

INCIDENCE OF PARKINSON'S DISEASE IN THE KICHEVO REGION IN NORTH MACEDONIA

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Abstract

Parkinson's disease (PD) is a multi-attribute neurodegenerative disorder combining motor and non-motor symptoms without well-defined diagnostic clinical markers. The presence of primary motor features (bradykinesia, rest tremor, rigidity and loss of postural reflexes) is the most characteristic signs of PD that are also utilized to identify patients in current clinical practice. Epidemiological studies on the incidence of PD are important to better understand the risk factors for PD and determine the condition's natural history. This paper examines the incidence and prevalence of DP in total and its variation by gender. We searched data for epidemiologic studies of PD from 2015 to 2021. The data were analyzed in general and by gender in particular, and referring to the official data on the population of the Kichevo region (30138 inhabitants), were determined whether a significant difference was present between the sexes. From the data obtained it was found that the total number of persons with Parkinson's disease from 2015 to 2021 resulted 1401 (4.65%). The number of women affected was 871 (2.89%), while the number of men was 530 (1.76%), that is, the number of women was higher than men for 341 (1.2%) cases. The incidence of PD in general in recent years (2019-2021) was increasing and significantly higher compared to earlier years (2015-2018).

Keywords: Parkinson's disease, incidence, symptoms, levodopa, neurodegeneration, Lewy bodies.

1. Introduction

The discovery of Parkinson's disease (PD) originated from James Parkinson, who described this disorder as "paralysis agitans" in 1817 (Parkinson, 1969). Since then, PD has been defined as a complex neurodegenerative disorder expressing various symptoms due to the dopaminergic neuronal cell death in the substantia nigra (SN) (Kalia and Lang, 2015). PD is identified as the second-most common neuropathological disorder after Alzheimer's disease associated with significant disability and decreased quality of life (Mhyre et al, 2012). The symptoms usually emerge slowly, and as the disease worsens, non-motor symptoms become more common [(Parkinson's Disease Information Page, 2016) (Kalia and Lang, 2015)]. The most obvious early symptoms are tremor, rigidity, slowness of movement, and difficulty with walking (Parkinson's Disease Information Page, 2016). Cognitive and behavioral problems may also occur with depression, anxiety, and apathy occurring in many people with PD (Han et al, 2018). Parkinson's disease dementia becomes common in the advanced stages of the disease. Those with Parkinson's can also have problems with their sleep and sensory systems [(Parkinson's Disease Information Page, 2016) (Sveinbjornsdottir, 2016)]. The motor symptoms of the disease result from the death of cells in the substantia nigra, a region of the midbrain, leading to a dopamine deficit (Parkinson's Disease Information Page, 2016). The cause of this cell death is poorly understood, but involves the build-up of misfolded proteins into Lewy bodies in the neurons [(Villar-Piqué et al, 2016) (Kalia and Lang, 2015)]. Collectively, the main motor symptoms are also known as Parkinsonism or a Parkinson syndrome (Kalia and Lang, 2015).

The prevalence of a disease reflects both the incidence and the duration of disease. The incidence of Parkinson's disease is linked to risk and protective factors [(de Lau and Breteler, 2006), (Bellou et al, 2016), (Harris, 2012)]. So, the cause of PD is unknown, with both inherited and environmental factors being believed to play a role (Kalia and Lang, 2015). Those with a family member affected by PD are at an increased risk of getting the disease, with certain genes known to be inheritable risk factors (Quadri, 2018). The most important risk factor is age, but the risk of Parkinson's disease also appears to be associated with industrial chemicals and pollutants, such as pesticides (Pezzoli and Cereda, 2013), solvents (Pezzoli and Cereda, 2013), and metals (Weisskopf et al, 2010), (Vlaar et al, 2018)] Conversely, smoking is associated with a decreased risk of Parkinson's disease (Li et al, 2015), but whether this association is causal is debatable (Ritz et al, 2014). The factors that affect disease duration are less well known, but increasing longevity also translates into longer disease duration [(Pringsheim et al, 2014) (Wanneveich et al, 2018)]. Therefore, as ageing and industrialisation increase globally and smoking decreases in some regions, the prevalence of Parkinson's disease seems poised to increase [(Dorsey, et al, 2007) (Rossi et al, 2018)]. Detailed estimates of the disease burden can help to evaluate the effect of these risk factors and inform efforts to prevent the disease and to care for and treat those affected by the condition.

Diagnosis of typical cases is mainly based on symptoms, with motor symptoms being the chief complaint. Tests such as neuroimaging (magnetic resonance imaging or imaging to look at dopamine neuronal dysfunction known as DaT scan) can be used to help rule out other diseases [(Armstrong and Okun, 2020) ("Parkinson's Disease Information Page", 2016)]. Parkinson's disease typically occurs in people over the age of 60, of whom about one percent are affected ("Parkinson's Disease Information Page", 2016) (Carroll, 2016)]. Males are more often affected than females at a ratio of around 3:2 (Kalia and Lang, 2015). When it is seen in people before the age of 50, it is called early-onset PD (Mosley, 2010). By 2015, PD affected 6.2 million people and resulted in about 117,400 deaths globally [(Vos et al, 2016) (Wang et al, 2016)]. The average life expectancy following diagnosis is between 7 and 15 years (Sveinbjornsdottir, 2016).

No cure for PD is known; treatment aims to reduce the effects of the symptoms [("Parkinson's Disease Information Page", 2016) (Samii et al, 2004)]. Initial treatment is typically with the medications levodopa (L-DOPA), MAO-B inhibitors, or dopamine agonists (Armstrong and Okun, 2020). This combination medication is used to treat symptoms of Parkinson's disease or Parkinson-like symptoms (such as shakiness, stiffness, difficulty moving). Parkinson's disease is thought to be caused by too little of a naturally occurring substance (dopamine) in the brain. Levodopa changes into dopamine in the brain, helping to control movement. Carbidopa prevents the breakdown of levodopa in the bloodstream so more levodopa can enter the brain. Carbidopa can also reduce some of levodopa's side effects such as nausea and vomiting. As the disease progresses, these medications become less effective, while at the same time producing a side effect marked by involuntary muscle movements (Sveinbjornsdottir, 2016). At that time, medications may be used in combination and doses may be increased (Armstrong and Okun, 2020). Diet and certain forms of rehabilitation have shown some effectiveness at improving symptoms [(Barichella et al, 2009) (Ahlskog, 2011)]. Surgery to place microelectrodes for deep brain stimulation has been used to reduce motor symptoms in severe cases where drugs are ineffective ("Parkinson's Disease Information Page", 2016). Evidence for treatments for the non-movement-related symptoms of PD, such as sleep disturbances and emotional problems, is less strong (Kalia and Lang, 2015).

Epidemiological studies on the incidence of PD are important to better understand both the risk factors for PD and determine the condition's natural history. As PD predominantly affects older adults, worldwide aging populations, especially in economically developed countries, will increasingly need to develop strategies to meet the health care needs of individuals with PD. Information on the variation in the incidence of PD between age groups and genders can be used to effectively direct these strategies to appropriate populations. Therefore, the synthesis of epidemiological data on PD incidence can help guide effective planning of medical services.

This systematic review provides an up-to-date synthesis of incidence studies of PD performed between 2015

and 2021, and builds on results by including an analysis of study quality and a descriptive analysis of the prevalence of Parkinson's patients in the city of Kichevo according to tests throughout the calendar year and gender categorization to compare gender differences.

2. Material

As material for identification of cases of Parkinson's disease (PD) in the district of Kichevo are used the statistical data provided by the Central Hospital of Kichevo (Department of Neurology), a permit obtained from the directorate of the aforementioned hospital.

Search strategies for studies on the incidence of PD were developed in consultation with an academic research librarian with expertise in systematic review. Databases were searched for PD incidence from 2015-2021 using terms specific to PD and restricted to studies of incidence and epidemiology.

Reviewers performed the data extraction using a standardized assessment form that included the following domains: region, target study population, definition of condition, data sources, diagnostic criteria, overall incidence, and incidence by gender. The incidence of Parkinson's disease (PD) was studied over a 7-year period (2015–2021) in the district of Kichevo, North Macedonia with a mean population of 30138 and were reported for 1401 persons diagnosed with Parkinson's disease. These data were processed to derive the incidence of the number of infected persons per 30138 inhabitants. Incidence in 30138 inhabitants. ($c = (a / b) \times 30138$).

We estimated overall incidence and prevalence as well as gender prevalence comparisons over the years. All data were then assessed and entered into evidence tables.

3. Results and discussion

During the years 2015 - 2021, 1401 patients are controlled in the hospital of Kichevo according to the data. It's valuated the general frequency in the Kichevo district, and we have also categorized it by gender (male and female). From the secured results, patients registered with this disease can be found in the following tables and graphs. But it is also worth mentioning that, due to civic negligence and carelessness to be in step with this neurological disease and the lack of medical check-ups, has made that every checked person unfortunately be diagnosed with Parkinson' disease.

Table 1. Frequency of individuals with Parkinson's disease

Years	Numerical frequency	Relative frequency (%)
2015	118	0.39
2016	106	0.35
2017	106	0.35
2018	114	0.38
2019	223	0.74
2020	318	1.06
2021	416	1.38
Total:	1401	4.65

The data of Table 1 are also presented graphically in Graph 2.

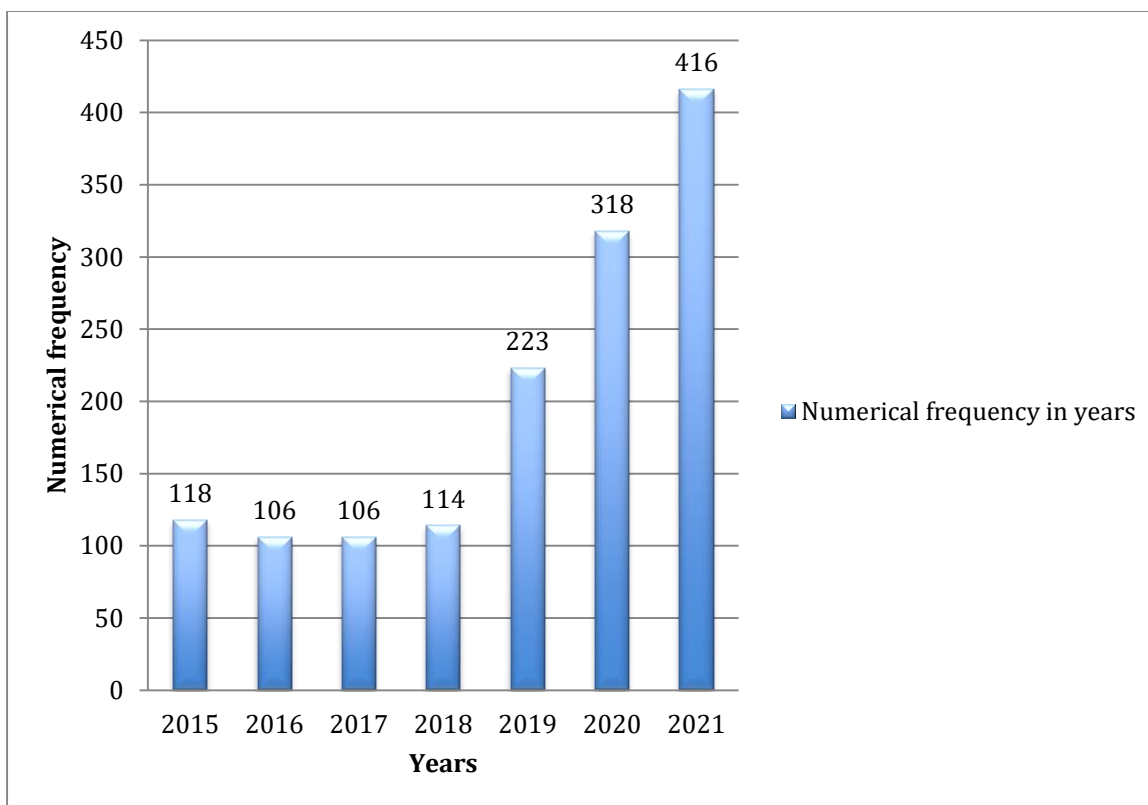


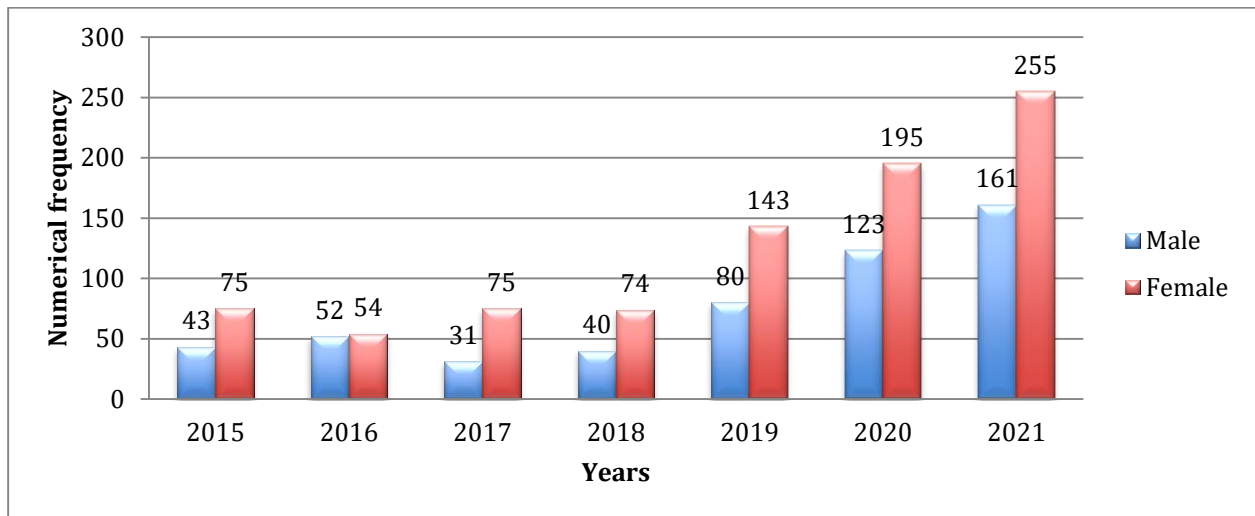
Fig 1. Numerical frequency of individuals with Parkinson's disease

In the table and graph above are presented descriptive data on the number of patients with Parkinson's in the region of Kichevo according to tests during a calendar year. Referring to the official data on the population of the city of Kichevo (30138 inhabitants, Wikipedia; https://sq.wikipedia.org/wiki/Komuna_e_K%C3%ABr%C3%A7ov%C3%ABs) has been calculated the total number of diseased from the total percentage of inhabitants. The data reflect the presence of Parkinson's patients in the Kichevo region, in the period 2015 - 2019, where: in 2015 there was a total of 118 (0.39%) with Parkinson's disease; in 2016 and 2017 the number of patients with Parkinson's was the same and reached 106 (0.35%); in 2018 there was a slight increase compared to previous years, where the total was 114 (0.38%). From the previous year in 2019 the number of cases with Parkinson's has doubled and reaches 223 (0.74%). In 2020 cases with Parkinson's disease have continued to increase to 318 (1.06%) and the increase in cases with Parkinson's has reached a maximum in 2021, where the number has increased to 416 (1.38%) cases. From the relevant data it is understood that, the frequency of Parkinson's disease the last two three years has been significantly increased several times compared to previous years. Also, according to the information received from the adequate staff, the mortality rate in recent years in the Municipality of Kichevo has increased significantly, and the reasons why are not yet known. It is thought that it comes as a result of pollution of the external environment, for hereditary genetic reasons, but it is thought that the cause is the lack of conditions in the hospital of Kichevo to diagnose and treat this disease in time, as well as the negligence of citizens. For this increase in the frequency of the disease, we think that, in addition to the above factors, the pandemic of SARS-CoV-2 (personal communications with relatives) has also had its affect.

Table 2. Frequency of Parkinson's disease divided by gender

Years	Numerical frequencies for females	Numerical frequencies for males	Relative frequency (%)	
			Female	Male
2015	75	43	0.25	0.14
2016	54	52	0.18	0.17
2017	75	31	0.25	0.10
2018	74	40	0.25	0.13
2019	143	80	0.47	0.27
2020	195	123	0.65	0.41
2021	255	161	0.85	0.53
Total:	871	530	2.89	1.76

The values of Table 2 are graphically presented in Graph 2 as well.

**Fig 2.** Numerical frequency of individuals with Parkinson's disease according to gender

From the results of the table and graph above, in terms of the frequency of Parkinson's patients across years divided by gender, it can be seen that for the last seven years, out of a total of 1401 patients, the total number of women affected by Parkinson's disease was 871 (2.89%), while for men the total number of people affected by Parkinson's disease was 530 (1.76%). So, from the relevant data it was found that the number of women with Parkinson's disease from 2015 to 2021 is higher than men for 341 cases ($871 - 530 = 341$) or 1.2% ($2.89\% - 1.76\% = 1.13\%$), ie close to once more than the male gender, these results are opposite to most of the data from different authors for different countries.

In terms of gender difference over the years, we have: for 2015 number of women were 75 (0.25%) and number of men were 43 (0.14%); in 2016 there were 54 females or (0.18%) and 52 males or (0.17%); in 2017 there were 75 (0.25%) females with Parkinson's and 31 (0.10%) males; in 2018, the number with DS in females was 74 (0.25%) and 40 (0.13%) in males. From the previous year in 2019 the number of cases with Parkinson's has doubled and reached 143 (0.47%) for females and 80 (0.27%) for males. In 2020 cases with Parkinson's disease have continued to increase to 195 (0.65%) for females and 123 (0.41%) for males and the increase in cases with Parkinson's has reached a maximum in 2021 where the number has increased to 255 (0.85%) for women and up to 161 (0.53%) for men.

4. Conclusions

Based on the secured data, the number of people affected by Parkinson's in the Kichevo region, during the period 2015 - 2021 is 1401 (4.65%).

In terms of disease frequency between years, the results were: 0.39% for 2015, 0.35% (human frequency) for 2016 and 2017, 0.38% for 2018, 0.74% in 2019, 1.02% in 2019 and 1.02 % at 12. for 2021.

Regarding the frequency of Parkinson's patients across years divided by gender, the total number of women affected by Parkinson's disease was 871 (2.89%), while for men it was 530 (1.76%) (from 2015 to year 2021 the number of females was higher than males by 341 or 1.2%).

The origin of Parkinson's disease in the Kichevo region is considered to be hereditary and genetics, as well as high neglect of civic for control and care over their health. Also the increase of cases with Parkinson's disease in recent years has been affected by the pandemic of SARS-CoV-2.

The lack of definite clinical markers for PD diagnosis has initiated the development of symptom-based guidelines for the identification and classification of PD patients. The most widely accepted clinical criteria are solely built on motor symptoms, although the successful implementation of dopaminergic therapy has pointed out the importance of non-motor features. The patients' quality of life and their degree of disability is highly affected by the presence of non-motor symptoms, and more importantly, their appearance can precede motor symptoms by several years. The first diagnostic criteria for PD have not considered NMS as significant features or used as a suggestion of alternative criteria, while in current guidelines, their presence is essential in PD diagnosis. The involvement of several NMS into novel guidelines has improved diagnostic accuracy and sensitivity, although early-stage identification is still challenging. One of the potential strategies is to identify molecular alterations that can be specified for the prodromal symptoms of PD. The use of smart devices and wearable sensors can also provide essential data to identify prodromal symptoms of PD by analyzing sleep (RBD), defecation (constipation) and mental health (depression). These could help to recognize earlier the disease initiation and develop novel neuroprotective therapies to improve PD remission.

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