Prevalence of Parkinson's Disease in Populations of African Ancestry: A Review

Aideen McInerney-Leo, MS; Katrina Gwinn-Hardy; and Robert L. Nussbaum
Bethesda, Maryland

There have been a number of studies looking at the prevalence of Parkinson's disease (PD) in different racial and geographical populations. Some of the earliest studies suggested a difference in the prevalence of PD in African Americans as compared with Caucasians. As such a difference would have important implications for healthcare and research into the etiology of PD, we undertook a review of published studies to determine whether evidence suggested that such a difference exists. We reviewed 20 studies that looked at incidence, prevalence, and percentages of neurology patients with PD and Parkinsonism in Africa and in African-American populations. Two of these were door-to-door studies that relied on questionnaires for initial ascertainment, another was performed by review of outpatient records of a large health maintenance organization, while the remainder were based on hospital admissions, diagnosis in the community, or death certificate reports. In the aggregate, these studies suggest PD may be less frequent among Africans and African Americans than among Caucasians, although the most well-designed study showed only a statistically insignificant reduction in the prevalence of PD among African Americans. Although an apparently lower disease frequency among people of African origin may have a basis in the pathobiology of the disease, nearly all of these studies were vulnerable to a variety of ascertainment biases, and many lacked stringent application of diagnostic criteria applied by specialists trained in movement disorders. We conclude that a difference in the prevalence of PD and Parkinsonism between black and other populations is unproven and will require additional well-designed studies to determine if previously reported ethnic differences in disease prevalence are real.

Key words: Parkinson's ■ Parkinsonism ■ African ■ prevalence ■ etiology

 From National Human Genome Research Institute (McInerney-Leo, Nussbaum) and National Institutes of Neurological Disorders and Stroke at the National Institutes of Health (Gwinn-Hardy), Bethesda, MD. Send correspondence and reprint requests for *J Natl Med Assoc.* 2004;96:974–979 to: Aideen McInerney-Leo, Medical Genetics Branch, National Human Genome Research Institute, Building 10, Room 3C710, 10 Center Drive, MSC 1253, Bethesda, MD 20892-1253; e-mail: amcinern@nhgri.nih.gov

INTRODUCTION

Parkinson's disease (PD) is a common progressive neurodegenerative disorder characterized clinically by bradykinesia, resting tremor, rigidity, and postural instability. Symptomatic response to L-DOPA therapy is also often used as an additional diagnostic criterion.[1] It affects 1–2% of the population over the age of 60 years, although the disease is seen in younger individuals as well.[2] A recent meta-analysis of studies to date suggests an overall annual incidence of 16–19/100,000.[3] In 1993, a review of the worldwide occurrence of PD reported that Asian and black African populations have the lowest prevalence rates of this disease in the world.[4] Reports to date have not only suggested that the prevalence rate is lower in black Africans but, in addition, that this rate is also lower in African Americans as compared to Caucasians. We have noted a deficiency of black families among volunteers for our ongoing studies on the genetics of PD. We, therefore, undertook a literature review in order to ascertain whether a reduced prevalence of PD among African Americans might be a contributing factor to there being fewer black individuals and families affected with PD in our study.

BACKGROUND

Most studies to date have focused on the prevalence as opposed to the incidence of PD. As prevalence is a function of both incidence and survival, the reduced average life expectancy among African Americans as compared to white Americans[5] could result in a significant inherent limitation of any measurement of prevalence of a disease affecting a predominantly older population. Most studies have examined the prevalence of PD through review of hospital records, physician registration, and review of death certificates. There have only been three community-based studies published to date: two door-to-door studies that looked at African and African-American populations in Nigeria and Mississippi, respectively, and one study that examined the prevalence of the disease in different racial

groups enrolled in a health maintenance organization in California. A synopsis of the studies to date is presented below.

Studies among Hospital Inpatients (United States)

The first study ascertaining individuals affected with PD through hospital admission records was published in 1972.[6] In this study, Kessler looked at all patients discharged with a diagnosis of PD or Parkinsonism from all Baltimore hospitals between 1965 and 1967. A physician without specialty training in neurology reviewed the charts to confirm the diagnosis, and the study did not specify which diagnostic criteria were being used to confirm the diagnosis. It was not stated how many of the patients had been examined by a neurologist during their hospital stay, but only 20% of those identified as having PD had been admitted for problems related to PD. All individuals identified as having PD in this population were visited by an interviewer who was not medically trained, and they completed a questionnaire that included a number of questions pertaining to the diagnosis of PD, lifestyle factors, and other health conditions. They reported that PD/Parkinsonism was significantly less common in blacks than in whites. The annual reported prevalence of 28 (per 100,000) in white males and 22.8 in white females was significantly higher than the 4.6 and 4.3 seen in black males and females, respectively. We do not know the ethnic, age, and gender breakdown of the total hospital population during that period.

In another study, medical records were reviewed for patients admitted over a 10-year period (1959–1969) to a charity hospital in New Orleans with a patient population that is 75% black.[7] They only included patients with unequivocal clinical evidence of PD and found that it occurred in 0.022% of black patients as compared with 0.146% of whites. The ages of the populations were not given, but if consistent with the national survival rates at the time,[5] it is likely that the average age of the patients was lower among the black population than the white.

The hospital-based studies do not address the differences in delivery and uptake of medical services between African Americans and whites. Without specialty training in neurology, interviewers would be far more likely to ascertain a patient with PD when the patient already knew he carried the diagnosis, having previously sought and received outpatient medical evaluation for neurological symptoms. It is also not apparent that a hospital setting is the best place to encounter patients with PD. In Kessler's study, only 20% of patients with PD were admitted because of problems related to the disease, and it is likely that as treatments further improve in the future even fewer PD patients will be admitted with disease-related problems.

Prevalence and Incidence Studies of PD in Black Populations

Study	Study Type	Sample Size	Number of Cases	Prevalence (per 100,000) Crude	Prevalence (per 100,000) Adjusted	Incidence (100,000) Adjusted
United States						
Kessler II, 1972	Community clinics, Baltimore	B W	1,183 87	8.67(F), 30.66(M) 121.47(F), 128.37(M)		
Paddison RM, 1974	Review records inpatients, New Orleans	B 333,280 W 112,878	74 165	22* 147*		
Schonberg et al., 1985	Door-to-door Mississippi	B 11,666 W 11,981	12 19	341 352	338 353	
Mayeux et al., 1995	Recipients of healthcare—NY	B W			57* 116*	
Van Den Eden et al., 2003	Kaiser Pts—CA	B 192,300 W 969,286	16 291			10.2 13.6
Africa						
Lombard et al., 1978	Zimbabwe, hospital admissions	B 82,453 W 34,952	17 33	20.6 94.4		
Schonberg et al., 1988	Door-to-door Igbo-ora, Nigeria	B 3,412	2		67	

* Statistically significant difference

Africa

Of the 750 inpatient and outpatient cases which Harries had seen in his neurology practice in Kenya over a five-year period,[8] he observed 27 cases of PD (~4% of neurology patients) with an age range of 45–60 years. A survey of patients admitted to the hospital over a one-year period in what was formerly known as Rhodesia revealed three patients with a diagnosis of PD,[9] accounting for less than 1% of all neurological admissions. Both these percentages were similar to those reported by Haddock in Ghana among 280 admissions and 192 outpatients.[10] Collomb who saw inpatients and outpatients over a 10-year period in Senegal[11] also reported that less than 1% of neurological admissions were due to PD. Interestingly, his observations of outpatients over time suggested that among patients with classical PD in 25% of cases, the disease seemed to progress more slowly in comparison to his previous clinical experience in England. Conversely, Cosnett's experience in Natal (South Africa) led him to conclude that though Parkinsonism was common, true PD was rare.[12] For his summary on Nigerian patients, Osuntokun[13] reviewed 13 years of records and found 107 cases of Parkinsonian syndrome (1% of neurological admissions). He observed that the peak incidence was in sixth decade and commented that liver disease was the cause of many of the early-onset cases. A later study by the South African neurologists Cosnett and Bill[14] involved reviewing records from all patients seen for neurological consultation during a seven-year period (1979–1985). Patients with Parkinsonian symptoms were classified as having PD or Secondary Parkinsonism (SP). They found PD in 0.15% of blacks and 2.3% of whites, whereas SP occurred in 0.5% of blacks and 1.15% of whites. Interesting is the fact that only 22.8% of black patients were over the age of 50 as opposed to 47.8% of white patients.

Osuntokun et al.[15] also did a later retrospective review of records. He reported seeing 217 patients with Parkinsonism in his neurology clinic over a 10-year period (1966–1976). Mean age of onset for idiopathic PD was 55.6 years, and it is particularly noteworthy that two patients with idiopathic PD volunteered a positive family history.

Lombard and Gelfand[16] conducted a retrospective survey of cases admitted with PD to Harare Hospital in Zimbabwe between 1973–1976 and compared them with the European admissions to Andrew Fleming Hospital in the same city between 1974 and 1976. Out of 82,000 admissions in a four-year period to Harare Hospital, 17 cases of PD were reported. This was significantly lower than the 33 cases that were seen in almost 35,000 patients admitted to Andrew Fleming Hospital.

Studies among Outpatients (United States)

Convinced that the approach of identifying patients through hospital admissions was limited, Kessler set about attempting to ascertain PD cases through neurologists and general health providers in the community within Baltimore.[17] In this study, a random sample of 6% of physicians in the community, of whom 25% were neurologists, were invited to be members of a PD panel. They were asked to register all patients that they had diagnosed with PD between 1967 and 1969 based on the four diagnostic criteria: tremor, rigidity, slowness, and immobility of the facies. Differences in incidence figures were seen, as they found 31 and 8.7 cases/100,000 in black men and women, respectively, as compared with 128 and 121 in white men and women. Such a study design, however, is open to ascertainment bias since socioeconomic factors could effect the likelihood that an African-American with symptoms of PD might seek out specialists in neurology most capable of making the diagnosis of PD. Furthermore, there is a documented reluctance among African Americans[18,19] and African-American physicians[20] to participate in clinical research, which, though understandable, could also lead to serious under-reporting of PD among African Americans.

In a separate study of two New York districts, Mayeux et al. counted all individuals with a diagnosis of PD who either had sought medical services at hospitals and doctors offices or had requested medical assistance from federal and state agencies between 1988–1993.[21] All individuals they identified were subsequently examined by a neurologist and only deemed to be affected if they had the necessary diagnostic criteria of bradykinesia and at least one other feature (muscular rigidity, resting tremor, or postural instability). Additional criteria included the presence of at least three of the following: history of unilateral onset, persistence of asymmetry of symptoms, history of improvement on levodopa, a progressive course or a history of levodopa-induced chorea. As there were clear diagnostic criteria for this study and every individual with a suspected diagnosis was examined by a neurologist, the diagnosis was clearly confirmed in individuals reported as affected. They reported a total prevalence rate of 107 per 100,000 and an average annual incidence of 13 per 100,000. Age-adjusted prevalence rates were lower for blacks (92 men and 55 women per 100,000) than for whites (172 men and 86 women) and Hispanics (187 men and 95 women). As comparable prevalence figures were seen in whites and Hispanics, socioeconomic factors and access to medical care were thought unlikely to account for the lower prevalence observed in blacks. The researchers speculated that the apparently reduced prevalence in

the black population was a function of reduced survival, as the number of deaths in the incident cohort was significantly greater for blacks than for any other ethnic group. However, the study by Mayeux et al. also found that black men over age of 75 years had the highest incidence rate of any group. It is therefore possible that the age of onset or age at diagnosis was delayed in this group. The reasons for such a delay are unknown and could include biological, economic, or social factors, acting alone or in combination. As with the hospital-based studies, both of these large community-based studies required that individuals were seeking medical care and, in the case of the latter study, already carried a diagnosis of PD.

The Harlem Aging Project[22] involved interviewing about their health status a probability sample of 164 elderly persons—65 years of age or over and living in central Harlem. Approximately, 97% identified themselves as black. Cognitive screening measure assessed cognitive functioning, neurological signs associated with PD or stroke, communication, ambulation, and mood. Nonmedical interviewers trained to conduct the survey administered the questionnaire but there were no follow-up exams by neurologists. Only 0.6% had received the diagnosis of PD, but 16.2% of the sample had three or more symptoms of PD; 7.5% had four or more symptoms. As neurologists were not involved in ascertainment or confirmation, the sensitivity and specificity of this study cannot be assessed. However, the results do suggest under-reporting of Parkinsonism.

Most recently, the incidence of PD was ascertained in patients followed at the Kaiser Permanente Medical Care Program of Northern California.[23] The population was representative of the general population in terms of race but had above average income and higher education levels than the general population. Clinical summaries were abstracted from the medical records by medical record analysts, and neurologists reviewed these summaries to ensure that the essential diagnostic criteria were present. No clinical examinations were performed to confirm reported symptoms. Although not statistically significant, these researchers did observe fewer cases of PD in blacks (10.2/100,000) than in non-Hispanic whites (13.6/100,000).

DEATH CERTIFICATES

A search of the 1988 mortality files, created by the National Center for Health Statistics (NCHS), looking for individuals who died with an ICD-9 diagnosis of PD revealed racial differences.[24] Whether PD was the underlying cause of death, a contributing cause, or just a diagnosis that people carried, whites had significantly higher rates than blacks. This study confirmed the findings of earlier reports that had mainly looked at census data from 1959–1961.[25-28] These studies were obviously limited by the fact that they relied both on a person carrying the diagnosis at the time of death and that death certificates were completed in a consistent fashion throughout the country.

COMMUNITY SURVEYS

All residents of Copiah County, Mississippi as of January 1, 1978 were visited by nonmedical lay-interviewers who administered an extensive questionnaire that included questions on the symptoms of PD among other topics.[29] Individuals who had features suggestive of PD were subsequently examined by a neurologist. Ninety-seven percent of the households, containing almost 24,000 residents, agreed to participate in the study. Although 49% of the total population was black and 50% was white, the study focused on individuals over 40 years of age, of whom 60% were white and 39% were black. A definitive diagnosis of PD required the presence of two or more of the following signs: resting tremor, bradykinesia, rigidity, parkinsonian gait or posture, retropulsion, masked facies, and micrographia. A possible diagnosis of PD required the presence of one of these cardinal signs and the equivocal presence of at least one other. They found 31 individuals—13 of whom were newly diagnosed as a result of the study—with PD or possible PD in this study. There were no differences in the occurrence of PD in blacks (12 cases in almost 3,600 over 40) as opposed to whites (19 cases in almost 5,400 over 40) when one looked at the total number of PD cases. However, when definite and possible cases were examined separately, it was found that whites had a greater proportion of definite cases than blacks. Fifty-eight percent of blacks and 32% of whites had not been diagnosed previously.

The same research group that carried out the door-to-door study in Copiah County sought to compare the prevalence of PD in Copiah County to its prevalence in Nigeria, on the assumption that West Africa was the ancestral origin for a large proportion of blacks residing in the United States, including Mississippi.[15] They chose a town in Nigeria with a stable population of 20,000. Over 99% of households cooperated and, of the 3,412 people over the age of 40, only two individuals were found to have PD. The authors felt that the reduced survival rates in Nigeria only partly accounted for the discrepancy in prevalence between locations and subsequently hypothesized that environmental agents were responsible for observed differences.

Postmortem Findings in an African Population

The only published postmortem survey for PD in Africa was carried out in West Africa.[30] This was not a true epidemiologic study. The researchers simply examined the brains of 94 patients who had been reported to be neurologically normal and found

nigral Lewy bodies accompanied by mild neuronal loss in five patients. The authors felt that this incidence was similar to the figures previously reported in the UK and USA.

Inherited Parkinson's Disease in Families of African Ancestry

None of the African studies intentionally ascertained whether a family history was present. Osuntokun did report that of the 217 patients with Parkinsonism seen in Nigeria over a 10-year period, two had volunteered a family history of PD. But we do not know whether the figure would have been higher had the question been asked to every patient.[15] A study looking for PD in first-degree relatives (FDRs) of affected PD patients found that it was two-and-a-half times more common in relatives of people with PD than controls.[31] In 19 cases, there was an FDR affected, and in three of these, there were two affected FDRs—one of which was an African-American family.

SUMMARY AND CONCLUSIONS

There are a number of possible explanations—some real, others factitious—for any observed differences in the prevalence of PD between groups of European origin and Africans or African Americans. First, we must consider that the differences in prevalence are real and the result of biological or environmental differences between populations. There is some evidence to suggest that PD may be milder or phenotypically different in African Americans. Specifically, there were fewer definite cases in the Copiah County study, while in South Africa, Cosnett found that though Parkinsonism was often seen, true PD was rare. Collomb suggested that PD in Senegal resembled PD in England but, in 25% of cases, deterioration was slower and patients survived for many years after diagnosis.[11] Unmeasured environmental factors could also contribute to the differences in prevalence rates; however, none of the studies reviewed here attempted to address the role of environment.

On the other hand, there are a number of ways that observed differences in disease prevalence could be artifactual due to biased study designs rather the result of some hypothetical but as-of-yet unidentified biological or environmental factors. Hospital- or outpatient-based studies are clearly not a reliable means of ascertaining incidence or prevalence of PD, because socioeconomic and cultural factors can be major sources of bias in ascertainment. The only studies that systematically determined prevalence were the door-to-door studies in Copiah County and Nigeria. In an area of Mississippi where there is an equal percentage of whites as African Americans, the total incidence of PD (which includes definite, probable, and possible) was equal in both populations, although 58% of African Americans and 32% of Caucasians had not been diagnosed previously. Definite PD was more common in whites than blacks. These community-based studies suggest that PD is likely to be underdiagnosed in general and, most especially, among African Americans. Thus, PD may be one of many chronic diseases that have been shown through health disparities research to be both underdiagnosed and inadequately treated in racial minorities.[32] Ironically, studies reporting a lower frequency of PD in African-American populations may lead to a reduction in the early diagnosis of the condition, as clinicians may not consider it as high on the list of differentials for this population.

Another confounding factor of all the reports including the Copiah County study is the fact that the risk for PD increases with age. According to 1978 life tables, the average life expectancy for blacks was 68.1 years, compared with 74.1 years in whites.[5] In a condition where age is a major risk factor, this is a noteworthy difference. Had African Americans lived longer at that time, the probable and possible cases may have become definite. The prevalence in Nigeria is reported to be much lower than in the United States. Once again, as prevalence is a function of incidence and survival, it is impossible to know whether Africans are less susceptible to PD or whether the higher mortality rates in Nigeria mean that people are dying before reaching an age where they would develop the condition. As long as African Americans have a shortened life expectancy in comparison to individuals of European ancestry, all prevalence studies must be corrected for the age profile of the populations being studied.

Recommendations for Future Studies

An accurate estimate of the prevalence of PD among African Americans relative to the prevalence in non-African Americans will require a community-based survey carried out by medically trained interviewers in a population with a similar proportion of black and white populations. Without a community-based study, there is the possibility that the prevailing idea that PD is less common among Africans or African Americans might bias ascertainment and serve as a self-fulfilling prophecy: as discussed previously, a cross-sectional study of a population such as this would only ascertain the prevalence of PD in these groups, while a long-term survey of the population would be needed to determine the incidence and phenotypic picture of PD in the different ethnic groups. Aside from a detailed neurology questionnaire and a follow-up exam by a neurologist specializing in movement disorders, the study should also include a family history. Ideally, a postmortem would be performed on all individuals who died during the study period. While we acknowledge that a long-term study would

have additional significant logistical difficulties due to loss to follow-up, etc., it is apparent that without such a thorough study, the true prevalence, incidence, and clinical course of PD among African Americans in the United States will remain unknown. Despite these challenges, the need to understand the phenotypic and epidemiological characteristics of PD and other neurodegenerative diseases among minority populations remains an important goal for clinical research.[33]

REFERENCES

1. Hughes AJ, Daniel SE, Kilford L, et al. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinicopathological study of 100 cases. *J Neurol Neurosurg Psychiatry.* 1992;55:181-184.

2. Tanner CM, Goldman SM. Epidemiology of Parkinson's disease. *Neurol Clin.* 1996;14:317-335.

3. Twelves D, Perkins KS, Counsell C. Systematic review of incidence studies of Parkinson's disease. *Mov Disord.* 2003;18:19-31.

4. Zhang ZX, Roman GC. Worldwide occurrence of Parkinson's disease: an updated review. *Neuroepidemiology.* 1993;12:195-208.

5. Arias E. United States life tables, 2000. *Natl Vital Stat Rep.* 2002;51:1-38.

6. Kessler, II. Epidemiologic studies of Parkinson's disease. II: a hospital-based survey. *Am J Epidemiol.* 1972;95:308-318.

7. Paddison RM, Griffith RP. Occurrence of Parkinson's disease in black patients at Charity Hospital in New Orleans. *Neurology.* 1974;24:688-690.

8. Harries J. Neurological disorders in Kenya. London: Oxford University Press, 1973.

9. Rachman I. Neurological disorders in Rhodesia. London: Oxford University Press, 1973.

10. Haddock D. Neurological disorders in Ghana. London: Oxford University Press, 1973.

11. Collomb H, Dumas M, Girard P. Neurological disorders in Ghana. London: Oxford University Press, 1973.

12. Cosnett JE. Neurological disease in Natal. London: Oxford University Press, 1973.

13. Osuntokun BO. Neurological disorders in Nigeria. London: Oxford University Press, 1973.

14. Cosnett JE, Bill PL. Parkinson's disease in blacks: observations on epidemiology in Natal. *S Afr Med J.* 1988;73:281-283.

15. Osuntokun BO, Bademosi O. Parkinsonism in the Nigerian African: a prospective study of 217 patients. *East Afr Med J.* 1979;56:597-607.

16. Lombard A, Gelfand M. Parkinson's disease in the African. *Cent Afr J Med.* 1978;24:5-8.

17. Kessler I. Epidemiologic studies of Parkinson's disease III: a community-based survey. *Am J Epidemiol.* 1972;96:242-254.

18. Shavers VL, Lynch CF, Burmeister LF. Knowledge of the Tuskegee study and its impact on the willingness to participate in medical research studies. *J Natl Med Assoc.* 2000;92:563-572.

19. Advani AS, Atkeson B, Brown CL, et al. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. *Cancer.* 2003;97:1499-1506.

20. Lynch GF, Gorelick PB, Raman R, et al. A pilot survey of African-American physician perceptions about clinical trials. *J Natl Med Assoc.* 2001;93 (12 Suppl):8S-13S.

21. Mayeux R, Marder K, Cote LJ, et al. The frequency of idiopathic Parkinson's disease by age, ethnic group, and sex in northern Manhattan, 1988–1993. *Am J Epidemiol.* 1995;142:820-827.

22. Teresi JA, Albert SM, Holmes D, et al. Use of latent class analyses for the estimation of prevalence of cognitive impairment, and signs of stroke and Parkinson's disease among African-American elderly of central Harlem: results of the Harlem Aging Project. *Neuroepidemiology.* 1999;18:309-321.

23. Van Den Eeden SK, Tanner CM, Bernstein AL, et al. Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. *Am J Epidemiol.* 2003;157:1015-1022.

24. Lanska DJ. The geographic distribution of Parkinson's disease mortality in the United States. *J Neurol Sci.* 1997;150:63-70.

25. Williams G, Kurland L, Goldberg I. Morbidity and mortality with Parkinsonism. *J Neurosurg.* 1966;24:138-143.

26. Kurland LT, Kurtzke JF, Goldberg ID, et al. Parkinsonism. Cambridge, MA: Harvard University Press, 1973.

27. Lux WE, Kurtzke JF. Is Parkinson's disease acquired? Evidence from a geographic comparison with multiple sclerosis. *Neurology.* 1987;37:467-471.

28. Kurtzke JF, Goldberg ID. Parkinsonism death rates by race, sex, and geography. *Neurology.* 1988;38:1558-1561.

29. Schoenberg BS, Anderson DW, Haerer AF. Prevalence of Parkinson's disease in the biracial population of Copiah County, Mississippi. *Neurology.* 1985;35:841-845.

30. Jendroska K, Olasode BJ, Daniel SE, et al. Incidental Lewy body disease in black Africans. *Lancet.* 1994;344(8926):882-883.

31. Marder K, Tang MX, Mejia H, et al. Risk of Parkinson's disease among first-degree relatives: a community-based study. *Neurology.* 1996;47:155-160.

32. Cohen JJ. Disparities in healthcare: an overview. *Acad Emerg Med.* 2003;10:1155-1160.

33. Hardy J, Singleton A, Gwinn-Hardy K. Ethnic differences and disease phenotypes. *Science.* 2003;300:739-740. ■