



Study of Treatment Pattern of Neurodegenerative Diseases in a Pakistani Context.

Alina Atif .

Abstract:

Introduction: Neurodegenerative disease is a multi-factorial disease which is attributed to the constant degeneration of the function and structure of central and peripheral nervous system. Alzheimer and Parkinson's diseases are common degenerative diseases all over the world including Pakistan.

Objectives: To find out the disease treatment pattern of neurodegenerative diseases (Alzheimer's disease and Parkinson's disease) in a Pakistani context. The study will help the practicing neuro physicians in Pakistan to get an insight about the findings.

Methodology: This study was conducted at private hospital of Karachi having 200 indoor patients from Dec 2020 to June 2021. Patients selected through convenience sampling by screening at two stages. At first the patients were screened at general OPD or ER. The attending physician then referred the cases to consultant physicians. After confirmation at this level the cases referred to the neurologist. A total of 146 patients were diagnosed for Alzheimer disease while 46 were diagnosed for Parkinson's disease.

Results: For this cohort 146 cases diagnosed as having Alzheimer's disease; female outnumber male and almost all were suffering from one or more other illness as well. Mild grade seen mostly during 50-59 years of age. 48 cases were diagnosed as Parkinson's disease, males affected more than female and most were in their fifties. In comparison to Alzheimer's disease, Parkinson's disease had a mild relationship with the independent variables for example motor symptoms and other comorbidity.

Keywords: Neurodegenerative disorders, Parkinsonism, Alzheimer disease.

Assistant Professor;
Department of Physiology.
Jinnah Medical &
Dental College.
Karachi.

*=corresponding author
alinaatif75@yahoo.com

Introduction:

Abbreviations and definitions:

SPECT: Single Photon Emission Computed Tomography

Unified Parkinson's Disease Rating Scale (UPDRS)¹: 4 parts
Part I: Mentation, Behavior, Mood. Part II: Activities of Daily Living (Determine for "on" or "off", indicating either a "good" or "bad" day, respectively.) Part III: Motor Examination. Part IV: Complications of Therapy (in the past week)

Neurodegenerative disease is a multi-factorial disease

which is attributed to the constant degeneration of the function and structure of central and peripheral nervous system. Alzheimer and Parkinson's diseases are common degenerative diseases all over the world including Pakistan. The neurodegenerative disease is the neurological disorder that eventually influences different bodily activities like walking, speaking, listening, movement, cardiac functions, breathing, balancing, dementia symptoms like difficulty in thinking and etc.¹ The studies show that there is a high relationship be-

tween age and neurological disease. Almost all over the world, the neurodegenerative disease affect aging population. However, due to accidents or severe injuries, medicinal action leads to eradicate the symptoms of neurodegenerative disease before aging or at early times.² The dementia symptoms also progress into neurodegenerative disease. Primarily, dementia is a psychological disease and many researchers confuse this term as neurodegenerative disease.³ Dementia has different types. Dementia is common in Pakistan and when left untreated gets converted into neurodegenerative disease like Parkinson and Alzheimer. This disease can be partially to fully cured depending on the age, causes, brain condition and treatment duration. Treatment is usually prolonged in older patients.⁴ However, due to different metabolic diseases like diabetes, hyperlipidemia, overweight and etc. Life challenges that cause to feel the individual deeply traumatic inside due to stress; depression, insomnia, anxiety etc. affect the prognosis of the disease.⁵ The global prevalence is about 6.5%. 4-5% are contributed by the low income countries inclusive of Pakistan. However, the global burden contributing percentage is high in high income countries like United States, United Kingdom, Australia, New Zealand etc. The 11 to 12% people of first world countries or high-income countries are suffering with the nerve cells degenerative disease.⁶

In Pakistan about 219 people per 100,000 individuals are suffering from Parkinson's disease and the trend is rising. The contributing factors are gender and age, depressive illnesses, exposure to drugs like pesticides, smoke, occupation, sedentary life style like consuming health deleterious diets, consuming alcohol etc.⁷ Furthermore, the demographic, geographic and socioeconomic conditions are also the main causes of disease advancement.

In today's era, the older adults are also experiencing Parkinson symptoms frequently than previous decades. Results of national study shows that older individuals of both genders are affected and Karachi and Peshawar have high occurrence rate of Parkinson disease.⁸ In rural areas, male population is more affected while in urban areas, females' population are affected more with Parkinson disease.⁹

Alzheimer disease is the common type of dementia disease that is growing very fast. China, Pakistan, India and other Asian countries have been reporting increasing

number of cases. In China, nearly nine million people are living with the neurodegenerative disease. In Pakistan, 75% neurological cases are Alzheimer and more common in older age group followed by traumatic brain injury. The dementia patients worsened into Alzheimer disease.¹⁰ Pakistan ranked 4th in Alzheimer and dementia mortalities accounting for 1.39% of yearly deaths during 2018 as per report by WHO.¹¹ The current statistics indicates that nearly two million people are living with Alzheimer disease; and underlying dementia is the common cause, with problem in thinking, memory and behavioral changes.¹¹

Another rare neurodegenerative disease in Pakistan is Amyotrophic lateral disease in which the nerve cells of brain and spinal cord are affected. This disease is the main type of motor neuron disorder and is developed under the age of 50 years. The damage in nerve cell and spine ultimately influences muscle movement that control movement and breathing. For this disease, the exact cause is still under investigation however, it is believed that this condition can be inherited, or may be associated with particular environmental factors that cause the incorrect manufacturing of nerve proteins or by chemical imbalance etc. The prevalence is more in men than women.¹² Another rare inherited neurodegenerative disease is the Huntington Disease in which the nerve cells rapidly breakdown leading functional disabilities including both physical and physiological. The common disabilities are eye movement, body movement inclusive of legs and body, difficulty in speaking etc. A rare disease in Asian countries including Pakistan but not uncommon in Western countries.¹³

Literature Review:

Alzheimer Disease: Alzheimer Disease is manifested by dementia which is characterized by the rapid loss of cognitive abilities over normal aging.¹⁴ The symptoms can be generally noticed by the change in mood and behavior. Physiologically, cerebral cortex and hippocampus are damaged in Alzheimer disease. Pathologically, neurofibrillary tangles, senile plaques or neuritic plaques are aggregated in affected tissues. This disease has two main features. In blood vessels of brain, neuritic plaques are formed due to the aggregation of amyloid beta peptides. The second common pathological change is neurofibrillary tangles which occurs to hyperphosphorylation of tau protein in the cytoplasm of neurons.¹⁵ Under normal condition, the tau protein func-

tions as nutrition transport. However, in pathological condition, the tau proteins in hyper-phosphorylated form develop tangles and are deposited leading to disturbances in normal cascade mechanism. The associated damages are nutritional deficiency in brain, micro vascular damage, oxidative stress leading to inflammation, abnormal mitochondrial function etc. Alzheimer disease can be hereditary, the familial Alzheimer disease usually have the autosomal dominant inherent pattern.¹⁶ To date, the three mutations in genes encoding genes associated to form amyloid precursor proteins have been identified. The presenilin-1 gene, presenilin-2 gene and amyloid precursor protein gene are the causal genes for early onset of Alzheimer disease. Usually, the non-hereditary disease occurs after the age of 65 years, common in female as compare to male.¹⁷

Traumatic brain injury leading to Alzheimer disease is more noticed in older adults and the changes are 2 to 3 times higher. The common sign and symptoms are memory loss, bad decisions due to poor judgment, taking relatively long time to finish the task, wandering and getting lost, loss things or misplacing things at odd places, mood and behavior changes, hallucination, paranoia, difficulty in learning new things, too high in outbursting of anger, using vulgar language, repetitive statements, frequent muscle twitching and blockage are the common symptoms.¹⁸ These symptoms can be controlled by medicinal therapy; the commonly prescribed medicines in mild to moderate conditions is cholinesterase Inhibitor which assists in managing behavioral changes.¹⁹ Donepezil, galantamine, memantine-donepezil, rivastigmine are the common medicines given to Alzheimer patients to recover memory loss, ability to perform tasks, improvement in speech, attention and judgment. At advanced stages, the aducanumab is given which is a monoclonal antibody and is administrated through intraperitoneal injections. This drug causes the removal of amyloid aggregates in brain.²⁰

Parkinson's Disease: Parkinson's disease is fundamentally a movement disorder. It may be idiopathic or of unknown origin. It is a progressive neurodegenerative disease affecting millions of people around the globe. This disease is caused by the loss of nerve cells in the substantia nigra which produces dopamine. The pathogenesis includes defective protein deposition and defi-

ciency in their clearance. The aggregates are the alpha-synuclein in Lewy bodies which deposited in intra-cells eventually causing less dopamine formation and release.²¹

Dopamine regulates some of the brain functions and nervous system to assist in controlling and coordinating body movements. Lack of dopamine is a disease condition, the brain doesn't perform normal to control movement leading to rigidity, slow movement, tremors and instability of body posture. The disease onset is usually after 50 years. There is a different hereditary condition that eventually leads to the development of Parkinson disease. The mutation in Alpha synuclein (SNCA) gene encodes the protein called alpha-synuclein and performs the function of repairing DNA damage repairing signaling kinase.²²

There are some genes that are associated with the lysosome function. The lysosome function is to digest waste products of cells. But in Parkinson disease, the lysosomal function is disturbed leading to decrease in the ability of catabolism activity of cells to breakdown alpha-synuclein. Current researches revealed the association between smoking and Parkinson disease. High caffeine intake is also more prone to develop Parkinson disease at older age. The smoking reduces the monoamine oxidase enzyme activity in the brain. Consequently, dopamine catabolism gets reduced.²³ In addition to this, there are five major pathways in brain coordinating and connecting other areas of brain with basal ganglia. They are motor, oculo-motor, associative, limbic and orbitofrontal circuits. These regions are involved in learning, movement and attention. In Parkinson disease, all these five brain regions get affected which physically explains the symptom of disease like difficulty in walking, imbalance body posture, difficulty in learning, speaking and thinking.²⁴

To date, there is no particular treatment for Parkinson's disease; the medicines are available just to improve symptoms. Dopamine agonists, monoamine oxidase inhibitors, levodopa are usually recommended therapies. The counseling therapy and physiotherapy help to improve muscle movement, following strict dietary regimen to further manage the deteriorating conditions. However, at advanced stage where medicinal therapy failed to improve symptoms, surgical intervention is recommended and microelectrodes are installed in substantia nigra for providing deep brain

stimulation (DBS). This therapy is quite helpful in resolving motor dysfunctions.²⁵

Methodology:

This study was conducted at private hospital of Karachi having 200 indoor patients from Dec 2020 to June 2021. Patients selected through convenience sampling by screening at two stages. At first the patients were screened at general OPD or ER. The attending physician then referred the cases to consultant physicians. After confirmation at this level the cases referred to the neurologist. A total of 146 patients were diagnosed for Alzheimer disease while 46 were diagnosed for Parkinson's disease.

During the said six months period a total of 4682 patients reported to the OPD and ER. Out of these patients, during the first screening (by junior doctors) 273 patients were referred to the consultant physicians. In the second screening (by the consultant physician) a total of 192 patients were finally diagnosed for having Parkinson or Alzheimer disease. Out of this total 192, 146 patients were diagnosed for Alzheimer disease while 46 were diagnosed for Parkinson's disease.

Alzheimer's disease: All patients above 40 who reported or experienced the signs and symptoms of the disease as per criteria defined by National Institute of Ageing were diagnosed as AD.²⁶ These includes memory loss, misplacing things, difficulty in remembering events that just occurred, confusion with place and time, losing track of dates, seasons and time, difficulty in completing routine functions, difficulty with conversations, trouble understanding visual images and spatial relationships, challenges in planning or solving problems, problems with in speaking, problems with in writing, change in mood and personality, poor decision-making.

Parkinson's disease:

Patients having following signs and symptoms were diagnosed as Parkinson's disease (PD): tremor, loss of automatic movements, rigid muscles, slowed movement (bradykinesia), impaired posture and balance, speech changes, writing changes.

Inclusions criteria: All patients above 40 who reported or experienced the following signs and symptoms of the disease: slowness of movement, speech changes, tremor, flatulence, hyposmia, dyskinesia

Exclusions criteria: Patients suffering from a) dementia, b) motor fluctuations at the first visit, co physical disabilities as a result of any other disease having the possibility of interfering with the diagnosis and rating of Parkinson's disease and d) Patients who were on non PD medications having the possibility of interfering the diagnosis of PD (e. g. extrapyramidal motor function).

History of repeated strokes with stepwise progression of parkinsonian features, History of repeated head injury, History of definite encephalitis, Oculogyric crises, Neuroleptic treatment at onset of symptoms, More than one affected relative, Sustained remission, Strictly unilateral features after 3 years, Supra-nuclear gaze palsy, Cerebellar signs, Early severe autonomic involvement, Early severe dementia with disturbances of memory, language and praxis, Babinski sign, Presence of cerebral tumor or communicating hydrocephalus on CT scan, Negative response to large doses of levodopa (if malabsorption excluded), MPTP exposure.

Results:

Alzheimer's disease: Female outnumbers male. Most common age group was 50-59 years old followed next in frequency by 80 years and above (28.08%). Among the major comorbid conditions hypertension (72.60%) was followed by diabetes (62.33%). Psychiatric illnesses (depression, agitation etc.) in totality were found to be 76.71%. Overall, as high as 77.40% patients were taking 1-3 drugs on a routine regular basis. 43.15% patients were taking physiotherapy at different intervals during a month. Patients (50%) were getting mental and social stimulation from within the family and friends. 45.89% patients were also getting counseling as well.

50-59 years patients were higher for mild (34.14%) of the disease. 80 years and above years patients were higher for moderate (37.10%) and severe (38.30%) grades of the disease. For mild grade the following major diagnostic measures were observed more frequently: Loss of spontaneity and sense of initiative (72.97%), Taking longer to complete normal daily tasks (64.86%), Trouble handling money and paying bills (62.16%). For moderate grade the following major diagnostic measures were observed more frequently: Difficulty carrying out multistep tasks, such as getting dressed (83.87%), Repetitive statements or movement

(83.87%), occasional muscle twitches problems coping with new situations (79.03%) and shortened attention span (69.35%). For severe grade the following major diagnostic measures were observed more frequently: Increased sleeping (91.49%), Difficulty swallowing (89.36%), Groaning, moaning, or grunting (82.98%).

In regression analysis the values of R (0.939), R² (0.882) and adjusted R² (0.876) indicate that the independent variables supports the dependent variable at 93.9%, 88.2% and 87.6% respectively. The Durbin-Watson value of 0.320 indicates that there is a strong positive relationship between the dependent variable and independent variables. The Sig (P) value of zero indicates that the result is significant and the model is a good fit.

Parkinson's disease: Males (60.87%) outnumber females (39.13%). Age group between 50-59 was most commonly (41.30%) followed next in frequency by 60-69 with 32.61% cases. Comorbid conditions identified were hypertension (58.70%), cardiac ailments (50%) and psychiatric illnesses (50%). More than half of the patients (56.52%) were taking 3-4 drugs at a time in their daily routine. 30.43% patients were given deep brain stimulation (DBT) as their treatment. 63.04% patients were getting physiotherapy 1-2 times a month. Among other supportive treatments mental and social stimulation were given to 69.57% patients. The signs and symptoms were muscular rigidity or stiffness (93.48%), 4-6 Hz rest tremor (93.48%), bradykinesia (73.91%), tiredness (100%), pain (84.78%), morning akinesia (71.74%), all patients had a day time sleep pattern of different duration (from less than 3 hours to more than 5 hours). Unified Parkinson's Disease Rating Scale (UPDRS) was used to assess the degree of involvement of Parkinson's disease. It was found that motor involvement was the most prominent (71.74%) according to the measurement scale. 73.981% patients had their first onset during 50 to 69 years of age. At the time of first SPECT (Single Photon Emission Computed Tomography) 93.48% patients were 50 – 69 years old. Disease duration at the time of first UPDRS was 5-7 years for 23.91% patients and less than 2 years for 15.22% patients.

In regression analysis the value of R (0.955), R² (0.912) and adjusted R² (0.880) indicate that the independent variables support the dependent variable at 95.5%,

91.2% and 88.0% respectively. The Durbin-Watson value of 1.484 indicates that there is a mild relationship between the independent variables and the dependent variable. The zero sig (P) value indicates that the result is significant and the model is a good fit.

Table No 1: Basic data :Alzheimer's disease

		n=146	Percent
Gender	Male	55	37.67
	Female	91	62.33
Age	40 - 49 Years	17	11.64
	50 - 59 Years	43	29.45
	60 - 69 Years	26	17.81
	70 -79 Years	19	13.01
	80 years and above	41	28.08
Comorbidity	Hypertension	106	72.60
	Cardiac ailments	79	54.11
	Diabetes	91	62.33
	Arthritic problems	86	58.90
	Peptic ulcer	55	37.67
	Psychiatric illnesses (depression, agitation etc.)	112	76.71
Drug therapy	1 to 3	113	77.40
	4 to 6	27	18.49
	More than 6	6	4.11
Physiotherapy	1-2 in a month	32	21.92
	3-4 in a month	17	11.64
	More than 4 in a month	14	9.59
	None	83	56.85
Other supportive treatment	Counseling	67	45.89
	Memory training	54	36.99
	Mental and social stimulation	73	50.00
	Physical exercise programs	47	32.19

TABLE 2: ALZHEIMER'S DISEASE (n=146): DURATION OF SUFFERINGS

		2-4 yrs. (mild)		3-9 yrs. (moderate)		10 yrs. or more (severe)		Total	
		n	%	n	%	n	%	n	%
Gender	Male	14	37.84	16	25.81	9	19.15	55	37.67
	Female	23	62.16	29	46.77	38	80.85	91	62.33
Age in years	40 – 49	7	18.92	8	12.90	2	4.26	17	11.64
	50 - 59	13	35.14	14	22.58	16	34.04	43	29.45
	60 - 69	9	24.32	9	14.52	8	17.02	26	17.81
	70 -79	8	21.62	8	12.90	3	6.38	19	13.01
	80 and above		0.00	23	37.10	18	38.30	41	28.08
	Total	37	100%	62	100%	47	100%	146	100

TABLE 3: ALZHEIMER'S DISEASE: DIAGNOSTIC MEASURES A: Mild Disease, B: Moderate Disease, C: Severe Disease

A: Mild Alzheimer's Disease (n=37)		
	n= 37	%
Mild memory loss	14	37.84
Poor judgment leading to bad decisions	7	18.92
Loss of spontaneity and sense of initiative	27	72.97
Taking longer to complete normal daily tasks	24	64.86
Repeating questions	21	56.76
Trouble handling money and paying bills	23	62.16
Wandering and getting lost	3	8.11
Losing things or misplacing them in odd places	9	24.32
Mood and personality changes	16	43.24
Increased anxiety and/or aggression	19	51.35

B: Moderate Alzheimer's Disease		
	n=62	%
Increased memory loss and confusion	32	51.61
Inability to learn new things	24	38.71
Difficulty with language and problems with reading, writing, and working with numbers	25	40.32
Difficulty organizing thoughts and thinking logically	27	43.55
Shortened attention span	43	69.35
Problems coping with new situations	49	79.03
Difficulty carrying out multistep tasks, such as getting dressed	52	83.87
Problems recognizing family and friends	23	37.10
Hallucinations, delusions, and paranoia	16	25.81
Impulsive behavior such as undressing at inappropriate times or places or using vulgar language	7	11.29
Inappropriate outbursts of anger	11	17.74
Restlessness, agitation, anxiety, tearfulness, wandering—especially in the late afternoon or evening	27	43.55
Repetitive statements or movement, occasional muscle twitches	52	83.87

**TABLE 3: ALZHEIMER'S DISEASE:
DIAGNOSTIC MEASURES C: Severe Disease**

Severe Alzheimer's Disease (n=47)		
	n=47	%
Inability to communicate	36	76.60
Weight loss	33	70.21
Seizures	21	44.68
Skin infections	29	61.70
Difficulty swallowing	42	89.36
Groaning, moaning, or grunting	39	82.98
Increased sleeping	43	91.49
Loss of bowel and bladder control	37	78.72

TABLE 4: ALZHEIMER'S DISEASE REGRESSION ANALYSIS: Model Summary ^b

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				Sig. F Change	Durbin-Watson	Sig (P) value
					R Square Change	F Change	df1	df2			
1	.939 ^a	0.882	0.876	0.26646	0.882	172.404	6	139	0	0.320	0
a Predictors: (Constant), COMORBIDITY, GENDER, DRUG THERAPY, OTHER SUPPORTIVE TREATMENT, PHYSIOTHERAPY, AGE											
b Dependent Variable: GRADE (DURATION OF SUFFERING)											

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics					Durbin - Watson	Sig (P) value
					R Square Change	F Change	df 1	df 2	Sig. F Change		
1	.955 ^a	0.912	0.880	0.20282	0.912	28.474	12	33	0.000	1.484	0
a. Predictors: (Constant), Disease duration at the time of first UPDRS, Deep Brain Stimulation, Motor Symptoms, Comorbidity, Age at the time of first SPECT, No of drugs taking, Physiotherapy, Age at the time of first onset of UPDRS, Day time sleep, Worst time of symptoms, Other supportive treatment, gender											
b. Dependent Variable: UPDRS											

TABLE 5: : Basic Information Parkinson's Disease

		n= 46	%
Gender	Male	28	60.87
	Female	18	39.13
Age of onset of PD	30 - 39	3	6.52
	40 - 49	6	13.04
	50 - 59	19	41.30
	60 - 69	15	32.61
	70 and above	3	6.52
Comorbidity	Hypertension	27	58.70
	Cardiac ailments	23	50.00
	Diabetes	21	45.65
	Arthritic problems	16	34.78
	Peptic ulcer	18	39.13
	Psychiatric illnesses (depression, agitation etc.)	23	50.00
No of drugs taking	1 to 2	13	28.26
	3 to 4	26	56.52
	5 to 6	7	15.22
	More than 6	0	
Deep brain stimulation	Insertion at one side	14	30.43
	None	32	69.57
Physiotherapy	1-2 in a month	29	63.04
	3-4 in a month	14	30.43
	More than 4 in a month	3	6.52
Other supportive treatment	Counseling	24	52.17
	Memory training	18	39.13
	Mental and social stimulation,	32	69.57
	Physical exercise programs	27	58.70

Table 6: Parkinson's disease. Signs and symptoms

		n= 46	%
Motor symptoms	Bradykinesia	34	73.91
	Muscular rigidity or stiffness	43	93.48
	4-6 Hz rest tremor	43	93.48
	Postural imbalance	24	52.17
Non-motor symptoms	Tiredness	46	100.00
	Depression	33	71.74
	Pain	39	84.78
Worst time of symptoms	Morning akinesia	33	71.74
	Other timings	13	28.26
Day time sleep	Less than 3 hours	23	50.00
	3-5 hours	17	36.96
	More than 5 hours	6	13.04
UPDRS	Part i: mentation, behavior, mood	23	50.00
	Part ii: activities of daily living (good or bad day)	21	45.65
	Part iii: motor examination	33	71.74
	Part iv: complications of therapy (in the past week)	7	15.22
Age at the time of first onset of UPDRS	30 - 39 years	3	6.52
	40 - 49 years	6	13.04
	50 - 59 years	19	41.30
	60 - 69 years	15	32.61
	70 years and above	3	6.52
Age at the time of first SPECT	50 - 59 years	22	47.83
	60 - 69 years	21	45.65
	70 years and above	3	6.52
Disease duration at the time of first updrs	Less than 2 years	7	15.22
	2-4 years	23	6.52
	5-7 years	11	23.91
	8-10 years	5	10.87

Discussion:

Neurodegenerative diseases are common diseases over the world and are frequently diagnosed in elderly population besides older population. The main reason is the social stresses, lack of self-care, poor nutritional diet. Even, in children the aggression is increased due to frequent usage of digital technology. These conditions eventually changes brain chemistry leading prognosis of neurodegenerative diseases before time. People should give proper time to exercise, taking proper eight hours sleep, taking proper diet, should avoid high carb and fat diets, keep body hydrated, thinking less and do more, can eventually cause to improve the electrophysiology of heart and brain leading proper functioning of other organs as well. Keeping away the digital technology, doing yoga or exercise in open air with silent mode help releases the stress and anxiety. Furthermore, also releases the endorphins in brain which is the happy hormone. This makes the person feels good. Doing so can significantly reduce the number of patients for neurodegenerative diseases along reducing the global burden for this disease.

Conclusion:

Alzheimer's disease: The disease was found more prevalent in females than males. Almost all the patients were also suffering from one or more other disease. Most affected (29.45%) age group for mild grade of Alzheimer's disease was people of 50-59 years, for moderate and severe grade 80 years and above were more frequent, Psychiatric illnesses were the most prevalent illness (76.71) among all. As high as 77.40% patients were taking 1-3 drugs. Mental and social stimulation from within the family and friend circle were received by 50% of the patients. The result concludes that the grade of suffering (mild, moderate, severe) in Alzheimer's disease has a positive relationship with associated disease, gender, age, drug therapy the patients are taking for other disease, other supportive treatments and physiotherapy.

Parkinson's disease: The disease is more prevalent on males were higher (60.87%) than the females (39.13%). The disease onset started for most of the patients (73.91%) after 50 years. This indicates that for elderly people proper preventive measures should be taken to stop the onset. More than half of the patients (56.52%) were taking 3-4 drugs on their routine. They

were also getting physiotherapy as well. In comparison to Alzheimer's disease, Parkinson's disease had a mild relationship with the independent variables (disease duration at the time of first UPDRS, deep brain stimulation, motor symptoms, comorbidity, age at the time of first SPECT, no of drugs taking, physiotherapy, age at the time of first onset of UPDRS, day time sleep, worst time of symptoms, other supportive treatment, gender.

Both the diseases are major diseases of the old age and are progressive in nature with age. In a Pakistani society where joint family is a norm rather than exception, with the help of family members the disease symptoms and their progression can be either slowed down or stopped altogether. However, poverty and financial constraints are major causes of worry and tension which are considered the basic reasons for onset. This constraints can be overcome through love, affection and tender care by the family members.

Financial disclosure statement:

This research did not receive any specific grant from

Conflict of interest: The authors declare none.

References:

1. Hou Y, Dan X, Babbar M, Wei Y, Hasselbalch SG, Croteau DL, Bohr VA. Ageing as a risk factor for neurodegenerative disease. *Nature Reviews Neurology*. 2019 Oct;15(10):565-81. <https://www.nature.com/articles/s41582-019-0244-7>
2. Chalazonitis A, Rao M. Enteric nervous system manifestations of neurodegenerative disease. *Brain research*. 2018 Aug 15;1693:207-13. <https://www.sciencedirect.com/science/article/pii/S0006899318300192>
3. Willis R, Zaidi A, Balouch S, Farina N. Experiences of people with dementia in Pakistan: Help-seeking, understanding, stigma, and religion. *The Gerontologist*. 2020 Jan 24;60(1):145-54. <https://academic.oup.com/gerontologist/article-abstract/60/1/145/5185650>
4. Leroi I, Chaudhry N, Daniel A, Dunne R, Eman S, Farina N, Husain N, Jafri H, Karim S, Kiran T, Khan M. A roadmap to develop dementia research capacity and capability in Pakistan: a model for low-and middle-income countries. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*. 2019 Jan 1;5:939-52. <https://www.sciencedirect.com/science/article/pii/S2352873719300915>
5. Nnanabu TC. Type 2 Diabetes and Alzheimer's Disease: Investigation Into the Genetic Linkages of Shared Pathological Molecular Mechanisms (Doctoral dissertation).

- <https://dash.harvard.edu/handle/1/37365629>
6. Guo X, He H, Qu Y, Liu J, Qu Q, Lyu J. Incidence of Alzheimer's Disease and Other Dementias: Results from the 2017 Global Burden of Disease Study. <https://www.researchsquare.com/article/rs-43686/latest.pdf>
 7. Taimur M, Shah MA, Ali M, Barry HD, Hussain SZ, Shahzad H, Rizwan A. Frequency of Cognitive Impairment in Patients with Parkinson's Disease. *Cureus*. 2019 May;11(5):e4733. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6649883/>
 8. Tufail M. Clinical features and risk factors of Parkinson's disease in a population of Khyber Pakhtunkhwa, Pakistan: a case-control study. *Neurodegenerative Diseases*. 2019;19(5-6):211-217. <https://www.karger.com/Article/Abstract/506742>
 9. Tanveer K, Attique I, Sadiq W, Ahmad A. Non-motor symptoms in patients with Parkinson's disease: a cross-sectional survey. *Cureus*. 2018 Oct;10(10) e3412. <https://www.ncbi.nlm.nih.gov/pmc/articles/pmc6281445>
 10. Noreen Z, DeJesus J, Bhatti A, Loffredo CA, John P, Khan JS, Nunlee-Bland G, Ghosh S. Epidemiological investigation of type 2 diabetes and Alzheimer's disease in a Pakistani population. *International journal of environmental research and public health*. 2018 Aug;15(8):1582. <https://www.mdpi.com/1660-4601/15/8/1582>
 11. Adamson MM, Shakil S, Sultana T, Hasan MA, Mubarak F, Enam SA, Parvaz MA, Razi A. Brain injury and dementia in Pakistan: current perspectives. *Frontiers in neurology*. 2020 Apr 30;11:299. <https://www.frontiersin.org/articles/10.3389/fneur.2020.00299/full>
 12. Fousiya Kunjumon Subaida, Diya Sarju, Binsha Malliyekal Abdulkhadar, Divya Venugopal. Amyotrophic Lateral Sclerosis (ALS) - A Case Report; *Indian Journal of Pharmacy Practice*, 2017: Vol 10 (2), Apr-Jun. 151-2.
 13. Munawar T, Bibi Y, Ahmad F. Ethnomedicinal Study of Plants used for Neurodegenerative Diseases: A Review: Ethnomedicinal study of plants used for Neurodegenerative Diseases. *Proceedings of the Pakistan Academy of Sciences: B. Life and Environmental Sciences*. 2020;57(3):13-26. <http://ppaspk.org/index.php/PPAS-B/article/view/3>
 14. Sidera Nadeem, Faheem Abbas. Factors Affecting Elder's Health in Pakistan: A Literature Review. *PJNM Vol-2 (3) Jul-Sep 2018*
 15. Jagust W. Imaging the evolution and pathophysiology of Alzheimer disease. *Nature Reviews Neuroscience*. 2018 Nov;19(11):687-700. <https://www.nature.com/articles/s41583-018-0067-3>
 16. Iqbal, K., Liu, F., Gong, C. X., & Grundke-Iqbal, I. (2010). Tau in Alzheimer disease and related tauopathies. *Current Alzheimer research*, 7(8), 656–664. <https://doi.org/10.2174/156720510793611592>
 17. Aanandhi MV, Niventhi A, Rujaswini T, Hemalatha CN, Praveen D. A Comprehensive Review on the Role of Tau Proteins in Alzheimer's Pathology. *Research Journal of Pharmacy and Technology*. 2018 Feb 1;11(2):788-90. <https://search.proquest.com/openview/7f244a2447e01ec3fd5a91300446129e/1?pq-origsite=gscholar&cbl=1096441>
 18. Lucke-Wold B. Understanding the link between traumatic brain injury and Alzheimer's disease. *Annals of translational medicine*. 2018 Nov;6(Suppl 1). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6291599/>
 19. Atri A. Current and Future Treatments in Alzheimer's Disease. *Semin Neurol*. 2019 Apr;39(2):227-240. doi: 10.1055/s-0039-1678581. Epub 2019 Mar 29. PMID: 30925615.
 20. Simon DK, Tanner CM, Brundin P. Parkinson disease epidemiology, pathology, genetics, and pathophysiology. *Clinics in geriatric medicine*. 2020 Feb 1;36(1):1-2. [https://www.geriatric.theclinics.com/article/S0749-0690\(19\)30063-1/abstract](https://www.geriatric.theclinics.com/article/S0749-0690(19)30063-1/abstract)
 21. Goldstein DS, Holmes C, Lopez GJ, Wu T, Sharabi Y. Cerebrospinal fluid biomarkers of central dopamine deficiency predict Parkinson's disease. *Parkinsonism & related disorders*. 2018 May 1;50:108-12. <https://www.sciencedirect.com/science/article/pii/S1353802018300592>
 22. Zeng XS, Geng WS, Jia JJ, Chen L, Zhang PP. Cellular and molecular basis of neurodegeneration in Parkinson disease. *Frontiers in aging neuroscience*. 2018 Apr 17;10:109. <https://www.frontiersin.org/articles/10.3389/fnagi.2018.00109/full>
 23. Peng W, Minakaki G, Nguyen M, Krainc D. Preserving Lysosomal Function in the Aging Brain: Insights from Neurodegeneration. *Neurotherapeutics*. 2019 Jul;16(3):611-634. doi: 10.1007/s13311-019-00742-3. Erratum in: *Neurotherapeutics*. 2019 Jul 24;: PMID: 31183763; PMCID: PMC6694346.
 24. Lie PP, Nixon RA. Lysosome trafficking and signaling in health and neurodegenerative diseases. *Neurobiology of disease*. 2019 Feb 1;122:94-105. <https://www.sciencedirect.com/science/article/pii/S0969996118301530>
 25. Elkouzi A, Vedam-Mai V, Eisinger RS, Okun MS. Emerging therapies in Parkinson disease—repurposed drugs and new approaches. *Nature Reviews Neurology*. 2019 Apr;15(4):204-23. <https://www.nature.com/articles/s41582-019-0155>