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The Incidence of Psychosis Among Parkinson's Disease Patients and Associated Factors: A Meta-Analysis

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Abstract

Introduction: Parkinson's-induced psychosis is rather prevalent, and it has continuously been linked to poor outcomes. Therefore, detecting this presentation early on, can enhance the quality of life of Parkinson's disease patients and is therefore a clinical and societal necessity. This systematic review and meta-analysis aimed to estimate the pooled incidence of induced psychosis or psychosis associated with neurodegeneration in Parkinson's disease.

Materials and Methods: PubMed, Scopus, and Cochrane Library were searched to identify studies reporting the prevalence of psychosis in Parkinson's disease patients. A random-effect meta-analysis was used to pool data from the included studies. The objectives, inclusion criteria, and methods of analysis for this review were specified in advance and documented in a priori protocol (PROSPERO reg. num. CRD42022318920).

Results: Twenty studies including 5,123 Parkinson's disease patients which explored the incidence of presenting symptoms of psychosis in Parkinson's disease patients were included in the final analysis. The meta-analysis showed that the incidence of psychosis among Parkinson's disease patients was 35%. A subgroup analysis was performed which showed that disease duration could explain the statistical heterogeneity in this meta-analysis.

Conclusion: This systematic review and meta-analysis revealed that psychotic disorders are highly prevalent among Parkinson's disease patients, indicating an urgent need for further studies to help develop better mechanisms of prevention, detection, and treatment of those disorders among Parkinson's disease patients in an effort to improve their quality of life.

Keywords: Parkinson's disease, Psychosis, Meta-analysis.

INTRODUCTION

Parkinson's disease (PD) is a well-known with a clinical disorder variety of etiologies and symptoms. It is neurodegenerative disease marked by the destruction of dopaminergic neurons in the substantia nigra of the midbrain, as well as the accumulation of fibrillar aggregates known as Lewy bodies. PD is estimated to affect at least 1% of the population over the age of sixty, with the majority of cases being idiopathic and only 10% of cases having a genetic origin, which is mostly observed in young individuals [1]. The presence of widespread slowing of movements (bradykinesia) and at least one other symptom of resting tremor or rigidity is the current definition of PD. A loss of smell, constipation, and mood disturbances are other common symptoms [1]. Appropriate therapy should be initiated at diagnosis using dopamine agonists, especially for the management of motor symptoms [2].

Psychosis is characterized by a group of psychiatric symptoms that culminate in a loss of contact with reality. It is a distinguishing element of schizophrenia and other psychotic disorders and a co-existing component of many substance use and mood disorders. Psychosis can cause a great deal of suffering for patients and caregivers which is why it has become a main therapeutic goal for clinical personnel [3]. According to the DSM-5, Schizophrenia Spectrum and Other Psychotic Disorders are characterized by "abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms" [4]. Although there is evidence for genetic risk factors in the pathophysiology of psychotic illnesses, primary psychotic disorders are considered neurodevelopmental

abnormalities and are thought to develop prenatally, whereas full-blown psychosis is associated with genetic or environmental factors [3]. Many conditions appear to predispose to psychotic episodes, including Parkinson's disease, Alzheimer's disease, brain tumors, severe depression or anxiety, and substance abuse [5]⁵.

Despite breakthroughs in neurology, the pathophysiology of psychosis in PD is still unknown. In the development of psychosis in PD, both external (i.e. drugs) and internal (i.e. the disease itself) variables appear to have a role [6]. Psychosis in PD is thought to be complex with alterations in multiple neurotransmitters and brain pathways being causal contributors [7]. Psychosis has become more common in people treated with dopamine agonists, which are commonly used to treat PD. Dopaminergic overactivity in the limbic system and cerebral cortex is thought to play a role in the development of psychosis. This theory was reinforced by the observed improvement of psychosis with atypical antipsychotics, which block dopamine receptors [7]. According to the literature, hallucination may be caused by either postsynaptic dopamine receptor sensitization in the mesolimbic/mesocortical system, alterations beyond the basal ganglia, or changes in the serotonergic system [8]. Other risk factors reported for the development of psychosis in PD patients include old age, sleep disturbance, dementia, and depression [9].

Parkinson's-induced psychosis (PDP) is rather prevalent and has been previously evaluated in a study where the pooled frequency of psychosis in PD patients was found to be around 20.7% [10;11]. Furthermore, PDP has continuously been linked to poor patient outcomes due to the disruption of patients' daily lives and lowered quality of life. Psychotic diseases are linked

to significant personal, social, and clinical burdens [12]. As a result, identifying at-risk patients, detecting this presentation early on, and enhancing the quality of life of PD patients is a clinical and societal necessity. The purpose of this study was to conduct a systematic review and meta-analysis of reported cases in order to establish the incidence and proportion of Parkinson's disease patients who go on to develop psychosis. Moreover, the etiology, risk factors, and pathophysiology of psychosis in these patients was discussed.

The objectives, inclusion criteria, and methods of analysis for this review were specified in advance and documented in an a priori protocol (PROSPERO reg. num. CRD42022318920) [13].

METHODS

The study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [14].

Search strategy and selection criteria

Studies published before March 2022 were searched using the following terms: ("Parkinson's disease" OR "PD") AND ("psychosis" OR "schizophrenia" OR "delusions" OR "hallucinations") in the following databases: PubMed, Scopus, and Cochrane Library. To supplement the automatic database search, the references of relevant articles were manually searched for eligible articles.

Studies including diagnosed Parkinson's disease patients whether undergoing treatment or not who later developed diagnosed psychotic disorders (such as schizophrenia, delusions, hallucinations, and other minor psychotic symptoms) were included. When multiple papers reported the same data, the complete data set was included. Review articles, meta-

analyses, systematic reviews, case reports, animal studies, and those reporting no measured incidence, insufficient data or were not available in English were excluded. There were no timeline restrictions.

After excluding duplicates and screening for eligibility, twenty-three studies were included, which included participants with PD who later developed a psychotic spectrum disorder, both diagnosed according to specific criteria.

Data extraction

The titles and abstracts of each article were reviewed by two reviewers independently. Articles that did not meet the inclusion criteria, or had at least one exclusion criterion, were excluded. The authors then reviewed the full texts of articles meeting the inclusion criteria. Disagreement in the search strategy was resolved by the senior author.

Included studies' relevant data were extracted including the first author's name; year of publication; study design; country; sample size; total number of cases and controls; participants' demographic and clinical information (age, gender, age at onset of PD, disease duration, and levodopa dose); criteria used to diagnose PD and psychosis; results; effect values with 95% Cis; and information required for quality assessment.

Quality assessment

Quality assessment was performed by using The Joanna Briggs Institute (JBI) critical appraisal tool [15] for each study. For cross-sectional studies, the quality score for analytical cross-sectional studies was based on eight items. In cohort studies, quality scoring was based on the JBI checklist of eleven items.

Meta-analysis

The R software of Meta 4 was used to conduct the meta-analysis of included studies. Q-test and inconsistency index (I²) statistics

were used to assess heterogeneities between studies. Random-effects models were used to compute results when heterogeneity was high $(p\text{-value} \text{ for } Q \text{ test} \leq 0.05 \text{ and } I^2 \geq 50\%)$, whereas fixed-effects models were used to compute results when heterogeneity was low $(p\text{-value} \text{ for } Q \text{ test} > 0.05 \text{ and } I^2 < 50\%)$. If the proportion of PD patients who developed psychosis was not stated in the study, it was calculated manually by reviewing tables and figures. Incidence of the disease was calculated through summation. Publication bias was assessed using a funnel plot, which was confirmed by Begg's and Rank Correlation tests.

The primary goal of this meta-analysis was to determine the incidence of psychotic diseases among the PD population. The secondary goal was to investigate possible factors that could influence this occurrence and their significance in contributing to its incidence.

RESULTS

Search criteria identified 3.406 articles of fifty-five which were eliminated duplicates. Titles and abstracts of the remaining 3,351 articles were reviewed. Four hundred and fifty-two articles that met the criteria for full text review. Subsequently, four hundred and thirty-two articles were excluded after full text review and the remaining twenty articles were eligible for inclusion in the meta-analysis. The PRISMA flowchart displayed in Figure 1 shows the selection procedure for included studies identified from the databases. Detailed characteristics of the included studies were summarized in **Table S1**. The meta-analysis included twelve cohort studies [16-23], consisting of 2,065 PD patients and eight cross-sectional studies [24-38] consisting of 3,783 PD patients, exploring the association between PD and risk of psychosis.

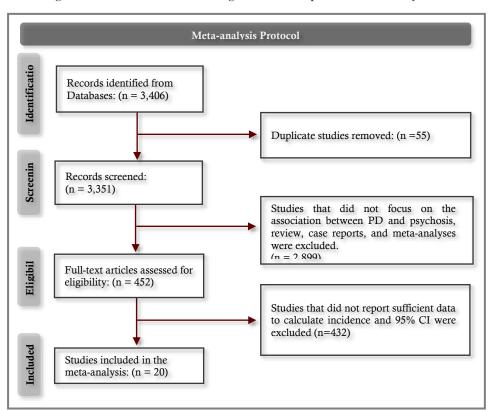


Figure 1: Flow of information through the different phases of meta-analysis.

Study Cases Total Prevalence 95% C.I. Forsaa et al 2010 230 137 0.60 [0.53; 0.66] Goetz et al 2011 38 60 0.63 [0.51; 0.74] Verbaan et al 2009 230 353 0.65 [0.60; 0.70] Ffytche et al 2016 115 423 0.27 [0.23; 0.32] Sonali et al 2019 141 386 0.37 [0.32; 0.41] Barrett et al 2017 33 101 0.33 [0.24: 0.42] Poletti et al 2012 213 805 0.26 [0.24; 0.30] Maier et al 2014 18 108 0.17 [0.11; 0.25] Pacchetti et al 2005 92 289 0.32 [0.27; 0.37] Zhong et al 2021 215 0.34 [0.28; 0.41] 74 Holroyd et al 2001 26 102 0.25 [0.18; 0.35] Factor et al 2011 63 500 0.13 [0.10; 0.16] Aarsland et al 1999 37 235 0.16 [0.12; 0.21] Weintraub et al 2006 34 130 0.26 [0.19; 0.34] Chou et al 2005 157 160 0.98 [0.94; 0.99] 0.26 [0.21; 0.32] Mack et al 2012 250 65 0.21 [0.16; 0.28] Lee et al 2012 41 191 Chendo et al 2021 51 92 0.55 [0.45; 0.65] Factor et al 2014 48 144 0.33 [0.26; 0.41] Solla et al 2011 89 349 0.26 [0.21; 0.30] Random effects model 0.35 [0.28; 0.43] Heterogeneity: $I^2 = 96\%$, $\tau^2 = 0.5337$, $\chi_{19}^2 = 493.76$ (p < 0.01) 0.2 0.4 0.6 0.8 0 1 Prevalence of CC

Figure 2: Forest plot of the incidence of Parkinson-induced psychosis in 20 studies. The figure shows the results of the meta-analysis using random effect model.

Quality of included studies

The quality of the studies was assessed using the JBI checklists for cohort and cross-sectional studies (**Table S2**). Of the total of 12 cohort studies, 4 studies were found to be high quality (JBI score 8 and above); 7 studies were fair quality (JBI score between 5 and 7 inclusive); of the 8 cross-sectional studies, 3 studies were found to be of high quality (JBI score 6 and above); 5 studies were of fair quality (JBI score between 3 and 5 inclusive); and one study was of poor quality (JBI score below 3).

Results of Meta-analysis

The incidence of the overall psychotic disorders in Parkinson's disease patients

A total of 20 studies were included which reported the incidence of psychosis among Parkinson's patients (**Table 1**). Based on the results of the random-effects method (**Figure 2**), the pooled incidence estimate of psychotic disorder in Parkinson's patients was 35% (95% CI; 28.0 - 43.0). A significant heterogeneity for this analysis was also found ($I^2 = 96\%$; p < 0.01).

Table 1. Distribution of studies on psychosis in Parkinson's disease based on year, study type, sample size, instrument, disease duration, levodopa dose, and incidence.

		instrument, disease duration, levodopa dose, and incidence.						
#	Author (year) (Reference number)	Study Type	Sample size	Psychosis Diagnostic Tool	PD Duration (y)	LEDD (mg)	Outcome (%)	
1	Forsaa et al (2010) [16]	Cohort	230	UPDRS	8.6	476	Psychosis (60)	
2	Goetz et al (2011) [19]	Cohort	60	RHI	9.0	480	Hallucination (63)	
3	Verbaan et al (2009) [20]	Cohort	353	DSM	12.7	736	Hallucination (65)	
4	Ffytche et al (2017) [21]	Cohort	423	UPDRS	NS	NS	Hallucination (27)	
5	Sonali et al (2020) [22]	Cohort	386	UPDRS	NS	NS	Hallucinations and Delusions (37)	
6	Barrett et al (2017) [23]	Cohort	101	SAPS	6.1	598	Hallucination (33)	
7	Aarsland et al (1999) [25]	Cross- sectional	235	UPDRS	8.8	463	Hallucination (16)	
8	Weintraub et al (2006) [26]	Cross- sectional	130	PPRS	7	442	Psychosis (26)	
9	Poletti et al (2012) [27]	Cohort	805	PPRS	9.9	NS	Hallucinations and Delusions (26)	
10	Maier et al (2014) [28]	Cohort	108	DSM	NS	NS	Schizophrenia (17)	
11	Pacchetti et al (2005) [29]	Cohort	289	DSM	8.37	840	Hallucinations and Delusions (32)	
12	Holroyd et al (2001) [33]	Cohort	102	UPDRS	9.7	630	Hallucinations and Delusions (26)	
13	Mack et al (2012) [31]	Cross- sectional	250	DSM	7.8	NS	Hallucinations and Delusions (26)	
14	Zhong et al (2021) [32]	Cohort	215	UPDRS	5.35	442	Hallucinations and Delusions (34)	
15	Chou et al (2005) [29]	Cross- sectional	160	NPI	11.8	NS	Hallucination (98)	
16	Lee et al (2012) [34]	Cross- sectional	191	PPRS	6.4	501.2	Hallucination (21)	
17	Factor et al (2011) [35]	Cohort	500	UPDRS	8.5	NS	Psychosis (13)	
18	Chendo et al (2021) [36]	Cross- sectional	92	NINDS/NIMH	15.9	856.9	Hallucinations and Delusions (55)	
19	Factor et al (2014) [37]	Cross- sectional	144	DSM	NS	NS	Hallucinations and Delusions (33)	
20	Solla et al (2011) [38]	Cross- sectional	349	DSM	9.6	487	Hallucinations and Delusions (26)	

Abbreviations: PD: Parkinson's Disease; LEDD: L-dopa equivalent daily dose; NS: not specified; UPDRS: Unified Parkinson's Disease Rating Scale; DSM: Diagnostic and Statistical Manual of Mental Disorders; MMSE: Mini Mental State Examination; PPRS: Parkinson Psychosis Rating Scale; SAPS: Scale for the Assessment of Positive Symptoms; RHI: Rubber Hand Illusion; NIMH: National Institute of Mental Health.

Of the included studies, some provided point prevalence while others provided period prevalence. A meta-analysis was conducted for each type to determine whether the type of study would affect the reported incidence. Based on the results of the random-effects method, the pooled incidence estimate of psychotic disorder in Parkinson's patients in cohort studies was 34% (95% CI; 25.0 - 45.0, $I^2 = 97\%$; p < 0.01) (**Figure 3**) while that for cross-sectional studies was 37% 95% CI; 26.0 -50.0, $I^2 = 94\%$; p < 0.01) (**Figure 4**).

Figure 3. Forest plot of the incidence of Parkinson-induced psychosis in 12 cohort studies. The figure shows the results of the meta-analysis using random effect model.

Study	Cases	Total	Prevalence	95% C.I.		
Forsaa et al 2010	137	230	0.60	[0.53; 0.66]	-	
Goetz et al 2011	38	60	0.63	[0.51; 0.74]		
Verbaan et al 2009	230	353	0.65	[0.60; 0.70]	-	
Ffytche et al 2016	115	423	0.27	[0.23; 0.32]	-	
Sonali et al 2019	141	386	0.37	[0.32; 0.41]	-	
Barrett et al 2017	33	101	0.33	[0.24; 0.42]	_ -	
Poletti et al 2012	213	805	0.26	[0.24; 0.30]	+	
Maier et al 2014	18	108	0.17	[0.11; 0.25]	-	
Pacchetti et al 2005	92	289	0.32	[0.27; 0.37]	-	
Zhong et al 2021	74	215	0.34	[0.28; 0.41]	- •	
Holroyd et al 2001	26	102	0.25	[0.18; 0.35]	-	
Factor et al 2011	63	500	0.13	[0.10; 0.16]	-	
Random effects model						
Heterogeneity: $I^2 = 97\%$, $\tau^2 = 0.5513$, $\chi^2_{11} = 351.31$ ($p < 0.01$)						
				0	0.2 0.4 0.6 0.8 1	
					Prevalence of CC	

Figure 4. Forest plot of the incidence of Parkinson-induced psychosis in 8 cross-sectional studies. The figure shows the results of the meta-analysis using random effect model.

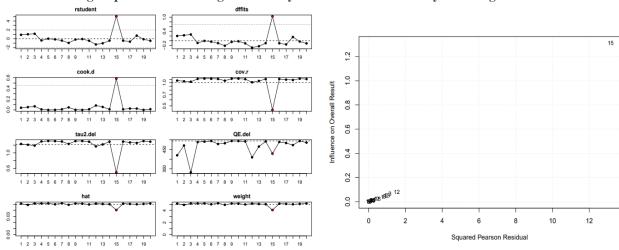
Study	Cases	Total	Prevalence	95% C.I.	
Aarsland et al 1999	37	235	0.16	[0.12; 0.21]	-
Weintraub et al 2006	34	130	0.26	[0.19; 0.34]	-
Chou et al 2005	157	160	0.98	[0.94; 0.99]	-
Mack et al 2012	65	250	0.26	[0.21; 0.32]	-
Lee et al 2012	41	191	0.21	[0.16; 0.28]	-
Chendo et al 2021	51	92	0.55	[0.45; 0.65]	
Factor et al 2014	48	144	0.33	[0.26; 0.41]	
Solla et al 2011	89	349	0.26	[0.21; 0.30]	-
Random effects mode			[0.26; 0.50]		
Heterogeneity: $I^2 = 94\%$, τ^2	= 0.5442 , χ	$\binom{2}{7} = 126$	6.03 (p < 0.01)	1	1 1 1 1
				0	0.2 0.4 0.6 0.8 1
					Prevalence of CC

Outliers and influential cases

The presence of outliers and influential cases may affect the validity of the conclusions of a meta-analysis. Outliers may receive considerably more weight, leading to distorted estimates. Therefore, a regression analysis was conducted to determine influential outliers. In **Figure 5**, Baujat plot

Pearson residual scatter plot identified study 15 (Chou et al. 2005) to be a potential outlier study that may have influenced the results. When excluding the study due to the reported influence on the overall result, the incidence of psychosis in Parkinson's patients dropped from 35% to 32% (95% CI; 25.0 – 39.0).

Figure 5. Influence and outlier plots showing two outlier cases which did not correspond to the bulk of the data. Weights plot shows the weight of a study in the overall meta-analytic average effect size.



Sensitivity Analysis

To further explore the possible source of heterogeneity in the analysis of the incidence of psychosis in Parkinson's disease patients, a sensitivity analysis was conducted on the duration of Parkinson's disease; levodopa-equivalent daily dose (LEDD); study design; and the quality of the included studies, to derive an estimate of the overall effect. A moderated regression analysis was conducted to investigate potential moderators which may have impacted the study's results (Table. 2). The cut-off points for both the disease duration and LEDD were based on the median value. When limiting the analysis to the duration of disease, the incidence of psychotic disorder was 61% for those who had the disease for more than 9 years, while being 26% in those who had it for less than 9

years. The observed difference in the magnitude of overall Parkinson-induced psychosis between the two groups was statistically significant (p < 0.01). The incidence of psychosis was 50% when subjects were prescribed LEDD of more than 495mg and 34% for those prescribed less than 495mg, wherein the observed difference was not statistically significant (p=0.21). The quality of included studies was also analyzed, showing that the incidence of overall psychotic disorder was 36% for high-quality and 39% for fair-quality studies; this difference was not statistically significant (p= 0.65). Finally, cohort studies showed a lower incidence (34%) compared to cross-sectional studies (37%); however, no statistical significance was found (p=0.91).

Table 2. Sensitivity analysis of all studies based on the duration of disease, levodopa-equivalent daily dose,

study design, and quality of the included studies

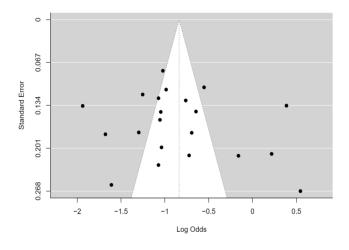
Subgroups	Studies (n)	Incidence (%) -	Heterogeneity across the studies		Estimate of Overall Effect		
			I^2	p-value	(p-value)		
	Disease Duration						
More than 9 years	6	61	97%	< 0.01	$X^2 = 12.77$, df = 1 ($p < 0.01$)		
Less than 9 years	10	26	95%	< 0.01			
Levodopa-equivalent Dose							
More than 495mg	6	50	98%	< 0.01	$X^2 = 1.56$, df = 1 ($p = 0.21$)		
Less than 495mg	7	34	95%	< 0.01			
High	6	36	94%	< 0.01	$X^2 = 0.87$, df = 2 $(p = 0.65)$		
Fair	9	39	98%	< 0.01			
Poor	1	21	NA	NA			
Cross-sectional	8	37	94%	< 0.01	$X^2 = 0.01$, df = 1 ($p = 0.91$)		
Cohort	12	34	97%	< 0.01	-		

Publication bias

The funnel plot in **Figure 6** was symmetric showing no evidence of substantial publication bias for the

prevalence of overall psychotic disorders in Parkinson's disease patients confirmed by Begg's test (p= 0.326).

Figure 6. Funnel plot of standard error by log odds showing publication bias for psychosis among Parkinson's patients.



DISCUSSION

This study systematically analyzed and reconstructed the estimated pooled incidence of psychosis among PD patients. A total of 20 studies on the incidence of psychosis incidence among PD patients were included in the systematic review and meta-analysis, and a subgroup analysis was conducted to determine potential factors that impact the incidence of Parkinson's-induced psychosis.

Psychosis incidence among PD patients

Overall psychosis was found to be very common among Parkinson's patients (35%) according this study. to systematic review included 73 main studies assessing psychosis incidence rates. It found that the median lifetime incidence of psychosis in the general population was 4.44% across these publications [39]. The results of this meta-analysis revealed that the incidence of psychosis in Parkinson's patients was significantly higher than the stated incidence in the general population. Psychosis patients are known to have a lower quality of life and are two to three times more likely to die at a younger age than the general population [40]. Therefore, the findings of this study highlight psychotic diseases as a major and urgent global public health concern among Parkinson's patients. The observed difference considerable psychosis severity between Parkinson's patients and the general population could be explained by several factors. Psychosis in PD is most likely complex, resulting from alterations various neurochemical in transmitters and brain structures. Despite breakthroughs in neurochemistry, pathophysiology of psychosis in Parkinson's disease is still unknown. Exogenous (drugs) and endogenous (related to the disease process itself) factors both play a role in the development of psychosis in people with

Parkinson's disease. According to research, the interaction of several neurotransmitters such as dopamine, serotonin (5-HT), and acetylcholine appears be to the most important. Dopamine has long been recognized as a key neurotransmitter in perceptual abnormalities. For instance, dopamine agonists are known to cause psychosis. As a result, dopamine receptor antagonists are extensively used antipsychotics. The use of dopamine agonists is one of treatments for Parkinson's disease symptoms which are thought to be caused by low or declining dopamine levels. It is thought that dopaminergic overactivity in the limbic system is implicated in the development of psychosis, this would explain why PD patients taking dopamine agonists are more likely to develop psychosis [41].

Determined outliers in the meta-analysis

One included publication (Chou et al. 2005) was shown to have influenced the overall outcomes of this meta-analysis in this study's regression analysis. The discovered outliers could be actual values resulting from natural population fluctuation, or they could be the consequence of faulty data entry, equipment issues, or other measurement errors. Upon deeper inspection, Chou et al. stated that their data were drawn from 2 trials involving the treatment of drug-induced psychosis with olanzapine causing the sample to be unrepresentative of the general Parkinson's disease population [30], thus, their findings could have been skewed.

Factors that impact the occurrence of psychosis among PD patients

According to the sensitivity analysis performed in this study, the incidence of psychosis was 58% when subjects were prescribed LEDD of more than 558mg, while it was 33% for those prescribed less than 558mg, indicating that people who take

higher doses of levodopa-equivalent drugs are more likely to develop psychosis, in which a statistical difference was also found. One study found that medications used to treat Parkinson's disease patients, such as dopamine agonists, can exacerbate or potentially cause psychosis [7]. However, anti-parkinsonian medications were not found to be a risk factor for psychosis in a recent investigation [42]. The association between drug dose and psychosis in Parkinson's disease is complicated and influenced by a variety of factors.

In relation to disease duration, the incidence of psychosis was reported to be higher in those who had PD for more than 9 years (63%) and a significant association was established. Longer disease duration being a risk factor for developing psychosis could be related to the larger cumulative doses of levodopa-equivalent drugs administered and older age. According to one study, psychosis in Parkinson's disease tends to develop later in the disease. However, it appeared that there may be a bimodal onset with earlyonset (5.5 years) associated with high drug and late-onset doses (>5.5)vears) due cognitive impairment [43]. Thanvi et al. discovered that hallucination may be caused by postsynaptic dopamine receptor denervation super-sensitivity in the mesolimbic/mesocortical system individuals with a disease duration of less than five years. Hallucinations may be mediated by alterations beyond the basal ganglia or by the serotonergic system in patients with a disease duration of more than five years [7]. In accordance, another metaanalysis investigating the risk of developing PDP found that it is influenced by the duration of the disease, Hoehn & Yahr stage, and the cognitive status of the patients [11].

This systematic review included both

studies that provided point prevalence and others that provided period prevalence which could affect results. Therefore, a subgroup analysis for each type was conducted reporting that cohort studies showed a lower incidence (34%) compared to cross-sectional studies (37%); however, no statistical significance was found (p= 0.91). This could be due to the fact that approximately 27% of patients with Parkinson's disease psychosis undergo remission based on the adjustment of drug regimen [44] therefore, missing states of relapse and remission between visits, which underestimated actual incidence.

No statistical association was found in the extent of psychosis incidence in PD patients between the different study design, quality, or LEDD taken. As a result, the difference is more of a chance of observation than an actual difference.

Strengths and Limitations

The current systematic review and metaanalysis had several advantages since a predetermined protocol for article selection, data extraction, and analysis was followed. Furthermore, two independent investigators extracted information from the included papers and assessed the quality of the studies, followed by a subgroup and sensitivity analysis based on the diagnostic criteria utilized, disease duration, LEDD, and study However, there were quality. some limitations to this review, including the fact that the subgroups and sensitivity analysis included a small number of articles; a subgroup that could potentially reduce the estimate's power; and that there was significant heterogeneity across the studies that could not be explained by the subgroup analysis.

Future research and clinical practice implications of the findings

This study has implications for future

clinical practice and research since it discovered a higher incidence of psychosis among PD patients when compared to the reported incidence in the general population, highlighting the fact that psychotic diseases should be a major and urgent global public health concern among PD patients, requiring additional robust studies to investigate possible explanations for the higher magnitude. Since no significant differences were found in the subgroup analysis, more research is needed to ascertain which factors influence the incidence of psychosis in Parkinson's patients. Involved sectors should give importance to the risk of PD patients developing psychosis, including better prevention strategies, which may include integrating mental health services for Parkinson's patients with existing healthcare services, which suggests using broader approaches to address the physical and mental health needs of Parkinson's patients.

CONCLUSION

In conclusion, the current systematic review and meta-analysis demonstrated that psychosis is extremely common among PD patients. More research into likely causes and risk factors for this increased incidence is required. Furthermore, comprehensive and informative research is urgently needed to support the creation of better methods for the prevention, diagnosis, and treatment of psychotic illnesses in Parkinson's patients.

Abbreviations

PD: Parkinson's disease; PDP: Parkinson's-induced psychosis; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis; JBI: Joanna Briggs Institute;

LEDD: Levodopa-equivalent daily dose; UPDRS: Unified Parkinson's Disease Rating Scale; DSM: Diagnostic and Statistical Manual of Mental Disorders; MMSE: Mini Mental State Examination; PPRS: Parkinson Psychosis Rating Scale; SAPS: Scale for the Assessment of Positive Symptoms.

Declarations

Ethics approval and consent to participate.

N/A

Consent for publication

N/A

Availability of data and materials

All data generated or analyzed during this study are included in this article.

Competing interests

The authors have no conflicts of interest relevant to disclose.

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Authors contributions

Alsharaeh, Alsalahat, and Khudairat conceptualized the study. Both Alsharaeh and Alsalahat contributed to writing of the full manuscript. The analysis was conducted by Alhajahjeh. The search, data extraction, and quality assessment were performed by Shuriquie, Alashoor, and Alquabeht. Alryalat supervised the project. All authors provided critical feedback, helped shape the research, and approved the final manuscript.

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حدوث الذهان في مرضى باركنسون والعوامل المرتبطة به: تحليل ميتا

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الملخص

الخلفية والأهداف: الذهان الناجم عن مرض باركنسون منتشر إلى حد ما ، وقد تم ربطه باستمرار بالنتائج السيئة. لذلك، فإن اكتشاف هذه الظاهرة في وقت مبكروبالتالي تحسين نوعية حياة مرضى الباركنسون هو ضرورة سريرية ومجتمعية. هدفت هذه المراجعة المنهجية وتحليل ميتا إلى تقدير الوقوع المجمع للذهان المُستحث أو الذهان المرتبط بالتنكس العصبي لمرض الباركنسون.

منهجية الدراسة: تم البحث في مكتبة PubMed و Scopus و Cochrane لتحديد الدراسات التي تشير إلى حدوث الذهان في مرضى باركنسون. تم استخدام تحليل ميتا لتجميع البيانات من الدراسات المشمولة. تم تحديد الأهداف ومعايير التضمين وطرق التحليل لهذه المراجعة مسبعًا وتم توثيقها في PROSPERO (CRD42022318920).

النتائج: تم تضمين عشرين دراسة بما في ذلك 5123 مريض بمرض باركنسون لاستكشاف حالات الإصابة بالذهان لديهم في التحليل النهائي. أظهر تحليل ميتا أن معدل الإصابة بالذهان بين مرضى باركنسون كان 35%. تم إجراء تحليل مجموعة فرعية يوضح أن مدة المرض يمكن أن تفسر عدم التجانس الإحصائي في هذا التحليل التلوي.

الاستنتاجات: كشفت هذه المراجعة المنهجية وتحليل ميتا أن الاضطرابات الذهانية منتشرة بشكل كبير بين مرضى مرض باركنسون، مما يشير إلى الحاجة الملحة لمزيد من الدراسات للمساعدة في تطوير آليات أفضل للوقاية من تلك الاضطرابات واكتشافها وعلاجها بين مرضى باركنسون في محاولة لتحسين نوعية حياتهم.

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