

# Role of Neuroimaging in Suspected Dementia Patients: Utilization of Structural Imaging Algorithmic-Based Diagnosis in Resource Limited Settings

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## Research Article

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# Abstract

## Background

In 2050, it is estimated that the number of dementia patients in the sub Saharan Africa is expected to reach 5.05 million, an increase of 136% from the previous estimate of 2.14 million. The objectives of the present study were to assess the neuroimaging findings and associated factors in dementia suspected patients.

## Method

A retrospective survey of the medical records of 121 suspected dementia patients whom presented to the Yehuleshet Specialty Clinic with subjective forgetfulness were reviewed. The study duration was between January 1, 2020 and December 31, 2021. Both descriptive and analytical statistics were used to analyze the data.

## Results

The mean age was 70.4 (1SD = 10.3) years. Sixty four (52.9%) participants were age below 70. Male accounted for 57.9%. Hyperlipidemia was the commonest (38%) identified vascular risk factor followed by prevalence of hypertension (32.2%) and diabetes mellitus (22.3%). HIV infection was observed in 3.3%. Low mean serum vitamin D level (below 20ng/mL) was observed in individuals with focal & global cortical atrophy and those with white matter hyperintensity. Fifty two (43%) participants fulfilled the clinical and imaging criteria of vascular cognitive impairment (VCI). Nearly quarter of the patients had imaging evidences of focal or global cortical atrophy. Eleven (9.1%) had imaging evidences of surgical causes of dementia. the presences of comorbid hypertension, previous stroke, and Parkinsonism were independent predictors of vascular dementia.

## Conclusion

The present study shows high burden of vascular cognitive impairment among individuals suspected of dementia. Furthermore, the presences of comorbid hypertension, previous stroke, and Parkinsonism were independent predictors of vascular dementia.

## 1. Introduction

According to 2017 report by World Health Organization (WHO) indicate that by 2050, 150 million persons will be living with dementia; more than 68% of persons with dementia will reside in LMICs by 2050 (1–3). Worldwide, dementia is the fifth leading cause of death and the second leading contributor to death from neurological diseases (4). Dementia care is expensive even in high income countries, according to recent estimate, > 818 billion USD is spent annually on dementia-related care globally and by 2028 the worldwide cost of dementia care is estimated to be > 2 trillion USD (5). The burden of dementia is sharply rising among African population. Dementia prevalence varies from 2.3–20.0% and incidence rates are 13.3 per 1000 person-years with increasing mortality in parts of rapidly transforming Africa (1).

According to a recent review by Rufus et al. 2021 (1), Alzheimer's disease, vascular dementia, and human immunodeficiency virus (HIV) associated neurocognitive impairment (HAND) are the most common dementia subtypes in Africa. Ethiopia is the second populous country in the African continent with more than 110 million populations. According to 2020 Human Development Report (HDR), the life expectancy at birth in Ethiopia in 2019 is 66.6 years (6). Thus, considering the ever increasing life expectance, population growth, and prevalent HIV infection and non-communicable diseases, the burden of dementia is expected to be high in Ethiopia.

Cognitive impairment resulting from brain vascular changes or injury is likely to be the most prevalent worldwide. There are sparse data on vascular cognitive impairment (VCI) in Africa. In sub-Saharan Africa, cognitive impairment from all causes was estimated to range from 6.3–25% in adults over 50 years of age (7). Accurate and timely diagnosis of dementia is important to guide management. In Africa due to lack of well validated cognitive assessment batteries and availability of accurate clinical and biological biomarkers, accurate diagnosis of dementia is a major challenge clinicians are facing in the continent. However, utilization of a structural neuroimaging, in combination with clinical assessment, has value in improving diagnostic accuracy of dementia in Africa (8–11).

The objectives of the present review was to assess the pattern of brain magnetic resonance image (MRI) findings in suspected dementia patients and also to identify factors associated with different dementia sub types.

## **2. Methods And Materials**

### **2.1. Study setting**

The study was conducted at Yehuleshet Specialty Clinic (YSC) in Addis Ababa, Ethiopia. Yehuleshet Specialty Clinic is a specialty clinic located at the heart of Addis Ababa. The clinic is equipped with SIEMENS 0.35 Tesla Magnetic Resonance Image (MRI) machine, Electroencephalograph, Nerve Conduction Study/Electromyography, and comprehensive laboratory service.

### **2.2. Study design and study period**

A retrospective survey of the medical records of 121 suspected dementia patients whom presented to the Yehuleshet Specialty Clinic with subjective forgetfulness were reviewed. The study duration was between January 1, 2020 and December 31, 2021.

### **2.3. Cognitive assessment of the study participants**

All 121 patients included in the present study visited YSC with subjective complain of forgetfulness and evaluated for dementia. Diagnosis of dementia and classification of the subtypes were made using the Diagnostic and Statistical Manual of Mental Disorders (DSM V) 5th edition (12). In addition to the clinical phenotypes, supportive brain MRI findings and laboratory results were used in dementia case ascertainment. All patients were evaluated, investigated, and diagnosed by board certified senior neurologists working at YSC (GZ, MZ, and BAA). A structured questionnaire was used to collect the demographic characteristics, clinical information, and laboratory investigations of suspected dementia patients.

### **2.4. Assessment of structural MRI of the study participants**

All (n = 121) brain MRI of study participants were reviewed and neuroimaging data were extracted and interpreted by a board certified neuroradiologist (YT). The structural MRI of all the patients with suspected dementia were assessed in terms of signal change on MRI and cerebral atrophy and classified in a systematic method using a structural MRI algorithm published by Harper L. et al, 2014 (9).

### **2.5. Ethical approval**

The study received ethical approval from City Government of Addis Ababa Health Bureau Ethical Clearance Committee (Protocol number: A/A/HB/3787/207). All patients' data were deidentified and pre coded in order to keep maximum patients data confidentiality. All the methods in the present study were performed in accordance with the relevant guidelines and regulations.

### **2.6. Statistical analysis**

The demographic characteristics, presenting symptoms, dementia risk factors, and laboratory results were described and presented using means, median, frequency, percentile, and standard deviation, and interquartile range using summary tables and graphs. Proportional associations between dependent variable and other variables were done using Chi square/Fisher exact test. Those variables with p value below 0.2 were included in the univariate and multivariate logistic regression analysis in order to identify independent predictors. All the results were presented using odds ratio (OR), and p value was set at < 0.05 as statistically significant.

### **3. Results**

#### **3.1. Characteristics and dementia risk factors of study participants**

In the present survey, total of 121 medical records of patients with suspected dementia were reviewed. The mean age was 70.4 (1SD = 10.3) years. Sixty four (52.9%) participants were age below 70. Male accounted for 57.9% (Table 1). All of the study participants (100%) presented to Yehuleshet Specialty Clinic with subjective forgetfulness. More than one third of the study participants reported some sort of motor (weakness, gait abnormality, and cranial nerves palsy) (36.4%), sensory symptoms (33.9%), and incontinence (33.1%). Neuropsychiatric symptoms were reported by thirty seven (30.6%) of the participants. In this review, quarter of the patients reported headache (22.3%) and joint pain (22.3%). Sleep disorders, fatigue, fall, and seizure were reported by 11.6%, 13.2%, 7.4%, and 8.3% respectively. In the present review, eleven (9.1%) study participants had clinical signs of Parkinsonism (Fig. 1). Cardiovascular, infectious, and metabolic risk factors for dementia were reviewed in the present study. Hyperlipidemia (38%) is the commonest cardiometabolic risk factor identified in dementia suspected patients, followed by hypertension (32.2%). Diabetes mellitus, cardiac disorders, and strokes were observed in 22.3%, 14.9%, and 11.6% of the study participants. HIV infection was observed in 3.3% of the study participants. Among metabolic risk factors of dementia, hypovitaminosis D was the prevalent one (67.7%, n = 42/62), followed by anemia (35.1%, n = 34/97). Vitamin B12 deficiency and hypothyroidism were observed in 16.7% and 9.5% of the study participants respectively (Table 1).

Table 1  
Baseline characteristics of study participants (n = 121)

| Variables  | Number (%)   |
|--|--------------|
| Age category   |              |
| Below 70 years   | 64 (52.9)    |
| Above 70 years   | 57 (47.1)    |
| Gender   |              |
| Male   | 70 (57.9)    |
| Female   | 51 (42.1)    |
| Brain MRI findings   |              |
| White matter hyperintensity (WMH)/small vessel disease (SVD)   | 52 (43)      |
| Global brain atrophy   | 17 (14)      |
| Temporal lobe atrophy  | 16 (13.2)    |
| Frontotemporal lobar atrophy   | 5 (4.1)      |
| Mixed pathology (cortical atrophy + WMH/SVD)   | 12 (9.9)     |
| Surgical causes of dementia*   | 11 (9.1)     |
| Age related changes  | 8 (6.6)      |
| Dementia risk factors  |              |
| Diabetes mellitus  | 27 (22.3)    |
| Hypertension   | 39 (32.2)    |
| Hyperlipidemia   | 46 (38)      |
| Cardiac disease  | 18 (14.9)    |
| Stroke   | 14 (11.6)    |
| HIV infection  | 4 (3.3)      |
| Anemia*  | 34/97 (35.1) |
| Hypovitaminosis D*   | 42/62 (67.7) |
| Vitamin B12 deficiency*  | 9/54 (16.7)  |
| Hypothyroidism*  | 7/74(9.5)    |
| *Surgical causes of dementia include: normal pressure hydrocephalus (NPH), sub dural hematoma (SDH), & brain tumor;<br>*The denominator for all the variable was (n = 121) unless specified otherwise. |              |

## 3.2. Neuroimaging findings in the study participants

All 121 patients with suspected dementia presented to YSC had brain MRI examination. White matter hyperintensity (WMI) and evidences of cerebral small vessel disease (SVD) were the commonest imaging findings in the present survey (43%). Seventeen (14%) of the study participants had imaging evidences of global cortical atrophy. Out of the total 121, twelve (9.9%) patients had mixed imaging features of cortical atrophy and WMH/SVD. Predominant temporal lobar atrophy and combined frontotemporal lobar atrophy were seen in 13.2% and 4.1% respectively. Surgical causes of dementia (NPH, SDH, and temporal lobe tumor) were observed in 9.1%. Eight (6.6%) patients had a normal age related subcortical white matter

changes (Table 1). In this review, mild variation was observed regarding the average serum vitamin D level among different neuroimaging findings. The lowest level of mean serum vitamin D was observed among individuals with surgical causes of dementia, followed by patients with mixed pathology (WMH and cortical atrophy). Low mean serum vitamin D level (below 20ng/mL) was observed in individuals with focal & global cortical atrophy and those with white matter hyperintensity/ SVD. Normal mean vitamin D level was observed in those with normal age related brain MRI changes (Fig. 2). Lower mean age was observed among patients with vascular dementia and those with normal age related MRI findings. In the present study, individuals with focal temporal lobe atrophy and frontotemporal lobar degeneration have higher mean ages (Fig. 3).

### **3.3. Comparison of vascular and non-vascular dementia subtype in the study participants**

In the present review, vascular dementia was observed in 43% of the study participants. Those patients age below 70 years have higher proportion of vascular dementia compared to those aged above 70 ( $p = 0.04$ ). No difference was observed between vascular dementia and non-vascular group ( $p = 0.47$ ). In this review, the prevalence of vascular dementia is higher in those participants with clinical signs of Parkinsonism compared to the non-vascular group (7.4% vs. 1.7%,  $p = 0.009$ ). No statistical difference was observed between the two groups regarding neuropsychiatric symptoms, seizure, fall, incontinence, and sleep disorders (Table 2). In the present study, the presence of hypertension was associated with the presence of vascular dementia ( $p = 0.009$ ). The presence of comorbid cardiac illness ( $p = 0.03$ ) and strokes ( $p = 0.02$ ) were associated with the presence of vascular cognitive impairments. Even though statistically not significant, the presence of comorbid HIV infection was associated with higher proportion of vascular dementia. No difference was observed between the two groups regarding the presences of diabetes, hyperlipidemia, and metabolic causes of dementia (anemia, vitamin B12, D deficiency, and hypothyroidism) (Table 2).

Table 2  
Association between dementia sub types and variables (n = 121)

| Variables   | Vascular dementia<br>N = 52 (43%) | Non-vascular dementia*<br>N = 69 (57%) | P value  |
|---|-----------------------------------|--|----------|
| Age category  |                                   |  |          |
| Below 70 years  | 33 (27.3)                         | 31 (25.6)                              | 0.04     |
| Above 70 years  | 19 (15.7)                         | 38 (31.4)                              |          |
| Gender  |                                   |  |          |
| Male  | 32 (26.4)                         | 38 (31.4)                              | 0.47     |
| Female  | 20 (16.5)                         | 31 (25.6)                              |          |
| Presenting symptoms   |                                   |  |          |
| Neuropsychiatric  | 14 (11.6)                         | 23 (19)                                | 0.45     |
| Seizure   | 7 (5.8)                           | 3 (2.50)                               | 0.09     |
| Parkinsonism  | 9 (7.4)                           | 2 (1.7)                                | 0.009    |
| Fatigue   | 6 (5)                             | 10 (8.3)                               | 0.63     |
| Motor symptoms  | 19 (15.7)                         | 25 (20.7)                              | 0.97     |
| Incontinence  | 21 (17.4)                         | 19 (15.7)                              | 0.13     |
| Fall  | 4 (3.3)                           | 5 (4.1)                                | 0.92     |
| Sleep disorders   | 5 (4.1)                           | 9 (7.4)                                | 0.56     |
| Diabetes mellitus   | 13 (10.7)                         | 14 (11.6)                              | 0.54     |
| Hypertension  | 26 (21.5)                         | 13 (10.7)                              | < 0.0001 |
| Hyperlipidemia  | 9 (15.7)                          | 27 (22.3)                              | 0.77     |
| Cardiac disease   | 12 (9.9)                          | 6 (5)                                  | 0.03     |
| Cerebrovascular diseases  | 10 (8.3)                          | 4 (3.3)                                | 0.02     |
| HIV infection   | 3 (2.5)                           | 1 (0.8)                                | 0.18     |
| Anemia  | 16/97 (16.5)                      | 18/97 (18.6)                           | 0.58     |
| Hypovitaminosis D   | 18/62 (29)                        | 24/62 (38.7)                           | 0.59     |
| Vitamin B12 deficiency  | 5/54 (9.3)                        | 4/54 (7.4)                             | 0.38     |
| Hypothyroidism  | 2/74 (2.7)                        | 5/74 (6.8)                             | 0.45     |
| *Non-vascular dementia includes: focal & global brain atrophy, mixed pathology, surgical causes of dementia, and others |                                   |  |          |

### 3.4. Logistic regression analysis between vascular dementia and covariates in the study participants

In the present review, multivariate logistic regression analysis showed the presences of clinical signs of Parkinsonism (Adjusted OR 2.37, p = 0.001), comorbid hypertension (Adjusted OR 4.59, p = 0.002), and the presences of stroke (Adjusted OR 4.57, p = 0.04) were associated with vascular dementia when adjusted for the covariates (Table 3). In univariate logistic regression analysis age below 70 years was associated with vascular dementia (Crude OR 2.12, p = 0.04); however, no

association was observed when adjusted for the covariates (Adjusted OR 2.37,  $p = 0.06$ ). Near significant association was found between the presences of seizure, incontinence and vascular dementia when adjusted for the other covariates. In univariate logistic regression analysis comorbid cardiac illness was associated with vascular dementia (Crude OR 3.15,  $p = 0.03$ ); however, no association was observed when adjusted for the covariates (Adjusted OR 2.91,  $p = 0.10$ ) (Table 3).

Table 3  
Logistic regression analysis of vascular dementia and covariates in the study participants

| Covariates  | COR  | 95% CI     | P value  | AOR   | 95% CI      | P value |
|---|------|------------|----------|-------|-------------|---------|
| Below 70 years  | 2.12 | 1.02–4.45  | 0.04     | 2.37  | 0.95–5.89   | 0.06    |
| Seizure   | 3.42 | 0.84–13.94 | 0.08     | 4.61  | 0.99–21.49  | 0.05    |
| Parkinsonism  | 7.01 | 1.44–34.01 | 0.01     | 18.33 | 3.28–102.30 | 0.001   |
| Incontinence  | 1.78 | 0.83–3.83  | 0.14     | 2.53  | 0.99–6.48   | 0.05    |
| Hypertension  | 4.31 | 1.91–9.70  | < 0.0001 | 4.59  | 1.76–11.97  | 0.002   |
| Cardiac disease   | 3.15 | 1.09–9.07  | 0.03     | 2.91  | 0.81–10.47  | 0.10    |
| Stroke  | 3.86 | 1.14–13.14 | 0.03     | 4.57  | 1.04–20.07  | 0.04    |
| HIV infection   | 4.16 | 0.42–41.23 | 0.22     | 5.24  | 0.35–78.14  | 0.22    |
| ¶ COR: Crude odds ratio; AOR: Adjusted odds ratio; CI: Confidence interval; HIV: Human immunodeficiency virus |      |            |          |       |             |         |

## 4. Discussion And Conclusion

The present study shows vascular cognitive impairment (VCI) as a dominant subtype, among individuals presented to Yehuleshet Specialty Clinic with subjective forgetfulness. Nearly, half of the study participants fulfilled the diagnostic criteria of vascular neurocognitive disorder (i.e vascular dementia) (12). This is consistent with previous scientific reports from other African countries (1, 13–17). Dementia is multi-factorial with many of these factors highly prevalent in sub Saharan Africa (SSA); namely: malnutrition, HIV infections, cardiovascular disease, and neurodegenerative disorders such as Alzheimer's disease (AD) (1, 13–17). In this review, the presences of comorbid hypertension, stroke, and clinical signs of Parkinsonism were independent predictors of vascular dementia.

Since recent decades, utilization of structural brain imaging is increasingly playing a role in differentiating underlying causes of dementia, with focal atrophy of the hippocampus and entorhinal/medial temporal lobe an early and sensitive marker for AD, and cortical and subcortical lacunar infarcts and white matter lesions, which is a characteristic neuroimaging hallmarks of vascular dementia (VaD) (7–9, 18–22). Likewise, the present study, nearly half of the study participants have the neuroimaging evidences of cortical and subcortical white matter lesions, which are related to cerebral small vessel disease (SVD). Furthermore, one third of the individuals have brain MRI evidences of neurodegenerative disorders; in the form of, global cortical atrophy, focal temporal lobe and frontotemporal lobar atrophy. Small-vessel disease is the main vascular cause of subcortical ischemic vascular dementia. Lacunar infarcts and ischemic white matter lesions are the main type of brain lesions, which are located predominantly subcortical in location and largely associated with VaD (7–9, 18–22). Brain MRI plays unarguably a central role in differentiating in some degree, vascular etiologies from neurodegenerative pathology as the cause of a patient's cognitive impairment (8, 9, 11, 23). The assessment of signal change using T2-weighted imaging or fluid attenuated inversion recovery (FLAIR) can be used to help identify vascular damage. Furthermore, the presence and global or focal lobar atrophy has (pathologically proven) positive predictive value for dementia, especially towards neurodegenerative causes such as AD (8, 9, 11, 23). Global cortical or focal lobar atrophy can be easily assessed by using T1-weighted imaging sequences (8, 9, 11, 23).

According to the Global Impact of Dementia 2013–2050 (3), the largest increases in projected numbers of people with dementia are expected to be in the low and middle income countries (LMIC). In 2050, it is estimated that the number of



dementia patients in the sub Saharan Africa is expected to reach 5.05 million, an increase of 136% from the previous estimate of 2.14 million (3). Thus, it is imperative for clinicians in Africa to improve our diagnostic accuracy and utilize every available asset including, imaging based diagnostic algorithm, in order to improve our dementia care service.

In the present review, the proportion of vascular cognitive impairment is high compared to the overall western studies which put AD as the commonest culprit among patients suspected to have dementia. Plethora of scientific evidences support the major role of vascular risk factors such as, hypertension & stroke in predisposing patients to VaD (1, 7, 10, 14, 15, 17, 24–26). The high prevalence of vascular dementia observed in this study is likely due to the high burden of traditional vascular risk factors were observed; namely, hypertension, hyperlipidemia, diabetes mellitus, and stroke. Among the current study participants, modest burden of infectious (eg. HIV) and metabolic causes of dementia (eg. hypovitaminosis D, vitamin B12, and anemia) were observed. This findings are consistent with previous regional and global reports (1, 6, 31, 10, 13, 15, 25, 27–30). These study results help us to guide our approach to patients with suspected dementia in searching for the underlying etiologies. Moreover, potentially treatable risk factors such as vascular, HIV, and metabolic disorders should be actively screened in all patients suspected of dementia in Ethiopia. This study has several limitations; the retrospective nature of the survey is the major caveat. In addition, the small sample size and lack of locally validated neuropsychological assessment tool are the other issues limiting the study generalizability. The present study shows high burden of vascular cognitive impairment among individuals suspected of dementia. Furthermore, the presences of comorbid hypertension, previous stroke, and Parkinsonism were independent predictors of vascular dementia. Future prospective controlled study is recommended to consolidate our results.

## Abbreviations

**MRI:** Magnetic resonance image;

**SMV:** Small vessel disease

**WMH:** White matter hyperintensity;

**YSC:** Yehuleshet Specialty Clinic

## Declarations

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**Ethical approval of the study protocol:** The study received ethical approval from City Government of Addis Ababa Health Bureau Ethical Clearance Committee (Protocol number: A/A/HB/3787/207). All patients' data were deidentified and pre coded in order to keep maximum patients data confidentiality. All the methods in the present study were performed in accordance with the relevant guidelines and regulations. As this is a retrospective medical chart review survey, a waiver for informed consent was received from City Government of Addis Ababa Health Bureau Ethical Clearance Committee.

**Availability of data and materials:** All data sets on which the conclusions of this manuscript rely are available as spread excel sheet document and available from the corresponding author on reasonable request.

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**Consent to publication:** Not applicable

**Author's contribution:** BAA has contributed in concept design, case ascertainment, data analysis, and manuscript writing up. BG, HT, and TG have contributed in data cleaning, data entry, and figure preparation. MZ and GZ have contributed in research supervisor, manuscript reviewing, and case ascertainment. YT has contributed in reviewing all the imaging data and final revision of the manuscript.

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## Figures

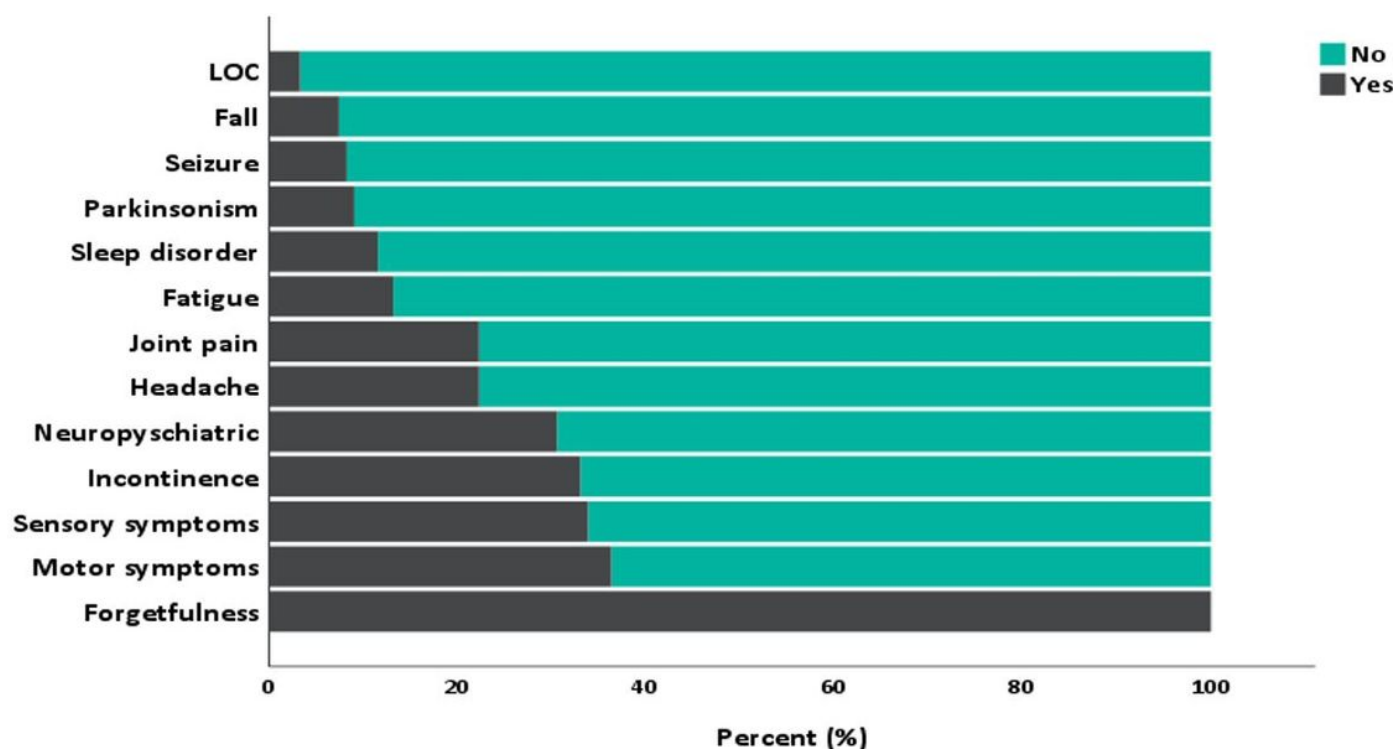


Figure 1

Bargraph showing distribution of clinical symptoms reported by study participants

LOC: Loss of consciousness

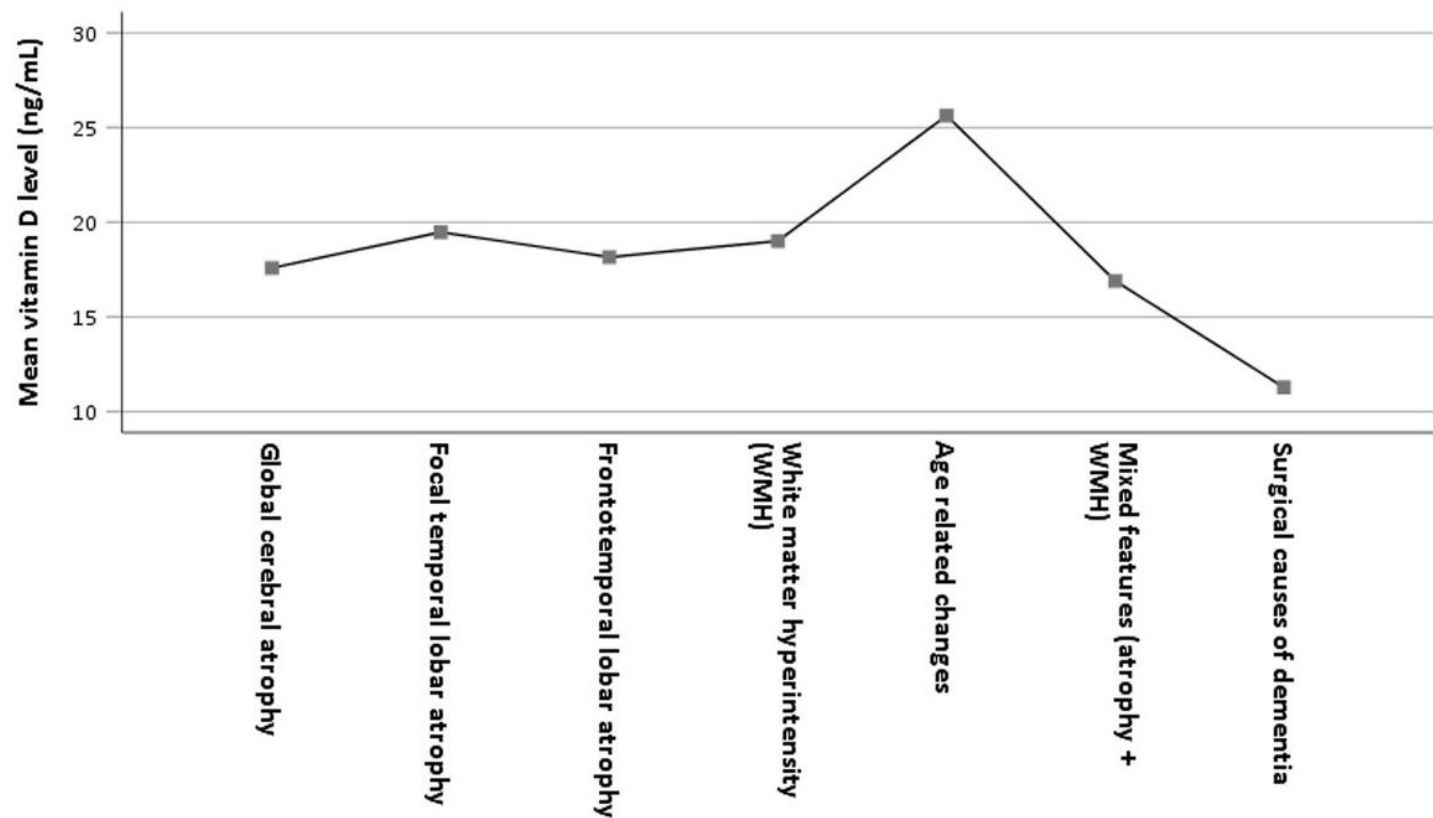


Figure 2

Line graph showing distribution of the mean vitamin D with neuroimaging findings

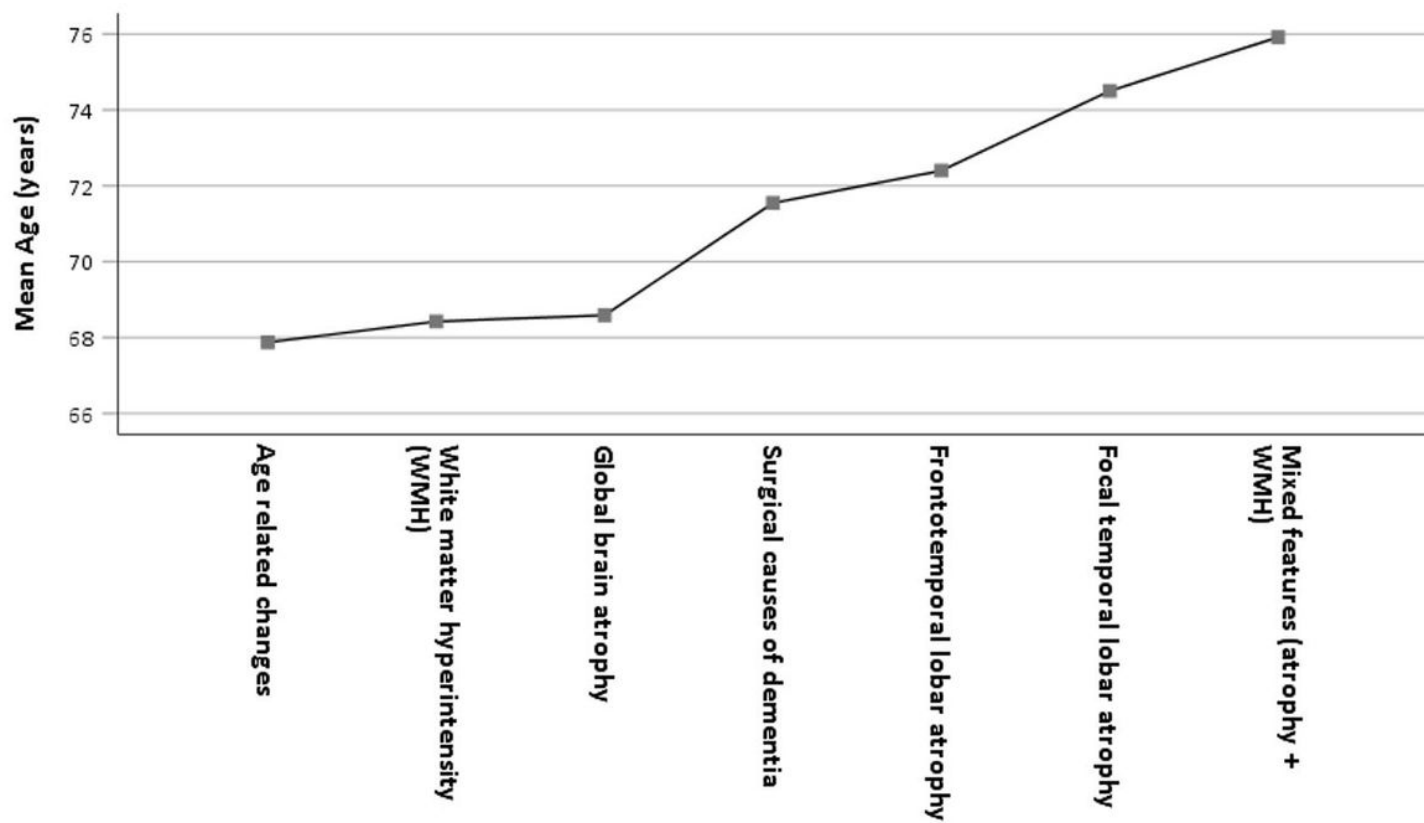


Figure 3

Line graph showing distribution of mean age with neuroimaging findings