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Exploring Epidemiological Factors and Risk Associations for Parkinson's Disease: A Study in India

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Abstract: This article investigates the epidemiological factors and associated risks contributing to the development of Parkinson's Disease PD with a specific focus on India. Parkinson's Disease is the second most common neurodegenerative disease which is quickly progressing into one of the most important neurological diseases in the world. Its symptoms have been found to occur due to degeneration of dopaminergic neurons in the substantia nigra and an increase of a protein called α - Synuclein. While genetics play a role in some cases, the majority of PD cases are sporadic. This study, based on a questionnaire survey conducted in India and distributed to 16 Indian adults, explores factors such as dairy consumption, caffeine intake, constipation, and medication use, shedding light on their potential associations with PD. While correlations are observed, further research is needed to establish causation. The findings emphasize the importance of awareness and monitoring of lifestyle choices to mitigate the risk of developing PD.

Keywords: Parkinson's Disease, Epidemiological Factors, Risk Associations, India, Neurodegenerative Disease

1. What is Parkinson's Disease?

Parkinson's Disease (PD) is the second most common neurodegenerative disease that more than 10 million people around the globe struggle with and it is the fastest growing neurological disorder in the world¹. It most prominently occurs in the ventral component of the substantia nigra (SN) pars compacta in the midbrain due to the death of dopaminergic neurons which causes a lack of dopamine in the brain. Dopamine is a neurotransmitter responsible for movement, motivation, memory, and a variety of other functions. This is the reason for the loss of motor control in the disease, where commonly hand tremors, muscle stiffness, and slowness of movement occur. The hallmark of the disease is the formation of α - Synuclein aggregates. Their spreading to surrounding cells is what is thought to cause the formation of Lewy bodies and subsequent cell death².

The percentage of Parkinson's disease patients with a first degree family member, i. e. a parent, with the disease is only reported to be around 15% and 90% of Parkinson's disease cases do not have a traceable genetic cause. The majority of cases of PD are sporadic, in that a variety of different factors caused them².

Understanding what factors and events can impact one's likelihood of having Parkinson's disease is important in prevention and awareness. Throughout my review of papers regarding risk factors of Parkinson's disease, I had realized the amount of research into the epidemiology of the disease in Asian countries, especially countries such as India, were few in number. So I decided to conduct one of my own in India, using a questionnaire formulated with the help of Dr. Praveen Sharma of Apollo Hospitals in Bangalore.

2. Literature Review

There have been many factors found statistically to correlate with increased incidence of Parkinson's disease.

Ethnicity, as a factor in the prevalence of Parkinson's disease has not been well defined but has been explored numerous times. White people have been found to have the highest prevalence of the disease, with 1, 671.63/100, 000, asians with 1, 138.56/100, 000, and black people with 1, 036.41/100, 000. Other studies have found that autopsies of Nigerian brains had a higher amount of Lewy bodies as compared to those in Europe and North America³.

Motor complications may vary according to ethnicity, with dyskinesia (involuntary muscle movement) and the wearing off phenomenon (decrease in effectiveness of levodopa) have been seen to be more common in North American and European patients and less with Asians. But the cause may be from the types of treatment administered in different countries and their effects. Non - motor symptoms, such as gastrointestinal symptoms like vomiting and nausea may be more common in East Asians. But there have been studies refuting these results as well.

Cognitive dysfunction is one issue seen in PD around the globe, with one's visuospatial, executive, and attention cognitive domains usually affected. This can coincide with other problems like depression, anxiety, hallucinations, etc. The presence of this has been shown to increase the risk of mortality in patients. Studies have shown that Black PD patients have an increase in risk of cognitive impairment and dementia, and the same with Hispanic patients. While Asian patients seem to report higher levels of cognitive impairment, dementia specifically was found to have a lower rate³.

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Associated Risk Factors:

This section will now only focus on the associated risk factors, and not on ethnicity, race, and culture as factors. Note that the correlations made are only associations, and have not been proven to be anything more.

Parkinson's disease has been found to more commonly occur in men, with men having almost a two - fold higher chance of having PD. This higher incidence is seen across all ethnicities and backgrounds, which may suggest possible hormonal determinants in the disease⁴. This is backed up by the fact that single nucleotide polymorphisms in many estrogen - related genes have been linked positively with Parkinson's disease. Studies have found an increased risk of PD when women undergo a surgical removal of their ovaries, and for those with PD, estrogen based hormone replacement therapy has been found to be effective in combating its symptoms. However, this does not confirm any neuroprotective properties of estrogen. The difference could also suggest an effect of the expression of Y chromosome genes or even differential expression of X chromosome genes in men which increases the risk of the disease⁵.

Dairy products such as milk have also been found to be a risk factor, with higher consumption of milk and other dairy products being positively correlated to having Parkinson's⁴. A study at Harvard found this to be specific to low - fat dairy⁶. With the topic of one's diet as a factor, alcohol abuse has also been found in some cases to cause a higher risk. But most studies have mixed results, some even finding an inverse relationship between AUD or alcohol use disorder and Parkinson's disease. Methamphetamine has also been correlated, and it has been shown that it binds to the presynaptic dopamine transporter, to increase dopamine outside the cells and cause dopaminergic cell death⁵.

Some pesticides are well known as risk factors for the disease, the most studied and understood are paraquat and rotenone. Most pesticides that have been associated with the

disease seem to be involved in causing oxidative stress which as discussed earlier can lead to dopaminergic cell death, which is part of the pathology of Parkinson's disease⁴.

Smoking is surprisingly associated negatively with having the disease, although the exact implications of this is still unknown. Smoking related cancers therefore do not seem to be much of a risk, but melanoma or skin cancer has been found to increase one's risk of PD by $44\%^4$.

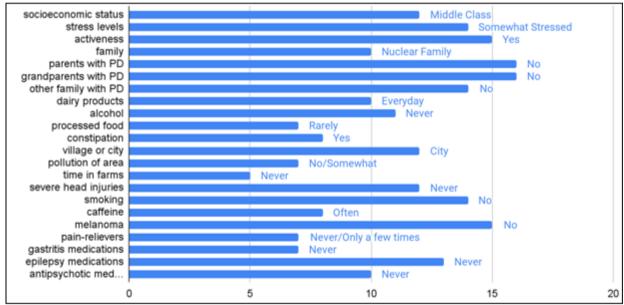
Finally and perhaps the most obvious, traumatic brain injury has been positively correlated with Parkinson's. The prevailing explanation for this is that it breaks down the blood - brain barrier in cells causing inflammation and mitochondrial dysfunction, as well as accumulation of α - Synuclein⁴.

The existing research is not very extensive and is not easily generalizable to the general public due to the specificity of the groups researched on. Thus the idea was to formulate a questionnaire for Indians with the disease with the research question in mind.

Research Question: What epidemiological factors play a role in increasing the risk of Parkinson's Disease?

3. Results

Out of the 16 participants, 9 were male and 7 were female, and their ages ranged from 53 - 79 with a mean of 70.06. The average age of diagnosis was 62.81 years. Their previous or current jobs were asked, and it was found that their average work hours per day were 7.82, but there seemed to be no correlation. Mode, a measure of central tendency, was used for the qualitative data received to see the highest frequency responses and therefore the most typical answer for a specific question. The table below represents the results for the short answer questions.



Graph 1: The modal response for 22 short answer questions

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^{*}The full questions are in the appendix

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There were also 5 long answer questions that cannot be easily represented through the use of mode or any other measure of central tendency. They, and their results, are summarized below.

The questions "How often do you visit friends" and "How often do you visit family?" were asked to investigate any social factors, and it was found that only around half still visited friends and the majority frequently were with their families. They were also questioned regarding the source of the water they have drunk, whether groundwater or surface water (i. e. from lakes, rivers, etc.), and the results showed that most from Bangalore, Karnataka drank from groundwater while most from Pune, Maharashtra drank from surface water which is already a well known fact. Most drunk from either groundwater or surface water for a majority of their lives. The sports they played was the final question asked, and there were a variety of different responses such as table tennis (which was the most common sport played among the sample), dance, no sport, and more.

Analysis:

From the data collected, participants seemed to be somewhat stressed, most had a high consumption of dairy products, constipation is somewhat common, as well as caffeine. Although the mode is not indicative of this, many participants were found to have taken medications for gastritis and psychosis in some form. One participant was in fact found to have taken pain relievers and antipsychotic drugs for a long period of time, and medications for gastritis and epilepsy a few times as well.

It is important to note that the usage of mode leaves out a few pieces of information. Questions such as "Have you spent time in fields/farms?" generated mixed results with many responding with "often", "sometimes", or "rarely" as well. Most did not have a history with melanoma, except for one, which may or may not be significant. Questions based on the participants' history of medications showed 5 who had taken medications for gastritis, 1 who had taken a medicine for epilepsy, and 5 who had taken antipsychotics.

Overall, the questionnaire suffered from a small and not very representative sample size. The majority of participants were middle or upper class and lived in cities, so the results were perhaps biased towards specific answers. The results were also very mixed, so it is hard to make many correlations between the responses collected and risk factors for Parkinson's disease.

Although based on the data collected, much assumptions cannot be formed, research has been done throughout the world (although unfortunately most excluding India) on what factors seem to be risks. As discussed earlier in this paper, high intake of dairy products and caffeine have been found to be correlated with PD. Surprisingly, most participants did not have family members with the disease and were the first in the family to at least be diagnosed with Parkinson's. Pain relievers and antipsychotics seemed to have the highest intake in this sample size, and could be factors. One thing to mention, is the difficulty in attributing

these results as mere coincidences or as being actual risk factors.

Evaluation:

In conclusion, many actions and habits seem to have some associations with the disease. Whether they are correlations, causes, or just simply associations is up for debate. According to the data collected, dairy, caffeine, and constipation seem to be the most strongly correlated with Parkinson's disease. Pain relievers and antipsychotics seem to have some associations with developing PD as well. Any conclusions beyond this are hard to make, but again using research carried out around the globe, exposure to certain pesticides like paraquat which could occur in farms can be a factor.

Taking into account these posited risks, it is important to be aware of one's level of dairy or caffeine intake, and any abnormal processes occurring within one's body. These findings are further confirmed by earlier research done in other countries, where similar results were found. Experiencing or doing any of these does not mean one will definitely get PD, rather it means one has a higher association with the development of the disease.

4. Conclusion

In conclusion, this study delves into the epidemiological factors and potential risk associations for Parkinson's Disease, particularly within the Indian context. While correlations with dairy consumption, caffeine intake, constipation, and medication use are noted, causative links remain unclear. The rising prevalence of PD underscores the urgency of extensive research to identify triggers and preventive measures. This study provides valuable insights, urging individuals to be mindful of lifestyle choices and fostering a heightened awareness of PD risk factors. However, more comprehensive investigations are essential to establish conclusive relationships between these factors and PD development.

5. Materials and Method

The questionnaire was created and distributed online through Google forms in, with a total of 33 questions, ranging from multiple choice to short answer questions. It was distributed to family members of mine, as well as to private online groups for Parkinson's disease in WhatsApp or Telegram. Distribution was also done with the help of the doctor, Dr. Praveen Sharma, to a few of his patients. The questionnaire was sent to around 20 people, and 16 participants responded, wherein 6 were from Karnataka, 5 from Maharashtra, 1 from Andhra Pradesh, 1 from Telangana, 1 from Uttar Pradesh, and 2 anonymous. The collection of data took place over exactly 2 weeks and participation was not mandatory. Mode was used as a statistical measure, as opposed to the mean and median, as it was found to be the best fit for looking at central tendency in such qualitative and non - numerical responses. The 28 short answer questions in the questionnaire are given below.

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Table 1: 28 short answer questions in the questionnaire

Short Answer Questions	Modal Response
What is your socioeconomic status?	Middle Class (12)
On average, how stressed do/did you feel on a daily basis?	Somewhat Stressed (14)
In high school, would you have described yourself as an active person?	Yes (15)
Have you lived, for most of your life, in a nuclear family (just father, mother, and siblings) or in a joint family (including other relatives)?	Nuclear Family (10)
Do you have parents with Parkinson's Disease?	No (16)
Do you have grandparents with Parkinson's Disease?	No (16)
Do you have any other family members with Parkinson's Disease?	No (14)
How often do you have dairy products (milk, cheese, yogurt, butter, ice cream)?	Everyday (10)
Do you drink alcohol?	Never (11)
Do you have processed food?	Rarely (7)
Have you dealt with constipation?	Yes (8)
Did you grow up in a village or a city?	City (12)
Do you live in a heavily polluted area?	No/Somewhat (7)
Have you spent time in fields/farms?	Never (5)
Have you had any severe head injuries in the past?	Never (12)
Do you or did you smoke?	No (14)
Do you consume caffeine (coffee, tea, soda/coke) often?	Often (8)
Do you have or did you have skin cancer / melanoma?	No (15)
Have you taken any anti - inflammatory drugs or pain relievers?	Never / Only a few times (7)
Have you taken any medications for gastritis?	Never (7)
Have you taken any medications for epilepsy?	Never (13)
Have you taken any antipsychotic medications?	Never (10)

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