

“Transferrin Saturation And Total Iron-Binding Capacity As Iron-Metabolism Biomarkers In Parkinson’s Disease: Evidence From An Indian Population”

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ABSTRACT

Background: Parkinson’s disease (PD) is a progressive neurodegenerative disorder characterized by dopaminergic neuronal degeneration in the substantia nigra pars compacta and Lewy body formation. Altered iron metabolism is increasingly implicated in PD pathogenesis; however, peripheral iron transport biomarkers remain insufficiently explored, particularly in Indian populations.

Objectives: This study aimed to evaluate transferrin saturation (TSAT) and total iron-binding capacity (TIBC) as peripheral biomarkers of iron metabolism in Parkinson’s disease and to determine their association with disease status.

Methods: A hospital-based case-control study was conducted including 100 clinically diagnosed PD subjects and 100 non-PD subjects which are age- and sex-matched. Serum transferrin, ferritin, TSAT, and TIBC were assessed using automated analyzers. TIBC and TSAT were calculated using standard biochemical formulas. Statistical analysis included independent sample t-test, univariate and multivariable binary logistic regression, and receiver operating characteristic (ROC) curve analysis.

Results: PD subjects showed significantly lower TSAT ($14.17 \pm 5.13\%$ vs. $28.76 \pm 8.10\%$, $p < 0.001$) and ferritin levels (53.91 ± 34.10 vs. 99.65 ± 82.85 , $p < 0.001$), whereas TIBC was significantly higher (88.28 ± 20.18 vs. 81.37 ± 11.20 , $p = 0.003$) compared to controls. In multivariable regression analysis, TSAT remained independently associated with PD (AOR = 0.659; 95% CI: 0.579-0.750; $p < 0.001$). ROC analysis demonstrated modest discrimination for TIBC (AUC = 0.631), while TSAT and ferritin showed inverse AUC values due to their lower distribution among PD cases.

Conclusion: Parkinson’s disease subjects exhibited significant alterations in peripheral iron transport markers. Reduced transferrin saturation emerged as an independent biomarker associated with PD, supporting systemic iron maldistribution and altered functional iron availability in disease pathophysiology.

Keywords: Parkinson’s disease; transferrin saturation; total iron-binding capacity; ferritin; iron metabolism.

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INTRODUCTION

Parkinson’s disease (PD) is the second most common neurodegenerative disorder and is clinically characterized by resting tremor, rigidity, bradykinesia, and postural instability. Neuropathologically, it is characterized by progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and the presence of Lewy bodies containing α -synuclein [1]. Although PD has a complex etiology, increasing evidence suggests that iron metabolism abnormalities play a significant role in disease pathophysiology.

Iron is an essential trace element required for mitochondrial respiration, dopamine synthesis, and neuronal function. However, dysregulated iron homeostasis can be detrimental due to iron’s redox activity, which promotes the generation of reactive oxygen species through Fenton and Haber-Weiss reactions [2]. Postmortem and neuroimaging studies have consistently demonstrated excessive iron

accumulation in the substantia nigra of PD patients, linking iron overload to oxidative stress, mitochondrial dysfunction, α -synuclein aggregation, and neuronal degeneration [3,4]. Ferroptosis, an iron-dependent regulated form of cell death, has also been implicated as an important mechanism linking iron overload to neurodegeneration [5].

Although central iron accumulation is a well-recognized feature of Parkinson’s disease, the role of peripheral iron metabolism remains insufficiently explored. Transferrin saturation (TSAT) and total iron-binding capacity (TIBC) are critical indicators of systemic iron transport and buffering capacity. TSAT represents the proportion of transferrin bound to circulating iron, whereas TIBC reflects the total capacity of transferrin to bind iron in serum [6]. Despite their clinical utility in iron-related disorders, TSAT and TIBC have received comparatively limited attention in Parkinson’s disease research, where most studies have focused on serum iron and ferritin with inconsistent results [7,8].

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Emerging evidence suggests that peripheral iron dysregulation may parallel central iron accumulation and contribute to systemic oxidative stress in PD [9]. India represents a particularly relevant population due to its diverse nutritional patterns, regional environmental exposure, and an increasing burden of Parkinson’s disease [10]. In addition, functional iron deficiency has been proposed as an important mechanism contributing to Parkinson’s disease pathobiology [11]. Impaired systemic iron homeostasis has also been reported previously in PD subjects, supporting the relevance of transferrin-related biomarkers [12]. Therefore, this study aimed to evaluate transferrin saturation and total iron-binding capacity as biomarkers of peripheral iron metabolism in Parkinson’s disease subjects from an Indian population.

MATERIALS AND METHODS

Study Design and Setting

A hospital-based case-control study was conducted in the Department of Biochemistry, Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh, India, in collaboration with the Department of Neurochemistry and Department of Neurology, Institute of Human Behaviour and Allied Sciences (IHBAS), New Delhi, India. The study was carried out over a period of one year.

Ethical Approval

The study was approved by the Institutional Ethics Committees of Santosh Deemed to be University and IHBAS, New Delhi. Written informed consent was obtained from all participants prior to enrolment in accordance with ethical principles outlined in the Declaration of Helsinki [12].

Study Population

A total of 200 participants aged 50-80 years were recruited from the Neurology outpatient department of IHBAS, New Delhi. Subjects were categorized into two groups:

- **Group I (Cases):** 100 clinically confirmed Parkinson’s disease subjects
- **Group II (Controls):** 100 age- and sex-matched healthy individuals

Diagnosis of PD was established using the United Kingdom Parkinson’s Disease Society Brain Bank Criteria [13].

Inclusion Criteria

- Subjects aged 50-80 years
- Clinically diagnosed Parkinson’s disease subjects

- Age- and sex-matched healthy controls

Exclusion Criteria

Participants were excluded if they had:

- Cerebral stroke, tumor, epilepsy, or head trauma
- Parkinson-plus syndrome
- Neurological disorders associated with dementia
- Chronic intake of drugs affecting cognitive processes
- Moderate to severe depressive disorder
- Refusal to provide informed consent

Sample Collection

Approximately 3 mL of venous blood was collected under aseptic precautions in plain vacutainers. Samples were transported to the laboratory within 30 minutes and centrifuged at 3000 rpm for 10-15 minutes. Serum was separated and stored at -20°C until analysis.

Biochemical Analysis

Biochemical investigations were performed on ERBA XL1000 Automated Biochemistry Analyzer (TransAsia Pvt. Ltd.), except ferritin which was measured on ARCHITECT i2000SR analyzer (Abbott Pvt. Ltd.).

Calculation of TIBC and TSAT

Total iron-binding capacity was calculated using transferrin concentration by applying a standard biochemical conversion:

$$\text{TIBC } (\mu\text{mol/L}) = 25 \times \text{Transferrin (g/L)}$$

Transferrin saturation was calculated as:

$$\text{TSAT } (\%) = (\text{Serum Iron} / \text{TIBC}) \times 100$$

Statistical Analysis

Statistical analysis was performed using SPSS software. Quantitative variables were expressed as mean \pm standard deviation (SD). Independent sample t-test was used to compare mean values between PD cases and controls. Binary logistic regression analysis was performed to evaluate crude (univariate) and adjusted (multivariable) associations between biomarkers and Parkinson’s disease. Receiver operating characteristic (ROC) curve analysis was applied to evaluate the discriminatory performance of biomarkers. A p-value < 0.05 was considered statistically significant.

RESULTS

In this study, samples of 100 PD patients and 100 controls were collected and assessed for the biochemical investigations. PD is a disorder of old age, and there is no differentiation based upon gender. Therefore, the findings of this study have been age and gender matched.

Socio-Demographic Parameters:

Table 1: Socio-demographic characteristics of PD Subjects and Non-PD subjects.

VARIABLES		GROUPS		P VALUE
		CASES (N=100)	CONTROL (N=100)	
Age	Mean (SD)	59.77 (7.40)	59.08 (7.14)	0.78
Gender	Male	60 (60.0%)	60 (60.0%)	1.00

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	Female	40 (40.0%)	40 (40.0%)	
Habitat	Rural	27 (27.0%)	42 (42.0%)	0.07
	Urban	73 (73.0%)	58 (58.0%)	
Alcohol	NO	80 (80.0%)	70 (70.0%)	0.10
	YES	20 (20.0%)	30 (30.0%)	
Smoking	NO	79 (79.0%)	82 (82.0%)	0.59
	YES	21 (21.0%)	18 (18.0%)	
Diet	NON-VEG	45 (45.0%)	42 (42.0%)	0.67
	VEG	55 (55.0%)	58 (58.0%)	

Metal Profile in PD and non-PD subjects:

The levels of heavy metals like iron and copper along with the iron profile observed in the serum of both PD and non-PD subjects are shown in Table 2. Serum transferrin levels were significantly high in PD subjects ($p < 0.05$). Transferrin saturation was a calculated value and was found to be lower in PD subjects, and the difference was statistically significant ($p < 0.05$). TIBC was a calculated value and was found to be higher in PD subjects compared to non-subjects, and the difference was statistically significant ($p < 0.05$). Serum ferritin was lower in PD subjects than non-PD subjects, and this difference was found to be statistically significant ($p < 0.05$).

TABLE 2: Metal profile (Serum Iron, Transferrin, Transferrin Saturation, TIBC, Ferritin) in PD Subjects and Non-PD subjects.

Variables	Groups	N	Mean (SD)	95% CI	p-value
Transferrin Saturation	Diseased	100	14.17 (5.13)	13.16 - 15.18	0.000
	Non-Diseased	100	28.76 (8.10)	27.17 - 30.35	
TIBC ($\mu\text{mol/L}$)	Diseased	100	88.28 (20.18)	84.32 - 92.24	0.003
	Non-Diseased	100	81.37 (11.20)	79.18 - 83.56	
Serum Ferritin ($\mu\text{g/dL}$)	Diseased	100	53.91 (34.10)	47.23 - 60.59	0.000
	Non-Diseased	100	99.65 (82.85)	83.41 - 115.89	

Regression Analysis:

Univariate (crude) binary logistic regression analysis showed that transferrin saturation, total iron-binding capacity, and ferritin were each statistically associated with Parkinson’s disease. Lower transferrin saturation was associated with higher odds of Parkinson’s disease (crude OR = 0.673). Total iron-binding capacity showed a positive association with Parkinson’s disease, while lower ferritin levels were also associated with Parkinson’s disease in the univariate analysis (Table 3).

Table 3: Crude (Unadjusted) Binary Logistic Regression Analysis of Iron Metabolism Biomarkers and Parkinson’s Disease

Variable	Crude Odds Ratio (OR)	95% CI	p-value
Transferrin Saturation (%)	0.673	0.605 - 0.748	< 0.001
Total Iron-Binding Capacity ($\mu\text{mol/L}$)	1.027	1.009 - 1.047	0.004
Ferritin (ng/dL)	0.972	0.962 - 0.982	< 0.001

In multivariable binary logistic regression analysis, transferrin saturation remained statistically associated with Parkinson’s disease after adjustment for total iron-binding capacity and ferritin (AOR = 0.659, 95% CI: 0.579-0.750; $p < 0.001$). Total iron-binding capacity and ferritin were not statistically significant in the adjusted model ($p > 0.05$) (Table 4).

While total iron-binding capacity and ferritin showed statistically significant associations in univariate analysis, these associations were not observed in the multivariable analysis. The adjusted model therefore identified transferrin saturation as the only variable that remained statistically significant among the iron metabolism markers evaluated.

Table 4: Adjusted Binary Logistic Regression Analysis of Iron Metabolism Biomarkers and Parkinson’s Disease

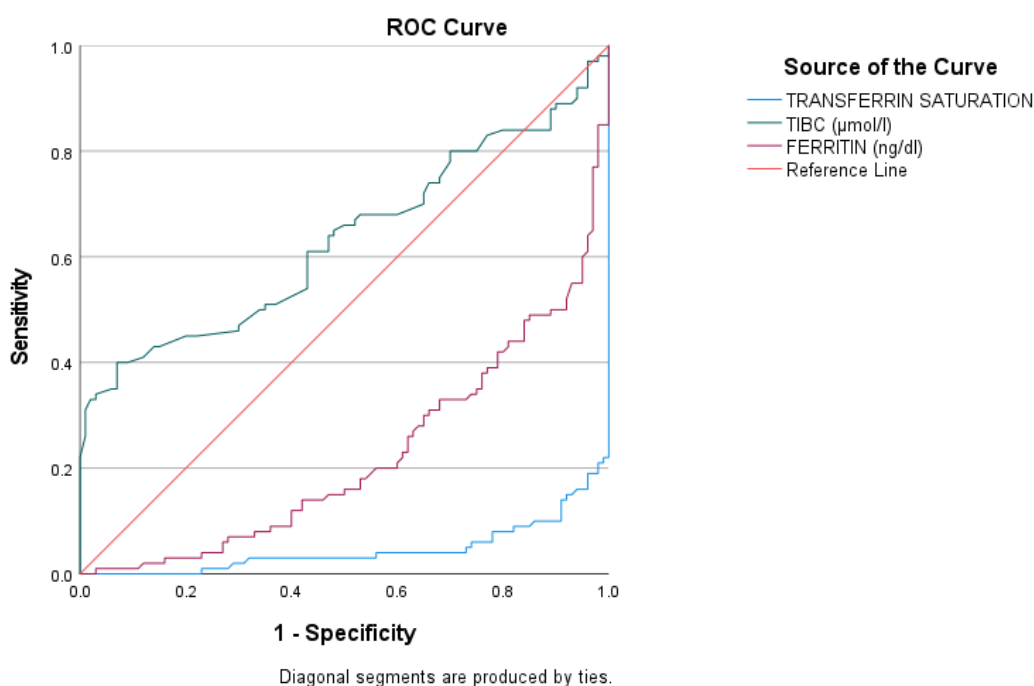
Variable	Adjusted Odds Ratio (AOR)	95% CI	p-value
Transferrin Saturation (%)	0.659	0.579 - 0.750	< 0.001
Total Iron-Binding Capacity ($\mu\text{mol/L}$)	0.97	0.936 - 1.006	0.104
Ferritin (ng/dL)	0.993	0.979 - 1.007	0.331

Receiver operating characteristic (ROC) Curve

ROC curve analysis revealed statistically significant discrimination for all three iron metabolism biomarkers ($p < 0.05$). Transferrin saturation and ferritin demonstrated AUC values below 0.5, indicating inverse discrimination relative to Parkinson’s disease status, whereas total iron-binding capacity showed modest discriminative ability with an AUC of 0.631 (Table 5).

Table 5. Receiver operating characteristic (ROC) curve analysis showing the area under the curve (AUC) for iron metabolism biomarkers in relation to Parkinson’s disease.

Test Result Variable	Area Under the Curve (AUC)	Standard Error	p-value	95% CI
Transferrin Saturation (%)	0.046	0.015	< 0.001	0.017 - 0.075
Total Iron-Binding Capacity ($\mu\text{mol/L}$)	0.631	0.04	0.001	0.553 - 0.710
Ferritin (ng/dL)	0.223	0.032	<0.001	0.159 - 0.286



Graph 1: Lower values of transferrin saturation and ferritin were associated with Parkinson’s disease; therefore, AUC values below 0.5 indicate inverse discrimination.

DISCUSSION

The present case-control study evaluated transferrin saturation and total iron-binding capacity as peripheral biomarkers of iron metabolism in Parkinson’s disease subjects from an Indian population. Since socio-demographic characteristics were comparable between PD subjects and controls, the biochemical differences observed are unlikely to be influenced by demographic confounding.

In this study, transferrin saturation was significantly reduced in PD subjects compared to controls, suggesting impaired systemic iron transport and reduced functional iron availability. This finding supports the concept that Parkinson’s disease may involve not only localized brain iron accumulation but also systemic iron dysregulation. Recent evidence has highlighted that iron mishandling occurs in both central and peripheral compartments,

reinforcing the hypothesis of iron maldistribution in PD [13]. Reduced TSAT may reflect altered transferrin-mediated iron delivery, which could contribute indirectly to oxidative stress and neuronal vulnerability. TIBC was significantly higher in PD subjects, indicating increased iron-binding capacity in circulation. Elevated TIBC combined with reduced TSAT suggests that compensatory transferrin upregulation may occur in response to decreased bioavailable iron. Similar alterations in serum iron-related parameters have been reported in idiopathic Parkinson’s disease, supporting the relevance of peripheral iron profile abnormalities [14].

Ferritin levels were also significantly lower in PD subjects compared to controls. Ferritin is an important marker of systemic iron storage, and reduced ferritin may indicate altered peripheral iron reserves or

redistribution of iron into other compartments. Evidence from previous investigations suggests that peripheral iron indices may not consistently mirror central iron deposition. Shen et al. reported that while blood iron may not differ significantly, cerebrospinal fluid iron levels may decrease in PD, supporting the possibility of compartmental redistribution [15]. Additionally, Chen et al. evaluated ferritin and transferrin receptor levels in plasma neural-derived exosomes and suggested that iron-related biomarkers may have diagnostic relevance in PD [16].

The present regression analysis demonstrated that TSAT, TIBC, and ferritin were associated with Parkinson’s disease in univariate analysis; however, after multivariable adjustment, only TSAT remained independently associated with PD. This indicates that transferrin saturation may represent a more sensitive marker of systemic iron transport disturbance compared to isolated indicators of iron storage or binding capacity. Several studies have reported variability in peripheral iron markers among PD subjects. Mariani et al. conducted a replication study and meta-analysis and observed that peripheral Fe and Cu parameters may not consistently differ across PD cohorts, indicating population-specific variations [17]. Mechanistically, altered expression of iron transport proteins such as divalent metal transporter-1 has been implicated in iron accumulation processes and may contribute to dysregulated iron trafficking in PD [18]. Furthermore, Tripathi et al. demonstrated that iron profile parameters could classify PD cases from controls with good diagnostic accuracy, supporting the possible utility of iron biomarkers in disease discrimination [19].

ROC curve analysis in the present study showed modest discrimination for TIBC, whereas TSAT and ferritin demonstrated inverse AUC values due to their lower distribution among PD subjects. This inverse discrimination indicates that lower TSAT and ferritin values are characteristic features of Parkinson’s disease. Overall, the findings support the potential clinical relevance of transferrin saturation as a peripheral biomarker of systemic iron transport dysregulation in Parkinson’s disease.

CONCLUSION

The present study demonstrated significant alterations in peripheral iron metabolism markers in Parkinson’s disease subjects compared to healthy controls. Transferrin saturation and ferritin were significantly reduced, whereas total iron-binding capacity was significantly increased in PD subjects. Although TSAT, TIBC, and ferritin were associated with PD in univariate analysis, only transferrin saturation remained independently associated with Parkinson’s disease after adjustment. These findings suggest that reduced transferrin saturation may serve as a clinically relevant peripheral biomarker reflecting altered systemic iron transport and iron maldistribution in Parkinson’s disease.

References

1. Kalia LV, Lang AE. Parkinson’s disease. *Lancet*. 2015;386(9996):896-912.
2. Ward RJ, Zucca FA, Duyn JH, Crichton RR, Zecca L. The role of iron in brain ageing and neurodegenerative disorders. *Lancet Neurol*. 2014;13(10):1045-1060.
3. Dexter DT, Wells FR, Agid F, et al. Increased nigral iron content in postmortem Parkinsonian brain. *Lancet*. 1987;2(8569):1219-1220.
4. Zecca L, Youdim MBH, Riederer P, Connor JR, Crichton RR. Iron, brain ageing and neurodegenerative disorders. *Nat Rev Neurosci*. 2004;5(11):863-873.
5. Stockwell BR, Friedmann Angeli JP, Bayir H, et al. Ferroptosis: A regulated cell death nexus linking metabolism, redox biology, and disease. *Cell*. 2017;171(2):273-285.
6. Uversky VN, Li J, Fink AL. Metal-triggered structural transformations, aggregation, and fibrillation of human α -synuclein. *J Biol Chem*. 2001;276(47):44284-44296.
7. Logroscino G, Marder K, Graziano J, et al. Altered systemic iron metabolism in Parkinson’s disease. *Neurology*. 1997;49(3):714-717.
8. Savica R, Grossardt BR, Ahlskog JE, et al. Iron deficiency anemia and Parkinson disease risk. *Neurology*. 2009;73(18):1381-1387.
9. Andrews NC. Disorders of iron metabolism. *N Engl J Med*. 1999;341(26):1986-1995.
10. Pringsheim T, Jette N, Frolkis A, Steeves TD. The prevalence of Parkinson’s disease: A systematic review and meta-analysis. *Mov Disord*. 2014;29(13):1583-1590.
11. Peikon I, Andrews NC. Isn’t it ironic? Functional iron deficiency at the core of Parkinson’s disease pathobiology. *J Clin Invest*. 2026;136(1):e202244.
12. Gangania MK, Batra J, Kushwaha S, Aggarwal R. Impaired systemic iron homeostasis and Parkinson’s disease. *J Med Sci Clin Res*. 2017;5(4):20855-20859.
13. Bolen ML, Menees KB, Dupreez AC, Gámez Tansey M. Iron mishandling in the brain and periphery in Parkinson’s disease. *NPJ Parkinsons Dis*. 2025;11:246.
14. Farhoudi M, Taheraghdam A, Farid GA, Talebi M, Pashapou A, Majidi J, et al. Serum iron and ferritin level in idiopathic Parkinson. *Pak J Biol Sci*. 2012;15(22):1094-1097.
15. Shen X, Yang H, Zhang D, Jiang H. Iron concentration does not differ in blood but decreases in cerebrospinal fluid in Parkinson’s disease. *Front Neurosci*. 2019;13:939.
16. Chen ZT, Pan CZ, Ruan XL, Lei LP, Lin SM, Wang YZ, et al. Evaluation of ferritin and TfR level in plasma neural-derived exosomes as potential markers of Parkinson’s disease. *Front Aging Neurosci*. 2023;15:1216905.
17. Mariani S, Ventriglia M, Simonelli I, Donno S, Bucossi S, Vernieri F, et al. Fe and Cu do not differ in Parkinson’s disease: a replication study plus meta-analysis. *Neurobiol Aging*. 2013;34(2):632-633.

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18. Xu HM, Jiang H, Wang J, Luo B, Xie JX. Over-expressed human divalent metal transporter 1 is involved in iron accumulation in MES23.5 cells. *Neurochem Int.* 2008;52(6-7):1044-1051.
19. Tripathi CB, Gangania M, Kushwaha S, Agarwal R. Evidence-based discriminant analysis: a new insight into iron profile for the diagnosis of Parkinson’s disease. *Ann Indian Acad Neurol.* 2021;24(2):234-238.