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The Frequency, Predictors and Health Impact of Post-Stroke Extrapyramidal Disorders (Clinical and Epidemiological Study)

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ABSTRACT

Background: Post-stroke extrapyramidal disorders (PSEDs) significantly impair functional outcomes but remain poorly characterized in stroke populations. Understanding the frequency, risk factors, and health impacts of PSEDs is essential for improving stroke management and rehabilitation strategies.

Objective: To assess the incidence, risk variables, and impact of post-stroke extrapyramidal illnesses on functional outcome in a hospital-based population.

Patients and Methods: This nested case-control study was conducted from October 2017 to September 2020. Among 1,971 acute cerebrovascular stroke patients screened, 167 met the inclusion criteria, divided into 69 cases with PSEDs and 98 controls without. Extensive neurological exams, brain imaging, and the Abnormal Involuntary Movement Scale (AIMS) were utilized to diagnose PSEDs. Risk factors were analyzed using logistic regression in IBM SPSS 21.0.

Results: PSEDs developed in 3.5% of the stroke patients. Significant risk factors included older age (OR = 1.067, 95% CI: 1.037–1.097), diabetes mellitus (OR = 4.476, 95% CI: 1.987–8.083), and deep lesion site (OR = 3.477, 95% CI: 1.683–7.184). Patients with PSEDs were more likely to exhibit dementia (47.8% vs. 19.4%, P = 0.006) and had worse functional outcomes as measured by the Barthel Index (82.6% with poor outcomes vs. 61.2% in controls, P = 0.003).

Conclusion: Post-stroke extrapyramidal disorders are associated with significant functional impairment and are more likely in patients with specific risk factors such as advanced age, diabetes, and deep brain lesions. Early identification and tailored management of these risk factors may improve outcomes in stroke patients at risk of PSEDs.

Keywords: Post-Stroke Extrapyramidal Disorders, Chorea, Dystonia, Parkinsonism, Barthel Index.

INTRODUCTION

Secondary movements after stroke are rare disorders, occurring in 1–4% of stroke patients [1]. They affect deep brain regions, including the thalamus (37%), basal ganglia (44%), and occasionally multiple locations across the motor circuit [2]. Examples of post-stroke extrapyramidal disorders (PSEDs) include dystonia, chorea with or without hemiballismus, tremor, parkinsonism, segmental or focal myoclonus, athetosis, choreoathetosis, and asterixis [3-5].

Post-stroke extrapyramidal disorders can result from lesions in cortical (primary motor, supplementary motor, and premotor areas), subcortical (basal ganglia, thalamus, and diencephalon), or cerebellar circuitry [2].

The pathophysiology of movement disorders is attributed to the interaction of diverse motor networks across multiple brain regions. A focal brain lesion may affect many neural networks, resulting in more than one type of movement disorder [6]. Conversely, the same type of abnormal movement can manifest with lesions in different locations [7]. The post-stroke remodeling phase is associated with increased activity in the contralesional hemisphere and decreased interhemispheric inhibition, which results in heightened cortical excitability and, consequently, the appearance of abnormal movements [8]. All PSEDs significantly affect post-stroke neurological impairment by exacerbating the neurological deficits associated with the primary focus of brain damage from the stroke, and as a consequence, these disorders substantially reduce the quality of life for stroke survivors [9].

Therefore, the purpose of this article was to explore the incidence, risk variables, predictors, and effects of PSEDs on endpoints as well as the necessity of early intervention to ensure that survivors live healthy lives.

PATIENTS AND METHODS

The current work was a nested case-control (NCC) study conducted in the stroke unit and neurology ward, with follow-up at the outpatient clinic of (blinded for review) from October 2017 to September 2020.

A total of 1,971 patients with acute cerebrovascular stroke (within one week) were initially recruited, of whom 69 patients who developed post-stroke extrapyramidal disorders (PSEDs) and 98 who did not develop PSEDs met the inclusion and exclusion criteria and were included in this study.

Exclusion criteria were patients with transient ischemic attack, stroke associated with other primary brain lesions such as brain tumors, cognitive impairments, unreliable informants, refusal to participate, known renal or hepatic issues, communication problems like sensory aphasia, and those experiencing or taking medications known to cause extrapyramidal manifestations, such as antipsychotics. Patients were categorized into ischemic and hemorrhagic stroke groups (cerebral and subarachnoid hemorrhage) based on their clinical presentation and neuroimaging results. All patients underwent CT and/or MRI brain scans to confirm their stroke diagnosis.

Socio-demographic details, hypertension, diabetes mellitus, heart disease, smoking, family history,

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and the number of prior strokes were collected from the patient or their caretakers. All patients underwent comprehensive neurological and general examinations as well as body mass index measurements at admission, with obesity diagnosed at scores ≥30 kg/m² [10]. Lipograms were performed after fasting for more than 14 hours, with serum values above 239 mg/dl and 200 mg/dl classified as hypercholesterolemia and hypertriglyceridemia, respectively [11]. Electrocardiography (ECG) and/or echocardiography were conducted (CON-TEC, model: ECG100G, China) to detect any arrhythmias or ischemia.

The Barthel Index (BI) [12], which categorizes stroke severity into three grades: extremely poor (full dependency, BI score ≤ 60), poor (aided independence, BI score 60-95), and good (minimal or no impairment, BI score ≥ 95), was used to assess all patients. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), with scores of 23 or below (or 21 for illiterates) indicating dementia [13].

The Abnormal Involuntary Movement Scale (AIMS) was used to serially assess all patients within six months from the onset to detect the emergence of PSEDs [14]. The AIMS assesses 12 different tasks evaluating involuntary movements throughout the body, rated on a scale from 0 (none) to 4 (severe). At the end of the six months, the BI was used to evaluate the progress of all cerebrovascular stroke (CVS) patients.

Sample size:

G*Power 3 software was utilized for the task [15]. To identify an effect size of 0.1 in the mean MMSE and BI, a calculated minimal sample of 167 stroke patients divided into two groups (69 with PSEDs and 98 without PSEDs) was necessary, with an error probability of 0.05 and 90% power on a two-tailed test.

Ethical considerations:

The study was done after being accepted by the Research Ethics Committee of the University Hospital (IRB: 500/1/21). All patients provided written informed consents prior to their enrolment. The consent form explicitly outlined their agreement to participate in the study and for the publication of data, ensuring protection of their confidentiality and privacy. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical methods

The researchers used IBM-SPSS 21.0 (IBM-SPSS Inc., Chicago, IL, USA) to process and analyse the data [16].

Means, standard deviations, and percentages were computed employing descriptive statistics. Chi-square test was performed to assess the variation in the distribution of frequencies between groups as a measure of significance. A separate t-test analysis was performed to compare the dichotomous data means. The odds ratio (OR), 95% confidence interval (CI), and p-value were used to investigate the independent predictors of extrapyramidal disorders in stroke patients using significant factors from the univariate and multivariate analysis. When the p-value was equal to or less than 0.05, it was judged significant.

RESULTS

Eligibility criteria didn't match 653 of evaluated patients. 69 cases out of the included 1,971 stroke patients (3.5%) went on to develop extrapyramidal illnesses **(Figure 1)**.

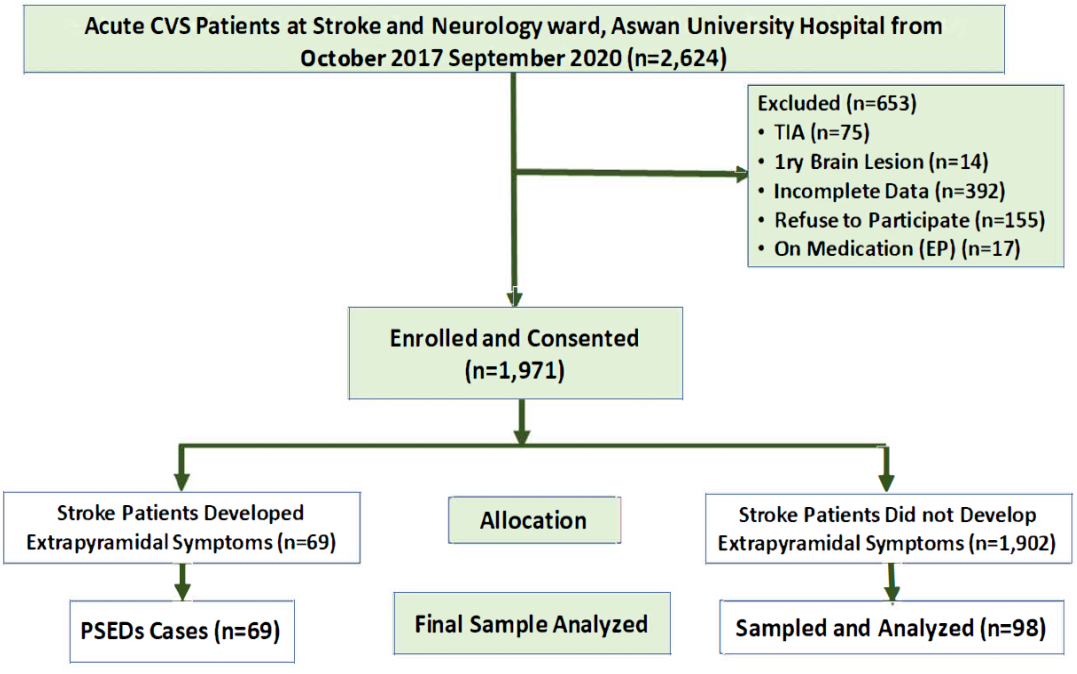

Figure 1: Flow Chart of the Studied Sample

CVS, Cerebrovascular stroke, PSEDs, Post-stroke extrapyramidal disorders.

Old age, male sex, hypercholesterolemia, diabetes mellitus, RBS, and obesity were recorded significantly more in PSEDs group. Some vascular risk factors; hypertension, smoking and ischemic heart diseases were detected in the two subtypes of stroke patients without significant differences (P>0.05) whereas, diabetes mellitus and hypercholesterolemia were recorded more significantly in PSEDs group (P<0.05). On the contrary, obesity was reported in 8.7% of PSEDs patients versus 21.7% in those without extrapyramidal disorders with difference that is statistically noteworthy (P=0.028) **(Table 1, Figure 2)**.

Table 1: Baseline Data and Risk Factors Comparisons among the Studied Stroke Cases

	Without PSEDs (n=98)	With PSEDs (n=69)	P-value
Age/years	57.69 ± 10.7	70.61 ± 12.9	**< 0.001****
Sex (Male/Female)	48/50	45/24	**= 0.038***
Smoking	29 (29.6%)	24 (34.8%)	= 0.218*
Hypertension	38 (38.8%)	27 (39.1%)	= 0.545*
IHD	47 (48%)	24 (34.8%)	= 0.062*
S. Cholesterol (mg/dl)	211.98 ± 46.1	234.33 ± 63.2	**= 0.009****
DM	13 (13.3%)	30 (43.5%)	**< 0.001***
RBS (g/dl)	130.96 ± 7.6	168.00 ± 12.5	**< 0.001****
Obesity	21 (21.7%)	6 (8.7%)	**= 0.028***

*Chi-square analysis was used to compare the frequency between the groups, **Independent t-test was used to compare the means among groups; IHD, Ischemic heart disease; S, Serum; DM, Diabetes mellitus; RBS, random blood sugar; PSEDs, Post-stroke extrapyramidal disorders

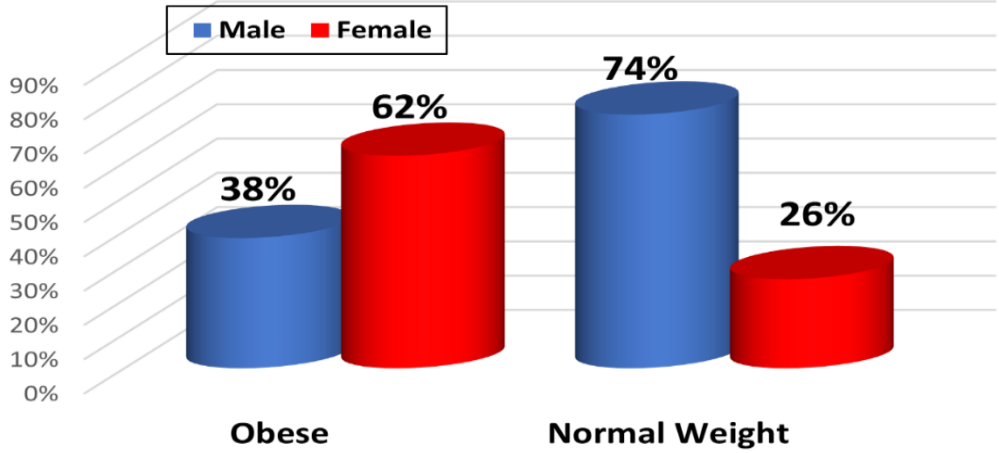

Figure 2: Weight Distribution Among the Studied Sample of Both Sexes.

Table 2 displayed poor/very poor Barthel Index and certain neuroimaging presentations, such as deeply located stroke, sphincter affection, gait disorders, cerebellar manifestations, or cognitive impairment, were associated with a significantly greater likelihood of PSEDs development**.**

Table 2: Clinical Data Comparisons among the Studied Stroke Cases

	Without PSEDs (n=98)	With PSEDs (n=69)	P-value*
Sphincter Affection	27 (27.6%)	33 (47.8%)	**= 0.007***
Gait Affection	74 (75.5%)	63 (91.3%)	**= 0.009***
Cerebellar Manifestations	2 (2.1%)	6 (8.7%)	**= 0.047***
Dementia	19 (19.4%)	33 (47.8%)	**= 0.006**
MMSE	25.21 ± 6.3	18.48 ± 3.9	**< 0.001****
Barthel Index:			
• **Poor/Very Poor**	46 (46.9%)	57 (82.6%)	**< 0.001***
• **Excellent**	52 (53.1%)	12 (17.4%)	
Recurrent Stroke	9 (9.2%)	9 (13%)	= 0.293*
Ischemic/Hemorrhagic Stroke	87/11	60/9	= 0.450*
Site of Lesion			
• **Superficial**	64 (65.3%)	22 (31.9%)	**< 0.001***
• **Deep**	34(34.7%)	47(68.1%)	

*Chi-square analysis was used to compare the frequency among groups, **Independent t-test was used to compare the means among groups, MMSE, Mini Mental State Examination; PSEDs, Post-stroke extrapyramidal disorders.

As regard PSEDs subtypes, about 2/5 of patients had chorea (39%), and the patients who had it were the youngest, followed by parkinsonian patients (26%), who had the oldest ages. Thirdly, dystonia (22%) **(Figure 3 and 4)**. The basal ganglia followed by parietal lobe were the commonest sites for lesions **(Figure 5 and 6)**.

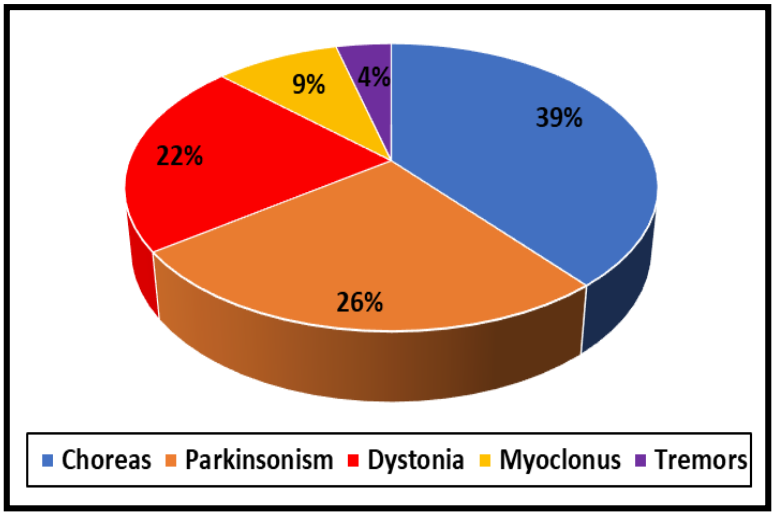

Figure 3: Distribution of the Studied Cohort According to Extrapyramidal Disorders Subtypes

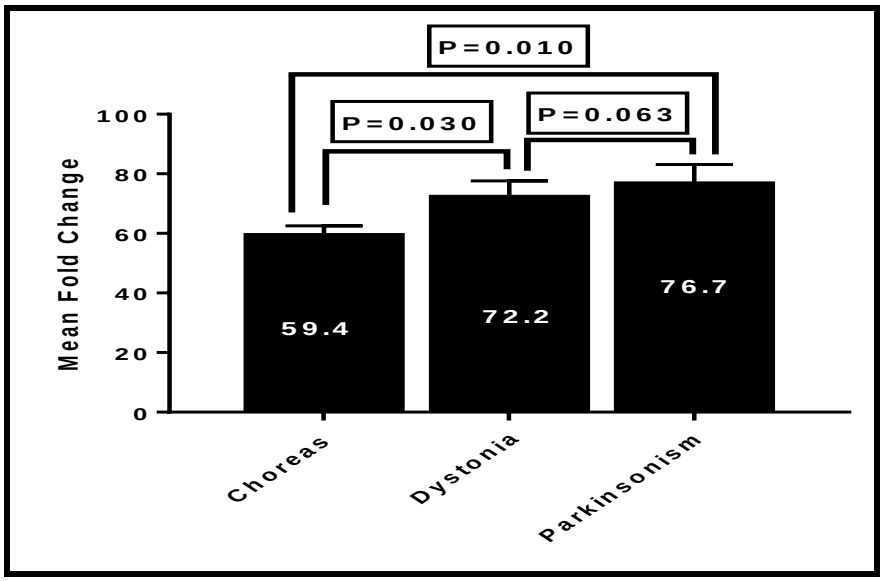

Figure 4: Age Difference between Extrapyramidal Subtypes.

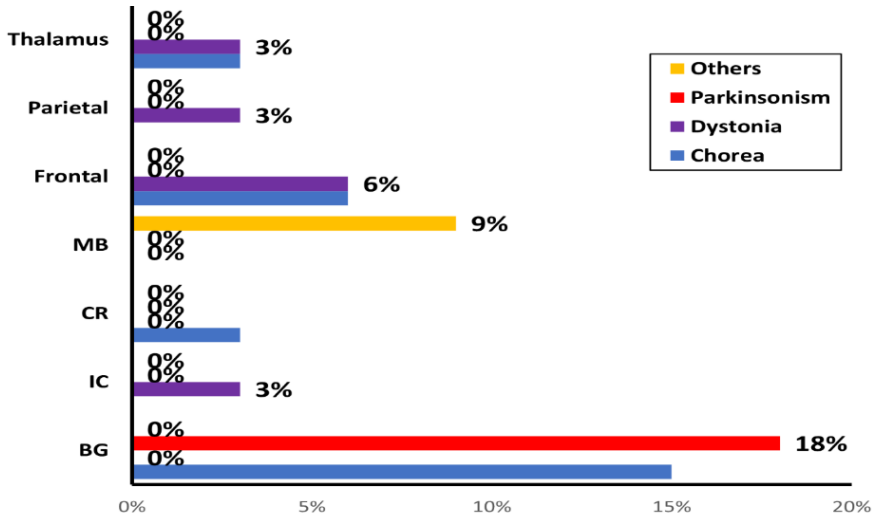

Figure 5: Commonest Lesion Sites of Extrapyramidal Subtypes
MB, Midbrain; CR, Corona radiata; IC, Internal capsule; BG, Basal ganglia

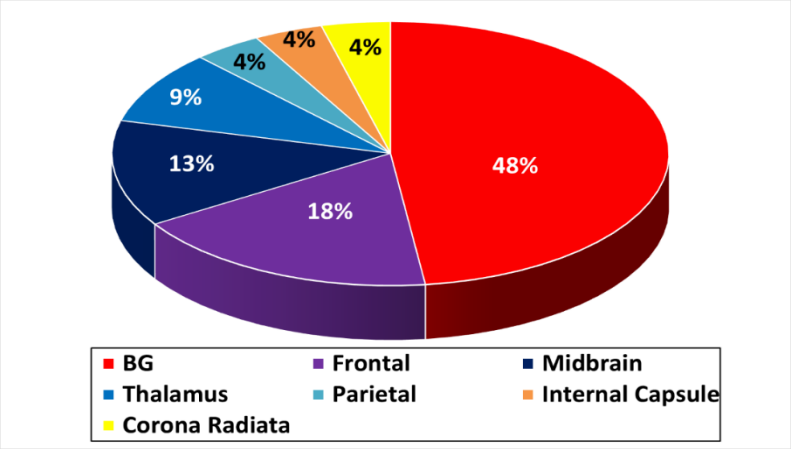

Figure 6: Distribution of Cases with PSEDs According to Lesion Site
BG, Basal ganglia

Eight independent predictors—diabetes mellitus, obesity, hypercholesterolemia, severe initial stroke (poor BI), old age, dementia, cerebellar symptoms, and deep lesion location—were accounted for in the final multivariate model after directing for age and sex. In other words, stroke patients presented with dementia, severe initial or deeply located stroke had triple risk of PSEDs. Moreover, patients with DM had quadruple risk of PSEDs. Also, patients with cerebellar manifestations were 14 times, more liable to have PSEDs. Finally, there were 64% and 10% probability of PSEDs with each point decent of BMI and MMSE, respectively [HR= 0.361 and 0.897, P = 0.023 and 0.001, respectively]. **(Table 3)**.

Table 3: Predictors of PSEDs among Stroke Patients: Logistic Regression Model

Variable	Univariate		Multivariate	
	OR (95% CI)	P-value	HR (95% CI)	P-value
Age/years	1.062 (1.035–1.090)	< **0.001**	1.067 (1.037–1.097)	=**0.001**
Sex (Male)	1.953 (1.036–3.683)	= **0.039**	1.381 (0.785–2.185)	= 0.164
Diabetes Mellitus	5.030 (2.368–9.681)	< **0.001**	4.476 (1.987–8.083)	< **0.001**
Obesity	0.349 (0.133–0.0918)	= 0.033	0.361 (0.123–0.674)	= **0.023**
S. Cholesterol Level	1.008 (1.002–1.014)	= **0.011**	1.007 (1.001–1.014)	= **0.028**
Poor BI-1 (Pre-)	5.370 (2.567–11.234)	< **0.001**	2.646 (1.124–6.229)	= **0.026**
MMSE	0.885 (0.835–0.938)	< **0.001**	0.897 (0.842–0.954)	= **0.001**
Dementia	3.811 (1.915–7.587)	< **0.001**	2.930 (1.413–6.077)	= **0.004**
Cerebellar Manifestations	4.571 (0.894–14.386)	= 0.068	14.094 (1.940–44.101)	= **0.009**
Deep Lesion Site	4.021 (2.088–7.744)	= **0.001**	3.477 (1.683–7.184)	= **0.001**

OR, Odd Ratio; CI, Confidence Interval; HR, Hazard Ratio; S, Serum; MMSE, Mini Mental State Examination; BI-1 (Pre-), Barthel Index at presentation; PSEDs, Post-stroke extrapyramidal disorder.

Evaluation of outcome of all stroke patients by BI after 6 months showed that in contrast to 61.2% of patients without PSEDs, 82.6% of patients with PSEDs had poor or very bad outcomes **(Figure 7)**.

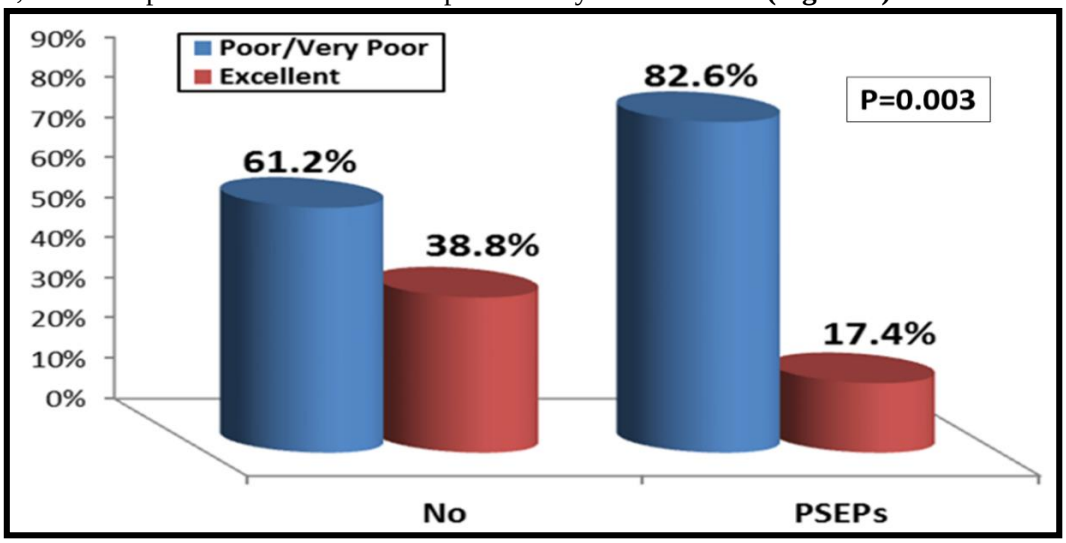

Figure 7: Prognostic Level (BI-2) of Extrapyramidal Cases versus non-Cases
BI-2, Barthel index after 6 months

DISCUSSION

In this study, the frequency of PSEDs was 3.5%, which aligns with the stated frequency range of 1-4% and is comparable to that reported by **Alarcón and colleagues** in 2004 (3.7%) [17,18].

Similarly, **Suri and colleagues** in their systematic review stated that old age and male sex were risk factors for the development of PSEDs; female obesity, which may act as a protective factor, might also play a role [19].

Among vascular risk factors, we identified hypercholesterolemia and diabetes as significant predictors for PSEDs. However, no notable differences were found between patients with PSEDs and controls in terms of other risk factors (hypertension, smoking, or coronary artery disease).

To our knowledge, no previous research has examined the relationship between PSEDs and body mass index (BMI). Our investigation, along with the study by **Park and colleagues** [20] found an inverse relationship between BMI and PSEDs. High levels of circulating and central insulin, which can be influenced by a high BMI, may reduce neurodegeneration in obese individuals, thus protecting them against the onset of PSED [21].

During our study, we observed that the most significant clinical presentations in individuals with PSEDs were sphincter affection, gait deviation, dementia, and cerebellar symptoms. These could be attributed to lesion positioning resulting in intracerebral circuit disruption or functional cortical disconnection, in addition to the impact of inflammatory mediators from the vascular insult or systemic issues related to decreased physical activity [22].

Myung and colleagues noted that PSEDs in patients with mild cognitive impairment (MCI) are a strong risk factor for the progression of MCI to non-Alzheimer dementia [23]. The dentato-rubro-olivary circuit (Guillain-Mollaret triangle), part of the cortico-cerebellar loop, may significantly influence cerebellar manifestations as a predictor of PSED development [7].

We found that deep lesions in the brain stem, basal ganglia, thalamus, or internal capsule were significant contributors to the emergence of PSEDs, and that these lesions were more frequently hemorrhagic than ischemic. Conversely, **Gupta and Pandey** reported that most cases with PSEDs were due to ischemic rather than hemorrhagic strokes [4].

Regarding PSED subtypes, chorea, parkinsonism, and dystonia were the most commonly observed in our patients. **Suri and colleagues** found that dystonia was the most common PSED, followed by chorea and myoclonus [19].

In contrast to patients with parkinsonism, who tended to be older, we discovered that individuals with post-stroke chorea were significantly younger. Conversely, **Suri and colleagues** stated that chorea was more prominent in older age, while dystonia tended to occur in younger patients [19].

Ovodiuk evaluated the quality of life of patients with PSEDs and documented that all extrapyramidal disorders significantly worsen neurological impairment after a stroke; they have a major detrimental effect on the quality of life of stroke survivors by exacerbating the neurological deficits related to the primary focus of brain injury [9].

CONCLUSION

Significant predictors of post-stroke extrapyramidal disorders include old age, diabetes mellitus, hypercholesterolemia, obesity, severe initial stroke, deeply located cerebral lesions, cognitive impairment, and cerebellar manifestations. The most common sites for lesions are the basal ganglia, followed by the parietal lobe. Early detection and intervention are crucial, as post-stroke extrapyramidal disorders significantly impact the outcomes and quality of life of stroke patients.

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