

# The Prevalence of Parkinson's Disease in an Arab Population, Wadi Ara, Israel

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**ABSTRACT:** **Background:** The prevalence of Parkinson's disease varies among ethnic and geographic groups around the world, being very low in China and high in Argentina. While the main etiology of the disease has yet to be determined, environmental, occupational and genetic factors seem to play important roles.

**Objectives:** To estimate the prevalence of PD in an Arab Muslim population in Israel, using the drug tracer approach.

**Methods:** We studied a Muslim Arab population living in a well-defined geographic area in Israel, with the majority located in two towns and two large villages. Of the approximately 115,000 residents, about 38% are under the age of 15 and 7.75% are older than 65. Drug tracer methodology was applied in this study. All those who were on anti-PD medication were identified and examined by a neurologist to confirm the diagnosis.

**Results:** The overall crude prevalence of PD in this population was low, 43.24/100,000, while the prevalence in the age group above 65 years was 477.32/100,000. Below this age, the prevalence was very low, 12.29/100,000. PD prevalence was higher in males than in females (ratio 1.17); 63% of male patients smoked cigarettes. The prevalence was found to be twice as high among the residents of rural areas, where most inhabitants work in agriculture.

**Conclusions:** The prevalence of PD among the Arab population in Israel is considered low and comparable to that reported in other Arab countries.

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**KEY WORDS:** Parkinson's disease, prevalence, Arab population, Wadi Ara, drug tracer approach

as 657/100,000 in Argentina [2]. A recent systematic review of PD in Arab populations [3] found only three epidemiological studies. Ashok et al. reported a crude prevalence rate of 31.4/100,000 in Benghazi (northeastern Libya) [4]; Al Rajeh et al., in a two-phase door-to-door study conducted in Thugbah, Saudi Arabia, found a crude prevalence rate of 22/100,000 [5], while Attia Romdhane et al. [6] found the prevalence of Parkinson's disease in Kelibia, Tunisia, to be close to that in the other two studies.

Different methods have been used to estimate the prevalence of PD, such as screening of clinical records and certificates, and two-phase door-to-door surveys in a specific community or drug tracer methodology, utilizing the consumption of L-dopa to calculate the prevalence of PD. Lai et al. [7] used the latter methodology with all anti-Parkinson medications to estimate the prevalence of PD in British Columbia, Canada.

Since very little data are available regarding the epidemiology of PD in Arabs, we undertook to estimate the prevalence of PD in an Arab Muslim population in Israel, using the drug tracer approach.

## SUBJECTS AND METHODS

This study was conducted in the population of Wadi Ara, Israel. This is a geographically well-defined area with a population of 113,322 residents insured by Clalit Health Services (the largest health management organization in Israel). All residents are Muslim Arabs living in two towns, Umm-El-Fahm and Baka-El-Garbia, and in two large villages, Kafr-Kara and Ara-Ar'ara. Wadi Ara is situated in the eastern part of Israel, 20 km from the coast and 10 km from Hadera, a city with an academic neurology department, and 45 km from major Israeli cities such as Haifa and Tel Aviv. The migra-

PD = Parkinson's disease

The prevalence of Parkinson's disease varies among different ethnic and geographic regions around the world. In door-to-door studies, the rate of crude PD prevalence was found to be as low as 15/100,000 in China [1] and as high

tion rate is negligible, with no migration inward and only minimal migration outward. Umm-El-Fahm is a relatively large town, where adult males work in garages, restaurants and construction in both their and other towns, such as Tel Aviv. The population of the town Baka-El-Garbia works in agriculture – in their own orchards or outside the town, in Jewish villages (moshavim and kibbutzim). This population is frequently exposed to pesticides, aerially spread on the nearby large fields by small airplanes. The population of the village Kfar-Kara works mainly in agriculture but a large number of residents are physicians, lawyers and teachers who work far from their village. The adult residents in the village Ar'ara are involved in agriculture.

**STUDY POPULATION**

The age of 3.4% of the studied population is 76–95 years, 3.35% are 66–75 years old, 4.75% are 56–65, 7.14% are 46–55 years old, 13.13% are 36–45, 15.3% are 26–35, 16.17% are 16–25, and 36.76% are younger than 15 years old [Table 1].

**METHODS**

This study applies drug tracer methodology to all anti-PD prescriptions. All drug prescriptions are recorded in the computer database of the Clalit Health Services pharmacy in this region. The anti-PD prescriptions included levodopa-carbidopa (Sinemet®), pergolide, selegiline, ropinirole, entacapone, bromocriptin, amantadin sulfate and anti-cholinergic drugs. To estimate the prevalence of PD from the number of patients taking levodopa-carbidopa alone, dopamine agonists or other anti-PD medications, one of the authors (M.R.), questioned every general practitioner regarding the indications for prescribing anti-Parkinson medications. Patients under the age of 50 being treated with bromocriptin to stop lactation or to control hyperprolactinemia were excluded from the study. Some of the patients were treated at the Movement Disorders Clinic of Hillel Yaffe Government Hospital in Hadera.

In the next step, the above-mentioned neurologist, who has experience in PD diagnosis, examined all the patients to confirm or refute the PD diagnosis. The diagnosis of Parkinson's disease was based on the presence of two or more of the four cardinal signs (resting tremor, rigidity, bradykinesia, postural instability) of PD in all subjects included in the study. Patients with drug-induced parkinsonism or post-encephalitis parkinsonism were excluded from the study. Questions on habits, occupation and known exposure to pesticides were put to the patients by a research assistant.

**RESULTS**

Of the 82 patients treated with anti-PD medications, 49 were diagnosed as suffering from PD; 33 subjects were excluded from the study. Resting tremor was the most fre-

**Table 1.** Age distribution and age-specific prevalence of PD in the Wadi Ara population

Prevalence/100,000	PD patients	% of population	Inhabitants	Age group (yrs)
290.24	11	3.4	3790	76–95
667.02	25	3.35	3748	66–75
132.22	7	4.75	5294	56–65
50.19	4	7.14	7969	46–55
13.65	2	13.13	14,652	36–45
NA	NA	68.23	79,545	< 35

NA = not available

**Table 2.** Population distribution and PD and gender prevalence among the inhabitants of Wadi Ara towns and villages

Prevalence/100,000	PD patients, M/F ratio	Inhabitants	Location
34.84	16 6/10 1.34	44,508	Umm-El-Fahm
73.39	27 18/9 1.78	34,899	Baka-El-Garbia
25.45	4 3/1 1.39	15,606	Kafr-Kara
18.54	3 2/1 3.12	10,278	Ar'Ara

PD = Parkinson's disease

quent sign of the disease. The crude prevalence of PD in this population is 43.24/100,000. The age-adjusted prevalence was 290.24/100,000 for those 76–96 years old, 667.02/100,000 for the 66–75 year old group, 132.22/100,000 for those 56–65 years old, 50.19/100,000 for those 46–55, and 13.65/100,000 for people aged 36–45 years. The prevalence of PD was 477.32/100,000 for people above 65 years of age and only 12.29/100,000 for people under this age [Table 1]. The overall prevalence of PD for males in this population was 46.49/100,000, whereas for females the rate was 39.74/100,000, yielding a male to female ratio of 1.17 [Table 2].

The prevalence of PD was low for residents living in Umm-El-Fahm (34.84/100,000), in Ara-Ar'ara (18.45/100,000) and in Kafr-Kara (25.45/100,000) but was much higher in Baka-El-Garbia (76.22/100,000). In Umm-El-Fahm, the prevalence of PD for males was 29.71/100,000 and for females 40.05/100,000 (a ratio of 1.34, in favor of females). In Baka-El-Garbia, PD prevalence was 93.23/100,000 for males and 53.32/100,000 for females (ratio 1.78); in Ar'Ara these values were 24.19/100,000 for males and 12.5/100,000 for females (ratio 1.93), while in Kafr-Kara the prevalence of PD was 12.47/100,000 for females and 38.97/100,000 for males (a ratio of 3.12, in favor of the males) [Table 2]. Sixty-three percent of the PD male patients were heavy smokers, while none of the female patients ever smoked.

In Baka-El-Garbia, four brothers suffering from autosomal recessive juvenile parkinsonism caused by mutations in the parkin gene were previously reported [8].

## DISCUSSION

The overall crude prevalence of Parkinson's disease in the Arab population in this region of Israel was as low as 43/100,000 and equal to that reported by Attia Romdhane et al. in the Kelibia area of Tunisia, where a door-to-door study was performed for the entire population of 34,874 persons [6]. However, this prevalence was higher than the 27/100,000 reported by Al Rajeh and colleagues [5] in a similar study in the Thugbah area of Saudi Arabia for 22,630 inhabitants, and the 31.4/100,000 rate reported in Benghazi, Libya for a population of 518,745 [4]. We assume that the prevalence of PD in our study might be an underestimate, since active case-finding efforts in communities detect as many as 10–40% of previously unrecognized PD cases [9,10]. We assume that some patients suffering from predominantly akinetic PD were missed from our study. However, our findings are quite sound, since the percentage of the elderly in this population is much higher than that in the other studies performed in Arab countries. This also reflects the good medical care provided in Israel, which leads to longevity.

Few studies have investigated the prevalence of PD. In Israel, Herishanu et al. studied the prevalence of PD in several kibbutzim in southern Israel. This Jewish population is unique [11,12] – living in rural communities, working mainly in agriculture, and receiving good medical care. The prevalence rate was found to be extremely high in this population. Another larger study examined the prevalence of the disease in the populations of every kibbutz in the country and also reported a high prevalence rate of 240/100,000 [13].

What could explain the differences in prevalence observed in Arab and Jewish populations in Israel? One possibility is a lower awareness of the symptoms of the disease among care providers (families and medical services) in Arab communities. We partially rule out such a possibility, since the medical services everywhere in Israel are of a high quality. However, families are not always aware that PD symptoms developing in the elderly are an expression of a disease (i.e., PD) and not an expression of the normal aging process. Another reason might be ethnic, since a low prevalence of the disease was already reported in other Arab populations in the Mediterranean basin (e.g., Tunisia, Lybia), as well as in other parts of the Middle East (Saudi Arabia).

A framework of the European Neuropsychopharmacology Task Force, which analyzed 39 studies conducted in selected European countries, reported a crude PD prevalence of 65.6–12,500 per 100,000. [14]. However, the causes of variation in the prevalence of PD in the different countries are still a matter of speculation. Although differences may be related to genetic, occupational or environmental factors, they may also be related to other factors, such as the use of different methodologies and diagnostic criteria in various studies.

In this study, we applied the drug tracer methodology, considering all anti-PD medications, mainly L-dopa compounds and all the dopamine agonists as well as anti-cholinergic agents and amantadin. This methodology is relatively new and only a few studies have used this approach to estimate the prevalence of PD in large populations [15].

However, there are disadvantages to this methodology as compared to a door-to-door study. According to several reports, the probability of omitting sub-clinical and/or misdiagnosing PD patients is about 12% [10,16,17], and about 20% of subjects were estimated to be over-diagnosed as PD and hence treated wrongly, with anti-Parkinson drugs, for extrapyramidal signs [18]. Nonetheless, drug tracer methodology has recently generated interest among many researchers for its feasibility and its ability to study very large populations within a short period and with a small team of researchers.

In our study, we examined every subject treated with an anti-Parkinson drug to confirm the diagnosis of PD. Only 60% of subjects were found to have PD; all were enrolled in the study. While this research revealed differences in the prevalence of PD between males and females in different areas of the studied region, in general, males slightly exceeded females by a ratio of 1.17. Epidemiological studies showed that men are at a greater risk of being afflicted with PD than are women [17,19,20]. There is no explanation for the increased risk in males [20]. The average standardized ratio of female to male is 1:3.5 for prevalence studies and 1:3.4 for incidence studies [21].

We found a high prevalence of PD in the town of Baka-El-Garbia, where the adult residents are agricultural workers. The prevalence of PD was twice as high as that in Umm-El-Fahm where the adult residents are not involved in agriculture. Epidemiological studies have pointed to an increased risk of PD in farmers and agricultural workers [20,22]. Moreover, Baka-El-Garbia is surrounded by large fields, where the population is continuously exposed to herbicides and pesticides dispersed in the air by small airplanes. Different studies showed that people exposed to pesticides have an increased risk of developing PD [20,22–24]. However, no conclusion has been drawn as to the specific agents that may be responsible [20]. A review of 31 publications evaluating the association between pesticides and PD concluded that such agents are risk factors for PD, and that herbicides, such as paraquat, specifically, increase the risk of PD.

The rate of cigarette smokers in this population is very high and is reflected in the fact that all the PD males in this study are cigarette smokers. This observation is in contradiction with previous studies stating that there is sufficient evidence to conclude that cigarette smokers stand a lower risk of developing PD [20,25].

In conclusion, this study demonstrates a low prevalence of PD in the Israeli Arab population (like that reported in

Arab countries in the region), in comparison with a relatively higher prevalence of PD in the Jewish Israeli population. Adult residents working in agriculture and exposed to pesticides are at risk of being struck with PD. The results of this study suggest that ethnic and environmental factors may play a part in the etiology of Parkinson's disease.

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