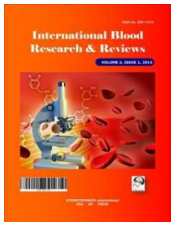

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ABO & Rh (D) Phenotypes and Alleles in the Patients with Parkinson's Disease among the North Indian Population

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Authors' contributions

This work was carried out in collaboration between all authors. Authors RS and AKV designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors AKK, RK and TK managed the literature. Author TBS helped in the statistical analyses of the study. Author VS provided the cases for the study. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Recent studies have pointed the association of blood groups with cognitive impairment and dementia. This study was planned to find the frequencies of ABO, Rh (D) alleles and examine the effect of their phenotype in the patients with Parkinson's disease (PD) in north Indian population.
Place and Duration of Study: The study was conducted in the Department of Biochemistry with the association of Department of Neurosurgery, Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), India for the period of September-2011 to August-2015.
Study Design: ABO and Rh alleles were determined in 240 patients with PD and 940 healthy individuals, which were selected as cases and controls respectively. Blood groups typing were

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done with rapid slide method. Allelic frequencies were calculated by using Hardy- Weinberg principle.

Results: Chi- Square (χ^2) test was significant for the comparison of various ABO blood groups in between cases and controls ($P < 0.001$). According to Z-test of proportion, the frequencies of phenotype A, B and allele I^A were not significantly altered in cases as compared to controls ($P > 0.05$). While, frequencies of phenotype AB and allele I^B were significantly increased and frequency of phenotype O and allele I^O were significantly decreased (all $P < 0.01$). The observed phenotypes of Rh (D) blood groups and frequencies of allele D and d were not significantly altered in cases when compared with controls ($P > 0.05$).

Conclusions: Study showed the increased frequencies of phenotypes B, AB and alleles I^B along with decreased frequencies of phenotype O and allele I^O among the patients with PD than normal population. It seems that the phenotypes AB and allele I^B may have the risk against the development of Parkinson's disease; while phenotype O and allele I^O may have the protective action.

Keywords: ABO blood group; Rh (D) blood group; Parkinson's disease; ABO alleles; Rh (D) alleles.

1. INTRODUCTION

The ABO blood group system is the most important blood type system (or blood group system) in human blood transfusion. In addition to the ABO system, the Rh blood group system can affect transfusion compatibility. An individual is either positive or negative for the Rh factor; this is denoted by a '+' or '−' after their ABO type. The genes of ABO blood groups are located on the chromosome 9q34.2 position [1-4]. ABO and Rh (D) blood groups distribution varies from different geographical area and races. ABO and Rh (D) blood groups distribution also varies from disease to disease. Its association with different diseases, like diabetes mellitus [5], coronary heart disease [6], pancreatic cancer [7], breast cancer [8], brain tumor [9], congenital neurosurgical diseases [10] dementia and cognitive impairment [11,12] has been reported.

Parkinson's disease (PD) is a second most common neurodegenerative disorder, which is characterized by bradykinesia, tremor, rigidity and increased oxidative stress [13,14]. It is a chronic and progressive neurodegenerative disorder of the brain. The motor symptoms of Parkinson's disease result from the death of dopamine-generating cells in the substantia nigra, a region of the midbrain. PD is more common in the elderly and incidence rises from 1% in those over 60 years of age to 4% of the population over 80 [13,14]. Till date, early diagnosis of PD from blood is not possible.

In 1966, Strang described the ABO blood groups distribution in the patients with PD among the Swedish population; while in 1970, Kak and Gordon reported ABO blood groups in the patients with PD among the population of Northern Ireland [15,16]. There is no study present in literature regarding association of ABO and Rh (D) blood groups (phenotypes and allelic frequency) in the patients with PD among the north Indian population. Thus, the present study was aimed to observe ABO & Rh (D) phenotypes and alleles in Parkinson's disease among the population of north India.

2. MATERIALS AND METHODS

This study was a Hospital based study, which was conducted in the Department of Biochemistry, Institute of Medical Sciences (IMS), Banaras Hindu University, (BHU), Varanasi, UP, India. Institutional ethical approval to carry out this study was taken. Self signed inform consent was taken from every studied subject.

240 patients with PD enrolled in the out patients department (OPD) of Sir Sunder Lal Hospital, IMS, BHU from September-2011 to August-2015 were taken as case group. A total of 960 normal healthy individuals were considered as control group. The cases and controls were matched in reference to ethnicity and races. All the studied subjects belonged to the different cities of the north India.

Blood was taken from finger pricks. ABO and Rh (D) blood groups were tested according to open slide method [17]. Allele frequencies of ABO and Rh (D) blood groups were calculated by Mourant et al. [18], method which is based on the Hardy Weinberg principles.

2.1 Statistical Calculations

The blood group phenotypes and frequencies, both were compared to each other with the use of both Chi-square test and Z- test of proportion for better clarification. The value of P ≥ 0.0 5 was considered as not-significant; while P < 0.05, < 0.01 and < 0.001 were considered as significant, high significant and highly significant respectively. M- STAT and SPSS (Version 16) software were used.

3. RESULTS

Observed phenotypes of ABO blood groups and allelic frequencies in the cases and controls are presented in Table 1.

Chi- Square (χ^2) test was significant regarding to comparison of altered ABO phenotypes in between cases and control groups (P < 0.001, Table 1). Z test of proportion was also calculated for evaluation of significance. Results showed that, the observed frequency of phenotypes A and B were not significantly altered in the cases as compared to controls. Observed frequency of phenotype AB was significantly increased, while phenotype O was significantly decreased in the cases than controls (Table 1).

Observed allelic frequency I^A was not significantly altered between cases and controls. However the frequency of allele B (I^B) was significantly increased and the frequency of allele O (I^O) was significantly decreased in the cases as compared to controls (Table 1).

Observed phenotype of Rh (D) factor and their allelic frequency were not significantly altered in the cases as compared to controls (Table 2).

4. DISCUSSION

The study included 240 patients with PD as cases, who came to the OPD of Sir Sunder Lal hospital, IMS, BHU, Varanasi during the period of September-2011 to August-2015. For the comparison purpose a total 960 healthy individuals were selected as controls in accordance of matched ethnicity and races.

There are number of studies present in the literature regarding ABO and Rh (D) blood group distribution among the normal population of north India. Out of which, four literature studies have been selected and grouped as group-I to IV for comparison purposes (Table 3). Sharan, 1970, (group-I), has reported ABO blood group distribution among the normal population of different districts of Bihar. According to him, the distribution of phenotypes A , B , AB and O has been observed as 21.55%,38.36%, 8.66%, 31.42% respectively [19], (Table 3). Yadav et al. [20], (group-II), have also reported the highest frequency of phenotype B followed by O, A, and AB in normal population of Bihar, (Table 3). Other studies by Chandra and Gupta, 2012, (group-III) and Gangwar et al. (group-IV), have reported the same patterns of ABO blood group distribution among normal population of Uttar Pradesh [21,22] (Table 3). Present study also represented the same patterns of ABO and Rh blood groups distribution among normal population of north India. The distribution of phenotypes A, B, AB, O, Rh^{+ve} and Rh^{-ve} were 21.04%, 35.94%, 8.44%, 34.58%, 94.89% and 5.10 % , respectively) (Tables 1 and 2).

In the present study, it is seen that the frequency of phenotype B (41.25 %) and AB (15.42 %) in patients with PD is higher than the frequency of these phenotypes in normal population (B-35.94% and AB-8.44%); while the frequency of phenotype O (22.50 %) is significantly decreased in PD patients as compared to controls (34.58%) as shown in Table 1. The difference in the distribution of phenotype A between patients with PD (20.83 %) and normal population (21.04%) is not-significant (Table 1).

Table 1. Representation of ABO blood group phenotypes and their allelic frequencies in the cases and controls

	Cases n = 240% (numbers)	Controls n = 960% (numbers)	Z- value (P-value)
Observed ABO phenotypes			
A	20.83 (50)	21.04 (202)	0.071 (0.471)
B	41.25 (99)	35.94 (345)	1.52 (0.064)
AB	15.42 (37)	8.44 (81)	3.25 (< 0.01)
O	22.50 (54)	34.58 (332)	3.58 (< 0.001)
Observed allelic frequency			
I^A	0.1995	0.1603	1.45 (0.073)
I^B	0.3389	0.2545	2.63 (0.004)
I^O	0.4615	0.5899	3.59 (< 0.001)

Z-value of proportion was calculated for observing of p-value. P-value < 0.05 was considered as significant. Another test, Chi- Square (χ^2) test was also used for the comparison of cases and controls (P < 0.001)

The difference of allelic frequency of allele I^A in the patients with PD (0.1995) and the normal population (0.1603) is not significant (Table 1) while the frequency of allele I^B is

significantly increased and the frequency of allele I^O is significantly decreased (Table 1) in patients of PD as compared to normal population.

According to the present study, the difference in the distribution of phenotypes of Rh (D), positive and negative in the patients with PD (94.59% and 5.42% respectively) and normal population (94.89% and 5.10% respectively) is statistically non-significant (Table 2). The allelic frequencies of allele D and d were 0.7673 and 0.2327 in the patients with PD and 0.7741 and 0.2259 in the normal population which is also statistically non-significant (Table 2).

When case group of present study was compared to selected literature groups I, II, III and IV, then above similar patterns of alteration in the distribution of ABO and Rh (D) blood group and their alleles has been observed (Tables 3 and 4).

Recent studies have reported that O blood group has protection against neurodegeneration and cognitive impairment in comparison to non O blood groups; while AB phenotype has higher incidence of cognitive deficiency [11]. Alexander et al., 2014, have also reported that blood group AB is associated with increased cognitive impairment [12]. Kak and Gordon, 1970, have reported that the incidence of phenotype B and AB were higher in the patients with PD as compared to controls [16]. In our present study, we also observed that the frequencies of the phenotypes B and AB and allele I^B are higher in the patients with PD than the normal population (Table 1). These values are also higher than the most of the previously reported studies on normal population of north India [19-22]

Table 2. Representation of Rh (D) blood groups and their allelic frequencies in the cases and controls

Variables	Cases (n = 240)		Controls (n = 960)		Sig.- value
	% (numbers)	Allelic frequency	% (numbers)	Allelic frequency	
Rh (D) positive	94.58 (227)	D = 0.7673	94.89 (911)	D = 0.7741	Non- significant
Rh (D) negative	5.42 (13)	d = 0.2327	5.10 (49)	d = 0.2259	

Table 3. Representation of ABO & Rh (D) blood groups and their allelic frequency distribution in the normal population of north India. Data were collected from different four literatures, which are named as group I, II, III and IV

Literature groups	Authors/ work place	Year	ABO & Rh (D) Blood group distribution (%)						Allelic frequencies	Reference
			A	B	AB	O	Rh (D) positive	Rh (D) negative		
I.	Sharan / Bihar N = 9257	1970	21.55	38.36	8.66	31.42	…	…	I^A = 0.1663 I^B = 0.2770 I^O = 0.5566	[19]
II.	Yadav et al. / Bihar N = 2500	2014	21.48	37.08	8.36	33.08	…..	…..	I^A = 0.1652 I^B = 0.2622 I^O = 0.5726 (Calculated)	[20]
III.	Chandra and Gupta. / UP N = 23320	2012	21.50	34.84	13.91	29.75	95.45	4.55	I^A = 0.1938 I^B = 0.2805 I^O = 0.5255 (Calculated)	[21]
IV.	Gangwar et al. / UP N = 15670	2012	21.94	35.66	9.73	32.67	95.76	4.24	I^A = 0.1729 I^B = 0.2601 I^O = 0.5670 (Calculated)	[22]
Present study, healthy population, N = 960		….	21.04	35.94	8.44	34.58	94.89	5.10	I^A = 0.1603 I^B = 0.2545 I^O = 0.5670	….

N = Total number of subjects, UP = Uttar Pradesh, Calculated = the values were calculated with the use of respective literature data

Table 4. Values of Z- test of proportion for the ABO and Rh (D) phenotypes and alleles, when different literature groups (I, II, III & IV) compared to cases group of present study

Compared groups	Z- value for ABO and Rh blood group phenotypes						Z- value for ABO and Rh alleles				
	A	B	AB	O	Rh^{+ve}	Rh^{-ve}	I^A	I^B	I^O	D	d
Cases with Group I	NS	NS	3.64***	2.95**	….	….	NS	2.11*	2.93**	….	….
Cases with Group II	NS	NS	3.63***	3.21***	….	….	NS	2.56**	3.31***	….	….
Cases with Group III	NS	2.07*	NS	2.44*	NS	NS	NS	2.00*	2.28*	NS	NS
Cases with Group IV	NS	1.98*	2.94**	3.34***	NS	NS	NS	2.76**	3.27***	NS	NS
Cases with present study controls	NS	NS	3.25**	3.58***	NS	NS	NS	2.63**	3.59***	NS	NS

** = P < 0.05, ** = P < 0.01, *** = P < 0.001, A P- value ≥ 0.0 5 was considered as non-significant; while < 0.05, < 0.01 and < 0.001 were considered as significant, high significant and highly significant respectively. NS = Non-significant*

(Tables 3 and 4). The frequency of phenotype O and allele I^O is significantly decreased in the patient with PD than the normal population. Thus, it seems that blood group B, AB and allele I^B have the increased risk for the development of Parkinson's disease; while blood group O and allele I^O may have the protective action.

5. CONCLUSIONS

The distribution of phenotypes B, AB and frequency of allele I^B is increased in the patients with PD as compared to normal population; while phenotype O and frequency of allele I^O is significantly decreased. Thus, it seems that the phenotypes AB, B and allele I^B may have the risk against the development of Parkinson's disease; while the phenotype O and allele I^O may have the protective action. It is also concluded that the distribution of Rh (D) phenotypes and their alleles does not alter in between patients with PD and normal population. More explorative studies are needed to prove this hypothesis.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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