student researcher.

Medical practitioners were responsible for all medical evaluations. The staff collected blood (the blood was used

to determine levels of protein, glucose and haemoglobin) from the participants, measures of height and weight (which were used to calculate Body Mass Index) were also obtained.

Administration of the International Neurobehavioural Test Battery was carried out at the beginning of the session. It was administered after the participants were screened for any condition that might affect neurocognitive test performance. Other questionnaires were administered after neuropsychological assessment.

### *Ethical consideration*

Ethical issues at all stages of the study were followed. Participants' consent was obtained after they read the study conditions, and they were not coerced into participating in the study. Participants were not physically or psychologically harmed.

Data from the study was handled by the researcher. The data was also coded. Participants' names were not used in the study. The study was approved by The University of Zambia Biomedical Ethics Committee (UNZABREC).

Approval to carry out the study in various clinics in Lusaka was obtained from the Ministry of Health.

### *Data analysis*

Data was analysed using the Statistical Package of Social Sciences (SPSS; Version 15.0). The raw data was converted into T-scores and deficit scores. The raw scores were corrected for Age, Education and Gender.

Descriptive analyses were performed for the independent and selected dependent variables. To determine whether malnutrition as a co-morbid factor affects neurocognitive performance, hierarchical multiple regression was used. To identify which neurocognitive domains are more affected by malnutrition as a co-morbid factor in HIV positive adults, Multiple Analysis of Variance was used. To determine whether both gender and nutritional status have an effect on neurocognitive performance Multiple Analysis of Variance was used.

## RESULTS

### *Response rate*

The study had managed to capture a total of 263 HIV positive participants. The response was thus 100%.

**Characteristics of the study**

**Table 1.** Effects of malnutrition as a co-morbid factor on neurocognitive functioning.

Variables	B	SE	$\beta$	p
<b>BMI</b>	0.189	0.127	0.100	0.139
<b>Protein</b>	-0.040	0.044	-0.061	0.364
<b>Glucose</b>	0.433	0.378	0.078	0.254
<b>Hb</b>	0.614	0.202	0.204	0.003
	<b>M1</b>	<b>M2</b>	<b>M3</b>	<b>M4</b>
.	0.010	0.014	0.020	0.060
-	0.010	0.004	0.006	0.040*
<b><math>\Delta F</math></b>	2.204	0.827	1.310	9.252*

SE = standard error,  $\beta$ = beta weight,  $\Delta F$  = F change, p= significant,  $R^2$  = variance, the p – values in M1 (model 1) represents only Body Mass Index (BMI), M2 (model 2) - protein, M3 (model 3) – glucose and M4 (model 4) haemoglobin only. Each nutritional variable has its own p value in all the 4 models.\*P<0.05.

From the regression, Haemoglobin levels accounted for a significant portion of the variance in model 4 ( $\Delta R^2=0.040$ ,  $\Delta F = 9.252$ ,  $p < 0.05$ ). It is can also be noted that haemoglobin has the strongest relationship with global mean T-scores ( $\beta = 0.204$ ,  $p < 0.05$ ).None of the models (1,2,3) were statistically significant.This means that the other three variables` (BMI, glucose, protein) contributions to the overall variance were very small.

**Table 2.** Effects of malnutrition as a co-morbid factor on individual neurocognitive domains.

Domain	value	F	p
<b>BMI</b>			
<b>Learning</b>	0.962	2.535	0.039
<b>Glucose</b>			
<b>Verbal fluency</b>	0.943	2.501	0.022
<b>Haemoglobin</b>			
<b>EF</b>	0.933	2.198	0.026
<b>Recall</b>	0.958	2.734	0.028
<b>Learning</b>	0.930	4.668	0.001

P =significant,  $\eta^2$ = effect size

MANOVA was run to determine the effects of malnutrition as a co-morbid factor on neurocognitive test domains. The table indicates that malnutrition as measured by BMI affected learning as a cognitive domain,  $F(2,262) = 2.535$ ,  $p = 0.039$ , Wilk Lambda = 0.962, partial eta squared = 0.019. Further analysis indicated that

The table indicates that glucose affected verbal fluency  $F(2,253) = 2.501$ ,  $p = 0.022$ , Wilk Lambda = 0.943, partial eta squared = 0.029.

The table also malnutrition as measured by haemoglobin affected a number of cognitive domains and these are learning  $F(2,259) = 4.668$ ,  $p = 0.001$ , Wilk Lambda = 0.930, partial eta squared = 0.036, executive functioning  $F(2,259) = 2.198$ ,  $p = 0.026$ , Wilk Lambda = 0.933, partial eta squared = 0.034 and recall  $F(2,259) = 2.734$ ,  $p = 0.028$ , Wilk Lambda = 0.958, partial eta squared = 0.021.

**Table 3:** Effects of both nutritional status and gender on neurocognitive functioning.

Variable	$\eta^2$	p
<b>BMI*gender</b>	0.031	0.29
		7
<b>Protein*gen</b>	0.032	0.31
		0
<b>Glucose*gen</b>	0.016	0.88
<b>der</b>		6
<b>Hemo*gende</b>	0.041	0.11
<b>r</b>		4

p = significant,  $\eta^2$ = eta squared

The table above shows that p value for the variables of gender and nutritional status are not statistically significant. Eta squared also ranged from 0.016 to 0.041. Partial Eta Squared represents the proportion of the variance in the dependent variables that can be explained by the independent variable. In this case the values represent a very small effect. The values represent about 1.6 per cent to 4.1 percent of the total variance.

## DISCUSSION

For the purposes of the current study a case of adult malnutrition as a co-morbid factor is represented by BMI, serum protein, random blood glucose level and haemoglobin level.

Results of the current study indicate that malnutrition as a co-morbid factor in HIV positive adults affects neurocognitive functioning in adults especially in haemoglobin states. The results also indicate that BMI, protein and glucose did not contribute significantly to the overall variance.

Previous studies have yielded similar results with regard to haemoglobin,<sup>17,18,19</sup> indicating that low levels of haemoglobin resulted in poor neurocognitive performance.

In terms of BMI, a number of studies<sup>20,21</sup> obtained results that were similar to the one obtained in the current study. BMI did not have an effect on cognition in middle aged adults.

In terms of neurocognitive domains affected by malnutrition as a co-morbid factor, previous studies<sup>15,22,23,24</sup> yielded results that were contrary to the one obtained in table 2, intellectual abilities, motor abilities, reasoning, SIP, executive functioning are affected malnutrition as a co-morbid factor as determined by BMI, protein and glucose.

The results in table 3 indicates that the interaction between gender and BMI, gender and protein, gender and glucose and gender and haemoglobin did not yield a significant effect on neurocognitive functioning. However contradicting results have been reported by a number of studies<sup>8,25,26,27,28</sup>, illustrating that gender and nutritional status have an effect on neurocognitive functioning in both adults and children.

The major limitation of the study was financial constraints which made the researcher omit the participants' lipid profile. Another limitation was lack of data from other parts of Zambia especially rural areas of Zambia. The data was collected from urban areas of Lusaka. It would have been very helpful to also analyze data from rural areas of Zambia for the purposes of generalization the results.

## CONCLUSION

Results obtained in the study seem to suggest that there is generally an effect of malnutrition as a co-morbid factor on neurocognitive functioning in HIV positive adults in

Lusaka particularly in low haemoglobin states. Malnutrition as a co-morbid factor did not seem to have an effect on global cognitive functioning when measures of BMI, protein and glucose were used to assess this variable.

On closer analysis of each neurocognitive domain, the effect of malnutrition as a co-morbid factor was observed mainly when hemoglobin, glucose and BMI were used to assess this effect. This effect was observed on a number of domains namely verbal fluency, learning, executive functioning and recall.

## ACKNOWLEDGMENTS

This research project was funded by the theNoradMasters Program (NOMA) in the department of psychiatry. The authors would like to express their gratitude to all individuals involved in this study.

## References

1. Saddock B. J. & Saddock V. A (2007) Kaplan & Saddock's Synopsis of Psychiatry. (10<sup>th</sup> Edi). Philadelphia. Lippincott Wilkins.
2. Kallings L. O. The first postmodern pandemic: 25 years of HIV/AIDS. *J. int. Med.*;2008.263 (3): 218-243.
3. UNAIDS (2010). Reports on the Global AIDS Epidemic, Geneva.
4. Annunziata P. Blood-brain barrier changes during invasion of the central nervous system by HIV-1: old and new insights into the mechanism. *Journal of Neurology* 2003; 250(8): 901-906.
5. Mattson M. P., Haughey N. J. & Nath A. Cell death in HIV dementia. *Cell Death and Differentiation*. 2005;12(1):893-904.
6. Woods S.P., Moore D.J., Weber E & Grant I. Cognitive Neuropsychology of HIV-Associated Neurocognitive Disorders. *Neuropsychol Rev*. 2009. 19: 152-168.
7. Heaton R.K., Grant I, Butters N, White D.A, Kirson D, Atkinson J. H, McCutchan J. A, Taylor M .J., Kelly M.D, Ellis R.J, Wolfson T, Velin R, Marcotte TM, Hesselink JR, Jernigan TL, Chandler J, Wallace M, Abramson I, and THE HNRC GROUP. The HNRC 500-Neuropsychology of HIV infection at different disease stages. *J Int Neuropsychol Soc*. 1995 1:231-251.
8. Hestad K.N., Menon A.J., Silalukey-Ngoma M, Franklin D.R., Imasiku L.M., Kalima K & Heaton

- R.K. Sex Differences in Neuropsychological Performance as an Effect of Human Immunodeficiency Virus Infection. A Pilot Study in Zambia, Africa. *J Nerv Ment Dis.* 2012; 200 (4): 336-342.
9. Robertson R. K., Nakasujja N., Wong M., Musisi S., Katabira E., Parsons T. D., Ronald A & Sacktor N. (2007). Pattern of neuropsychological performance among HIV positive patients in Uganda. *BMC Neurology*, 7(8), 1471.
  10. Sztam K. A. (2010) HIV and Nutrition. St Louis. Mosby. Zambia Demographic Health Survey 2007. Implemented by the Central Statistical Office (CSO) Ministry of Health. Tropical Diseases Research Centre, University of Zambia & Macro International Inc 2009.
  11. Kalanda B., Mamimine P., Taela K., Chingandu L. & Musuka G. Implementation of regional and international HIV and AIDS prevention, treatment, care and support conventions and declarations in Lesotho, Malawi and Mozambique. *Educational Research and Review.* 2010. 5 (9): 465-470.
  12. Asenso- Okyere K., Aragon C., Thangata P., Andam K & Mekonnen D.A. HIV and AIDS and farm labor productivity: A review of recent evidence in Africa. *J Dev Agric Econ.* 2010; 2(12): 406–415.
  13. Williams S. R. (1997) Nutrition and Diet Therapy. (8<sup>th</sup> Ed). St Louis. Mosby.
  14. White J. W & Wolraich M. Effects of Sugar on behavior and mental performance. *Am J Clin Nutr.* 1995; 62 ( Suppl) 242S- 95
  15. Liewellyn D.J., Langa K.M., Robert P. Friedland P.R. & Lang I.A. Serum albumin concentration and cognitive impairment. *Curr Alzheimer Res.* 2010; 1; 91-96.
  16. Ng T., Feng L., Niti M. & Yap K.B. Albumin, haemoglobin, BMI and cognitive performance in older adults. *Age and Ageing.* 2008; 37: 423- 429.
  17. Peters R., Burch L., Warner J., Beckett N., Poulter R & Bulpitt C. (2008). Haemoglobin, anaemia, dementia and cognitive decline in the elderly, a systematic review. *BMC geriatrics*, 8, 18.
  18. Beard J. L., Hendricks M. K., Perez E. M., Murray – Kolb L. E., Berg A., Vernon – Feagans L., Irlam J., Isaacs W., Slve A., Tomlinson M. (2005). Maternal iron deficiency anaemia affects postpartum emotions and cognition. *J Nutri*, 135, 267–272.
  19. Ward M. A., Carlsson C.M., Trivedi M. A., Sager M. A., Johnson S.C. (2005). The effect of body mass index on global brain volume in middle-aged adults: a cross sectional study. *BMC Neurology*, 5, 23.
  20. Gorospe E.C & Dave K. J. (2007). The risk of dementia with increased body mass index. *Age and Ageing*, 36, 23–29.
  21. Hoorwig J., Stanfield J. P. (2008). The effects of Protein Energy Malnutrition in Early Childhood on Intellectual and Motor abilities in Later Childhood and Adolescence. *Development Medicine*, 18(3), 350 –380.
  22. Cournot M., Marquie' J.-C., Ansiau D., Martinaud C., Fonds H., Ferrie' res F., Ruidavets J.B. (2006). Relation between body mass index and cognitive function in healthy middle-aged men and women. *Neurology*, 67, 1208.
  23. Sabia S., Kivimaki M., Shipley M. J., Marmot G. M., & Singh-Manoux A. (2009) Body mass index over the adult life course and cognition in late midlife: the Whitehall II Cohort Study. *Am J Clin Nutr* , 89, 601–607.
  24. Castel H., Shahar D., Harman-Boehm I. (2006). Gender Differences in Factors Associated with Nutritional Status of Older Medical Patients. *Journal of the American College of Nutrition*, 25 (2), 128–134.
  25. Gur R.I , Turetsky B.I., Matsui M., Yan M., Bilker W., Hughett P., Gur R. E. (1999). Sex Differences in Brain Gray and White Matter in Healthy Young Adults: Correlations with Cognitive Performance. *Journal of Neuroscience*, 19(10), 4065–4072.
  26. Hamid J. J. M., Mitra' z A.K., Hasmiza H., Pim C.D., Ng L.O., Manan W.W.M. (2002). Effect of Gender and Nutritional Status on Academic Achievement and Cognitive Function among Primary School Children in a Rural District in Malaysia. *Mal J Nutr*, 17(2), 8.
  27. Widenhorn-Müller K., Hille K., Klenk J., Weiland U. (2008). Influence of Having Breakfast on Cognitive Performance and Mood in 13 to 20 Year-Old High School Students: Results of a Crossover Trial. *Pediatrics*, 122–279.