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Clinical series of Parkinson's disease in KwaZulu-Natal, South Africa: Retrospective chart review

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ABSTRACT

Background: There is limited data on Parkinson's disease (PD) in South Africa.
Methods: Demographic and clinical information was extracted from the hospital records of patients who were coded as PD (International Classification of Diseases, 10th revision, G20) from 2002 to 2016.PD was diagnosed using the United Kingdom Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria (UKBBC).
Results: 414 patients met the criteria, 194 Indian, 130 Black, 16 Mixed Ancestry and 74 White patients. Median age at onset was 60 years, 53% were male and 20% had early onset PD (EOPD). There were no differences between the ethnic groups for the male: female ratio, age at onset, frequency of EOPD, family history, clinical phenotype and disease severity. Dyskinesia and neuropsychiatric symptoms were more frequent in Indian and White patients ($p < 0.001$). PD referral centre prevalence was 23/1000 neurological cases for the period 2002–2016. Referral centre prevalence of PD was 2.8 times higher in White compared to Black patients. Our study demonstrates an increase in referral centre prevalence of PD since the last clinical series in 1988 and an age related increase in prevalence.
Conclusions: PD prevalence is increasing. The clinical profile of PD in Black patients is similar to the other ethnic groups. This study highlights the need for health care resource allocation to neurodegenerative disorders in an ageing African continent.

1. Introduction

PD is a neurodegenerative disorder of ageing characterised by the presence of tremor, rigidity, bradykinesia and postural instability [1]. Ten million persons are affected by PD worldwide [2]. As the number of persons aged 60 years and older is increasing in developing countries, the burden of PD will increase as well [3].

There are no incidence studies of PD in Sub-Saharan Africa (SSA) and epidemiology of PD in South Africa (SA) is undescribed [4]. The 2016 mid-year population of South Africa was estimated to be 56 million persons with 45 million (81%) of the population being Black African [5], however over the past 30 years the largest number of Black African PD patients reported in a study is 35 [6]. Supplementary Table 1 [6–12].

KwaZulu-Natal (KZN) is the second most populous province in the country with a population of 11 million [5].

The last clinical series of patients with PD in KZN was published in 1988; this is the only study that reported on PD hospital prevalence in a South African setting [7]. Fourteen PD cases were identified with lower prevalence rates in Black compared to White and Indian patients (1.5, 23.1 and 12.6 PD cases per 1000 neurology consultations respectively). Since then there has been a demographic and political transition in SA where life expectancy is now higher in Black Africans and hospital access is less limited [13].

Our study reports on a significant number of Black Africans in South Africa (130 PD cases) whose clinical profile has not been previously described; and compares this group to the other ethnic groups from the same province. Our Neurology centre provides a service for a population of over 11 million individuals.

2. Materials and methods

We conducted a retrospective chart review of all out patients attending the Neurology Clinic with an International Classification of Diseases, 10th revision (ICD 10) code of G20 (Parkinson's disease) for the period September 2002–September 2016.

Our hospital, Inkosi Albert Luthuli Central Hospital (IALCH) has an electronic record keeping system. The record of patients for Neurology

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outpatients begins in 2002. At each consultation, notes are reviewed by staff trained in ICD 10 coding and the patient is given an ICD 10 code for each visit. ICD 10 code for Parkinson's disease is G20. Using this filter all patients with an ICD 10 code of G20 from 2002 to 30 September 2016 were searched for on the database.

The outpatient charts of all the patients extracted from the search were analysed. The charts were reviewed by a Neurologist who runs the Movement disorder Clinic since 2011.

PD cases were defined according to the United Kingdom Parkinson's Disease Society Brain Bank Clinical diagnostic criteria (UKBBC). Patients were excluded if they were coded as PD but whose chart revealed presence of exclusion criteria according to the UKBBC.

Demographic and clinical information was recorded for all patients. The self- reported ethnicity was recorded.

We used age at onset (AAO) < 50 years for early onset PD (EOPD). Family history (FH) was defined as a history of PD in a first degree relative. The Hoehn and Yahr scale and where available the Unified Parkinson's Disease Rating Scale (UPDRS) Part 3 was used to describe disease severity.

Referral centre prevalence of Parkinson's disease was calculated as the number of new PD cases compared to the number of new neurology cases for the period of the study. Clinical phenotypes of PD were described as tremor dominant, akinetic rigid or mixed [1,14]. The levodopa equivalent daily dose (LEDD) was calculated for each patient [15]. The frequency of non- motor symptoms (NMS) of anosmia, constipation, orthostatic hypotension, REM Sleep Behaviour Disorder (REMBD) and neuropsychiatric symptoms (NPS) were assessed from clinic records. Signs or reported symptoms of apathy, anxiety, depression, hallucinations or cognitive decline were included in NPS [16].

The study was approved by the Biomedical Research Ethic Committee of the University of KwaZulu- Natal (BE557/16). No consent was required due to the retrospective design of the study.

3. Data analysis

Continuous data is summarized as medians and interquartile ranges and frequencies (percentages). The Kruskal-Wallis test was used to compare the differences among group medians. Chi square tests or Fisher's exact test as appropriate were used for nominal variables. A multi-variable model including both ethnicity and LEDD was then used to determine the relationship between dyskinesias and ethnicity. A P value < 0.05 was used as statistically significant. Data was analysed using Stata V13.1 statistical software.

4. Results

Of the 18,121 neurology outpatients seen in the review period 642 charts were coded as G20 and reviewed. Four hundred and fourteen patients fulfilled the criteria for PD and had sufficient information for analysis (Fig. 1).

There were 134 patients who had Parkinsonism due to causes other than PD (secondary, Parkinson-Plus syndromes or heredodegenerative

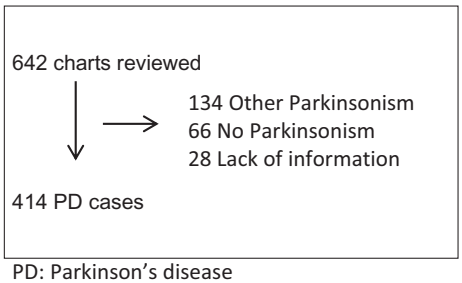

Fig. 1. Flow diagram for G20 search.

Table 1
Demographic and clinical characteristics of 414 PD cases.

Age, years	67 (60–74)
Male: Female	1:1.12
Duration of disease at first visit, months	27 (12–66)
Duration of follow up, months	27 (7–63)
AAO, years	60 (52–66)
EOPD: n (%)	84 (20)
FH: n (%)	28 (7)
H&Y first visit	2
H&Y last visit	2 (2–3)
UPDRS 3 for 60 patients:	42 (30–51)
Tremor dominant: n (%)	184 (44)
Akinetic Rigid: n (%)	31 (8)
Mixed: n (%)	199 (48)
Dyskinesia: n (%)	91 (22)
LEDD mg	575 (400–800)

Variables are reported as median (interquartile range) or number (percentage)
n: number
AAO: age at onset
EOPD: early onset Parkinson's Disease FH: family history
H&Y: Hoehn and Yahr
LEDD: levodopa equivalent daily dose

Parkinsonism). Vascular Parkinsonism and drug induced Parkinsonism were the most frequent secondary causes (50 and 21 patients respectively). Twenty seven patients had features of Parkinsonian Plus disorders (5 Progressive Supranuclear Palsy, 12 Multiple System Atrophy, 11 Dementia with Lewy bodies). Eleven patients had structural causes on neuroimaging (3 patients had space occupying lesions, 5 patients had normal pressure hydrocephalus and 3 had hydrocephalus). Four patients had Parkinsonism related to HIV. Three patients fulfilled the criteria for Frontotemporal dementia with Parkinsonism and one patient had Wilson's disease. The other 16 patients had atypical Parkinsonism but could not be further classified. Sixty six patients had no features of Parkinsonism and 28 patients fulfilled the criteria for PD but were excluded due to lack of information.

The demographic and clinical characteristics of the 414 PD patients are summarized in Table 1

The median AAO was 60 years, 53% were male, 20% of the cohort had EOPD and 7% of patients reported a positive FH of PD. Most of the patients had Mixed PD phenotype (48%), 44% had Tremor Dominant PD and only 8% had Akinetic Rigid PD. Median UPDRS 3 for 60 patients was 42 (30–51). The median duration of disease at first visit was 27 months. Medications used for motor symptoms of PD were dopamine agonists, COMT inhibitors, MOA-B inhibitors, anticholinergic agents, and amantadine. Deep brain stimulation was performed on 2 patients.

Neuroimaging was done for 263 patients (CT 110 and MRI 153), these were performed mostly on patients who had atypical signs for PD or vascular risk factors. The MRI findings of this cohort have not been included in the analysis for this present study, but will be reported separately.

The misdiagnosis rate in our series was 31% (200 patients diagnosed as PD who had another diagnosis).

The most frequently reported NMS were NPS (37%) and constipation (26%). Orthostatic hypotension was found in 6 patients (1%) and REMBD in 20 (5%) of patients.

PD referral centre prevalence was 2.3% of all neurological cases for the period 2002–2016. PD prevalence increased with increasing age. (Fig. 2).

Table 2 summarises the demographic and clinical comparisons between the four ethnic groups.

Of the 414 PD cases 194 were Indian, 130 Black, 16 Mixed Ancestry and 74 White. There were no statistically significant differences in the male: female ratio, AAO, frequency of EOPD, FH frequency, clinical phenotype and disease severity at first and last visit between the four ethnic groups.

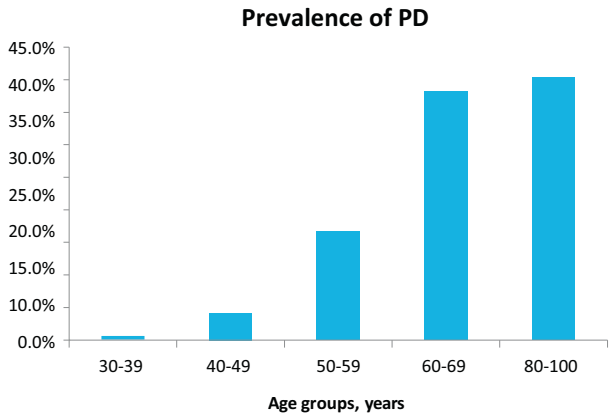

Fig. 2. Prevalence of PD by age groups.

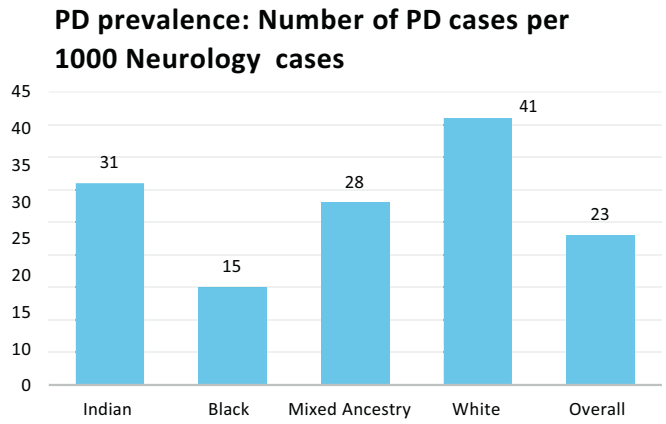

Fig. 3. Hospital prevalence of PD in each Ethnic group and overall hospital PD prevalence.

There was a statistically significant difference in the frequency of dyskinesia (Indians > Whites > Mixed ancestry > Black) and reported NPS (Whites > Indians > Mixed ancestry > Black), with $p < 0.001$.

LEDD was also higher in Indian and White patients compared to Mixed ancestry and Black patients ($p < 0.001$). Both ethnicity and LEDD were significantly associated with dyskinesias; therefore the association between ethnicity and dyskinesias was assessed using multivariable logistic regression model after adjusting for LEDD. In the adjusted analysis, both ethnicity and LEDD remained independently associated with dyskinesias. However the only ethnic groups which differed were Black and Indian ($p = 0.001$). There was no longer a difference between Black and White patients after adjusting for LEDD.

NPS were more frequently reported in White and Asian patients (54% and 42% respectively) compared to Black patients (23%).

PD referral centre prevalence was 2.8 times higher in White compared to Black patients. Referral centre prevalence of PD in each ethnic group and overall PD prevalence is shown in Fig. 3.

5. Discussion

This study reports on the clinical characteristics of 414 PD cases over 14 years. Of these, 130 patients were Black African. This is a substantial number of cases and gives the medical community a rare glimpse into Parkinson's disease in Black Africans; and compares their clinical motor and non- motor profile to White, Indian and Mixed ancestry PD cases from the same hospital.

Population based studies are difficult in our resource limited setting. However, we used our large database of patients to investigate the clinical characteristics of PD in our setting. Strength of our study is the use of clearly defined criteria for PD diagnosis and that all patients are seen by a Neurology team at the clinic.

We found a higher referral centre prevalence of PD compared to the study in 1988 [7]. This phenomenon of increase in prevalence of PD over time was described by Hoehn and Yahr [17]. However, we found that referral centre prevalence of PD was still higher in White compared to Black patients. Whether this is true or an underreporting requires community based studies as socioeconomic and cultural differences may underreport prevalence in a hospital setting [18,19]. There are five hospital prevalence studies in other regions of Sub-Saharan Africa which report prevalence of PD in an outpatient setting [4]. The hospital prevalence in Cameroon, Nigeria and Tanzania report a similar

Table 2
Comparisons of clinical profile in the four ethnic groups.

Ethnicity	Indian	Black	Mixed ancestry	White	P value
N, (%)	194 (47)	130 (31)	16 (4)	74 (18)	
Age, years	67.5 (60–73)	65 (59–72)	68.5 (64–77)	69.5 (63–76)	0.031[a]
Males: n, (%)	92 (42)	70 (32)	12 (5)	45 (21)	0.061
AAO, years	59 (51–65)	59 (52–68)	62.5 (60–70)	60 (50–69)	0.217
EOPD: n, (%)	42 (22)	23 (18)	1 (6)	18 (24)	0.326
FH: n, (%)	16 (8)	6 (5)	1 (6)	5 (7)	0.650
Clinical phenotype, n					0.291
TD	76	66	8	34	
AKR	19	6	0	6	
Mixed	99	58	8	34	
Dyskinesia: n (%)	57 (29)	12 (9)	2 (13)	20 (27)	< 0.001[a]
Adjusted for LEDD					< 0.001[a]
LEDD mg	600 (400–800)	412.5 (300–600)	437.5 (350–600)	600 (400–1000)	< 0.001[a]
Anosmia: n (%)	13 (7)	11 (9)	2 (13)	6 (8)	0.8
Constipation: n (%)	45 (23)	33 (25)	6 (38)	23 (31)	0.4
OH: n (%)	4 (2)	0 (0)	1 (6)	1 (1)	0.2
REMBD: n (%)	9 (5)	6 (5)	1 (6)	4 (5)	0.90
NPS: n (%)	82 (43)	30 (23)	1 (31)	37 (51)	< 0.001[a]

N: number
AAO: age at onset
EOPD: early onset Parkinson's disease FH: family history
TD: tremor dominant AKR: akinetic rigid
LEDD: levodopa equivalent daily dose OH: orthostatic hypotension
REMBD: Rapid eye movement behaviour disorder
[a] Statistically significant.

frequency to our study (2.96%, 1.47% and 2.2% respectively).

The large number of Indians in our cohort reflects the demographics of the province where KZN has the largest number of Indians in South Africa [5].

AAO, number of EOPD, clinical phenotype and M: F ratio of our patients is in keeping with that described in Nigeria and Western populations [14,20–22]. Lower AAO in other SA studies is likely due to a difference in methodology as those studies recruited patients with EOPD and a positive family history and life expectancy in SA is higher in 2016 than in 2002–2012 [5,9,11].

The higher frequency of dyskinesia in Indian and White patients can be attributed to higher LEDD in these groups. All patients were assessed by a Neurology team of Consultants and Neurology trainees with equal access to medications at a single centre, therefore medication access could not have accounted for the difference in LEDD.

After removing the effect of LEDD, Indian patients still had a higher frequency of dyskinesia compared to Black patients. This may be attributable to genetic differences in dopamine receptors and BDNF haplotypes [23–25]. Dopamine receptor DRD2 haplotype is associated with dyskinesia [25].

NPS were also reported less frequently by Black patients. This may be due to differences in perceptions of ageing in Black communities or a milder disease in Black patients [26,27]. Formal testing is needed to investigate if true differences exist. This is a limitation of the study.

The frequency of non-motor symptoms is lower than that found in recent studies; this may be due to the duration of the study period which included patients from 2002 when Neurologists did not routinely enquire about non motor symptoms [16].

Our patients had more access to neuroimaging and PD medications compared to that reported in Ghana, Nigeria and Ethiopia [23,28,29].

Limitations of our study are that is a retrospective study and assessment methods may not be identical and uniformly applied to all study participants. To overcome this limitation all charts were reviewed by a Neurologist using clearly defined criteria. Another limitation is the referral bias which is inherent with hospital based series, however we demonstrated an increase in prevalence over time and an increase in prevalence with age compared to other studies with a similar design in Sub-Saharan Africa. This enables us to provide information to health care planners to allocate more resources to the field of neurodegenerative disorders.

6. Conclusion

Prevalence studies in South Africa are challenging. Despite its limitations, this hospital based study allowed us to report on a large number of patients with PD from different ethnic groups. We found no differences in the clinical phenotypes of PD between Black, Indian, White and Mixed ancestry patients. PD in our setting is common. As a single disease, PD accounted for 3% of our Neurology consultations. As Africa undergoes a demographic transition, we are going to see a surge in PD and health services have to plan to treat the broader spectrum of ageing disorders.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2019.03.023.

Conflicts of interest

The authors declare that there are no conflicts of interest related to this research. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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