

**Systematic Review**

Prevalence of Parkinson's disease in Pakistan – A Systematic Review

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ABSTRACT

Numerous epidemiological investigations pertaining to Parkinson's disease (PD) have been carried out on a global scale during the course of time. While each research documented an increase in the frequency and incidence rate of PD as individuals age, there were variations in the overall estimations seen across various nations. **Objective:** The purpose of this study is to provide a thorough analysis of PD incidence and prevalence rates in Pakistan. **Methods:** Google Scholar, Medline, and Embase were used to look for studies which reported the incidence of PD around the world. The searches were limited to English-language studies about people that happened between 1965 to 2023. **Results:** A total of 7 studies were conducted on Parkinson's disease in Pakistan. Muhammad Tufail et al. in a cross-sectional study observed a heightened prevalence of Parkinson's disease, with 600 patients identified in Khyber Pakhtunkhwa (KPK). In a cross-sectional study conducted in Lahore, 85 cases of PD were identified within a hospital setting. Fifty cases in a cross-sectional study were conducted at a Hospital in Rawalpindi. Saira et al. performed an observational study at Islamabad Hospital and found the prevalence of PD. We estimated the overall frequency of PD in Pakistan was 1016 cases in this systematic review. Males were more diagnosed with PD as compared to females. **Conclusions:** The data from the studies reviewed here indicate that PD increased in Pakistan during the last decade. While males were dominant in this study which is not different from across the globe.

INTRODUCTION

After Alzheimer's disease, Parkinson's disease (PD) is the second most prevalent neurodegenerative illness. James Parkinson first characterized PD in the renowned "Essay on the Shaking Palsy" in 1817. The cardinal indications of Parkinson's disease are all associated with motor dysfunction and consist of resting tremor, bradykinesia, stiffness, and impairment of postural reflexes. Additional presentations include psychological symptoms including worry and sadness, as well as dysautonomic symptoms such as low blood pressure and constipation, abnormal sensations, muscle spasms, impaired sense of smell, and a skin condition called seborrheic dermatitis. The

manifestation of cognitive decline may become evident as the disorder progresses [1]. Parkinson's disease (PD) is characterized by two pathological features: The substantia nigra pars compacta (SNpc) experiences a reduction in dopaminergic neurons, while misfolded α -synuclein aggregates into Lewy bodies (LBs) in the cytoplasm. Many dopaminergic neurons in the SNpc have already been destroyed by the time patients are initially identified, and neurodegeneration has progressed to other parts of the central nervous system. Most patients' etiology remains unclear, however in 5%–10% of instances, several genetic factors have been shown to be responsible for the illness.

Replacing dopamine is the mainstay of current Parkinson's disease (PD) therapy, while deep brain stimulation (DBS) and other alternate methods are appropriate for advanced stages of the condition. The current therapies provide excellent control of motor symptoms, but they do not stop the disease's development, neurodegeneration, or growing impairment [2]. It is debatable to what extent genes and environmental/lifestyle factors contribute to the pathophysiology of Parkinson's disease. Age is the single biggest risk factor for Parkinson's disease (PD), with a median age at onset of 60 years [3, 4]. Differences in the frequency of characteristics such as coffee use, usage of postmenopausal hormones, and smoking habits may have an effect on the incidence. The frequency seems to be greater in males (1.3 to 2.0 times higher) compared to females [3]. Mitochondrial abnormalities, genomic instability, telomere dysfunction, epigenetic alterations, autophagy-lysosomal systems and the ubiquitin-proteasome and other age-related biological dysfunctions may contribute to neuronal death in this and other neurodegenerative illnesses [5, 6]. Society is greatly impacted by Parkinson's illness. This disease's incidence and prevalence have increased dramatically over the last 20 years, for causes that are still a mystery [7-9]. The impact of Parkinson's disease on an individual is profound. The protracted nature of degenerative diseases can extend for decades. The estimated incidence rates of PD in industrialized nations vary from 8 to 18 per 100,000 annually, with a general population prevalence of 0.3%, a 60–80 year prevalence of 1.0%, and an 80+ year prevalence of 3.0% [2]. A diagnosis of Parkinson's disease (PD) affects around one million Americans. However experts predict that 1.2 million new instances of PD will appear by 2030. The number of Americans diagnosed with Parkinson's disease each year approaches 60,000, according to new data [10]. Between 65 and 12,500 cases per 100,000 people and 5 to 346 cases per 100,000 person-years, respectively, are the estimated prevalence and incidence rates of PD in Europe [3]. Approximately 400,000 annually individuals in Pakistan are afflicted with PD [6]. The etiology of Parkinson's disease is complex and includes both hereditary and environmental components, as well as the natural consequences of becoming older. The risk of Parkinson's disease may vary between Asian and non-Asian populations due to differences in genetics and environmental exposures [7].

There has been little research on Parkinson's disease in Pakistan, and no study has yet looked at the country's general prevalence. Thus, the primary goal of this systematic review is to identify the total prevalence of Parkinson's disease in Pakistan.

METHODS

A systematic literature analysis was conducted utilizing the Google Scholar, Medline and EMBASE databases to identify worldwide studies that investigated the frequency rates of PD. The MeSH terms used in the search included "Parkinson," "Parkinson's disease," "Epidemiology," "Incidence," and "Prevalence." The search parameters included the human population, specifically targeting adults, with a need for English language publications spanning from 1965 to 2023. Additionally, a comprehensive search was conducted to identify the citations of the included works as well as published pertinent reviews. Studies with clear diagnostic criteria, population-based studies, case-control studies, and hospital-based studies with Pakistani people over the age of 18 were all considered. Cross-sectional studies that showed the incidence rates of PD were also included. The things that were ruled out were: similar publications (in this case, more complete, thorough, and reliable sets were chosen); data that was used in more than one study; nursing homes and social welfare homes for the old; and diagnostic criteria that were not clear or common. Geographical area of study, diagnosed cases, gender, age, type of study, source of study and publication year were extracted from the studies. The diagnostic evaluation, research design, response rate, and sample size were the four main criteria used to systematically assess the quality of all relevant studies.

RESULTS

From the databases of Google Scholar, Sciondirect, PubMed, and Embase, a grand total of 214 citations were found during our first search. Following the removal of irrelevant or incomplete entries and duplicates, 85 records were left. The incorrect methodology and findings led to the exclusion of 35 further publications. Figure 1 shows that 27 records were eliminated after further full-text assessment according to the inclusion and exclusion criteria.

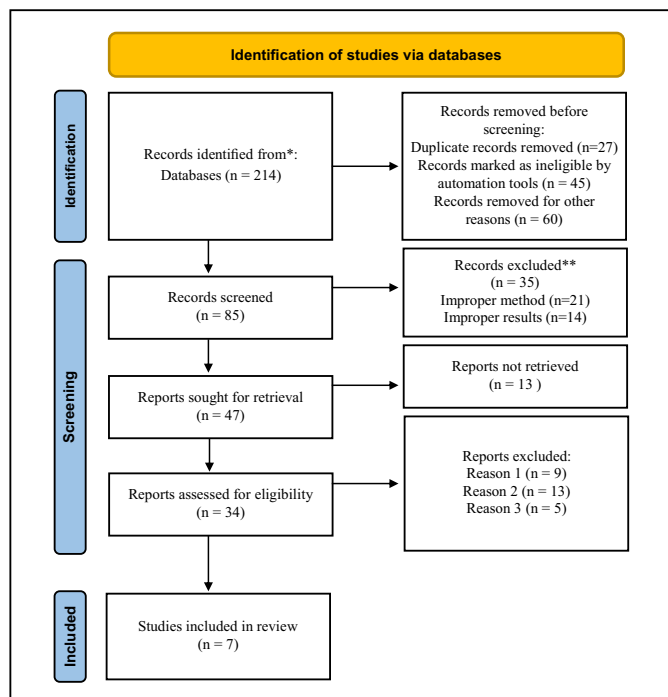


Figure 1: Flow diagram of study identification. Reason 1: Not based on Pakistan; Reason 2: overlapped data in different studies; Reason 3: conducted in unrepresentative population.

This systematic evaluation could include a total of seven records (Table 1). First authors, locations, types of investigations, sources, and publication years of the included studies are detailed in Table 1. The tables also provide the number of diagnosed PD patients. A total of 7 studies were conducted on Parkinson's disease in Pakistan. Muhammad Tufail et al. in a cross-sectional study observed a heightened prevalence of Parkinson's disease, with 600 patients identified in Khyber Pakhtunkhwa (KPK). The male patients were 78% (n=648) while female patients were 22.0% (n=132). The patients' age distribution was categorized as follows: 2.0% (n=12) between 18 and 30 years, 27.0% (n=162) between 31 and 50 years, and 71.0% (n=426) aged 51 and above. The research spanned various cities in Khyber Pakhtunkhwa (KPK) and included Parkinson's disease patients from 12 districts within the region. In a cross-sectional study conducted in Lahore, 85 cases of PD were identified within a hospital setting. The average age of the participants was 57.6 years, with the youngest individual being 35 years old and the oldest 77 years old. Notably, the higher prevalence of PD in men, comprising 82% (n=70), compared to women, who accounted for 18% (n=15) of the observed cases. Examining fifty cases within a cross-sectional study at a Rawalpindi hospital, we found a distribution of 62% (n=31) males and 38% (n=19) females. The age distribution revealed 40% (n=20) within the 48 to 57 years range, 34%

(n=17) aged between 58 and 67 years, and 26% (n=13) representing cases above the age of 67. Saira et al. conducted an observational study at Islamabad Hospital, determining the prevalence of Parkinson's disease (PD) among 62 cases. The study revealed an average age of 62 years, ranging from 33 to 80 years. Males constituted the majority (n=46, 74.1%) compared to females (n=16, 25.8%). In a hospital setting in Karachi, Khealani reported 80 PD patients. Among these, 63% (n=50) were males and 37% (n=30) were females. The mean age at disease onset was 54 years. Suliman Khan conducted a door-by-door study, identifying fourteen cases of Parkinsonism. The prevalence of all types of Parkinsonism among individuals aged 50 years and above was 0.55/100, increasing to 1.7/100 among those aged 65 years and above. Specifically for PD, the prevalence among individuals aged 50 years and above was 0.53/100 for males and 0.3/100 for females. Among participants aged 65 years and above, the prevalence rates were 1.31% for males and 1.21% for females. From August 2019 to February 2020, a descriptive cross-sectional research was conducted at Jinnah Postgraduate Medical Centre, Karachi, in the Neuro-medicine Ward. The prevalence of PD was determined to be 70 cases, comprising 44 male and 26 female patients. Of these patients, over 62.86% were between the ages of 50 and 60, while the remaining 37.14% were aged between 61 and 70. The male-to-female ratio was determined to be 1.69:1, suggesting a higher number of males compared to females in the reported instances. In this systematic review, we determined that the overall frequency of Parkinson's disease (PD) in Pakistan was estimated to be 1016 out of them 947 (93.2%) patients who visited the hospital while 69 (6.8%) patients were found in door-to-door survey. Our data indicated a greater incidence of Parkinson's disease among men 88.5% (n=900) in comparison to females 11.4% (n=116).

Table 1: Prevalence of PD disease according to location, type and source of study, and year.

Location	Prevalence of PD (N)	Type of Study	Study Setting	Year	Reference
Lahore	85	Cross-sectional	Hospital	2018	Mukhtar S et al., [12]
KPK	600	Case-control	Hospital	2020	Tufail M et al., [11]
Rawalpindi	50	Cross-sectional	Hospital	2016	Imtiaz N et al., [13]
Islamabad	62	Observational	Hospital	2016	Saad S et al., [14]
Karachi	80	Cross-sectional	Hospital	2006	Khealani BA et al., [15]
Lower Dir & Malakand	14	Cross-sectional	Population	2016	Khan S et al., [16]
Karachi	70	Cross-sectional	Hospital	2022	Moolchandani J et al., [17]

DISCUSSION

Only seven studies of PD prevalence were found. There were only a few studies conducted on PD disease in Pakistan. In our literature review studies, the total number of PD cases was 1016 patients. Out of 1016, 947 (93.2%) patients who visited the hospital while 69 (6.8%) patients were found in a door-to-door survey. In our systematic review, the lowest prevalence of Parkinson's disease was observed in Lower Dir and Malakand cities, with a reported count of 14 cases, while the highest prevalence was documented in Lahore city, totaling 85 cases. A community survey-based study in Brazil reported similar results in 86 (7.2%) PD patients [18]. Benito-León J et al., did a comprehensive study in Spain, going from door to door, and found a greater occurrence of Parkinson's disease in 1.8% (n=118) out of 6395 people with Parkinson's disease [19]. There is considerable heterogeneity in the worldwide occurrence of Parkinson's disease. There are more reasons that may be attributed to this variation. The discrepancy in prevalence estimates may be due to the disparity in survival rates seen across various countries. One such element that might contribute to the variation in the incidence of illnesses is the use of epidemiological research that depends on medical data. The applicability of this research to the broader population may be restricted since individuals with subclinical disease, who were unlikely to seek medical intervention, were excluded. The existence of undiagnosed Parkinson's disease (PD) in the population may be seen from the data offered by several research using 2-phase door-to-door surveys. These studies have shown a prevalence of PD ranging from 12% to 69% [19-23]. In our systematic review, the PD patients most age group was 50 - 70 years. Previously published literature results are not in agreement with our results. According to one comprehensive analysis, the greatest incidence occurs between the ages of 70 and 79, however this might be due to the difficulties of detecting extremely old people [24]. A recent Italian study conducted a thorough examination of a randomly selected group of 6,000 individuals between the ages of 65 and 84. The study found a much-increased occurrence of a certain condition in these age ranges compared to previous research, with rates ranging from 220 to 670 cases per 100,000 individuals annually. Furthermore, the incidence of this condition doubled between the ages of 75 and 79, as well as between 80 and 84 [25]. An additional study indicated that the occurrence was higher in men. A 1.5-2-fold increase was found in some investigations, with the largest study finding no gender difference [26]. Men with Parkinson's disease (PD) outnumbered women in the majority of the research that we have analyzed here. According to a prior comprehensive analysis, there were 12 994 (41%) fewer

women with PD overall than there were males (1800-29%). In fact, the fact that women are less likely to develop PD is one of the most well-documented gender disparities in PD [27]. In all age categories, males had a higher incidence of Parkinson's disease (41.1/100 000 yearly) than women (21.7/10 000 annually), according to Baldereschi et al. 10. This has been verified in further research [28-30]. Furthermore, males are more likely than women to have PD (around 30/10 000 vs 24/10 000, respectively)[30-32]. Men are up to twice as likely as women to get Parkinson's disease (PD), according to some research [33-35].

CONCLUSIONS

This research reviewed clinical studies investigating PD prevalence. According to the statistics analyzed here, Pakistan has shown an upsurge in PD during the last ten years. Nonetheless, the study's predominant gender was male, which is consistent with global trends.

Authors Contribution

Conceptualization: YAJ,

Methodology: ABK, ASS, SS, YAJ

Formal analysis: ASS, SS, YAJ

Writing-review and editing: HNR, AK

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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