International Journal of Otorhinolaryngology and Head and Neck Surgery
*Braimah OE et al. Int J Otorhinolaryngol Head Neck Surg. 2019 May;5(3):537-544*
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

**Original Research Article**

DOI: http://dx.doi.org/10.18203/issn.2454-5929.ijohns20191719

# Olfactory identification in HIV positive adults living in Benin city, Nigeria

**Oghogho E. Braimah*, Ngozi C. Onyeagwara**

Department of Ear, Nose and Throat, Head and Neck Surgery, University of Benin Teaching Hospital, Benin City, Edo State. Nigeria

**Received:** 31 January 2019
**Revised:** 14 March 2019
**Accepted:** 18 March 2019

***Correspondence:**
Dr. Oghogho Eloghosa Braimah,
E-mail: og_odes@yahoo.com



## ABSTRACT

**Background:** Olfactory function has been shown to be impaired in human immunodeficiency virus (HIV) infection. The advent of anti-retroviral therapy has resulted in prolonged survival of these patients requiring increased focus on factors that affect their quality of life including olfaction.
**Methods:** The study was conducted at the University of Benin Teaching Hospital, Benin city. Consenting adult HIV positive patients were assisted to fill a proforma after which they had rigid nasendoscopy done to rule out peripheral causes of anosmia such as nasal infections, nasal polyps and tumours. The brief smell identification test (BSIT) scratch and sniff tests were then administered to those included in the study. The same procedure was repeated with consenting HIV negative subjects serving as control.
**Results:** There was a statistically significant difference between olfactory identification ability of HIV positive and HIV negative adults (p=0.001). Cases were 2.92 times likely to have abnormal smell identification abilities than controls.
**Conclusions:** Olfactory identification ability is reduced in PLWHA relative to the HIV negative population.

**Keywords:** BSIT, HIV, Nasendoscopy, Olfactory identification, PLWHA

## INTRODUCTION

Olfaction has been described as "the neglected sense."[1] It serves many practical functions such as appreciating the taste of food, aiding communication between mother and child, and is an essential occupational tool for professional wine tasters, chefs, and perfumers.[2-4]

Olfaction is important for detecting danger and is especially important to fire fighters, gas shop attendants and homemakers.[1,5] Unpleasant odours adversely affect social interactions, and people with olfactory impairments may become isolated for fear of them or their environment being smelly and this, going undetected by them.[2,3]

Homemakers may have increased conflict with their spouse and families due to under- or over-seasoning of meals as a result of their impaired taste. They may also be accused of poor hygiene and laziness because of late detection of unpleasant smells in the house. This could have far-reaching consequences for the future of the sufferer especially in the African cultural setting which is patriarchal, and the homemaker is often the wife.[5]

Olfactory dysfunction therefore does not only reduce a person's enjoyment of life, it may also endanger the sufferer, distort feeding habits, result in job losses, increase social isolation, threaten family harmony and increase the risk of depression.

HIV infection is a global pandemic affecting tens of millions of people worldwide.[6,7] Two thirds of new cases of HIV infection are in Sub-Saharan Africa and Nigeria being its most populous country has the second largest number of HIV positive patients in the world.[6,7] HIV infection is associated with many deleterious multi-systemic effects including reduction in cognitive and neurosensory function, olfaction being one.[8] This olfactory impairment, negatively affects the quality of life of affected patients and in addition to all the problems associated with olfactory loss may specifically contribute to malnutrition and poor compliance with anti-retroviral drugs in these patients.[9-11] It may also predict the subsequent development of neurocognitive impairment (NCI) in these patients.[12]

While studies show that olfactory impairment is found in people living with HIV/AIDS (PLWHA), there is currently no consensus as to whether this is as a result of HIV virus itself, the immunosuppression it causes or its treatment. This study sought to assess the olfactory identification abilities in PLWHA and to assess the effects of HIV/AIDS and/or its treatment on the olfactory functions of these patients.

The process of olfactory identification requires the down-up process of sensory functioning and up-down process of cognitive abilities.[13] Beyond odour perception; memory, cognitive processing speed, decision making, verbal retrieval and level of education significantly affect olfactory identification performance.[14-16]

Many experts agree that all patients with HIV will benefit from screening for neurocognitive impairment (NCI) prior to commencing highly active anti-retroviral therapy (HAART) and there is currently no screening tool applicable across practice settings; current screening tests are complicated to administer and lack sensitivity for milder forms of HIV associated neurocognitive disorder (HAND).[17,18] Olfactory identification (Ol) may serve this need.[12]

Cross-cultural smell identification test (CC-SIT) is a scratch and sniff test designed based on the original University of Pennsylvania Smell Identification Test (UPSIT). It consists of 12 micro-encapsulated odourants impregnated onto a card which are released by scratching.[19] The objective of this study was to compare olfactory identification abilities in PLWHA and HIV negative adults in Benin city, Nigeria. It was also to ascertain if CD4 count and/or HAART use were related to olfactory identification ability in PLWHA.

## METHODS

The study was conducted in the University of Benin Teaching Hospital (UBTH) Benin City, Nigeria. It was a hospital based prospective comparative cross-sectional study. The study population comprised of both old and new patients who were 18 years and above and less than 65 years with confirmed HIV positive result who attended HIV clinic in UBTH. The control population were HIV negative individuals who are 18 years and above and less than 65 years attending the well/ screening clinic in UBTH Centre for Disease Control (CDC) clinic.

HIV positivity was determined by having a positive result on both Alere Determine™ HIV-1/2 test Kit (USA) and Trinity Biotech Uni-Gold™ HIV test kit (Ireland). In cases of discordant results, Chembio HIV 1/2 STAT PAK™ (USA) was used as a tie-breaking test. The control population was adult HIV negative attendees of the well/ screening clinic in UBTH CDC who were carrying out their routine yearly health screening.

Patients with history of head trauma, nasal disease/allergy, upper respiratory tract infection in the last 2 weeks and intra-cranial tumors were excluded from the study.

Sample size was determined using a formula for minimum sample size determination when comparing two proportions.[20] Total minimum sample size calculated was 84 in each arm making a total of 168 patients.

Simple random sampling of patients was done via balotting with the clinic booking register used as a sampling frame. Duration of the study was from August 2017 to January 2018.

Interviewer administered proforma form was used with the aid of a research assistant. Information retrieved from the proforma included; socio-demographic information, duration of diagnosis of HIV (old patient or new patient), whether on HAART or not, date of commencement of HAART (for old patients), type and dosing of HAART, history of nasal disease, head injury, smoking history, history suggestive of allergy and other medications the participant may be taking.

Anterior rhinoscopy was done for all participants by the researcher using thudicum speculae. A zero degrees Hopkins rod endoscope illuminated with a portable light source was then used by the researcher to examine the nasal cavities in three passes to exclude nasal pathologies.

The BSIT was then administered to each participant. The participant's score was based on the number of odourants correctly identified.

For the cases, CD4+ count done at index clinic appointment (on the same day) were retrieved and documented for each participant and record of lowest (nadir) CD4+ count pre-HAART commencement retrieved from the participants case note. Control participants were presumed to have CD4+ cell counts normal for the general population.

***Data analysis***

Data analysis was done using IBM SPSS Statistics version 21.0. Tables were used to present results. Descriptive statistics were used and categorical variables were compared in both groups using Chi squared and Fischers exact tests.

BSIT scores were grouped into normal and abnormal using the normative values in the BSIT administration manual.

Bivariate and multivariate logistic regression model were used to assess for determinants of olfactory identification. P value <0.05 was considered significant.

***Ethical approval***

Written informed consent was obtained from all participants in the study. Approval to carry out the study was obtained from the Health Research and Ethics Committee of the University of Benin Teaching Hospital, Benin City.

## RESULTS

***Sociodemography***

There were 86 case study participants and 86 control study group, giving a male to female ratio of 1:4.2 for both groups. The age range of participants was from 20 years to 64 years. Average age was 41.2 years for the cases and 39.3 years for the control group. Table 1 shows that the modal age group was 40-44 years for both cases and controls. The differences in age (years) was not statistically significant (p=0.786).

The number of cases (18 (20.0%)) who had primary education was 6 times higher than those in the controls (3 (3.5%)). However, the proportion of the controls (69 (80.2%)) who had tertiary education was 4 times higher than those of the cases (24 (27.9%)). The difference in level of education was statistically significant (p<0.001).

**Table 1: Socio demographic data of study participants (n=86).**

| Characteristics | Study group | | Test statistics | P value** |
|---|---|---|---|---|
| | Cases | Control | | |
| | N (%) | N (%) | | |
| **Sex** | | | | |
| Male | 16 (18.6) | 17 (19.8) | 0.037 | 0.846 |
| Female | 70 (81.4) | 69 (80.2) | | |
| **Age group (years)*** | | | | |
| 20-29 | 12 (14.0) | 15 (17.4) | 1.726 | 0.786 |
| 30-39 | 25 (29.1) | 27 (31.4) | | |
| 40-49 | 31 (36.0) | 31 (36.0) | | |
| 50-59 | 12 (14.0) | 7 (8.1) | | |
| 60+ | 6 (7.0) | 6 (7.0) | | |
| **Education** | | | | |
| No formal | 5 (5.8) | 4 (4.7) | 51.764 | <0.001+ |
| Primary | 18 (20.9) | 3 (3.5) | | |
| Secondary | 39 (45.3) | 10 (11.6) | | |
| Tertiary | 24 (27.9) | 69 (80.2) | | |

*Mean (SD) age: Cases = 41.2 (11.0) years, Control = 39.3 (10.7) years, **Chi-square test, +Fisher's exact test.

**Table 2: $CD4^+$ count of the HIV positive cases (n=86).**

| Variables | Frequency | Percentage (%) |
|---|---|---|
| **Latest $CD4^+$ count*** | | |
| <200 | 7 | 8.2 |
| 200-349 | 16 | 18.6 |
| 350-499 | 18 | 20.9 |
| 500+ | 45 | 52.3 |
| **Lowest (nadir) $CD4^+$count**** | | |
| <200 | 26 | 30.2 |
| 200-349 | 26 | 30.2 |
| 350-499 | 18 | 20.9 |
| 500+ | 16 | 18.7 |

*Mean (SD) = 533.2 (256.7), **Median (Interquartile range) = 315.5 (151.5-441.0).

The median (interquartile range) duration of diagnosis of HIV infection among the cases was 8.5 (2.8-10.0) years with majority (53 (61.6%)) of the cases in the range 1–10 years.

Among the case study group, 79 of the 86 (91.9) of the cases had used HAART of which a higher proportion (47 (59.5%)) used 3TC, ZDV and NVP.

The median (interquartile range) duration of use of HAART among those who had been on HAART was 8.0 (5.0-10.0) years with majority (55 (69.6%)) of the cases in the range of 1-10 years.

The latest mean (standard deviation) CD4+ count was 533.2 (256.7) with more than half 45 (52.3%) of the cases having a CD4+ count of 500 and above. Also, more than 80.0% of the cases had recorded a nadir (pre-HAART) CD4+ count of less than 500 with a median (interquartile range) CD4+ count of 315.5 (151.5-441.0) (Table 2).

***Olfactory identification***

Twenty six (30.2%) of the cases had normal olfactory identification compared to 48 (55.8%) of the control. Overall, 74 (43.0%) of the study participants had normal olfactory identification. Table 3 shows that the difference in olfactory identification abilities between cases and controls was statistically significant with a p-value of 0.001.

Four (57.1%) of the respondents with latest CD4+ cell count less than 200 had abnormal olfactory identification ability compared with 13 (81.3%) of those with $CD4^+$ count between 200-349, and 33 (73.3%) of those with CD4 count of 500 and above. The association between latest $CD4^+$ count and olfactory identification ability was not statistically significant (p=0.333) (Table 4).

**Table 3: Frequency distribution of olfactory identification ability of the study participants.**

| Olfactory identification (BSIT score) | Study group | | Total | Test statistics* | P value |
|---|---|---|---|---|---|
| | Cases | Control | | | |
| | N (%) | N (%) | N (%) | | |
| **Normal** | 26 (30.2) | 48 (55.8) | 74 (43.0) | 11.479 | 0.001 |
| **Abnormal** | 60 (69.8) | 38 (44.2) | 98 (57.0) | | |
| **Total** | 86 (100.0) | 86 (100.0) | 172 (100.0) | | |

*Chi-square test.

**Table 4: Olfactory identification ability and $CD4^+$ count of the study participants.**

| $CD4^+$ count | Olfactory identification ability | | Total (n=86) | Test statistics | P value |
|---|---|---|---|---|---|
| | Normal (n=26) | Abnormal (n=60) | | | |
| | N (%) | N (%) | N (%) | | |
| **CD4+ count latest** | | | | | |
| <200 | 3 (42.9) | 4 (57.1) | 7 (100.0) | 3.552* | 0.333 |
| 200-349 | 3 (18.8) | 13 (81.3) | 16 (100.0) | | |
| 350-499 | 8 (44.4) | 10 (55.6) | 18 (100.0) | | |
| 500+ | 12 (26.7) | 33 (73.3) | 45 (100.0) | | |
| **CD4+ count lowest** | | | | | |
| <200 | 12 (46.2) | 14 (53.8) | 26 (100.0) | 7.705** | 0.053 |
| 200-349 | 7 (26.9) | 19 (73.1) | 26 (100.0) | | |
| 350-499 | 6 (33.3) | 12 (66.7) | 18 (100.0) | | |
| 500+ | 1 (6.3) | 15 (93.8) | 16 (100.0) | | |

*Fisher's exact test, **Chi-square test.

Overall, more than 50% of the participants had abnormal olfactory identification ability irrespective of their lowest (nadir) CD4 count. Among respondents with CD4 count of 500 and above 93.8% (15) had abnormal olfactory identification ability. The association between lowest CD4 count and olfactory identification ability was not statistically significant (p=0.053).

Fifty five (69.6%) of the cases who were on HAART had abnormal olfactory identification ability compared to 5 (71.4%) of those who were not on HAART. The association between HAART use and olfactory identification ability was not statistically significant (p=0.920).

**Table 5: Unadjusted and adjusted (logistic regression model) predictors of abnormal BSIT score among the participants.**

| Variables | Unadjusted OR (95% CI) | Adjusted OR (95% CI)+ |
|---|---|---|
| **Study group** | | |
| Cases | 2.92 (1.56-5.46) | 2.02 (0.94-4.31) |
| Control* | 1 | 1 |
| **Sex** | | |
| Male | 2.34 (1.02-5.40) | 2.58 (1.07-6.22) |
| Female* | 1 | 1 |
| **Age group (years)*** | | |
| 20-29 | 2.38 (0.59-9.54) | 3.22 (0.70-14.95) |
| 30-39 | 1.63 (0.46-5.82) | 2.12 (0.53-8.56) |
| 40-49 | 2.22 (0.63-7.79) | 2.54 (0.64-10.02) |
| 50-59 | 1.56 (0.36-6.69) | 1.49 (0.31-7.19) |
| 60+* | 1 | 1 |
| **Education** | | |
| No formal | 1.52 (0.38-6.01) | 1.54 (0.34-6.97) |
| Primary | 2.43 (0.89-6.57) | 2.09 (0.66-6.61) |
| Secondary | 3.74 (1.74-8.08) | 2.90 (1.20-7.04) |
| Tertiary* | 1 | 1 |

$R^2$= 13.6% to 18.2%, *Reference category, +Adjusted for sex, age and education level.

**Table 6: Unadjusted and adjusted (logistic regression model) predictors of abnormal BSIT score among the cases.**

| Variables | Unadjusted OR (95% CI) | Adjusted OR (95% CI)+ |
|---|---|---|
| **Sex** | | |
| Male | 2.12 (0.55-8.19) | 1.87 (0.34-10.16) |
| Female* | 1 | 1 |
| **Age group (years)*** | | |
| 20-29 | 10.00 (1.03-97.50) | 3.62 (0.22-60.40) |
| 30-39 | 6.33 (0.92-43.62) | 3.13 (0.35-28.45) |
| 40-49 | 6.86 (1.03-45.60) | 4.95 (0.59-41.85) |
| 50-59 | 1.43 (0.18-11.09) | 0.79 (0.08-8.23) |
| 60+* | 1 | 1 |
| **Education** | | |
| No formal | 0.10 (0.01-1.09) | 0.12 (0.01-2.15) |
| Primary | 0.65 (0.18-2.36) | 0.95 (0.18-5.15) |
| Secondary | 1.60 (0.49-5.16) | 1.76 (0.42-7.29) |
| Tertiary* | 1 | 1 |
| **CD4+ count latest** | | |
| <200 | 0.49 (0.09-2.49) | 2.67 (0.18-39.85) |
| 200-349 | 1.58 (0.38-6.51) | 2.97 (0.44-19.90) |
| 350-499 | 0.46 (0.15-1.42) | 2.22 (0.47-10.36) |
| 500+ | 1 | 1 |
| **CD4+ count lowest (nadir)** | | |
| <200 | 0.08 (0.01-0.68) | 0.06 (0.01-0.75) |
| 200-349 | 0.18 (0.02-1.64) | 0.11 (0.01-1.35) |
| 350-499 | 0.13 (0.01-1.26) | 0.12 (0.01-1.36) |
| 500+ | 1 | 1 |
| **HAART use** | | |
| On HAART | 1 | 0.59 (0.06-6.20) |
| Not on HAART | 1.09 (0.20-6.02) | 1 |
| Constant | | 1.40 |

$R^2$= 24% to 34%, *Reference category, +Adjusted for sex, age, education level, CD4 counts and HAART use.

***Predictors of olfactory identification ability***

Twenty four (72.7%) of the male study participants had abnormal olfactory identification ability compared to 74 (53.2%) of the female participants. The association between sex and olfactory identification ability was statistically significant (p=0.042).

Forty two (42.9%) of the participants who had tertiary education had abnormal olfactory identification ability, followed by 37 (37.8%) of those with secondary level of education. The association between level of education and olfactory identification ability was statistically significant (p=0.005).

Cases were more likely to have abnormal olfactory identification than controls (unadjusted OR (95% CI) 2.92 (1.56-5.46), adjusted OR (95% CI) 2.02 (0.94-4.31) (Table 5).

As shown in Table 6, among the cases, after adjustment for other variables in the model, only lowest (nadir) CD4 count of <200 (OR=0.06 (95% CI: 0.01-0.75) was significantly associated with having abnormal olfactory identification ability.

## DISCUSSION

Sex was statistically significant in determining olfactory identification ability in this study, with females performing better than males. This finding has been relatively consistent across different studies and is present from childhood.[21-23] It is theorized that this may be due to female advantage in verbal processing or due to hormonal influences.[22,23]

In the same vein, level of education differed significantly between cases and controls in this study with the control group having most participants (80.2%) with tertiary level of education compared with just 27.9% of cases. This difference which was statistically significant was likely due to the fact that the well clinic which was used as source for the control population was more likely to be attended by educated and well to do individuals with good health seeking behaviour.

The lowest (nadir) CD4+ count among cases was >500 cells/ $mm^3$ in only 19.7% of patients compared with 52.3% at the time of this study. This reflects the effect of HAART causing improved immunity in these patients and has been demonstrated elsewhere.[5,21,24]

Of the HIV positive cases 69.8% had abnormal smell compared to 44.2% of controls which was statistically significant (p= 0.001, OR 2.02 95% CI (0.94-4.31)). Reduced olfaction in HIV positive patients has been documented in several studies.[5,21,25-28] In Ilorin, Nigeria Alabi and co-workers found complaints of Anosmia in 30.3% of HIV positive adults while in Ibadan a study in HIV positive women found the prevalence of olfactory dysfunction using TDI score on Sniffin sticks test to be 39.8%.[5,28] These values are much lower than the prevalence of 69.8% found in this study but close to the 68.9% found in the identification component of the TDI score in HIV positive adults in another hospital in southern Nigeria.[21]

Latest CD4+ count did not correlate with olfactory identification ability in this study, and lowest (nadir) CD4+ count with a p value of 0.053 did not meet the criteria for statistical significance using chi-squared test of association. This is similar to findings by Zucco in Italy and Fasunla in Ibadan and highlight the role of the HIV virus in OI impairment independent of disease severity.[21,27,29] It is contrary to findings in Italy where OI scores worsened with reducing CD4+ count.[30] That study however did not use the WHO staging system and employed a different methodology.

Abnormal olfactory identification in HIV is thought to arise as a result of CNS infection with the virus and attendant cognitive impairment.[29] Studies in PLWHA show that despite plasma control HIV once in the CNS continues to exist in CNS reservoirs and replicate at slow rates in brain tissue.[8,31,32] This CNS infection is thought to occur in the first few days to weeks of infection with HIV.[31-34] A study in Abuja, Nigeria showed prevalence of neurocognitive impairment in early HIV to be as high as 31%.[35] This may explain why CD4+ count often does not correlate with OI.[29] In a study which measured levels of neurofilament protein light (NFL), a marker of axonal injury, in patients with HIV, it was found that NFL levels rose in pre-HAART patients with CD4+ count of <250 cells/$mm^3$ and below.[36] Recent research suggests that early commencement of HAART in acute HIV infection may prevent neuroinvasion by the virus and so prevent HAND.[37] This study did not show a statistically significant relationship between HAART use and olfactory identification ability. This was also similar to findings in the aforementioned study in Ibadan where HAART use correlated with reduced threshold but not with olfactory identification or discrimination.[21] Benea and co-workers noted that HAART therapy has resulted in PLWHA developing less severe forms of HAND but not in its prevalence and theorized that this might be due to irreversible brain injury prior to initiating HAART, persistent CNS infection and continued viral replication or even possible neurotoxicity of HAART drugs themselves. In fact, HAND continues to progress in patients on HAART.[37,38]

Disruption of adult neurogenesis contributes at least in part to the CNS effects of HIV and the olfactory bulb being the most distal part of the rostral migratory stream will be affected earliest by this disruption and so olfactory loss occurs quite early in the course of illness. This pattern is seen in HIV infection of the CNS and other neurodegenerative disorders.[38.39] Therefore OI may be prognostic for the development of HAND before

clinical symptoms become apparent and severity, onset and progression of HAND may be reliably followed using olfactory identification tests.[27,29,38] This may signal the end of the search for an ideal screening test in the early detection of HAND in HIV positive patients as HAND is associated with shortened survival in PLWHA.[37,40]

## CONCLUSION

This study showed that HIV positive patients have impaired olfactory identification ability and were 2.92 times likely to have abnormal smell identification than controls.

The relationship between olfactory identification ability in participants with HIV and CD4+ count was not statistically significant. The use of HAART in cases did not affect olfactory identification ability in this study.

## ACKNOWLEDGMENTS

Prof. Richard Doty and Sensonics International who donated some of the test kits used in this study.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Benignus VA, Prah JD. Olfaction: Anatomy, Physiology and Behavior. Environ Health Perspect. 1982;44:15–21.
2. Doty RL, Kamath V. The influences of age on olfaction:a review Front Psychol. 2014;5:20
3. Croy I, Negoias S, Novakora L, Landis BN, Hummel T. Learning about the functions of the olfactory system from people without a sense of smell. PLoS ONE 2012;7(3):e33365.
4. Croy I, Mohr T, Weidner K, Hummel T, Junge Hoffmeister J. Mother-Child bonding is associated with the maternal perception of the child's body odour. Physiol Behav. 2019;198;151-7.
5. Fasunla AJ, Daniel A, Nwankwo U, Kuti KM, Nwaorgu OG, Akinyinka OO. Evaluation of Olfactory and Gustatory Function of HIV Infected Women. AIDS Res Treatment. 2016;(2016):2045383.
6. World Health Organisation. HIV/AIDS Factsheet No 360 Nov. 2015 WHO media centre. Available at http://www.who.int/mediacentre/factsheets/fs360/en/. Accessed on 23 March 2016.
7. National Agency for the Control of AIDS. National HIV/AIDS Epidemiology and Impact Analysis (NHEIA) Reports. Federal Republic of Nigeria; 2014
8. Lindl KA, Marks DR, Kolson DL, Jordan-Sciutto KL. HIV associated neurocognitive disorders: pathogenesis and therapeutic opportunities. J Neuroimmune. Pharmacol. 2010;5:294-309.
9. Amali A, Sazgar A, Langeroudi M, Saedi B. Olfactory disorders in HIV positive patients. Otolaryngol Head Neck Surg. 2012;147(2):252.
10. Heald AE, Schiffman SS. Taste and smell, neglected senses that contribute to the malnutrition of AIDS. NC Med J. 1997;58:100-4.
11. Graham CS, Graham BG, Bartlett JA, Heald AE, Schiffimann SS. Taste and smell losses in HIV infected patients. Physiol Behav. 1995;58:287-93
12. Vance D, Humphrey S. A-14 A Brief Olfactory Detection Test of HIV-Associated Neurocognitive Disorder: Three Case Studies. Arch Clin Neuropsychol. 2014;29(6):508-9.
13. Richardson, JTE, Zucco, MG. Cognition and olfaction: A review Psychol Bull. 1989 May;105(3):352-60.
14. Hummel T, Whitcroft KL, Andrews P, Altundag A, Cinghi C, Costanzo RM, et al. Position paper on olfactory dysfunction Rhinol Suppl. 2017 54(26):1-30.
15. Larsson M, Nilsson LG, Olofsson J, Nordin S. Demographic and cognitive predictors of odor identification-Evidence from a population-based study. Chem Senses. 2004;29:547-54.
16. Fagundo AB, Jiménez-Murcia S, Giner-Bartolomé C, Islam MA, de la Torre R, Pastor A, et al. Modulation of Higher-Order Olfaction Components on Executive Functions in Humans. PLoS ONE. 2015;10(6):e0130319.
17. Pozniak A, Rackstraw S, Deayton J, Barber T, Taylor S, Manji H, et al. HIV-associated neurocognitive disease:case studies and suggestions for diagnosis and management in different patient subgroups. Antivir Ther. 2014;19(1):1-3.
18. Antinori A, Arendt G, Grant I, Letendre S, Muñoz-Moreno JA, Eggers C, et al. Assessment, diagnosis, and treatment of HIV-associated neurocognitive disorder:a consensus report of the mind exchange program. CID. 2012;21;56(7):1004-17.
19. Doty RL, Marcus A, Lee WW Development of the 12-item Cross-Cultural Smell Identification Test. Laryngoscope. 1996;106(3);353-6.
20. Jaykaran C, Tamoghna B. How to Calculate Sample Size for Different Study Designs in Medical Research. Indian J Psychol Med 2013;35(2):121-6.
21. Fasunla AJ, Nwankwo U, Adebayo AM. Association between Sex, CD4 Cell Counts, Antiretroviral Medications, and Olfactory and Gustatory Functions of HIV-Infected Adults Otolaryngol Head Neck Surg. 2017:194599817733664.
22. Wehling EI. Cognitive and Olfactory Changes in Aging. Dissertation for the degree philosophiae doctor (PhD) University of Bergen, 2009.
23. Pinto JM, Schumm LP, Wroblewski KE, Kern DW, McClintock MK. Racial Disparities in Olfactory Loss Among Older Adults in the United States J Gerontol A Biol Sci Med Sci. 2014;69(3):323–9.

24. Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, LeBlanc S, et al. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy:differences in rates, nature, and predictors. J Neurovirol. 2011;17:3–16.
25. Hornung DE, Kuntz DB, Bradshaw CB, Siepel DM, Kent PF, Blair DC, et al. The Olfactory Loss That Accompanies an HIV infection. Physiol Behav 1998;64:549-56.
26. Brody D, Serby M, Etienne N, Kalkstein DS. Olfactory identification deficits in HIV infection Am J Psychiatry. 1991;148:248-50.
27. Vance DE. Olfactory and psychomotor symptoms in HIV and aging potential precursions to cognitive loss. Med Sci Monit. 2007;13:801-1.
28. Alabi BS, Salami AK, Afolabi A, Dunmade D, Aremu SK, Olawunmi O, et al. Otolaryngologic Manifestations Among Hiv/Aids Patients in a Nigerian Tertiary Health Institution: An Update Intl. Arch. Otorhinolaryngol. 2010;14(4):398-403.
29. Zucco GM, Ingegnen G. Olfactory deficits in HIV infected patients with and without AIDS dementia complex. Physio Behav. 2004;80:669-74.
30. Lehrner JP, Kryspin Exner I, Vetter N. Higher Olfactory threshold and decreased Odor identification ability in HIV infected persons. Chem Senses. 1995;20:325-8.
31. Spudich SS, Ances BM. Neurologic Complications of HIV Infection. Top Antivir Med. 2017;25(2):69-76.
32. Dahl V, Gisslen M, Hagberg L, Peterson J, Shao W, Spudich S, et al. An Example of Genetically Distinct HIV Type 1 Variants in Cerebrospinal Fluid and Plasma During Suppressive Therapy. J Infect Dis. 2014;209(10):1618-22.
33. Robertson KR, Su Z, Margolis DM, Krambrink A, Havlir DV, Evans S, et al. A5170 Study Team. Neurocognitive effects of treatment interruption in stable HIV-positive patients in an observational cohort. Neurology. 2010;74(16):1260-6.
34. Custodio N, Escobar J, Altamirano J. Dementia associated with infection by human immunodeficiency virus type 1. An Fac Med. 2006;67(3):1.
35. Akolo C, Royal W, Cherner M. Neurocognitive impairment associated with predominantly early stage HIV infection in Abuja, Nigeria. J Neurovirol. 2014;20(4):380-7.
36. Krut J, Mellberg T, Price RW, Hagberg L, Fuchs D. Biomarker Evidence of Axonal Injury in Neuroasymptomatic HIV-1 Patients. PLoS One. 2014;11;9(2):e88591.
37. Spudich SS, Ances BM. CROI 2017: Neurologic Complications of HIV Infection Top. Antivir Med. 2017 25(2):69-76.
38. Liang X, Ding D, Zhao Q, Guo Q, Luo J, Hong Z. Association between olfactory identification and cognitive function in community dwelling elderly: the Shanghai aging study. BMC Neurol. 2016;16:199.
39. Doty RL. Olfactory dysfunction in neurodegenerative diseases: is there a common pathological substrate? Lancet Neurol. 2017;16(6):478-88.
40. Benea CL, Petrescu A, Moroti-Constantinescu R 2012. HIV Encephalopathy - Now and Then, In:Miscellanea on Encephalopathies, Dr. Radu Tanasescu (Ed.), Croatia. Available at: https://www.intechopen.com/books/miscellanea-on-encephalopathies/hiv-encephalopathy-now-and-then. Accessed on 23 March 2016.

**Cite this article as:** Braimah OE, Onyeagwara NC. Olfactory identification in HIV positive adults living in Benin city, Nigeria. Int J Otorhinolaryngol Head Neck Surg 2019;5:537-44.