

Original Research Article

SEXUAL DIMORPHISM IN DEMENTIA AND ALZHEIMER DISEASES - A NEUROPSYCHIATRIC HOSPITAL BASED STUDY

ABSTRACT

Dementia which is a highly neglected syndrome in Nigeria is an umbrella of term that houses a group of diseases and illnesses that affect your thinking, memory, reasoning, personality, mood and behavior. Alzheimer's disease which is the leading cause of dementia disproportionately affects women than men. The objective of the study is to investigate gender and age differences in dementia and AD. This study retrospectively analyzed eighty-two (82) consecutive patients' folder who had been diagnosed with dementia and AD in Rivers State Neuropsychiatric Hospital Rumuigbo, Port-Harcourt from the year 2014 to 2020. The result obtained showed that the mean age for dementia and AD for males and females were 68.44 ± 8.96 and 70.74 ± 12.98 respectively. It was observed that the females are likely to develop dementia and AD the males, with the prevalence rate of 59 (72.0%) for females while 23 (28.0%) were males respectively. The analysis of comorbidities showed that hypertension and depression were major risk factors in males while depression was a major risk factor in females. There was high risk of association between smoking and dementia in males while Alcohol was a high-risk factor for dementia in females. Early detection plays a major role in the management of dementia and AD, this study therefore advocates for campaign to educate people about the danger of this sickness and set plan for proper management which will go along way reducing the stigmatization that comes with dementia.

Keywords: Dementia, Alzheimer, Gender, Age, Prevalence

INTRODUCTION

Dementia which was previously seen as a western world problem has gradual become a serious stigma for people in the Low and Middle-income countries. Dementia describes a syndrome of cognitive impairment that affects memory, cognitive abilities and behavior, and significantly interferes with a person's ability to perform daily activities. Alzheimer's disease is the most common form of dementia, accounting for approximately 60–70% of cases [1]. While age is the strongest known risk factor, dementia does not exclusively affect older people and is not an

inevitable consequence of ageing. The most commonly recognized risk factors are mid-life hypertension, low educational attainment, and diabetes mellitus and tobacco use [2]. Other risk factors include physical inactivity, obesity, unbalanced diets, and harmful use of alcohol as well as mid-life depression, social isolation and cognitive inactivity. According to [3], dementia currently affects approximately 50 million people worldwide; a number that is projected to grow to 82 million by 2030 and 152 million by 2050. AD is one of the leading causes of death in the world, currently ranked sixth. Every 65 seconds, someone in the United States develops AD. Approximately 5.7 million Americans suffer from Alzheimer's, of which almost 2/3 are women [4]. Every, sixty -five seconds, another person develops Alzheimer disease, and of these newcomers, roughly two-thirds will be women. For a woman over sixty, the risk of developing Alzheimer's is twice that of developing breast cancer (Shriver). Clinical studies indicate that Alzheimer's disease (AD) disproportionately affects women in both disease prevalence and rate of symptom progression, but the mechanisms underlying this sexual divergence are unknown [5]. If this is Left unaddressed, dementia could represent a significant barrier to social and economic development. Improvements in population health responses have the potential to reduce the number of new cases by 10–20%.

[6] carried out a cross- sectional community base study in South Africa to investigate the prevalence of dementia. The estimated prevalence was 0.12% for those aged 65 and more. Of the 1051 subjects, 68.6% were female participants and 69.8% had less than seven years of education. Dementia risk was associated with older age and symptoms of depression, but not with sex. The association with education was not significant when controlled for by age.

In Nigeria, sadly, little or no attention is given to mental health disorders. Dementia victims are labelled witches or mentally derailed. The level of awareness on mental health issues is poor and

fraught with lots of misconception. Dementia is highly neglected; hence no plans are made to help people living with dementia. Therefore, the study sought to investigate the sexual dimorphism, age differences and the associated risk factors in dementia patients.

MATERIALS AND METHODS

RESEARCH DESIGN: This retrospective, observational study was done in Neuro-Psychiatric Hospital Rumuigbo, Rivers State. We retrospectively analyzed consecutive patients' folders who had been diagnosed with dementia from the year 2014 to 2020.

DATA COLLECTION: We reviewed folders of dementia patients and collected data on socio-demographic characteristics (age and gender), comorbidities (hypertension, diabetes mellitus, Lifestyles (smoking, alcohol), Family history.

Ethical Protection:

To ensure ethical protection of subjects, no names of the subjects were taken. The data was held with strict confidentiality and purely for academic purposes.

DATA ANALYSIS

The data collected were analyzed by standard statistics methods guided by specific objectives and hypothesis of this research study. Descriptive characteristics of the data were analyzed using tables, frequencies, graphs and simple percentages. The inferential statistics were analyzed using the Chi-square statistics at the 0.05 level of significance. This technique was adopted due to the need to establish a relationship between the predictor and criterion variables. The Statistical

Package for the Social Sciences (SPSS) software technology version 20.0 was used to perform the analysis.

RESULTS

The data obtained from eighty-two (82) patients' case files of both male and female with dementia from Neuro Psychiatric hospital Rumuigbo from 2014-2020 were analyzed as shown below.

Table 1: Descriptive characteristics of Demographic and Associated Risk Factors:

Variable	Male	Female
Sex	23 (28.0)	59 (72.0)
Age	68.44±8.96	70.74±12.98
Comorbidities	No	Yes
Diabetes	57 (69.5)	25 (30.5)
Depression	44 (53.7)	38 (46.3)
Hypertension	77 (93.9)	5 (0.1)
Life Style	No	Yes
Smoke	68 (82.9)	14 (17.1)
Alcohol intake	46 (56.1)	36 (43.9)
Family history of AD	72 (87.8)	10 (12.2)

A total of 82 dementia cases were analyzed for the following variables namely sex, age, comorbidities (Diabetes, Depression and Hypertension), life style and family history. The sex variable reveals that out of the total cases of eighty-two (82) dementia patients, 23 cases representing 28.0% were males while 59 cases representing 72.0% were females. The mean age

for dementia diagnosis was 68.44 ± 8.96 for males and 70.74 ± 12.98 for females. Diabetes, Depression and Hypertension as underlying conditions associated with dementia. 25 patients representing 30.5% has diabetes whereas 57 patients representing 69.5% do not have such condition; 38 patients (46.3%) have depression while 44 patients (53.7%) do not have and 5 patients (0.1%) have hypertension whereas 77 patients (93.9%) do not have such medical condition. 14 patients (17.1%) smoke while 68 patients (82.9%) do not. Also, 36 patients (43.9%) indulge in alcohol intake while 46 patients (56.1%) do not indulge. 10 patients (12.2%) have family relatives that were diagnosed with Alzheimer disease whereas 72 patients (87.8%) do not.

Table 2: Yearly Distribution of Diseases and Sex

Year	Diagnosis (%)		Sex (%)		Total
	AD	Others	Male	Female	
2014	7 (8.54)	0 (0)	1 (4.3)	6 (10.2)	7 (8.5)
2015	7 (8.54)	2 (2.44)	2 (8.7)	7 (11.9)	9 (11.0)
2016	14 (17.07)	2 (2.44)	5 (21.7)	11 (18.6)	16 (19.5)
2017	14 (17.07)	3 (3.65)	5 (21.7)	12 (20.3)	17 (20.7)
2018	11 (13.41)	2 (2.44)	5 (21.7)	8 (13.6)	13 (15.9)
2019	7 (8.54)	1 (1.22)	2 (8.7)	6 (10.2)	8 (9.8)
2020	10 (12.2)	2 (2.44)	3 (13.0)	9 (15.3)	12 (14.6)
Total	70 (85.37)	12 (14.63)	23 (28.0)	59 (72.0)	

This shows the yearly distribution of dementia with sex from 2014 to 2020. A total of 82 data were collected over a period of 7 years from 2014 to 2020. The diagnosis was broadly segmented into two namely Alzheimer's disease (AD) and others (Vascular dementia, VAD and Lewy body dementia, LWD). In the year 2014, there were 7 recorded cases of dementia representing 8.5%. All the 7 cases were AD. Out of the 7 cases, 1 (4.3%) was a male while 6 (10.2%) were females. In 2015, 9 cases were recorded, 7 (8.54%) of the cases were AD while 2 (2.44%) were others.

2(8.7%) were males while 7(11.9%) were females. In 2016, 16 cases were recorded. 14(17.07%) were AD while 2 (2.44%) were others. Out of the 16 cases 5 (21.7%) occurred in males while 11 (18.6%) occurred in female. In 2017, 17 cases were recorded. 14 (17.07%) were AD while 3(3.65%) were others out of the 17 cases, 5 (21.7%) occurred in males while 12 (20.3%) occurred in females. A total of 13 cases were recorded in 2018, 11 (13.41%) were AD while 2 (2.44%) were others. 5 (21.7%) occurred in males while 8 (13.6%) occurred in female. In 2019, 8 cases were recorded. 7 (8.54%) were AD while 1 (1.22%) were others. 2 (8.7%) occurred in male while 6 (10.2%) occurred in females. And finally, in 2020, 12 cases were recorded. 10 (12.2%) were AD while 2 (2.44%) were others; 3 (13.0%) were males while 9 (15.3%) were females.

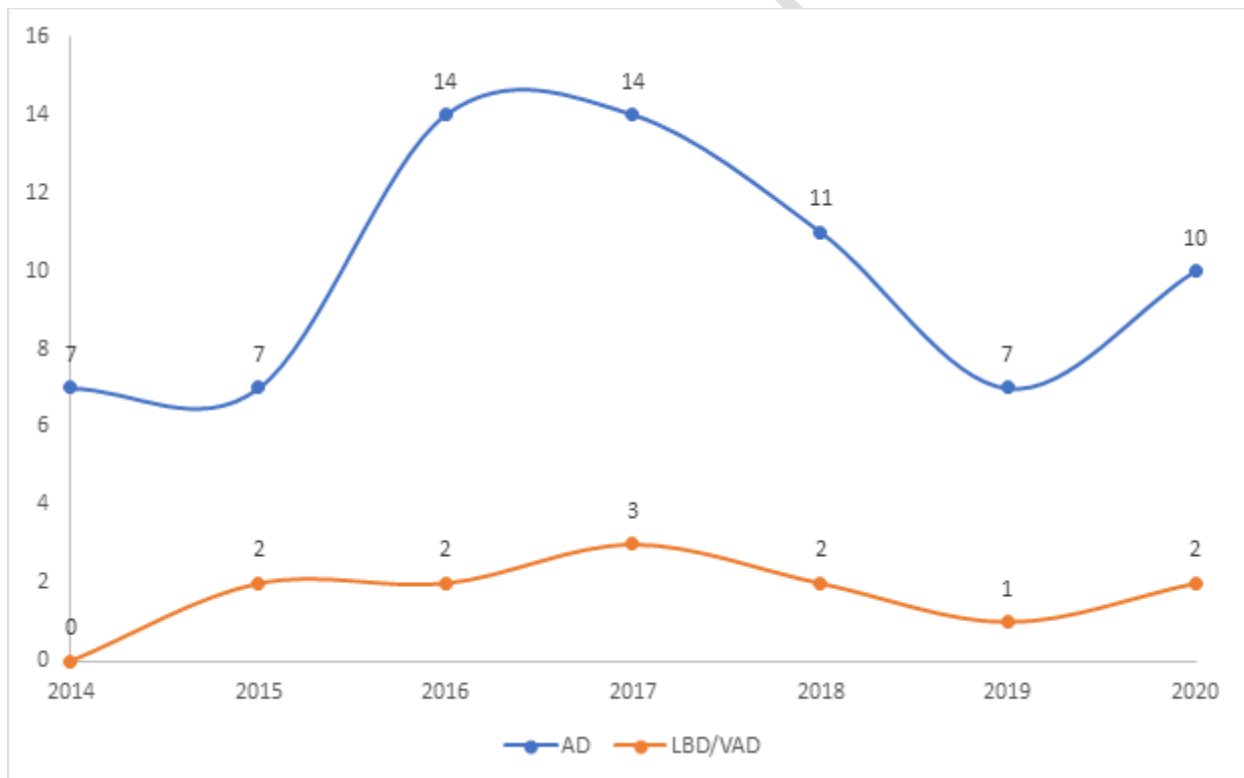


Figure1: Yearly distribution of dementia types (AD; Alzheimer's diseases, LBD; Lewy body dementia, VAD; vascular dementia)

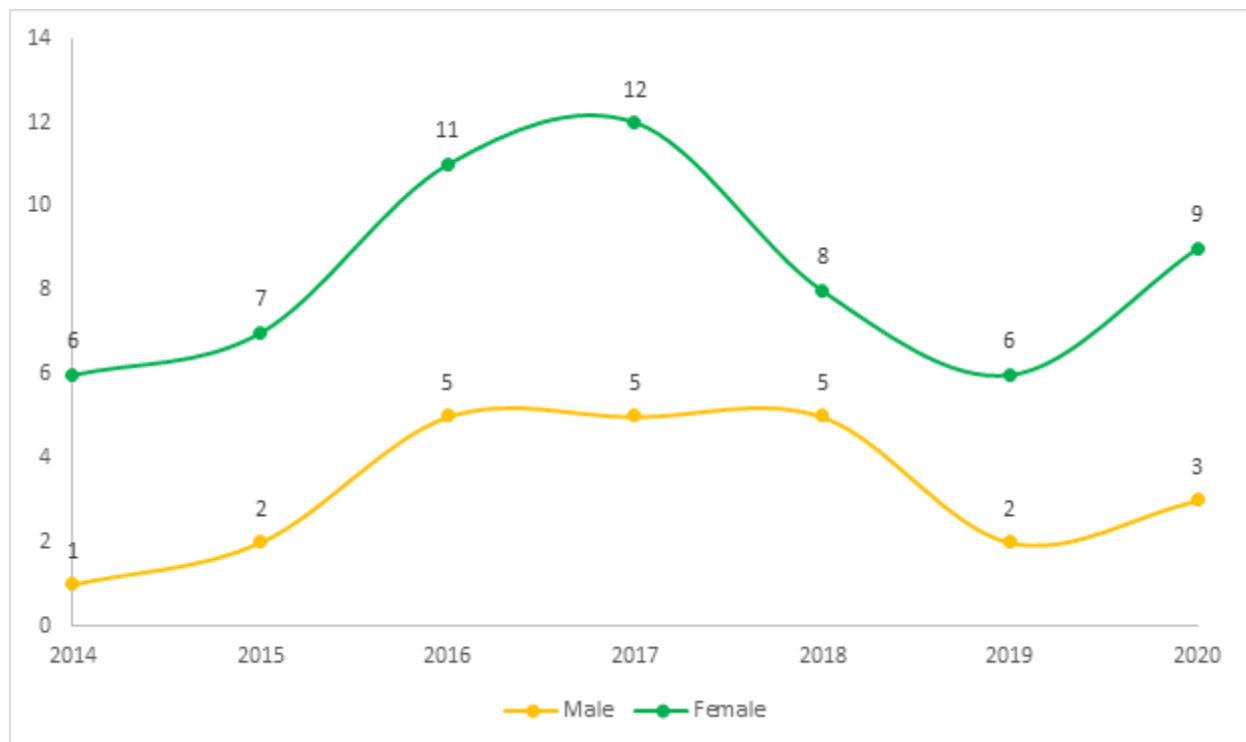


Figure 2: Yearly distribution of dementia types by sex

Table 3: Disease type and Sex

Disease	SEX		Chi-square		
	Male	Female	χ^2 -Value	df	P-value
AD	17	53	3.356	1	0.067
	24.3%	75.7%			
Others	6	6			
	50.0%	50.0%			
TOTAL	23	59			
	28.0%	72.0%			

This compared the sex- associated distributional difference in the type of dementia and found out that of the 82 patient data collected 70 of the patient had Alzheimer's disease of which 17

(24.3%) were males whereas 53 (75.7%) were females while 12 patient have other types of dementia (vascular and lewy bodies dementia) of which 6(50.0%) were males and 6(50.0%) were females.

Table 4: Disease type associated with diabetes

SEX	DIABETES		Chi-square		
	No	Yes	χ^2 -Value	df	P-value
Male	15	8	0.278	1	0.598
	65.2%	34.8%			
Female	42	17			
	71.2%	28.8%			
TOTAL	57	25			
	69.5%	30.5%			

This showed that 25(30.5%) patients have diabetes of which 8(34.8%) were males and 17(28.8%) were females whereas, 57(69.5%) patients do not have diabetes of which 15(65.2%) were males and 42(71.2%) were females (χ^2 [df=1]=0.278;P=0.598).

Table 5: Disease type associated with hypertension

SEX	HYPERTENSION		Chi-square		
	No	Yes	χ^2 -Value	df	P-value
Male	12	11	0.028	1	0.866
	52.2%	47.8%			
Female	32	27			
	54.2%	45.8%			
TOTAL	44	38			
	53.7%	46.3%			

Table 6: showed that out of the 82 patients data collected 5(6.1%) patients have hypertension of which 1(4.3%) was a male and 4(6.8%) were females. 77(93.9%) patients do not have hypertension of which 22 representing 95(7%) were males and 55 representing (93.2%)were females(χ^2 [df=1] =0.171;P=0.679).

Table 6: Disease type associated with depression

SEX	DEPRESSION		Chi-square		
	No	Yes	χ^2 -Value	df	P-value
Male	22	1	0.171	1	0.679
	95.7%	4.3%			
Female	55	4			
	93.2%	6.8%			
TOTAL	77	5			
	93.9%	6.1%			

This table showed that out of 82 patients data collected 38(46.3%) patients have depression and 44(53.7%) do not. 11(47.8%) males have depression and 12(52.2%) do not whereas 27(45.8%) females have depression and 32(54.2%) do not (χ^2 [df=1] =0.028;P=0.866).

Table 7: Disease type associated with smoking

SEX	SMOKING		Chi-square		
	No	Yes	χ^2 -Value	df	P-value
Male	16	7	4.031	1	0.095
	69.6%	30.4%			
Female	52	7			
	88.1%	11.9%			
TOTAL	68	14			
	82.9%	17.1%			

This table showed that out of the 82 patients data collected 14(17.9%) patients smokes of which 7(30.4%) were males and 7(11.9%) were females whereas 68(82.9%) patients do not smoke of which 16(68.6%) were males and were 52(88.1%) were females ($\chi^2[df=1] = 4.031; P=0.095$)

Table.8: Disease type associated with alcohol intake

SEX	Alcohol Intake		Chi-square		
	No	Yes	χ^2 -Value	df	P-value
Male	14	9	0.296	1	0.587
	60.9%	39.1%			
Female	32	27			
	54.2%	45.8%			
TOTAL	46	36			
	56.1%	43.9%			

Table 8 shows that 36 patients representing (43.9%) patients took alcohol and out of the 36, 9(39.1%) were males and 27(45.8%) were females. 46 patients representing (56.1%) do not take alcohol of which 14(60.9%) were males and 32(54.2%) were females ($\chi^2[df=1]=0.296; P=0.587$).

Table 9: Disease type associated with family history

SEX	Family History		Chi-square		
	No	Yes	χ^2 -Value	df	P-value
Male	22	1	1.838	1	0.175
	95.7%	4.3%			
Female	50	9			
	84.7%	15.3%			
TOTAL	72	10			
	87.8%	12.2%			

Table 9 shows that out of the 82 patients data collected, 10(12.2%) patients have a family history of dementia and of which 1(4.3%) was a male and 9(15.3%) were females whereas, 72(87.8%) patients do not have a family history of dementia of which 22(95.7%) and 50(84.7%) were males and females respectively ($\chi^2[df=1]=1.838;P=0.175$).

DISCUSSION

Dementia cases are seen to occur in both male and female of varying age bracket but with high level of disparity. Age remains the greatest risk factor for dementia and the prevalence in population aged 60years and older is vastly increase when compared to other ages [4]. Multiple studies have shown that the incidence of dementia occurs more in women than in male, meaning that there are more women at greatest risk based on age. It is known that women have a greater prevalence of Alzheimer disease (AD) than men, at least partly because women live longer [7, 8]. Sex differences in biological factors (sex hormones), health factors (cardiovascular risk), and social factors (education levels) are hypothesized to contribute to sex differences in dementia risk [9, 10].

From the study a total of 82 patient data were collected and out of 82 patient data collected, 59 (72.0%) were females while 23 (28.0%) were males. This study reveals that dementia and Alzheimer is highly prevalent in females than in males. This finding agrees with [11] who conducted a study in Nigeria to investigate the prevalence and occurrence of dementia. His study revealed a higher prevalence of dementia in females than in males. Also, [12] who investigated the prevalence and occurrence of dementia among patients aged 65 years and above in Cataloma (Spain) revealed that patients with dementia cases were mostly women. Many studies noted females had higher incidence rates of dementia and AD than males, especially in the oldest age

groups [13, 14] while other studies demonstrated no significant gender differences [15]. Some previous studies have also found a higher incidence of dementia and AD in females, especially in those suffering from dementia at age 85 or those suffering from AD at age 80 [13, 14], which may be partially explained by the neuroprotection effects of estrogen among females until menopause [16]. It is also hypothesized that the longer female life expectancy may be another possible interpretation with respect to the higher incidence of dementia and AD among females [17].

In the present study, the mean age analysis of the onset of dementia was 68.44 ± 8.96 for males and 70.74 ± 12.98 for females. This simply means that the mean age for dementia diagnosis is lower in male than in female. This finding is in line with [18] who conducted a study in Taiwan to investigate the age, gender, incidence and prevalence of dementia and Alzheimer's disease. His study revealed that the mean age for dementia was significantly lower in male than in female. The proven fact about Alzheimer is that the gene responsible for this disease is already in the brain decades before the onset. Our study revealed that age is not alone a factor but there are some variables that predispose female to Alzheimer disease and this is supported by [18] who reported that dementia and AD are not natural processes of ageing. Although the incidence of dementia and AD begins to elevate sharply after 65 years [19, 13], a meta-analysis suggested that the incidence of dementia and AD increased slowly or plateaued after age 90 [20].

Regarding the comorbidities, Diabetes, Depression and Hypertension, 25 patients representing 30.5% have diabetes whereas 57 patients representing 69.5% do not have such condition; 38 patients (46.3%) have depression while 44 patients (53.7%) do not have and 5 patients (0.1%) have hypertension whereas 77 patients (93.9%) do not have such medical condition. This is indicative of the fact that depression and diabetes were associated with an increased risk of

dementia as compared to hypertension. Our study revealed that hypertension and diabetes were major risk factor in Males while depression is a risk factor in Females. This finding is in accordance with [21] whose work on systematic review on the risk and protective factors for Alzheimer disease and cognitive decline showed that for medical factor diabetes, depression and traumatic brain injuries in males were all associated with increased risk of Alzheimer disease. Also, [22] identified that depression, hypertension, diabetes, arthritis and atherosclerosis significantly increased the risk of Alzheimer disease.

Furthermore, our study indicates that for life style 14 patients (17.1%) smoke while 68 patients (82.9%) do not. Also, 36 patients (43.9%) indulge in alcohol intake while 46 patients (56.1%) do not. This reveals that both smoking, and alcohol intake is associated with the risk of dementia. This finding is in line with [11] who opined that history of alcohol intake is a significant risk factor for dementia in Nigeria. [21] also identified that smoking and alcohol indulgence were all risk factors associated with dementia. Although smoking and alcohol intake has been recorded as a risk factor and this can only account for the males because males are more addicted to smoking and alcohol than females, but the present study showed that smoking is a majority risk factor in Males while Alcohol is a major risk factor in Females.

For family history, the study revealed that out of the 82 cases that were studied, 10 patients (12.2%) have family relatives that were diagnosed with Alzheimer disease whereas 72 patients (87.8%) do not. This study showed that family history is a risk factor in Females than in males, which a proven evidence that dementia could be hereditary since genes can be inherited from parents. This finding is in line with [23] whose work reveals that all genotypes of APOE e4 allele are associated with an increased risk of Alzheimer's disease whereas APOE e2/2, e2/3 and e3/3 were found to be marginally significant protective factors for Alzheimer's disease.

The incidence and prevalence of dementia was higher in female 59 (72.0%) than in male 23(28.0%) and this is because females are care givers and are prone to depression. This study also revealed that Alzheimer's disease 70 (85.4%) is the leading cause of dementia. These findings are well supported by [24] who opined that of all cases of dementia, Alzheimer's disease has the highest incidence than other rare forms. More so, [18] reported in his study that female consistently had a higher incidence and prevalence of dementia and Alzheimer's than males.

The reason women are disproportionately affected by this disease is not fully known but could be attributed to the fact the women are more vulnerable to stress, anxiety and depression. Majority of females were emotionally traumatized and sexually abused during the early and late stages of their lives which lead to sleep deprivation and decline in cognitive function. Hormonal imbalance which causes decline in estrogen is another recognizable factor why females are at high risk of developing dementia and Alzheimer disease more than their male counterpart.

Furthermore, a trend was also observed in the data indicating that the incidence and prevalence of dementia increased progressively from 2014 through 2016 and climaxed at 2017 with total recorded cases of 17. Then a decline was observed in 2018 and further declined in 2019 and then an increase was seen in 2020. These could be because of poor recording of dementia cases and the negligence in this disease. In Nigeria, the sharp increase observed in the year 2020 could be because of the rise in anxiety and depression due to Covid-19 pandemic, and this affected more females than males.

CONCLUSION

Alzheimer disease is tagged as an old age problem and therefore receives little or no attention. Females suffering from this disease are stigmatized and the family are advised not to waste their

resources. The gender disparity in dementia and AD is alarming, therefore strategic plans to help women suffering from this condition is highly recommended because dementia is not just a natural ageing problem but a progressive distortion in the brain tissues caused by accumulation of hormonal imbalances, emotional trauma, abuse and other stress related conditions that females encountered at different stages of their life time.

REFERENCES

1. WHO (2017). Global action plan on the public health response to dementia 2017–2025. Geneva: World Health Organization; 2017.
2. WHO (2018). World Health Organization 2015: The epidemiology and impact of dementia: current state and future trends. Geneva: (WHO/MSD/MER/15.3; http://www.who.int/mental_health/neurology/dementia/dementia_thematicbrief_epidemiology.pdf , accessed 17 April 2018).
3. WHO (2020). Common forms of dementia. <https://www.who.int/newsroom/factsheet> , accessed 17 April, 2020
4. Alzheimer's Association (2017). Alzheimer's disease facts and figures. *Alzheimers Dement*; 16(3):391-460. doi:10.1002/alz.12068
5. Daniel W. Fisher, David A. Bennett, and Hongxin Dong (2018): Sexual dimorphism in predisposition to Alzheimer's disease. *Neurobiology of Aging*; 70: 308–324.
6. De-Jager, Celeste A, Msemburi, William, Pepper, Katy, Combrinck, Marc I (2017). Dementia Prevalence in a Rural Region of South Africa: A Cross-Sectional Community Study. *Journal of Alzheimer's Disease*; 60(3) pp. 1087-1096, 2017

7. Chêne G, Beiser A, Au R, et al. (2015). Gender and incidence of dementia in the Framingham Heart Study from mid-adulthood. *Alzheimers Dement.*; 11(3):310-320. doi:10.1016/j.jalz.2013.10.005
8. Hebert LE, Scherr PA, McCann JJ, Beckett LA, Evans DA. Is the risk of developing Alzheimer's disease greater for women than for men? *Am J Epidemiol.* 2001;153(2):132-136. doi:10.1093/aje/153.2.132
9. Carter CL, Resnick EM, Mallampalli M, Kalbarczyk A. Sex and gender differences in Alzheimer's disease: recommendations for future research. *J Womens Health (Larchmt).* 2012; 21(10):1018-1023. doi:10.1089/jwh.2012.3789
10. Rocca WA, Mielke MM, Vemuri P, Miller VM. (2014). Sex and gender differences in the causes of dementia: a narrative review. *Maturitas*; 79(2):196-201. doi:10.1016/j.maturitas.2014.05.008
11. Adedoye Davies, Asa Auta, Martin Sixtus Ezejimofor, Ayo Oyedokun, Michael O. Harlay, Igor Ruddan, Kit Yee Chan (2019). Prevalence of dementia in Nigeria: A systematic review of the evidence *Glob Health Rep.*; 3: e2019014. doi:10.29392/joghr.3.e2019014.
12. Anna Ponjoan, Josep Garre-Olmo, Jordi Blanch, Ester Fages, Lia Alves-Cabreros, Ruth Martí-Lluch, Marc Comas-Cufí, Dídac Parramon, María García-Gil, Rafael Ram. (2019): Epidemiology of dementia: prevalence and incidence estimates using validated electronic health records from primary care. *Clinical Epidemiology*, 11 217–22
13. Eratne D., S. M. Loi, S. Farrand, W. Kelso, D. Velakoulis, and J. C. Looi (2018). "Alzheimer's disease paper 1: clinical update on epidemiology, pathophysiology and

diagnosis,” *Australas Psychiatry*, vol. 26, no. 4, pp. 347–357, 2018. View at: [Publisher Site](#) | [Google Scholar](#)

14. Christopher R. B., C. Kaneshiro, J. Yun Jang, A. R. Chandra, N. L. Pedersen, and M. Gatz (2018). “Differences between women and men in incidence rates of dementia and Alzheimer’s disease,” *Journal of Alzheimer’s Disease*, vol. 64, no. 4, pp. 1077–1093
15. Fiest K. M., N. Jetté, J. I. Roberts et al., (2016). “The prevalence and incidence of dementia: a systematic review and meta-analysis,” *Canadian Journal of Neurological Sciences*, vol. 43, no. 1, pp. S3–S50, 2016. View at: [Publisher Site](#) | [Google Scholar](#)
16. Li R., J. Cui, and Y. Shen (2014). “Brain sex matters: estrogen in cognition and Alzheimer’s disease,” *Molecular and Cellular Endocrinology*, vol. 389, no. 1-2, pp. 13–21, 2014. View at: [Publisher Site](#) | [Google Scholar](#)
17. Mielke M., P. Vemuri, and W. Rocca (2014). “Clinical epidemiology of Alzheimer’s disease: assessing sex and gender differences,” *Clinical Epidemiology*, vol. 6, pp. 37–48, 2014. View at: [Publisher Site](#) | [Google Scholar](#)
18. Chih-Ching Liu, Chung-Yi Li, Yu Sun, Susan C. Hu (2019). Gender and age differences and the trend in the incidence and prevalence of Dementia and Alzheimer's disease in Taiwan: A 7- year National population-based study”, *BioMed Research International*, vol. 2019, Article ID 5378540, 12 pages
19. Prince M., D. Acosta, C. P. Ferri et al., (2012). “Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 dementia research group population-based cohort study,” *The Lancet*, vol. 380, no. 9836, pp. 50–58, 2012. View at: [Publisher Site](#) | [Google Scholar](#)

20. Gao S, Hendrie HC, Hall KS, Hui S. (1998). The relationship between age, sex, and the incidence of dementia and Alzheimer disease: a meta-analysis. *Arch Gen Psychiatry*; 55:809-815.[Google Scholar](#)
21. John Williams, Plassman BL, Burke J, Benjamin S (2010). Preventing Alzheimer's disease and cognitive decline: Evid Rep Technol Assess; (193): 1-727. PMID: 21500874; PMCID: pmc4781578.
22. Tan Lan, Wei Xu, Jin-Tai Yu (2016). Meta-analysis of modifiable risk factors for Alzheimer's disease. *Neurology*; 86(16 supplement) PI. 096.
23. Rachna Jain, Nikita Jain, Akshay Aggarwal, D. Jude Hemanth (2014). Convolutional Neural Network based Alzheimer's disease Classification from Magnetic Resonance Brain Images. *Cognitive Systems Research*; doi: <https://doi.org/10.1016/j.cogsys.2018.12.015>
24. Kit-Yee Chan, Wei Wang, Jing-Jing Wu, Li Liu, Evropi Theodoratou, Josip Car (2013). Epidemiology of Alzheimer's disease and other forms of dementia in China: vol.381, issue 9882, p2016-2023, DOI: [https://doi.org/10.1016/50140-6736\(13\)60224](https://doi.org/10.1016/50140-6736(13)60224)