

Parkinson's Disease in A Kurdish Population

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ABSTRACT:

BACKGROUND :

Parkinson's disease (PD) is a neurodegenerative disorder of the central nervous system characterized by resting tremor, bradykinesia, cogwheel rigidity, and impairment of postural reflexes. It appears that certain environmental factors are involved.

OBJECTIVE:

The aim of the present work is to study the age, gender, residency, family history of patients with Parkinson's disease in Kurdish population.

PATIENTS AND METHODS:

A cross sectional survey study conducted in outpatient clinic at Shar hospital, a teaching hospital in Sulaymania city, during the period between the first of October 2014 and first of February 2015. Thirty five patients diagnosed idiopathic Parkinson's disease by a neurologist include in this study. Data was collected in outpatient in one hospital Shar teaching hospital in Sulaymania city.

RESULT:

Mean age of patients of Parkinson's disease 65 years, disease started in male earlier than female in Kurdish population in Sulaymania. We found that 22 cases (62.9%) of total cases were male and 13 cases (37.1%) of all cases female, male was affected more than female. Male to female ratio was (1.7:1).

There was statistically significant difference between cases who were living in urban area and who were living in rural area in regarding age but no significant difference regarding to gender.

There is statistically significant difference in family history distribution in different age groups.

Patients with family history positive of Parkinson's disease affected the disease in earlier ages.

There was statistically significant difference between age groups for smoking

CONCLUSION:

Male was more affected Parkinson's disease than female, male with earlier ages in Kurdish population. Patients living in rural area and patients with positive family history of Parkinson's disease affected by the disease in earlier ages.

KEY WORDS: parkinson, kurd.

INTRODUCTION:

Parkinson's disease (PD) is a neurodegenerative disorder of the central nervous system characterized by resting tremor, bradykinesia, cogwheel rigidity, and impairment of postural reflexes. The syndrome was first described by the British physician James Parkinson in An Essay on the Shaking Palsy published in 1817. The eponymous designation was given some years later by Jean-Martin Charcot, the famous director of Paris's Salpêtrière Hospital.⁽¹⁾

Parkinson's disease has been defined as a clinico-pathological entity, in which progressive levodopa-responsive Parkinsonism is associated, at autopsy, with neuronal loss and the presence of eosinophilic intracytoplasmic Lewy bodies in specific central and autonomic nervous structures. These include particularly the pigmented brainstem monoaminergic nuclei, the substantia nigra (dopaminergic) and locus caeruleus (noradrenergic).⁽²⁾

The prevalence of PD in most countries is around 180/100,000. Overall, incidence rises steadily with age, although recessive forms become less frequent with age. Average age at onset is about 60 years, with fewer than 5% of cases starting before age 40.⁽⁵⁾

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PD is generally considered a disease of late middle age with the average age of onset at around 60 years of age. There are cases of "early-onset" Parkinson's disease with patients developing symptoms prior to the age of 40.⁽⁶⁾

More men than women are diagnosed with PD by a ratio of approximately 2:1.⁽⁷⁾

People who lived with the disorder for 15 or 20 years had only a slightly shorter life expectancy than those without the disease.⁽⁹⁾

It appears that certain environmental factors are involved. Prior living in a rural area has been implicated as a possible risk factor for PD, particularly in the early onset type. Researchers began to wonder if an exogenous neurotoxin, possibly environmental in origin, could be responsible for the development of the disease. In the last few years, a series of epidemiological studies have suggested that PD is more prevalent among individuals who live in rural area.⁽¹⁰⁾

A protective effect of smoking and coffee drinking has emerged in some epidemiologic studies but is marginal. A number of studies have found that people who smoke cigarettes are less likely to develop Parkinson's disease than those who don't.⁽¹¹⁾

While previous studies have found that cigarette smoking and coffee consumption are associated with a lower risk of Parkinson's disease, research on alcohol consumption and PD risk has shown conflicting data.⁽¹³⁾

Having a parent or sibling with Parkinson's disease is thought to nearly double patient's risk of developing the disease. Five to 10 percent of people who have Parkinson's disease also have a family member with parkinson.⁽¹⁴⁾

Unilateral onset and persisting asymmetry of the cardinal motor features are diagnostic hallmarks of Parkinson's disease, differentiating it from similar but distinct parkinsonian disorders.⁽¹⁵⁾

The governorate of Sulaymaniya is located in the northeast of Iraq, on the border with Iran. Sulaymaniya hosts the fertile plains of Sharazur and Bitwen, which give way to hills and the Zagros mountain range in the northeast. The area: 17,023 sq km (3.9% of Iraq). Population: 1893617 (6% of total). Gender Distribution: Male: 50% Female: 50%. Geo Distribution: Rural: 30% Urban: 70%.²⁰

The aim of the present work is to study the age, gender, residency, family history of patients with Parkinson's disease in Kurdish population.

PATIENTS AND METHODS:

Design:

Design of the study was a cross sectional survey study with analytic elements.

Setting:

Study was conducted in outpatient clinic at Shar hospital, a teaching hospital in Sulaymania city, during the period between the first of October 2014 and first of February 2015.

Patient:

Thirty five patients diagnosed idiopathic Parkinson's disease by a neurologist include in this study; the patients were considered as cases of idiopathic Parkinson's disease when they met proposed diagnostic criteria (The Queen Square Brain Bank Criteria) for Parkinson's disease.⁽²¹⁾

Data collection and analysis:

A questionnaire form had been formed and prepared to be proper for data collection.

All questionnaire forms were filled by the researcher by obtaining data from the patients themselves and their relative and clinical examination of patients in outpatient clinic in Shar teaching hospital in Sulaymania.

Variables:

- Age of patients of Parkinson's disease
We divided patients according according to their age into 3 categories, below 60, 60-70, and above 70 years.
- Gender of patients of Parkinson's disease
- Patients were living in urban area or rural area
- Smoking in patients of Parkinson's disease
- Alcohol use in patients of Parkinson's disease
- Family history of Parkinson's disease

Statistical analysis:

Data were coded and fed on computer. Analysis was done on SPSS (Statistical Package for Social Science Analysis, Version 21). For the determination of statistical significance among different variables, a descriptive statistics like mean and SD (Standard Deviation) together with analytic statistics like Chi-square (χ^2) test & t-test have been done when appropriate. P-values less than 0.05 were considered significant. The results were presented in the form of frequency graphs.

RESULTS:

Our data was collected by filling formed questioner for idiopathic Parkinson disease in outpatient clinic in Shar teaching hospital in Sulaymania city during period 1st. of December 2014 to 1st. of February

2015 in cross sectional survey study, statistical significance was considered whenever the P-value was equal or less than 0.05. Study found that:

Age group :

We divided all cases into 3 age groups, The age of cases with Parkinson's disease in this study ranged from (42-80) years with a mean $\pm$ SD (65.09 $\pm$ 9.33) years, we have 9 cases (25.7%) of all cases below 60 years in which the youngest one was 42 years old, 8 cases (88.9%) of them were male and 1case (11.1%) was female. Ages of 10 of our cases (28.6%) were between (60-69) years, 5 cases (50%) were male and 5 cases (50%) were female. Ages of 16 cases (45.7%) of all cases were above 70 years, 9 cases (56.3%) were male and 7 cases (43.75%) were female (Fig. 1).

Gender:

We found that 22 cases (62.9%) of total cases were male and 13 cases (37.1%) of all cases female, male was affected more than female. Male to female ratio was (1.7:1).

Duration of the disease:

We divided duration of the disease into three category, we found that median duration of the disease was 10 years, the duration of the disease ranged between (1-15) years, with minimal duration 1 year and maximum duration 15 years, duration of 26 cases of total cases were in between (1-4) years, 18 cases (69.2%) were males and 8 cases (30.8%) were females. Duration of disease of 7 cases (20.0%) was between (5-9) years, 4 cases (57.1%) were male and 3 cases (42.9%) were female. The duration of the disease of 2 cases 5.7% were in between (10-15) years and all were females. We found that high percentage of duration of disease of male cases in between (1-4) years and numbers of cases duration in between (10-15) years, all are female. There was no statistically significant difference between male and female regarding duration of the disease, shown in (Fig.2).

Residency (Urban or Rural) area:

We divided residency of patients in to urban area and rural area, 19 cases (54.3%) were living in urban area, 12 cases (63.2%) were male and 7 cases (36.8%) were female, ages of 6 cases (31.6%) were below 60 years, ages of 2 cases (10.5%) in between (60-69) years and ages of 11 cases (57.9%) were

above 70 years of all who living in urban area. 16 cases (45.7%) living in rural area, 10 of cases (62.5%) were male and 6 cases (37.5%) were female, ages of 3 cases (18.8%) are below 60 years, ages of 8 cases (50%) in between (60-69) years and ages of 5 cases (31.3%) above 70 years of who were living in rural area. There was statistically significant difference between cases who were living in urban area and who were living in rural area in regarding age but no significant difference regarding to gender, as shown in (Fig.3).

Smoking in patients of Parkinson's disease:

Twenty cases (57.1%) smokers, ages of 7 cases (35%) are below 60 years, ages of 2 cases (10%) were in between (60-69) years and ages of 11 cases (55%) were above 70 years of whose smokers. 15 cases (42.9%) were non-smokers, ages of 2cases (13.3%) were below 60 years, ages of 8 cases (53.3%) were between (60-69) years, ages of 5 cases (33.3%) were above 70 years. There was statistically significant difference between age groups for smoking, shown in (Fig.4).

Alcohol use in patients of Parkinson disease:

Three cases (8.6%) were using alcohol, ages of 2 cases (66.7%) below 60 years and ages of one case 33.3% of alcohol user was above 70 years. 32 cases (91.4%) are not alcohol user, ages of 7 cases (21.9%) were below 60 years, ages of 10 cases (31.3%) in between (60-69) years and ages of 15 cases (46.9%) were above 70 years. Statistically there was no significant difference between age groups for alcohol use, shown in (Fig.5).

Family history:

Family history in 3 cases (8.6%) positive for Parkinson disease, 2 cases (66.7%) were males and one case (33.3%) was female, ages of all three cases (100%) are below 60 years, 32 cases (91.4%) with negative family history, 20 cases (62.91%) were males and 12 cases (37.5%) were females, ages of 6 cases (18.9%) were below 60 years, ages of 10 cases (31.3%) were in between (60-69) years and ages of 16 cases (50%) above 70 years. There is statistically significant difference in family history distribution in different age groups, but not statistically significant according to gender, shown in (Fig.6).

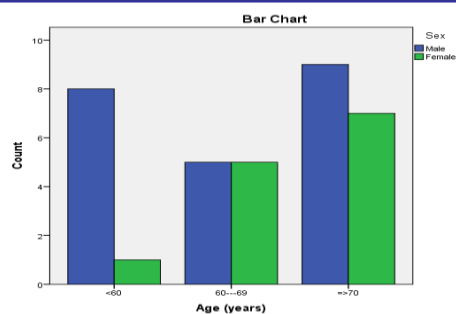


Fig. 1: Age of patients according to gender.

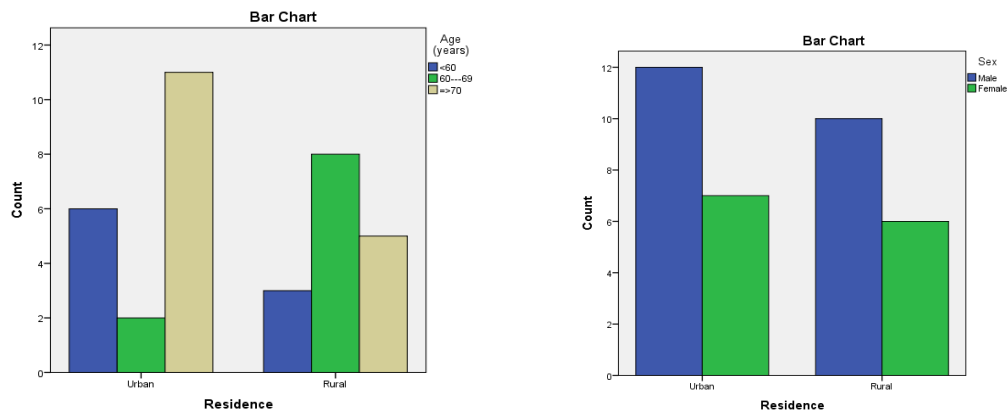


Fig. 3 :- Residency of patients according to age groups and gender.

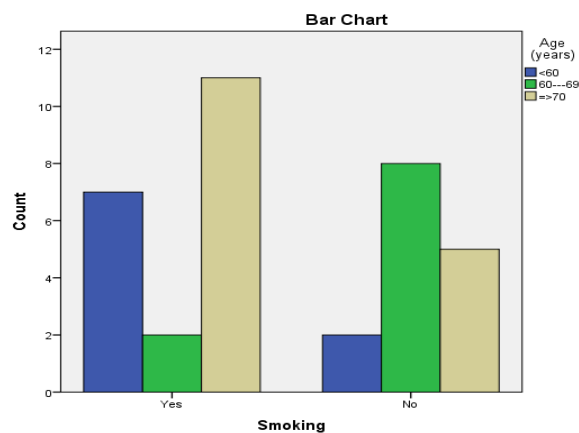


Fig. 4 Distribution of Smoking according to age groups.

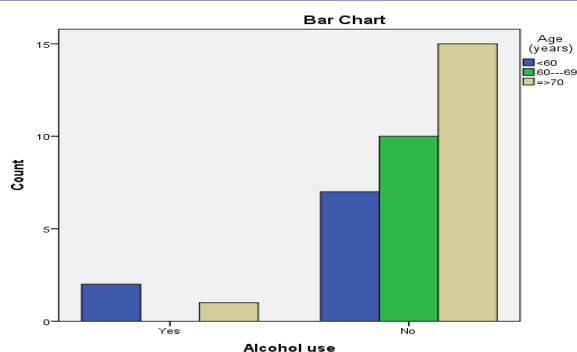


Fig. 5 Alcohol use in different age groups.

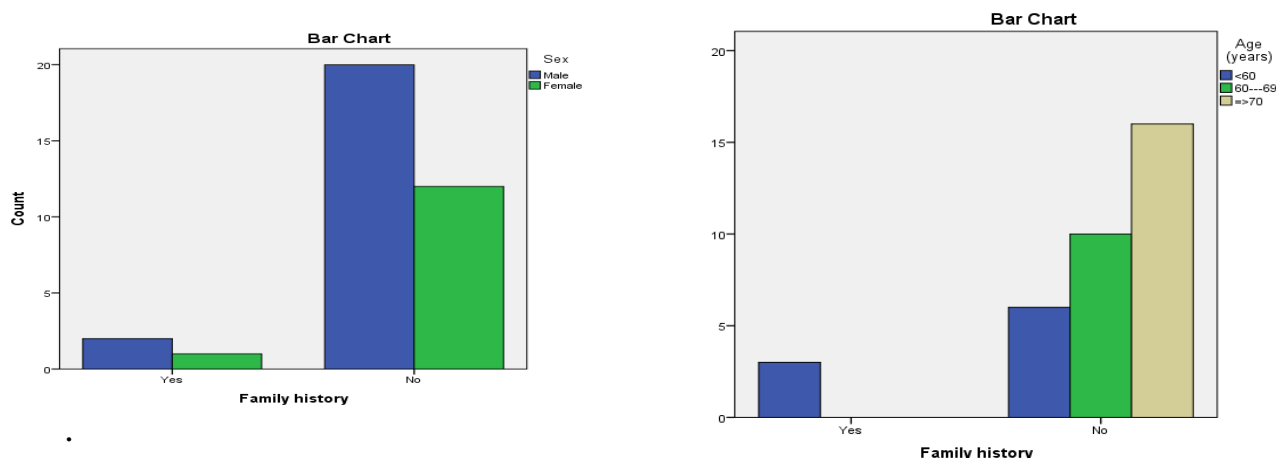


Fig 6: Distribution of Family history in different age groups and gender.

DISCUSSION:

There are several studies reported on idiopathic Parkinson disease in literature, several aspects of disease had been studied in many cities in the world, also many studies were done between several population, a variety of studies in Iraq for many aspects of idiopathic Parkinson disease were done specially in Baghdad and on Arabs population. We did our study on idiopathic Parkinson disease in Sulaymaniya city and between Kurdish populations for many aspects of the diseased patient.

We found mean age of the patients was 65 years, in similar studies in Arabs, Turkish, Persian, Swedish and Chinese population state that with small difference in mean age around 60 to 65 years in different population this is the ages which expected in Parkinson disease, Parkinson disease was known to be a disease of peoples who was completed their life. (23, 24, 25, 26, 27, 28, 29, 30, 31)

Male patients more affected in earlier ages than females in Kurdish population as in, as similar studies were done with same result male affected earlier as in Arabs, Turkish, Persian, Swedish and Chinese population, Parkinson disease had multiple causes and many causes are exposure to environmental and occupational toxins, in Kurdish population there are male predominance in many aspects of life as working in general and working in farms specially, in military and many other aspects, therefore males have more chance to exposure to toxins and affect Parkinson disease earlier. (25, 26, 30, 31, 32, 33, 34)

as in Kurdish population conservative community female mostly remain in home because religious factors in one aspect and in other aspect difference in nature of work as female mostly work and doing fine, clean, and often in side home works in versus male work in mechanic, driving, in farm, military

and many other hard works, therefore male had very high chances for exposure to occupational and environmental toxins by which affected disease more.^(27, 30, 31, 35, 36, 37, 38)

We found that number of patients of Parkinson disease in urban area or in sulaymania city more than numbers of patients in rural area as in may be due to lack of environmental difference between city and its rural area, as till now in many region in Sulaymania city they use underground water for drinking, urbanization and migration from rural area to center of city, development of transportation and communication causes loss of clear cut limitation between city and rural area, as many people are living in city and rural area at same time, lower awareness of the symptoms of the disease among care providers (families and medical services) in rural area, eradication of many rural area during war, increase rate of pollution in Sulaymania and chance of trauma and falling were more in city all these factors lead to increase number of affected people in urban area in reverse to study which stated number of affected patient more in rural area.^(39, 40, 41, 42, 43, 44)

Patients who were living in urban area in our study become old ages more than who were living in rural area, in as similar result found in similar studies, as medical care more present in urban area as patients take treatment properly for chest infection, people more oriented regarding their disease, vaccination against viral infection present, and improved survival as the result of introducing effective symptomatic therapy and decrease or delayed mortality from other disorders, over all in center of city health care more which cause patients with Parkinson disease survive for longer time.^(45,46, 47)

Smoking was common among people and it used frequently by males more than female may related to orientation of female for smoking bad effects and socially female not accepted to smoke in reverse to male who they allowed to smoke cigarette without social limitation. Generally we couldn't determine protective effect nor bad effect of smoking, as in similar study as stated that smoking has no role in Parkinson disease in contrast to older studies conclude that cigarette smokers stand a lower risk of developing PD or confirmed protective effect of smoking.^(50, 51, 52) The special availability of tobacco in Sulaymania region as tobacco was one of the most common agricultural product in this region and smoking

remain without any protective or beneficial effect.^(45, 52, 53)

Family history robust factor for the disease and it became more important specially among younger ages in patients of Parkinson disease as in our study we had younger patients with family history such as studies in Arabs, Turkish, Persian, Swedish and Chinese population confirm that family history, first and second degree relatives, had important role in Parkinson's disease specially if it was assisted by environmental factors in form of gene-environmental reaction.^(54, 55, 56, 57, 58, 59, 60, 61)

CONCLUSION:

Mean age of patients of Parkinson's disease 65 years, disease started in male earlier than female in Kurdish population in Sulaymania. Male was more affected Parkinson's disease than female, male with earlier ages in Kurdish population. Number of patients living in urban area more than rural area, there was significant difference between urban and rural area according to age in which patients in urban area age of onset older than who were living in rural area. Patients with family history positive of Parkinson's disease affected the disease in earlier ages.

REFERENCES:

1. Suchowersky O and Furtado S. parkinson's disease: etiology and treatment. Continuum, 2004;10:15-16.
2. Quinn N, Bhatia K, Brown P, et al. Movement disorders in: Clarke C, Howard R, Rossor M, et al. *Neurology A Queen Square Textbook*. Blackwell Publishing; 2009:155-57.
3. Quinn N. movement disorders in: John W. scadding and Nicholas A. losseff *Clinical neurology*. 4th Ed. London; 2011 Hodder, Arnold : 426-67.
4. De Lau LM, And Breteler MM. Epidemiology of Parkinson's disease, *Lancet Neurology*, 2006;5: 525-35.
5. Campenhausen V , Bornschein B, Wick R, et al. Prevalence and incidence of Parkinson's disease in Europe. *Neuro psycho pharmacology*, 2005;15:473-90.
6. Mehanna R, Moore S, Hou JG, et al. Comparing clinical features of young onset, middle onset and late onset Parkinson's disease. *Journ Parkreldis*, 2014;20:530-34.
7. Miller IN, and Golomb AC. Gender differences in parkinson's disease. *Movement disorder*, 2010;25: 2695-703.

8. Roos RA, Jongen JC and van der Velde EA. Clinical course of patients with idiopathic Parkinson's disease. *Movement Disorder*, 1996;11:236-42.
9. Jankovic J, and Kapadia AS. Functional decline in Parkinson's disease, *Arch Neurology*, 2001;58:1611-15.
10. Henrique B, Ferraz, Andrade LAF, Tuma V, et al. rural or urban living and parkinson's disease. *Arq Neuro-psiquiatr*, 1997;54:37-41.
11. Papapetropoulos S, Singer C, Villar JM. et al. Does cigarette smoking provide clinically significant neuro protection among patients diagnosed with Parkinson's disease? *Movement Disorder*, 2005;20:641-42.
12. Palacios N, Gao X, O'Reilly E. et al. Alcohol and risk of Parkinson's disease in a large prospective cohort of men and women, *Movement Disorder*, 2012;27:980-87.
13. Ritz B, Lee PC, and Lassen CF. Parkinson's disease and smoking revisited, *Arah OA. Neurology*, 2014; 83:1396-402.
14. Kenborg L, Lassen CF, Ritz B, et al. Lifestyle, family history, and risk of idiopathic Parkinson's disease, *Am J Epidemiol*, 2015;181:808-16.
15. Scherfler C, Seppi K, Mair KJ, et al. Left hemispheric predominance of nigrostriatal dysfunction in Parkinson's disease, *Brain a journal of neurology*, 2012;10:1-7.
16. Wirdefeldt K, Gatz M, Reynolds CA, et al. Heritability of Parkinson's disease in Swedish twins: a longitudinal study. *Neurobiol Aging*, 2011;32:1923-29.
17. Klein C And Schlossmacher MG. The genetics of Parkinson's disease: implications for neurological care. *Nature Clinical Practice Neurology*, 2006; 2:136-46.
18. Williams DR and Litvan I. Parkinsonian Syndromes. *Continuum*, 2013;19:1189-95.
19. Neil Lava (2015) *WebMD* the Stages of Parkinson's Disease, <http://www.webmd.com/parkinsons-disease/guide/parkinsons-stages>. [veiwed 6.9.2015].
20. NGO (2015) Sulaymaniyah Governorate Profile. <http://www.ncciraq.org/images/infobygov/SulaymaniyahGovernorateProfileNCCI.pdf> [veiwed 2.9.2015].
21. Gelb DJ, Oliver E, and Gilman S. Diagnostic criteria for Parkinson's disease. *Arch Neurol*, 1999;56:33-39.
22. Hughes AJ, Daniel SE, Kilford L, et al. Accuracy of clinical diagnosis of idiopathic Parkinson's disease. A clinico-pathological study of 100 cases. *JNNP*, 1992;55:181-84.
23. Reeve A, Simox E, Turnbull D. Ageing and Parkinson's disease in Sweden: Why is advancing age the biggest risk factor? *Science Direct*, 2014;14:19-30.
24. Al Rajeh S, Bademosi O, Ismail H, et al. A community survey of neurological disorders in Arabia. *Neuro epidemiology*, 1993;12:164-78.
25. Alrefai A, Hababbi M, Alkhawajah M, et al. prevalence of Parkinson's Benamer HT, de silva R, Siddiqui KA, et al. Parkinson's disease in Arabs: asystematic review. *Movement Disorder*, 2008;23:1205-10.
26. Linder J, Stenlund H, Forsgren L. Incidence of Parkinson's disease and Parkinsonism in northern Sweden. *Movement Disorder*, 2010;25:341-48.
27. Campenhausen SV, Bornschein B, Wick R, et al. Prevalence and incidence of Parkinson's disease in Europe. *European Neuro psychopharmacology*, 2005;15: 473-90.
28. Checkoway H and Nelson LM. Epidemiologic approaches to the study of Parkinson's disease etiology. *Epidemiology*, 1999;10: 327-36.
29. Gokolp MA, and Hanagasi H. Prevalence of Parkinson's disease in Baskale, Turkey. *Neurological sciences*, 2015; 36:411-13.
30. Woo J, Lau E, Ziea E, Chan DK, et al. prevalence of Parkinson's disease in a Chinese population. *Acta Neurol Scand*, 2004;109:228-31.
31. Benjamin C.L. Lai, and Joseph K.C. Tsui. Epidemiology of Parkinson's disease. *BCM J*, 2001;43:133-37.
32. Twelves D, M.Perkins KS, and Counsell C. Systematic review of incidence studies of Parkinson's disease. *Movement Disorders*, 2003;18:19-31.
33. disease in Northern Jordan. *Clin Neurol Neurosurg*, 2009;111:812-15.
34. De Lau LM and Breteler MM. Epidemiology of Parkinson's disease. *The Lancet Neurology*, 2006;5: 525-35.
35. Khedr EM, Al Attar GS, Kandil MR, et al. Epidemiological study and clinical profile of Parkinson's disease in the Assiut Governorate, Egypt: a community- based study. *Neuro epidemiology*, 2012;38:154-63.

36. Hani T.S., Rajith de Silva, Khurram A. et al. Parkinson's disease in Arabs: A systemic review. *Movement Disorder*, 2008;23:1205-10.
37. Lubomski M, Rushworth RL, Will lee, et al. Sex differences in Parkinson's disease. *Journal of clinical Neuroscience*, 2015;22:73-81.
38. Hobson P, Meara J, and Ishihara Paul L. The estimated life expectancy in a community cohort of Parkinson's disease patients with and without dementia, compared with the UK population. *Journal of Neurology, neurosurgery and Psychiatry*, 2010; 81:1093-98.
39. Broussolle E, Thobois S. Genetics and environmental factors of Parkinson's disease. *Rev Neurol*, 2002 ; 158:11-23.
40. Gorell JM, Johanson CC, Ribicki BA Person EL, et al. The risk of Parkinson's disease with exposure to pesticides, farming, well water, and rural living. *Neurology*, 1998;50:1346-50.
41. Allam MF, Del Castillo AS, and Navajas RF .Parkinson's disease risk factors: genetic, environmental, or both? *Neurol Res*. 2005;27:206-8.
42. Nalls MA, Mclean CY, Rick J, et al. Diagnosis of Parkinson's disease on the bases of clinical and genetic classification. *Lancet Neurology*, 2015;14:971-73.
43. Goldman SM. Environmental toxins and Parkinson's disease. *Annu Rev Pharmacol Toxicol*, 2014;54: 141-64.
44. Rhodes SL, Fitzmaurice AG, Cockburn M, et al. pesticides that inhibit the ubiquitin-proteasome system: effect measure modification by genetic variation in SKP1 in Parkinson's disease. *Environ Res*, 2013;126: 1-8.
45. Costello S, Cockburn M, Bronstein J, et al. Parkinson's disease and residential exposure to Maneb and Paraquat from agricultural applications in the central valley of California. *Am.J Epidemiological*, 2009; 169: 919-26.
46. Dick FD, De Palma G, Ahmadi A, et al. Environmental risk factors in Parkinson's disease and Parkinsonism: the Geo Parkinson study. *Occup Environ Med*, 2007;64: 666-72.
47. Willis AW, Evanoff BA, Lian M, et al. Geographic and ethnic variation in Parkinson's disease. *Neuroepidemiology*, 2010;34:143-51.
48. Ascherio A, Chen H, Weisskopf MG, et al. Pesticide exposure and and risk for Parkinson's disease. *Annals of neurology*, 2006;60:197-203.
49. Frigerio R, Sanft KR, Grossardt BR, et al. Chemical exposures and Parkinson's disease. *Movement Disorders*, 2006;21:1688-92.
50. Ritz B, Ascherio A, Checkoway H, et al. pooled analysis of tobacco use and risk of Parkinson's disease. *Arch neurol*, 2007;64:990-97.
51. Jay M. Gorell, Edward L. Pererson, Benjamin A. et al. Multiple risk factors for Parkinson's disease. *Journal of the Neurological sciences*, 2015;358:251- 361.
52. priyadarshi A, Khuder SA, schaub EA, et al. Enviromental risk factors and Parkinson's disease: a meta-analysis. *Environmental Research*, 2001;86:122-27.
53. . Behari M, Srivastava AK, Das RR, et al. Risk factors of Parkinson's disease in Indian patients. *Journal of the Neurological sciences*, 2001;190:49-55.
54. Elahe Elahi. A study on Parkinson's disease in Iranian patients. *Genetics in the 3rd Millenium*, 2009;7: 1749- 52.
55. Almubarak BR, Bohlega SA, Alkahairallah TS, et al. Parkinson's disease in Saudi patients: agenetic study. *PLoS one* 2015;10:158-63.
56. Chishti MA, Bohlega S, Ahmed M, et al. T313M PINK1 mutation in an extended highly consanguineous Saudi family with early-onset Parkinson's disease. *Arch Neurol*, 2006; 63:1483-85.
57. Lohmann E, Dursun B, Lesage S, et al. Genetic bases and phenotypes of autosomal recessive Parkinson's disease in Turkish population. *Europian journal of neurology*, 2016;19:769-75.
58. Babak Emamalizadeh, Abolfazl Movafagh, Mojdeh Akbari. RIT2, a susceptibility gene for Parkinson's disease in Iranian population. *Neurobiology of aging*, 2014;35:27-28.
59. Healy DG, Falchi M, O'Sullivan SS, et al. Phenotype, genotype, and worldwide genetic penetrance of LRRK2-associated Parkinson's disease. *Lancet Neurol*. 2008;7:583-90.
60. Li Z, Lin Q, Huang W, and Tzeng CM. Target gene capture sequencing in Chinese population of sporadic Parkinson's disease. *Medicine (Baltimore)* 2015;94:835-38.
61. Ji- Feng Guo, Kai Li, Bei- Sha Tang, et al. polygenic determinants of Parkinson's disease in a Chinese population. *Movement Disorder*, 2015;36:1765- 69.

62. Munhoz RP, Espay AJ, Litvan I, et al. Long duration Parkinson's disease: Role of lateralization of motor features. *Science Direct*, 2013;19:77-80.
63. Goneru EG, van't Hof M, and Hans J. Symptoms and duration of the prodromal phase in Parkinson's disease. *Movement Disorders*, 1997;12:871- 76.
64. Macleod AD, Taylor KSM, and Counsel CE. Mortality in Parkinson's disease: a systematic review and meta-analysis, *Movement Disorders*, 2014;29:1615- 22.
65. Chen H, Zhang SM, and Schwarzschild MA. Survival of Parkinson's disease patients in a large prospective cohort of male health professionals, *Movement Disorders*, 2006;21:1002- 7.
66. Brabo NC, Minett CT, and Ortiz KZ. Fluency in Parkinson's disease: disease duration, cognitive status and age. *Arq. Neuropsiquiatr*, 2014;72 :70-77.
67. Cubo E, Martin PM, Martin-Gonzalez JA, et al. Motor laterality asymmetry and non-motor symptoms in Parkinson's disease. *Movement Disorder*, 2010;25:70-75.