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RESEARCH ARTICLE

EPIDEMIOLOGICAL STUDY OF NEURODEGENERATIVE PARKINSONISM IN "HAZRATBAL BLOCK" A SPECIFIC REGION OF KASHMIR VALLEY - NORTH INDIA - A LONGITUDINAL COHORT STUDY

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ABSTRACT

Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder, commonly found in males above the age of 60. Increased life expectancy due to better health care and aging population will see a proportional rise in case of PD in India during next three decades making it a major health problem. ***Objectives****:* There was no well designed longitudinal study on PD from Kashmir, North-India. Therefore, we planned to determine the prevalence, type of PD & associated probable risk factor for PD in the Kashmir valley, North India, on a stratified random sampling through a door-to-door survey. ***Material and Method:*** A prospective community - based study was conducted over a period of three years from May 2010 – May 2013 after obtaining approval from the Institutional Ethical Committee & informed written consent. The study population consisted of all subjects above 7 years of age. The screening was conducted in 2 stages, initially a validated questionnaire was pretested and subjects were interviewed & clinically examined by team of Doctors. In later stage, cases with both typical and atypical features of PD underwent detailed examination by a neurologist at SMHS Hospital, a tertiary referral centre and requisite investigation done wherever deemed necessary. ***Results:*** The total number of subjects screened were 13710, out of them 39 were found to have PD, with overall prevalence of 0.28 % (280/100,000). The peak prevalence of PD was in the age group of 70-79 years with male prepondance M:F ratio (1.4:1) , Predominant symptom was Tremor (74.4%) followed by bradykinesia. The distribution of parkinsonism in our study was idiopathic PD 59%, drug induced PD 17.9%, Parkinson plus syndrome 15.4% and vascular Parkinsonism in 7.7%. The Prevalence of PD was more in rural population compared to urban. Exposure to agricultural chemicals, Pesticides, and prolonged well water consumption were also possible risk factors for PD. ***Conclusion:*** The prevalence of PD in our part of world is less as compared to Europe and western world. This study documents the epidemiological data of PD in Kashmir valley (Hazratbal Block). It represents varied geographical, social, economic, cultural ethnicity among rural/urban population. There is low literacy rate, predominant rural population and insufficient health infrastructure where PD poses an invisible but major health problem for policy makers.

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INTRODUCTION

Parkinson's disease (PD) is one of the most common age related neurodegenerative disease (Benjamin, 2001). It is estimated that approximately 6.3 million people suffer from PD worldwide. Among hospital based series of 2,43,021 new patient, 27% had neurological disorders, of which 20% had movement disorders and PD was the third common neurological disorder and the commonest movement disorder (86.5%) (Das, 1996). Out of the world's 580 million elderly (over 60 years), 60% live in developing countries and 22% live in India.

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Caring of this increasing elderly population with increase in age related disease (PD and Alzheimer's) can be very challenging. This is because of the fact that 80% of elderly Indians live in rural areas, 73% are illiterate, 60% are women and 60% live below the poverty line. Moreover in a study it has been projected that 6 out of 10 most populous countries of the world are in Asia (China, India, Indonesia, Pakistan, Bangladesh and Japan). The number of PD patients in these countries is expected to increase from 2.57 million in 2005 to 6.17 million in 2030 (Muthane, 2007). The only solace that PD has a low prevalence in India and Asian countries except in the small ethnic Parsi community of Mumbai (Tan Louis, 2013; Bharucha *et al*., 1988). PD is a slowly progressive disorder with no identifiable cause. Due to degeneration of *substantia nigra* neurons, there is depletion of dopamine neurotransmitter

which disturbs the transmission of signals between substantia nigra and the next relay station of the brain, the *corpus striatum*, which is responsible to produce smooth purposeful movement. It is diagnosed clinically by four major symptoms - *tremors* (hands, arms, legs, jaw and head), *rigidity* (stiffness of limbs and trunk), *bradykinesia* (slowness of movement) and *postural instability* (impaired balance). There is always a diagnostic dilemma as a single patient may not have all the symptoms at single point of diagnosis. Hence frequent follow up is necessary over the long period to have complete picture. Neurologists in principle have agreed that presence of two symptoms is enough for clinical diagnosis of PD. There are other conditions which mimic PD with additional neurological symptoms and are called atypical Parkinsonism – e.g. multiple system atrophy (MSA), progressive supranuclear palsy (PSP), striatonigral degeneration etc. The term Parkinsonism is also used where the aetiology of above symptoms are known, such as Parkinsonian signs due to stroke, infection, neuroleptic drugs and sometimes toxic agents.

Epidemiology of PD is beneficial in two ways for India. It provides highly probable risk factors for developing PD which can guide to achieve a clue of aetiology if further evaluated. Secondly India is a multi-ethnic country with genetic diversity and it needs proper healthcare planning and better investigative infrastructure for research into the aetiology of PD. With increased life expectancy and better healthcare, India is going to have huge disease burden due to PD in future. But so far, there is no prospective study to estimate its incidence and mortality except one (Das *et al*., 2010**).** Most of the epidemiological factors associated with PD have been obtained from case – control studies. However, in recent years, more prospective cohort studies have recorded sufficient data on PD to study the risk or protective factors in PD. Till date no epidemiological study exclusively on the prevalence of Parkinsonism has been undertaken in this part of the world. Our study is the maiden endeavor as regards the prevalence of Parkinsonism and will help us to understand the magnitude of this problem in this part of the world.

Aims and Objectives: The Primary objectives is to study the Prevalence of Parkinsonism as, Idiopathic Parkinson's disease, Drug induced Parkinsonism & Parkinson's plus Syndrome.

MATERIALS AND METHODS

A prospective community - based study was conducted over a period of three years from May 2010 – May 2013 after obtaining approval from the Institutional Ethical Committee & written informed consent. The study population consisted of all subjects above 7 years of age. The screening was conducted in 2 stages, initially a validated questionnaire was pretested and subjects were interviewed & clinically examined by team of Doctors. In later stage, cases with both typical and atypical features of PD underwent detailed examination by a neurologist at SMHS Hospital, a tertiary referral centre and requisite investigation done wherever deemed necessary.

Sampling Methods

The sample size was determined by using multistage sampling. The village / Mohalla was selected by simple random sampling method (using lottery method) , while as subsequent sample was taken by cluster random sampling. Three villages /Cluster at a random from each four zones were selected that comprised a population of 16,107. Among selected clusters /villages, survey was conducted by visiting each household and sample size was determined by population aged more than 7 years, which was 13,710 was taken considering inclusion criteria. Diagnosis of Parkinson's disease was established by adopting the Euro-Parkinson's collaborative study (Mc de Rijik, 1997).

Criteria

- Resting tremor
- Bradykinesia
- Rigidity
- Postural instability (festenant gait)

Positive Respones to Levodopa

Drug Induced Parkinsonism (Schrag, 2000): Dopamine receptor blocking drugs had been started within six months of onset of symptoms and taken for at least six months.

Vascular Parkinsonism

If two of the following were present

- History of stroke
- Abrupt onset with stepwise progression
- Hypertension
- Wide based gait with small steps
- Cognitive decline
- Pseudobulbar or pyramidal signs

Diagnostic Criteria for Parkinson Plus Syndrome

Clinical Features of Dementia Associated with Parkinson's Disease (Emre Murat, 2003)

Cognitive Features

- **Attention:** Prominent impairment with fluctuation.
- **Memory:** Moderate impairment, retriveval deficits with relative spared storage.
- **Executive Feature:** Severely impaired.
- **Visuospatial Feature:** Early and substantial impairment.
- **Language:** Impaired word finding and verbal fluency.

Behavioural Features

- Apathy
- Hallucination
- Delusion
- Depressive symptoms

Motor Functions

- Symmetrical involvement
- Prominent postural instability or gait disorder
- Tremor dominance less frequent.

Statistical Methods

Data was described as mean +_ SD and Mean. Metric data was compared by using Students T test, where as nonmetric data was compared by Mann Whitneys U test and Chi square test.

Data analysis was performed with SPSS & Microsoft Excel software.

OBSERVATION AND RESULTS

Total number of subjects screened were 13,710, out of which 39 were found to have parkinsonism, yielding a total prevalence of 0.28% (280/100,000), (Table 1). 56.9% belonged to rural area, whereas 43.1% belongs to urban area & the difference was statistically insignificant with p value >0.05, (Table 2). A total of 39 (0.28%) subjects were found to have parkinsonism, out of them 23 (0.33%) were males & 16 (0.24%) were females. Resting Tremor was predominant symptom followed by Bradykinesia, Rigidity & Postural instability, (Table 3). Idiopathic PD was the commonest type found in 59%, drug induced PD 17.9%, Parkinsons plus syndrome 15.4% & vascular PD in 7.7% respectively (Table 4). The distribution of PD across the age shows that maximum number of subjects were in the age group of 70-79 yrs (n=22) followed by > 80 years (n=8) & subsequently followed by 60-69 years (n = 5) & < 60 years age group (n=4), (Table 5). The Forgetfulness was present in 15.4% cases, Pesticide Exposure 48.7%, history of old stroke 7.7%, well water consumption 5.1% & smoking in 17.9% of cases. The difference was statistically insignificant with value of > 0.05 (Table 6).

DISCUSSION

Till date no epidemiological studies exclusively on the prevalence of Parkinsonism has been undertaken in this part of the world, and our neuroepidemological study is the first of its kind to study the prevalence and magnitude of this problem in this part of the world. The various studies conducted in Asian countries concluded that prevalence of Parkinson's disease were lower than that of western countries. Such differences may be due to documented differences in prevalence of genetic polymorphism associated with Parkinson's disease or due to differences in environmental factor. In our study prevalence of Parkinsonism was found to be 0.28% (280/100,000) which was lower as compared to the studies conducted in the western world. The prevalence rate was directly proportional to male gender. Among the studies conducted in India Bharucha *et al.* found the highest prevalence of Parkinson's disease in Parses community of Bombay (328.3/100,000). Similarly a study conducted in Karnataka by Gori Devi *et al.* showed the crude prevalence rate of Parkinson's disease was 6/100,000. A similar study was conducted by SK Das *et al.* in Karnataka found the crude prevalence rate per lac of Parkinson's disease to be 52.85. Das *et al.* also found crude prevalence rate of Parkinson's disease in Bengal as 16/100,000.

Weerask Muangpaisan *et al* (2009) found the prevalence of Parkinson's in Asia and concluded a standardized all age prevalence of 51.3 to 176.9/100,000 population in a door to door study and concluded that prevalence of Parkinson's disease in Asian countries where slightly lower than that in western countries. Worldwide prevalence rate ranges from 57/100,000 in China (1985) to 371/100,000 in Sicily (Morgante, 1992). A prevalence of 347/ 100,000 was reported in the population over age 40 years in Copiah County, Missippi (Schoenberg, 1985). Based on the US population of 1950, the cumulative life time risk of Parkinsonism was estimated at 2.4% (Kurland, 1958).

MC de Rijik *et al*. (1997) found the prevalence of Parkinsonism of 2.3% and 1.6% for Parkinson's disease in subject 65 years and older. One recent study in Holland found prevalence of Parkinsonism to be 1.4% (14/1000) people over age 55 years and 4.3% (43/1000) in the population 85years and older (De Rijik, 1995). In our study we found 39 subject with Parkinsonism, 23 effected by idiopathic Parkinson's disease (59%), 7 cases of drug induced Parkinsonism (17.9%), 6 cases of Parkinson's plus syndrome (15.4%) and 3 cases of vascular Parkinsonism (7.7%). Some results of our study like drug induced Parkinsonism (17.9%) and vascular Parkinsonism (7.7%) was in agreement with the results found the Schrag *et al* (2000), but idiopathic Parkinson's disease which was 59% in our study was less was compared to the study done by Schrag *et al* (2000). In our study, the peak prevalence were in the age group of 70-79 years which was in accordance with the study conducted by D. Alessandro *et al*. (1998), Kis *et al*. (2002) who reported a peak prevalence at the age of 70-79 years. In our study the prevalence was more in males than female with M: F ratio of 1.4:1. Which is in accordance with the world literature. In our study, the predominant symptom was resting tremor (74.4%) followed by bradykinesia (59%), rigidity (59%) and postural instability (41%), Which was in accordance with the study conducted by Lie Gan Chia *et al*. (1992) where Tremor was seen in 77% of patients with leading symptoms and usually involves the hand in (75%). In males the predominant symptom was unilateral resting tremor mostly involving right arm and hand, where as majority of the female patients had combination of symptoms which was consistent with the western data. In our study poly- smptomatic form in female was possibly due to less disease awareness and social constraints among females.

Our study has shown Parkinson's disease was more common in rural residents which was in accordance with the world literature. In our study 21 (53.8%) of Parkinson's patients were rural residents and 18 (46.2%) were urban residents. However the difference in prevalence between rural and urban population of Parkinson's disease was statistically insignificant. JP Huble *et al*. (1993) in their study have found rural residency including years of rural living as standard predictor of Parkinson's disease. Three previous studies in North America and one study in Hong Kong, although all using different methods have reported similar results. Woo J *et al*. (1989) in a case control study in Hong Kong found that rural living increase the risk five folds compared with those who hasnever lived in rural areas. Morane Jimenez *et al*., (1994) found in their study, 70.3% of Parkinson's disease patients and 61.5% controls are rural residents but more Parkinson's disease patients (56.8%) than controls (34.5%) living in rural areas (population of >50 years of age). In our study 47.8% of males (n=11) and 50% (n=8) female patients had exposure to these chemicals (herbicdes, insecticides, fungicides and rodenticides) during farming, orchard spraying and vegetable cultivation. A few number of patients could recall the nature of chemicals used and it would belong to organochlorine group of compounds. In our study exposure to agricultural chemicals was statistically insignificant in female patients which can be explained by less number of patients exposure to these chemicals possibly because in our set up due to religious and cultural background, majority of females remains indoors. Lion HH, Tsai Mac *et al*. (1991) in their study have found use of herbicides, pesticides as a risk factor for Parkinson's disease. A large study conducted by Enrico Granieri *et al*. (1989) has revealed a significantly higher

Table 1. Prevalence of Parkinsonism among the screened population

Total screened population (> 7 years)	No. of Parkinsonism patients	Prevalence per 100	Prevalence per 100000
13710	39	0.28%	280/100000

Table 2. Socio- demographic Characteristics

		MALE		FEMALE		TOTAL		P Value
	8-20	n	%	n	%	n	%	
Age (Yr)	21-39	2574	37.3	2486	36.5	5060	36.9	0.224 (NS)
	40-59	1417	20.5	1426	21.0	2843	20.7	
	≥ 60	694	10.0	730	10.7	1424	10.4	
Residence	Rural	3934	57.0	3862	56.8	7796	56.9	0.824 (NS)
	Urban	2973	43.0	2941	43.2	5914	43.1	

Table 3. Diagnostic Criteria

	MALE		FEMALE		TOTAL		
	n	%	n	%	n	%	P Value
Resting Tremor	19	0.28	10	0.15	29	0.21	0.00 (Sig)
Rigidity	14	0.20	9	0.13	23	0.17	0.00
Bradykinesia	12	0.17	11	0.16	23	0.17	0.00
Postural instability	8	0.12	8	0.12	16	0.12	0.00
Parkinsonism	23	0.33	16	0.24	39	0.28	0.00

Table 4. Disease status across Gender

	MALE		FEMALE		TOTAL	
	n	%	n	%	n	%
Idiopathic PD	14	60.9	9	56.3	23	59.0
Drug induced PD	2	8.7	5	31.3	7	17.9
Parkinson plus syndrome	5	21.7	1	6.3	6	15.4
Vascular PD	2	8.7	1	6.3	3	7.7

Table 5. Disease status across Age

	<60 Years		60-69 Years		70-79 Years		>80 Years	
	n	%	n	%	n	%	n	%
Idiopathic PD	2	50.0	4	80.0	14	63.6	3	37.5
Drug induced PD	2	50.0	0	0.0	3	13.6	2	25.0
Parkinsons plus syndrome	0	0.0	1	20.0	2	9.1	3	37.5
Vascular PD	0	0.0	0	0.0	3	13.6	0	0.0

Table 6. Parkinsonism across studied parameters

		Male		Female		Total		P value
		n	%	n	%	n	%	
Forget fullness	No	19	82.6	14	87.5	33	84.6	0.681 (NS)
	Yes	4	17.4	2	12.5	6	15.4	
Old Stroke	No	21	91.3	15	93.8	36	92.3	0.781 (NS)
	Yes	2	8.7	1	6.3	3	7.7	
Pesticide Exposure	Yes	11	47.8	8	50.0	19	48.7	0.895 (NS)
	No	12	52.2	8	50.0	20	51.3	
Well water Consumption	No	22	95.7	15	93.8	37	94.9	0.794 (NS)
	Yes	1	4.3	1	6.3	2	5.1	
Smoking / Alcohol Intake								0.465
	No	18	78.3	14	87.5	32	82.1	
	Yes	5	21.7	2	12.5	7	17.9	

incident rates among Parkinson's disease in agricultural workers. These results would give support to the hypothesis of a possible casual role of environmental factors that are mainly linked to the agriculture. Case control studies in China, Spain and Canada have found a relationship between an increased risk of Parkinson's disease and pesticides and industrial chemical exposure. Semchuk and co-worker (Karen, 1993) and Hubble and associated (Hubble, 1993) also found significant risk of pesticides, herbicide exposure and Parkinson's disease.

In our study we also found that 4.3% (n=1) of male and 6.3 (n=1) of female patients were found to drink well water which is one of the risk factor for developing Parkinson's disease, but it was statistically insignificant.

Koller *et al*. (Koller, 1990), Tanner *et al*. (1987), Jimenez *et al*. (1992) and Morane *et al*. (25) also found that well water drinking was one of the risk factor for developing Parkinson's disease.

Conclusion

The prevalence of PD in our part of world is less as compared to Europe and western world. Though the occurrence of PD is low in Asia and India, the rapid increase in the size of the population will create more number of PDs in future. Since the cause of PD is not conclusively known till date, all possible preventive steps should be undertaken to protect from undesirable effect of various epidemiological factors. This needs many more case control and cohort studies across India in many cities because of presence of genetic and ethnic diverse population and different socio economic picture in different parts of our country. Robust health infrastructure and health-care is the need of the hour and future also. The contribution of such study gives an insight into various epidemiological factors from different geographical area of India which will ultimately decide the general and specific health policy of each state and geographical division of India.

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