



Original Article

Hematological Profile of Patients with Dementia in South Punjab

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ABSTRACT

Objectives: A case-control study was conducted to find the prevalence of abnormal blood indices and electrolytes in patients with dementia.

Material & Methods: The levels of erythrocytes, leukocytes, platelets, electrolytes, and ESR were determined from the biochemistry lab. A t-test was applied to see the significance of the difference between each dementia patient group (Alzheimer Disease-AD, Parkinson's Disease-PD, and Frontotemporal Dementia-FTD) with the control group for each CBC and electrolyte parameter.

Results: In each patients' groups (AD, PD, and FTD), the mean value of every erythrocyte was lower than the normal range. A significant difference existed for each erythrocyte between dementia patients and controls, except MCHC. Low levels were observed in neutrophils in all groups of dementia including control group. Very high levels were observed in ESR in all groups of dementia. Significant differences existed in the WBC levels between controls and AD as well as PD patients, in platelets between the control group and FTD patients, and in ESR in each group of dementia patients vs. control group. Normal values observed in all groups of dementia patients as well as in the control group. Significant differences existed for sodium and potassium levels between the control group and frontotemporal dementia cases.

Conclusion: We found low levels in erythrocytes in cases of Alzheimer disease, Parkinson's disease, and frontotemporal dementia. Age-related changes to hematological indices especially related to RBCs, and inflammatory mediators like cytokines, hamper the microcirculation in the cerebral tissue leading to micro-infarcts or microbleeds which cause neuronal insults and parenchymal damage.

Keywords: Alzheimer Disease-AD, Parkinson's Disease-PD, Frontotemporal Dementia-FTD, Erythrocytes, Leukocytes, Electrolytes.

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INTRODUCTION

The current study was performed on dementia patients from the South Punjab Population of Pakistan to assess and compare the levels of erythrocytes, leukocytes, and electrolytes with the healthy control group. Dementia is a neurological disorder common in the elderly population. People suffer from cognitive and behavioral

changes and a varying degree of memory impairment. Up to 18% of the population (around 50 million people) of the world goes into neuropsychiatric disorders. They deteriorate in their thinking, memory, emotional and social behavior. 70% of the dementia of the world is attributed to Alzheimer's disease. This disease taxes heavily on the economy and psychology of the caretakers and families of the patients.¹⁻³ Common neurodegenerative diseases are Alzheimer's disease (AD), Huntington's disease, Frontotemporal dementia (FTD), and Parkinson's disease (PD).

The many causes of dementia include hypothyroidism, vitamin deficiencies, chronic alcohol abuse, brain tumors, subdural hematomas, psychiatric, depression, traumatic brain injury, infections (HIV), and chemotherapy-related cognitive dysfunction.¹⁻⁴

Dementia prevails in the elderly and goes proportionally with advancing age. Over 94 years of age, nearly 58% of people get dementia. Dementia is not always irreversible. Newer interventions are helpful. The highest degree of clinical expertise is crucial to manage and properly recognize the neuropsychiatric symptoms of dementia.⁴ People with dementia develop symptoms due to neurochemical, neuropathological, and genetic factors. They develop Apraxia, which is an inability to perform previously learned tasks. The impaired executive function of judgment, reasoning, planning, and Agnosia. The cerebral cortex suffers from inflammation, following injury. Synaptic function and metabolism of neurons decline to lead to cognitive impairment.⁵⁻⁶ Dementia's early phase slowly progresses and goes overlooked. The patient is forgetful, generally confused in time and space. In the middle phase, the symptoms are more defined and obvious to the caregivers. Patients experience uneasy swallowing of food, dysequilibrium, speech problems, confusion, or memory. They also report an inclusive of unease in swallowing and eating, having balance

problems, language and speech difficulties, memory impairment, forgets names or events, changes in behavior, restlessness, wandering around and repeatedly questioning), forgetfulness of people's names and recent events. They often require more help with problem-solving, communication, and attention. During the last phase, memory disturbance is marked. Cannot identify nearby relatives, places, or events. There is aggressiveness, crying, or anger.⁷⁻⁸

In clinical practice, behavioral and psychiatric disorders exhibit a variety of cognitive and non-cognitive symptoms. Patients ultimately develop behavioral or psychiatric symptoms in over 90% of the cases of dementia. The behavioral and psychological symptoms of dementia (BPSD) includes hallucinations, anxiety, depression, agitation, disinhibition, elation, apathy, irritability, delusions, aberrant motor behavior, and appetite or sleep changes. The BPSD tends to have a poor outcome in psychiatric patients as hospital stay and health care costs come into play in the long-term sequelae of the disease. It involves the misuse of drugs, agitation, or distress of the caregivers and the patients as well.⁹⁻¹¹ Symptoms in patients either exist simultaneously or occur individually. In clinical practice, it is better to group the symptoms of BPSD patients for estimation of prognosis, the response of treatment, and the natural course of disease¹⁰⁻¹¹. The dementias have some risk factors. Age is the biggest risk factor. Symptoms increase as the age advances. First-degree relatives of Alzheimer's patients have a higher risk. The genetic component apoE4 (Apolipoprotein E) has a role to play. Other risk factor includes lifestyle, diabetes, and hypertension, the intensity of mental engagement through life, play significant role.⁹

Cortical and sub-cortical types of dementia is a classification used by Psycho-neurolinguistics. Cortical dementia (CD) includes Alzheimer Disease (AD), Frontotemporal Dementia (FTD),

Creutzfeldt-Jakob disease (CJD) while Subcortical dementia (SCD) includes Progressive supranuclear palsy, Parkinson's Disease (PD) and Huntington's Disease (HD).^{9,12} Parkinson's disease is a progressive neurodegenerative disorder that occurs when substantia nigra cells start dying. There is no test that persistently differentiates PD from other neuropsychiatric disorders. History and examination remain the mainstay for diagnosis. The patient has slowness and difficulty of movements and rigidity of limbs. PD can also be caused due to infarctions of the cerebrum, or its degeneration like, multiple system atrophy or progressive supranuclear palsy.¹³ Frontotemporal dementia (FTD) is another progressive neurodegenerative disorder when atrophy of frontal and temporal lobes occurs. Here the patient has all the common neurodegenerative symptoms along with personality change, bizarre effect, and aphasia.¹⁴ Alzheimer's disease includes the affected area affected in Alzheimer's is the medial temporal and temporoparietal cortex. It starts with memory loss. There is amyloid protein deposition outside neurons and neurofibrillary tangles inside the cells that contribute to senile plaque formation. Amyloid plaques are formed by extracellular deposition of A β .¹⁵

MATERIALS AND METHODS

Study Design, Setting & Population

A case-control study was conducted during 2018-2019, at Bahauddin Zakariya University (BZU), Multan, Pakistan, to find the prevalence of abnormal blood indices and electrolytes in patients with dementia disease.

Inclusion Criteria

The dementia patients (N = 35) and the healthy individuals as the control group (N = 15) were enrolled from South Punjab. Following groups of dementia patients were included: Alzheimer Disease (AD), Parkinson's Disease (PD) and

Frontotemporal Dementia (FTD). Patients belonged to Kot Addu, Taunsa, Multan, Shujabad, Dera Gazi Khan, and Bahawalpur stations.

Diagnosis of Dementia

The diagnosis of dementia was done via either MRI or CT scans. In some of the patients, the PET or SPECT scans were also conducted for the diagnosis.

Exclusion Criteria

Patients suffering from malignancies not will to become part of the study.

Blood Sampling

Blood samples of dementia patients were collected from Fatima Medical Center, Multan. The blood samples of healthy controls were also collected from Fatima Medical Center, Multan.

Laboratory Testing

The blood samples were sent to the biochemistry laboratory of Fatima Medical Center. The levels of erythrocytes, leukocytes, platelets and ESR were determined through the complete blood count (CBC) test in both patients' groups as well as in control group. Serum electrolytes (Sodium & Potassium) were also determined from biochemistry laboratory tests.

Data Collection & Analyses

The data was collected for the information on age, gender, location, medication intake, existence of diabetes mellitus (DM). The descriptive statistics including frequencies, mean values, minimum/maximum values were analyzed via SPSS version 25. Each parameter of CBC and electrolytes were compared with the normal ranges.

Statistical Analyses

A t-test was applied to see the significance of difference between each dementia patient group (AD, PD & FTD) with the control group for each CBC and electrolyte parameter. A p-value less than 0.050 was considered the significant.

RESULTS

Age of the Patients

The mean age of the dementia patients was 70 years, whereas, the mean age of the control group was 65 years.

Gender Distribution

There were more female patients (62.85%) as compared to male patients (37%). Majority of the patients were from rural areas (51.4%).

Clinical Information

Table 1 shows the complete detail of information for both groups. The control group was not taking any medication. Dementia patients were on medication. Both group individuals were not diabetic. The included dementia patients people were not having any other diseases. However, they were found the intake of the following drugs for dementia: Donepezil, Memantine, Quetiapine,

Table 1: Sociodemographic Information of Dementia Patients and Controls.

Parameters	Dementia Group N=35	Control Group N=15
Age (years)	Mean: 70; Minimum:60; Maximum:80	Mean: 65; Minimum: 50; Maximum: 80
Gender	Male: 13 (37%); Female: 22 (62.85%)	Male: 7 (46%); Female: 8 (53.3%)
Location	Rural: 18 (51.4%) Urban: 17 (48.5%)	Rural: 6 (40%) Urban: 9 (60%)

Risperidone, Donecept, Valium, Methylcobalamin, Alzilo, Sinemet and PK-Merz.

Comparison of Erythrocytes

Table 2 shows the mean values of each erythrocyte in each group of dementia patients including a control group. The control group was having normal values of almost all parameters except, hematocrit and MCHC. However, in dementia patients' groups (Alzheimer Disease, Parkinson's Disease and Frontotemporal Dementia) mean value of every erythrocyte parameter was lower than the normal range. A significant difference existed (p value<0.050) for each erythrocyte parameter between each dementia patient group (AD, PD, and FTD) and control group (**Table 3**), except MCHC (between controls and AD group).

Table 2: Comparison of Mean Values of Erythrocytes between of Dementia Patients and Controls.

Erythrocytes	Control Group N=15	Alzheimer Disease (AD) Patients N=12	Parkinson's Disease (PD) Patients N=12	Frontotemporal Dementia (FTD) Patients N=11
Hemoglobin (g/dL) Normal Range: 13.5 – 17.5	13.7 ± 1.64	7.19 ± 0.928	8.90 ± 1.308	10.42 ± 0.681
Hematocrit (%) Normal Range: 42-52 (male), 37 – 47 (female)	40.6 ± 4.376	27.03 ± 4.027	23.38 ± 1.481	26.4 ± 2.79
Red Blood Cells (×10 ⁶ /μL) Normal Range: 4.5 – 5.9 (male), 4.1 – 5.1 (female)	4.87 ± 0.533	2.76 ± 0.608	2.97 ± 0.531	3.06 ± 0.485
Mean Cell Volume (fL) Normal Range: 80 – 94	87.4 ± 4.656	71.95 ± 4.094	77.48 ± 1.187	70.09 ± 2.213
Mean Corpuscular Hemoglobin (pg)	29.3 ± 1.790	25.09 ± 1.195	25.63 ± 2.029	25.2 ± 2.188

Normal Range: 27.5 – 33.2				
Mean Corpuscular Hemoglobin Concentration (g/dL) Normal Range: 33.4 – 35.5	32.89 ± 0.981	32.89 ± 1.249	31.51 ± 1.180	31.70 ± 1.494

Table 3: Comparison of Erythrocytes via. t-Test.

Erythrocytes	Control Group vs. Alzheimer Disease (AD) Patients		Control Group vs. Parkinson's Disease (PD) Patients		Control Group vs. Frontotemporal Dementia (FTD) Patients	
	p- value	t- test; df	p- value	t- test	p- value	t- test
Hemoglobin (g/dL)	< 0.0001	12.24;25	< 0.0001	8.24; 25	< 0.0001	6.22;24
Hematocrit (%)	< 0.0001	11.90;25	< 0.0001	28.28;25	< 0.0001	16.30;24
Red Blood Cells (million cells/cmm)	< 0.0001	9.60;25	< 0.0001	9.21;25	< 0.0001	8.87; 24
Mean Cell Volume (fL)	< 0.0001	9.03;25	< 0.0001	7.71;25	< 0.0001	11.37;24
Mean Corpuscular Hemoglobin (pg)	< 0.0001	6.98;25	< 0.0001	4.99;25	< 0.0001	5.25;24
Mean Corpuscular Hemoglobin Concentration (g/dL)	1.000*	0.0;25	0.0028	3.30;25	0.0217	2.45;24

*Insignificant

Comparison of Leukocytes

Table 4 shows the mean values of each leukocyte and ESR in each group of dementia patients including a control group. Normal ranges were observed between white blood cells, eosinophils, and platelets in all groups of dementia patients including the control group. Low levels were observed in Neutrophils in all groups of dementia patients including the control group. Very high levels were observed in ESR in all groups of dementia patients. According to t-test, significant differences (p-value < 0.0001) were existed in the WBC levels between the control group and AD as well as PD patients. A significant difference (p-value < 0.0001) existed in platelets between the

control group and FTD patients. However, significant differences (p-value < 0.0001) existed for ESR in each group of dementia patients vs control group (**Table 5**).

Comparison of Electrolytes

Table 6 shows the mean values of sodium and potassium in each group of dementia patients including the control group. Normal values observed in all groups of dementia patients as well as in the control group. Significant differences existed for sodium and potassium levels between the control group and frontotemporal dementia cases (p values: 0.0011 & 0.0009) (**Table 7**).

Table 4: Comparison of Mean Values of Leukocytes, Platelets & ESR between of Dementia Patients and Controls.

Leukocytes	Control Group N=15	Alzheimer Disease (AD) Patients N=12	Parkinson's Disease (PD) Patients N=12	Frontotemporal Dementia (FTD) Patients N=11
White Blood Cells ($\times 10^3/\text{mm}^3$) Normal Range: 4 – $11 \times 10^3/\text{mm}^3$	7546.66 ± 1044.62	9442.85 ± 901.03	8654.54 ± 1860.84	8320.0 ± 1599.16
Neutrophils (%) Normal Range: 49 – 74	3.60 ± 1.40	4.14 ± 1.40	4.00 ± 1.00	3.50 ± 1.17
Eosinophils (%) Normal Range: 0 – 6	2.93 ± 1.03	3.28 ± 1.20	2.90 ± 1.22	2.50 ± 1.08
Platelets ($\times 10^6/\text{L}$)	193620 ± 40582.37	199178.57 ± 48574.92	224818.18 ± 46363.38	25100 ± 61029.04

Normal Range: 150 – 450				
ESR Normal Range: 0 – 10 (mm/1 st hour)	12.06 ± 4.13	117.35 ± 7.94	106.72 ± 10.14	80.70 ± 10.77

Table 5: Comparison of Leukocytes, Platelets & ESR via. t-Test.

Leukocytes	Control Group vs. Alzheimer Disease (AD) Patients		Control Group vs. Parkinson's Disease (PD) Patients		Control Group vs. Frontotemporal Dementia (FTD) Patients	
	p- value	t- test; df	p- value	t- test	p- value	t- test
White Blood Cells (/mm)	< 0.0001*	4.97;25	< 0.0001*	1.95;25	0.148	1.49;24
Neutrophils (%)	0.3288	0.99;25	0.412	0.83;25	0.849	0.19;24
Eosinophils (%)	0.422	0.81;25	0.9453	0.069;25	0.313	1.03;24
Platelets	0.745	0.32;25	0.0741	1.86;25	< 0.0001*	8.46;24
ESR	< 0.0001*	44.51;25	< 0.0001*	33.01;25	< 0.0001*	22.65;24

*significant

Table 6: Comparison of Mean Values of Sodium & Potassium between of Dementia Patients and Controls.

Electrolytes	Control Group N=15	Alzheimer Disease (AD) Patients N=12	Parkinson's Disease (PD) Patients N=12	Frontotemporal Dementia (FTD) Patients N=11
Sodium (mmol/L) Normal Range: 136-145	138.8 ± 0.5	138.5 ± 0.6	139 ± 0.7	138 ± 0.6
Potassium (mmol/L) Normal Range: 3.6-5.2	4.4 ± 0.2	4.3 ± 0.4	4.6 ± 0.5	4.7 ± 0.2

Table 7: Comparison of Sodium & Potassium via. t-Test.

Electrolytes	Control Group vs. Alzheimer Disease (AD) Patients		Control Group vs. Parkinson's Disease (PD) Patients		Control Group vs. Frontotemporal Dementia (FTD) Patients	
	p- value	t- test; df	p- value	t- test	p- value	t- test
Sodium (mmol/L)	0.165	1.41;25	0.35	0.93;25	0.0011	3.70;24
Potassium (mmol/L)	0.404	0.84;25	0.16	1.41;25	0.0009	3.77;24

DISCUSSION

The study reported that the mean of each erythrocyte (hemoglobin, hematocrit, RBC, mean cell volume-MCV, mean cell hemoglobin-MCH and MCHC) was lower than the normal range. Whereas, the control group was having normal values of almost all parameters except, hematocrit and MCHC. Except for MCHC, the significant difference existed for each erythrocyte parameter between each dementia patient group (Alzheimer Disease-AD, Parkinson's Disease-PD, and Frontotemporal Dementia-FTD) and control group. Hemoglobin was associated with increased risks of

microbleeds and consequently dementias in a number of studies. Winchester et al also¹⁶ reported low hemoglobin ranges in Alzheimer's disease. Although, poor cognitive function is reported from anemia, however, Winchester et al¹⁶ did not find any causative impact on cognitive performance from low red blood cells. Wolters et al¹⁷ mentioned the risk of dementia, including Alzheimer's, associated with both low and high serum levels of hemoglobin, as there were differences in the integrity of white matter and perfusion of cerebral tissue. Anemia is associated with the risk of developing any type of dementia in 34%

and Alzheimer's dementia in 41% cases.¹⁸ In older persons, cognition was impaired in patients with higher or lower levels of hemoglobin, and the risk of developing Alzheimer's dementia was higher.¹⁹ We observed the normal ranges in white blood cells, eosinophils, and platelets in all groups of dementia patients including the control group. Low levels were observed in neutrophils in all groups of our dementia patients including the control group. Very high levels were observed in ESR in all groups of dementia patients. ESR tends to go up in advancing age and is more marked in females with dementia. Significant differences existed in the WBC levels between the control group and Alzheimer's cases as well as Parkinson's cases. A significant difference also existed in platelets between the control group and Frontotemporal dementia cases. We observed normal values in all groups of dementia patients as well as in the control group. Significant differences existed for sodium and potassium levels between the control group and frontotemporal dementia patients.

Dementia and cognitive impairment are secondary to cerebral infarction. Infarcts arise in the brain when there are vascular disturbances (embolism, spasms, bleeding, or low blood indices like hemoglobin or hematocrit). It is known that higher hemoglobin levels pose more risk of stroke than normal levels. As the age advances, there is more incidence of anemia ranging from as low as 4.2% to as high as 28%. There is little literature to support this though²⁰. With advancing age, the incidence of Alzheimer and other forms of dementia increases exponentially. The role of anemia as a cause of dementia is controversial.¹⁹ CBC is generally advised in patients for identification of reversible dementia. Upon post mortem studies of demented human brains, the levels of potassium measured intracellularly were in contradiction to other studies. The raised intracellularK⁺ were indicating exposure of astrocytes to A β .²⁰ Cellular potassium was lower in other studies.²¹ When compared to other studies our study contradicts their results, as we had normal levels of sodium and potassium ions in the brain cells of demented patients. Our patients of the study were receiving

treatment for their dementia. It is likely that correction of dementia brought the levels of these electrolytes back to normal. Dementia is found in patients that have either high or low hemoglobin. Cerebrovascular accidents cause dementia in these people who exhibit lower connectivity to brain infarcts. This, however, is still unclear, how hemoglobin relates to dementia.¹⁹ In Parkinson's disease, iron plays a significant role. It was found accumulated in the substantia nigra.²¹ Patients of PD were found to have a progressive reduction in hemoglobin content which also related to the peripheral metabolism of iron and indicated the severity of the disease.²³ Inflammatory cytokines have a deleterious effect on erythropoietin leading to worsening of anemia with the increasing cytokine.²⁴ The hematological indices and electrolytes show the level of cognitive dysfunction and it can also be used as a diagnostic biomarker for dementia progression in the patients of the South Punjab Population, but there is a limitation in our study that all patients were on the treatment for dementia.

CONCLUSION

We found deranged erythrocytes in cases of Alzheimer disease, Parkinson's disease and in frontotemporal dementia. Age related changes to hematological indices especially related to red blood cells, and inflammatory mediators like cytokines, hamper the microcirculation in the cerebral tissue leading to micro-infarcts or micro bleeds which cause neuronal insults and parenchymal damage, resulting in a progressive deterioration in cognition, memory, coordination and behavior of the individuals.

RECOMMENDATION

Adherence to the golden rules of health, physical activity and maintenance of healthy diet throughout life can lead to dementia free life. This was the study from single center on limited data.

LIMITATIONS OF THE STUDY

Larger studies are required to establish the complete hematological profile of demented people.

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Additional Information

Disclosures: Authors report no conflict of interest.

Ethical Review Board Approval: The study was conformed to the ethical review board requirements.

Human Subjects: Consent was obtained by all patients/participants in this study.

Conflicts of Interest:

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Faiza Khalil	Study design and methodology.
2.	Noureen Samad	Paper writing, referencing, and data calculations.
3.	Sohaib Hassan	Data collection and calculations.
4.	Muhammad Ali Qureshi	Analysis of data and interpretation of results etc.
5.	Ahsan Numan	Literature review and manuscript writing.