REVIEW

The impact of clinical scales in Parkinson's disease: a systematic review

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Abstract

Background: Parkinson's disease is one of the non-curable diseases and occurs by the prominent loss of neurotransmitter (dopamine) in substantia nigra pars compacta (SNpc). The main cause behind this is not yet identified and even its diagnosis is very intricate phase due to non-identified onset symptoms. Despite the fact that PD has been extensively researched over the decades, and various algorithms and strategies for early recognition and avoiding misdiagnosis have been published. The objective of this article is to focus on the current scenario and to explore the involvement of various clinical diagnostic scales in the detection of PD.

Method: An exhaustive literature review is conducted to synthesize the earlier work in this area, and the articles were searched using different keywords like Parkinson disease, motor/non-motor, treatment, diagnosis, scales, PPMI, etc., in all repositories such as Google scholar, Scopus, Elsevier, PubMed and many more. From the year 2017 to 2021, a total of 451 publications were scanned, but only 24 studies were chosen for a review process.

Findings: Mostly as clinical tools, UPDRS and HY scales are commonly used and even there are many other scales which can be helpful in detection of symptoms such as depression, anxiety, sleepiness, apathy, smell, anhedonia, fatigue, pain, etc., that affect the QoL of pateint. The recognition of non-motor manifests is typically very difficult than motor signs.

Conclusion: This study can give the beneficial research paths at an early stage diagnosis by focusing on frequent inspection of daily activities, interactions, and routine, which may also give a plethora of information on status changes, directing self-reformation, and clinical therapy.

Keywords: Parkinson's disease (PD), Motor and non-motor symptoms, Diagnostic scales, Systematic review

Introduction

The correct diagnosis and appropriate treatment of brain impairment are needed for effective monitoring of PD. The diagnosing process of brain disorders is tedious and profoundly costly. Parkinson's disorder is one of the major issues in the family of neurodegenerative disorders that essentially influences the population above 60 years. The precise cause of PD is still unfamiliar, but our researchers are working hard to figure out what are the causes behind the lack of dopaminergic neurotransmitters in the

SNpc [1]. These dopamine neurons may play a significant function in the control of many brain processes, such as behavioral and voluntary gestures [2]. Basically, SNpc is a part of the basal ganglia that control the body movement signals and works with the cerebellum to send impulses back and forth for movement signals, related to the spinal cord [3]. In addition, the reason for the deficit neurons of SNpc demonstrates the build-up of proteins (aSyn) into Lewy bodies of nerve cells [4]. Also, it has been observed that PD can occur due to a single or combination of factors like gene mutation, toxins, side-effects of drugs, rural living, trauma, aging, sex, and many more.

The Parkinsonian syndrome (PS) is categorized into motor symptoms (MS) and non-motor symptoms (NMS) as shown in Table 1. Generally, MS appear early than

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Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 2 of 10

NMS, but in some cases NMS may appear early and even earlier than the beginning of MS affirming the diagnosis [5]. In addition, NMS can have a greater influence on the quality of life (QoL) [6] from MS and is associated with significantly less well-being. NMS was seen in about 90% of patients with PD at all phases of the disease [7]. The social and economic consequences of PD have a considerable impression on a patient's QoL [8]. Because of the progressive appearance of signs [9], prognosis, and therapies vary significantly from other non-degenerative variants in their early stages, identifying management issues for a correct diagnosis is difficult or indecisive [10, 11]. With increasing clinical experience, the accuracy can be improved and also demonstrated that even the correct identification is missed in approximately 20% of cases because most of the cases are confused with other disorders [12].

While no particular treatment has been found for PD [13], medications can help to control manifestations. Mostly treatment includes pharmacologic strategies (L-Dopa arrangements recommended with or without other medications) and non-pharmacologic methods (for example workout, physical education,

occupational, speech rehabilitations, and nourishment [14]). PD can be treated with verbally guided dopamine precursor, levodopa (L-Dopa) [15] and even with combination of some other agents (COMT receptors, MAO-B agents, dopamine agonists (DA), and non-dopaminergic agents [16]). If the condition does not lead to treatment, surgery may be appropriate option. Another alternative is deep brain stimulation (surgery of either subthalamic core or globus pallidus), which showed to be effective in the treatment of patients suffering from PD motor problems [17].

In the diagnosis of early PD detection, there are several ways such as imaging-based, scale-based measurement, signal-based, and computer-aided methods. So, in this systematic review the effect of motor and non-motor based scales for detection has been discussed and also elaborated with its features. After the brief introduction, the paper is divided into following sections: "Review methodology" explains the methodology of the paper and "Role of clinical scales" covers the role of scales in diagnosis of PD. Section "Discussion" discusses the overview of this systematic review article and research gaps. Lastly, conclusion of the paper is given in "Conclusion".

Table 1 Motor/non-motor symptoms

Symptom type	Features
Motor symptoms	
Bradykinesia [18]	Affects up to 98% of Parkinson's Patients Motor planning amplitude disruptions are reduced
Tremor [19]	Approximately 75% of PD patients are affected by tremor Includes rest tremor, action tremor, and mixed tremor Trembling of one or both hands at rest is a symptom Also affects the chin, lips, face, and legs
Muscular rigidity [20]	Muscle resistance during passive mobilization is unable to relax normally Creates muscle pain
Postural reflex and gait disturbance [21]	People with PD can fall up to 40% of the time About 10% of people can experience weekly falls The number of drop-downs is related to the seriousness of PD Shorter stride length, which can get shorter over time
Non-motor symptoms	
Autonomic dysfunction [22]	Affects 70% to 80% of patients Have a high level of morbidity and pain Includes sexual problem, dysregulation of swallowing, gastrointestinal disorders, cardiac regulation problem, orthostatic hypotension, entrail, and bladder irregularities
Sleep dysfunction [23]	Affecting 64% of PD patients Fatigue, REM sleep pattern disorder, muscle spasms, prolonged morning sleepiness, sleep disorder, and sleep fragmentation are all forms of sleep disturbances Sleep dysfunctions are multi-factorial that includes nocturnal and diurnal symptoms Sleep in PD is characterized by decreased sleep performance and an elevated number of awakenings
Sensory dysfunction [24]	Includes pain, olfactory disturbance, and visual dysfunction
Neuropsychiatric [25]	Includes depression, anxiety, apathy and psychosis Despite the lower prevalence rates, roughly 30–40% of patients with PD experience severe depressive manifests

Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 3 of 10

Review methodology

This article investigates the state-of-the-art on clinical scales that are related to PD's detection. The main aim of pertinent literature review is to analyze and identify the different clinical scales from the reported studies in the domain of early PD detection for future research. So, we execute the Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) [26] methodology for this article and discussed in Fig. 1. We searched total 451 articles with different keywords like Parkinson disease, motor/non-motor, UNDRESS, H&Y, review, diagnosis, scales, etc., in different repositories such as Google scholar, Scopus, Elsevier, Pub Med and many more. After this step, we removed the duplicate articles and left articles were 406. The screened articles were analyzed on behalf of title and abstract. Then, filtration criteria were applied that included exclusion–inclusion points. In exclusion criteria, we excluded the articles related to multimodal criteria (means used with some other modality or combination with other processing technique), we analyzed various NMS symptom based articles, UPDRS, review articles (already published), papers in English language and published paper on scales only. Based on these requirements, full-text articles were accessed (104) and lastly, a total 24 selected articles were used for this systematic review.

Role of clinical scales

For clinical evaluation, valid measuring instruments for rating the severity of disease symptoms, stage of disease, ability to determine everyday functional activities, and symptomatic response to medication are needed for PD therapeutic interventions [13]. Thus, it was probably the discovery of new techniques in the management of PD that led to the design of new scales focusing on specific points of PD based on the required assessment [27]. For the assessment, there are several meaningful MS/NMS-based measurement scales that propose to evaluate the different cardinal manifestations for the early detection of PD. Different community-clinicians use PD rating scales (by assigning a score to them) as a clinical method to evaluate MS/NMS exercises, but the basic scales MDS-UPDRS [28] and HY are mostly used as discussed in Table 2 [29]. It is also observed that these methods are cheapest and convenient-to-use as compared to other methods.

In addition to basic diagnostic scales, there are many other measurement scales that are highly recommended to reach the complexity of NMS [31] and also used to identify the specific symptoms of PD like Depression, Anxiety, Autonomic dysfunction, cognitive dysfunction, Sleep, Apathy, smell, Anhedonia, Fatigue, Pain, etc. (as shown in Table 3). It is noteworthy that non-motor assessment is even more difficult to give a clear clinical
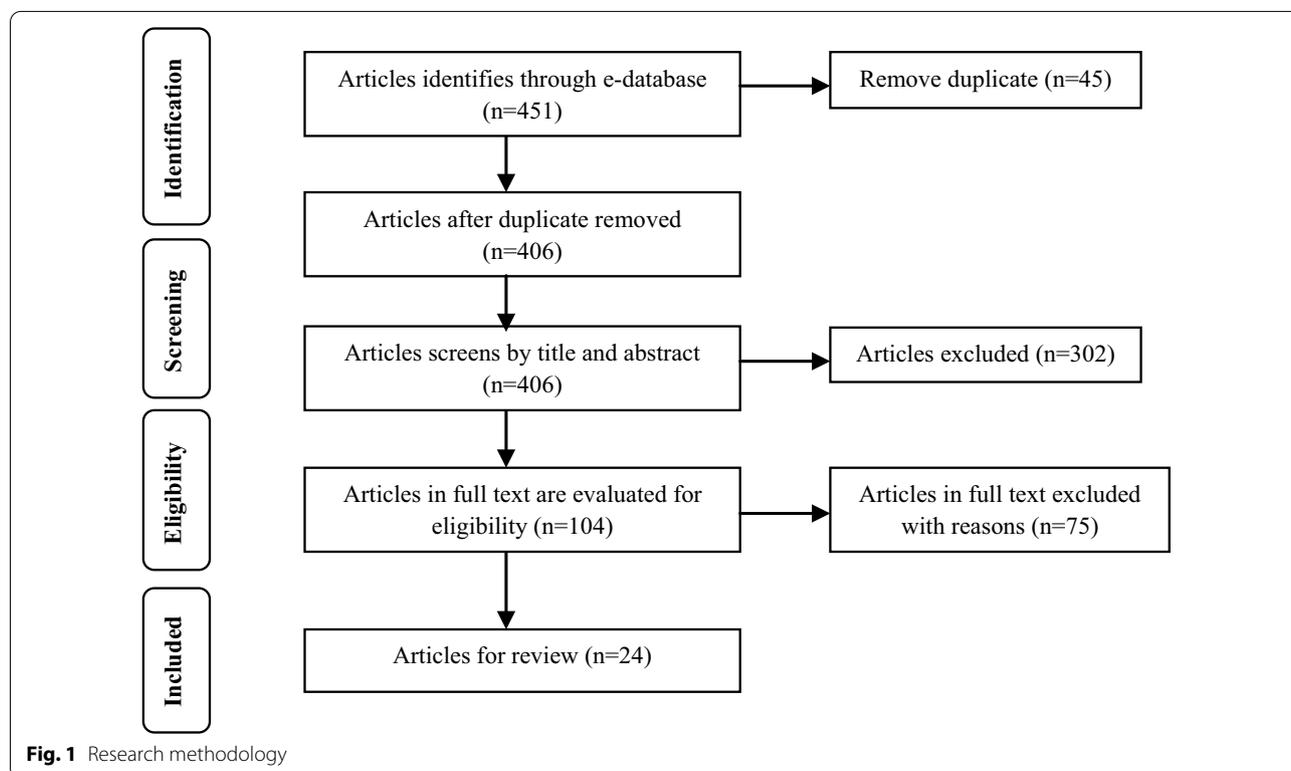

Fig. 1 Research methodology

Table 2 Scales used in diagnosis of PD symptoms

Scale name	Range/features	Problems	
UPDRS Subscale Part-I	Includes mentation, mood and behavior Range from 0 (normal) to 16 (each item graded from 0 to 4)	Intellectual impairment	Motivation/initiative
		Thought disorder	Depression
UPDRS Subscale Part-II	Self-evaluation of activities of daily living Range 0 to 52 (Each item scored from 0 to 4)	Using utensils and cutting food	Getting into bed and fixing the bedclothes
		Drooling	Drop-down
		Swallowing	Steady
		Handwriting	Walking
		Voice or speaking	Right arm tremor
		Habiliment	Left arm tremor
		Sanitation	Sensory difficulties
UPDRS Subscale Part-III	Evaluation of motor functions Range 0 to 108 27 items (each item grades from 0 to 4)	Items 1 to 5 (resting tremor)	Item 23 (arising from a chair)
		Items 6 and 7 (action tremor)	Item 24 (posture)
		Items 8 to 12 (Stiffness)	Item 25 (gait)
		Items 13 and 20 (Bradykinesia)	Item 26 (postural stability)
		Item 21 and 22 (speech and facial expressions)	Item 27 (body bradykinesia)
UPDRS Subscale Part-IV	Used for complications of therapy Range items from 32 to 35 for dyskinesia Items 36 to 39 for motor/ clinical fluctuations Items 40 to 42 for intestinal, autonomic, and sleep problems	Item 32 (Duration of dyskinesia)	Item 38 (Undetermined-OFF)
		Item 33 (Disability)	Item 39 (Time OFF)
		Item 34 (Pain)	Item 40 (Gastrointestinal problems)
		Item 35 (Early Morning)	Item 41 (Sleep Disturbances)
		Item 36 (Predictability)	Item 42 (Orthostasis)
		Item 37 (Unpredictable OFF)	
HY Part-V [13]	Sub-Part of UPDRS Scale	Stage-0	No indication of disease
		Stage-1	Side effects on one side just (one-sided)
		Stage-1.5	Side effects one-sided and also including the neck and spine
		Stage-2	Indications on the two sides but no disability of balance
		Stage-2.5	Gentle side effects on the two sides, with when the 'pull' test is performed (the specialist stands behind the individual and requests that they keep up their balance when pulled in reverse)
		Stage-3	Impairment of balance, gentle to moderate disease, physically independent
		Stage-4	Extreme inability, but still at the same time ready to move or balance without assistance
		Stage- 5	Requiring a bed-rest or wheel-chair if assisted

Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 5 of 10

Table 2 (continued)

Scale name	Range/features	Problems	
SEADL Scale Part–VI [30]	Range 0–100% Demonstrates the 'Schwab and England' method for determining independency on everyday living activities under ON/OFF states Higher scores indicate to better useful independency	100%	Totally independent, efficient to do all activities without gradualness, trouble or disability
		90%	Totally independent, efficient to do all exercises with some slowness, trouble or impairment, Activities may take double time as long to finish
		80%	Many drills are self-contained, although certain tasks take double time, Aware of potential problems and a desire to slow down
		70%	Not entirely self-sufficient, more problems with activities that can take three to multiple times as long, may take enormous part of day for tasks
		60%	Can do most exercises, but very slowly and with much exertion, however a few tasks are unthinkable
		50%	More reliant, Help needed with half of tasks, Trouble with everything
		40%	Very needy, can help with all activities but can manage few alone
		30%	With exertion, occasionally do a couple of tasks alone or starts alone, much assistance require
		20%	No task can do alone; can help in some slight with some chores. Severe invalid
		10%	Helpless and completely dependent on caretaker
		0%	Vegetative controls like swallowing, bladder and bowel functions

UPDRS Unified Parkinson Disease Rating Scale, *HY* Hoehn and Yahr Scale, *SEADL* Schwab and England Activities of daily living

Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 6 of 10

Table 3 Other NMS scales

S. no.	NMS problems	Different scales of NMS	Features
1	Monitoring for NMS	NMS-Q	There are 30 items in all Self-sufficient and a yes/no answer
		NMS-S	Physician administered 9 domains and having 30 items Needs rating of frequency (1–4)/severity responses (0–3)
2	Quality of Life	PDQ-39	Assess 39 item Clinical administrated and covered by questionnaire
3	Autonomic dysfunction	SCOPA	Includes 25 items No cut-off value is defined
4	Cognitive dysfunction	PD-CRS	Getting 7 activities that are administered by a clinician Checking for memory issues
		SCOPA:CS	Having 10 tasks, clinician-administered
		MoCA	To detect mild cognitive impairment and PD dementia
5	Depression	Ham-D	Multiple versions of scale exist, but commonly version of 17 items is mostly used Self-administered, clinician-administered, and semi-structured forms are all available
		BDI	Employs 21 items, self-completed, multiple choice answers
		MADRS	Consists of 10 items, clinician-administered Not usually used
		GDS	Anxiety screening service for senior citizens, self-report, yes or no screening instrument
6	Anxiety	STAI	Diagnosing anxiety and differentiating it from depressive disorders
7	Sleep	PDSS	Having 15 items, self-completed
		SCOPA: SS	Identifying and evaluating the degree of daytime sleepiness Uses self-completed 12 items Looks at signs from the preceding month as well
		PSQI	Consists of 19 items, self-completed with monitoring of previous month symptoms
		ESS	A self-completed 8-item questionnaire with 0–3 rating on each item was used to determine the degree of daytime sleepiness For pathologic sleepiness, a cut-off of 10/11 is used
		ISCS	Consists of 6 items, clinician-administered
		SSS	Calculating magnitude at a certain point in time
8	Apathy	AES	Based on an 18-item Likert scale 4 items scored solely by the patient, 1 item scored solely by the rater
		AS	Abridged AES, which was developed for PD and has a 4-point Likert scale of 14 items, was used in treatment trials Patient's score (items are read to patient)
		LARS	In therapy trials, 33 items are used to screen for apathy Structured interview with yes/no
9	Anhedonia	SHPS	Followed by 14 items, self-completed
10	Smell	AHRS	Ability to smell by asking questions
		UPSI	To quantify the olfactory function
11	Fatigue	FSS	After reading each phrase, the applicant must circle or round a number between 1 and 7 Self-administered, 9-item A low value implies that the argument is not entirely true, while a high value indicates that it is
12	Pain	DN4	Interview problems and physical measurements are used A score of > 4 was deemed positive on the test
		VAS	To determine the severity of the pain It varies from 0 (no pain) to 10 (extreme pain)

NMS-Q NMS Questionnaire, *NMS-S* NMS scale, *PDQ-39* PD questionnaire, *SCOPA* Scales for Outcomes in PD, *PD-CRS* PD Cognitive Rating Scale, *SCOPA-CS* SCOPA-Cognitive subscale, *MoCA* Montreal Cognitive Assessment, *Ham-D* Hamilton Depression Index, *BDI* Beck Depression Inventory, *MADRS* Montgomery–Asberg Depression Rating Scale, *GDS* Geriatric Depression Scale, *STAI* State–Trait Anxiety Inventory, *PDSS* PD Sleep Scale, *SCOPA-SS* Scales for Outcomes in PD- sleep subscale, *PSQI* Pittsburgh Sleep Quality Index, *ESS* Epworth Sleepiness Scale, *ISCS* Inappropriate Sleep Composite Score, *SSS* Stanford Sleepiness Scale, *AES* Apathy Evaluation Scale, *AS* Apathy Scale, *LARS* Lille Apathy Rating Scale, *SHPS* Snaith–Hamilton Pleasure Scale, *AHRS* Argentina Hyposmia Rating Scale, *UPSIT* University of Pennsylvania smell identification test, *FSS* Fatigue Severity Scale, *DN4* Douleur Neuropathique-4 Questionnaire, *VAS* visual analogue scale

Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 7 of 10

description of than motor issues because it involves a subjective assessment and patient cooperation, which is sometimes difficult to get. These evaluations include the analysis of disease staging, QoL, activities of daily living, impairment, disability, and other specific aspects. In general, the questionnaire-based assessment method used for NMS and those attempting to address whole-complex NMS differs from those specifically for those attempting portions of resolution of side-effects. Still, there is little evidence on the psychometric characteristics of most of these instruments used for this disease, and some are beneficial only for a specific group of individuals [27].

Discussion

Parkinson's disorder is one of the major issues and occurs due to the death of dopaminergic neurotransmitters of SNpc. The progression of the symptoms often varies from person to person to the diversity of the disease. The influence of PD on a person's life is immense on both social and economic levels. Even, it has been also observed that motor signs appear sooner than non-motor but in some cases, non-motor manifestations may appear early and confirm the diagnosis even before the beginning of motor manifests. The identification management problems for accurate diagnosis are very challenging or indecisive part due to the gradual appearance of symptoms, prognosis, and similarity with other non-degenerative disorders. In general, influenced people are given L-Dopa with agonists or inhibitors.

In early phases, before undergoing medications or scans, scales can help in diagnosis of early symptoms evaluation because these imaging evaluations are expensive and may produce some side-effects. Even these clinical scales can help the researchers and practitioners to start their work with these scales for detection of PD because these are easy to handle and convenient. The scale's assessment depends upon the rating score and it lies between the 5-point range from 0 to 4 ('0' = no problem, '1' = mild difficulties, '2' = moderate difficulties, '3' = high levels of difficulties, and '4' = extreme difficulties). The accuracy of scales also depends upon the patients' response because sometimes patient is unable to give answer in that case caretaker may respond. The severity of disease can be evaluated from the total score. Mostly for motor and non-motor symptoms, UPDRS and HY scales are used, but for particular assessment of symptom, there are many other non-motor scales. Secondly, in later stages of Parkinson's disease, these scales can help in providing the information of progression of disease.

In this systematic review process, the motor and non-motor scales have been discussed. Therefore, it has been analyzed that UPDRS and HY scales are largely used as

clinical tools, but also these scales have some limitations which are further modified according to the demand of the nature. Some of the drawbacks have been noted by the Movement Disorders Society (MDS), including vague questions, insufficient instruction, and exclusion of essential components of NMS. Their findings led to the creation of a new version of the MDS-UPDRS, which addresses issues with the UPDRS and allows for improved identification of minor alterations and impairments [32]. Even it is also found that HY staging scale only reflects the motor complications of disease (especially the matter of balance/gait) [29]. There are many other NMS scales for particular symptom identification in PD. The paper has discussed the 12 subtypes of NMS scales; each category has been further including the different types of scales for particular symptom diagnosis.

The first subtype is monitoring for NMS that includes two types of scales (NMSS and NMSQ) and the problems analyzed by these two scales are cardiac, fatigue, apathy, vision issues, memory issues, sexual, gastrointestinal, urinary, and so on [33]. Both the NMSQ and NMSS load grades exhibit a strong inverse relationship with patient's QoL [34]. The second subtype is the quality of NMS that includes PDQ-39 scale which is a clinically and psychometrically admissible indication of the key components of health, functioning, and impairment [35]. The third subtype is autonomic dysfunction that involves SCOPA-AUT scale which is a specific instrument designed to assess autonomic function for PD patients and targeting the regions with 7 items of gastrointestinal, 6 items of urinary incontinence, 3 items of cardiovascular, 4 items of thermoregulatory, 1 item of pupillomotor and 4 items of sexual (2 for men and 2 for women) [36]. Also these symptoms have great impact on PD patient's daily life functioning [37].

The fourth type is cognitive dysfunction that includes three scales (PD-CRS, MoCA and SCOPA:CS) which is used to access cortical and subcortical functions [38]. PD-CRS: including naming and copy drawing of a clock, verbal memory, attention, working memory, visuo-spatial functions, alternating, and action fluency [39]. The MoCA has also been demonstrated to be effective in distinguishing healthy controls from PD patients with various cognitive stages (no cognitive impairment, moderate cognitive impairment, or dementia) [40]. The fifth subtype involves depression that includes four types of scales (Ham-D, BDI, MADRS, and GDS), the symptom of depression affecting 40% (approx.) of PD patients [41]. The sixth subpart Anxiety that has one scale STAI, composed of two subscales (STAI-state and STAI-trait) [38]. Anxiety affects 12–57% of PD patients [42]. The seventh subpart is sleep having six scales (PDSS, SCOPA: SS, PSQI, ESS, ISCS, and SSS) and sleep disturbances affect

Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 8 of 10

the QoL of PD patient [43]. Sleep disturbances create the problems like insomnia, daytime sleepiness, sleep-walking, and overlap parasomnia [44, 45]. The eighth subpart is Apathy and contains three scales under apathy (AES, AS, and LARS); between 17 and 50% of PD patients develop apathy during the course of the disease. Apathy affects the behavioral disturbance and also creates the intellectual impairment, level of consciousness, and emotional distress problems [46]. Anhedonia, the ninth component, is described as a reduced ability to enjoy pleasure. It is regarded as a fundamental symptom of severe depression, with 30–40% of those with PD experiencing substantial depression [47]. The tenth subpart is Smell that includes two scales (AHRS and UPSI). Smell impairment in PD patients ranges from 75 to 95%. The 11th subpart belongs to Fatigue and screened by FSS. Patients are asked to rate how each item describes their fatigue from 1 ("strongly disagree") to 7 point (s) ("strongly agree"). Total FSS score is obtained by dividing the sum of all item scores by 9 [36]. The 12th subpart is Pain that involves two types of scales (DN4 and VAS) which affects around 67.6% of PD patients. DN4 pain is used to distinguish between the presence and absence of neuropathic pain. On the other hand, VAS identifies the pain score in the last 24 h.

Research gaps

1. The most common method used in detection is questionnaire-based data analysis, but there is a problem of data inconsistency because sometimes the patient is unable to give an answer or response in that case caretaker can handle or give the response.
2. Even it is found that these scales are not fit for both clinical diagnoses and research because sometimes these are only useful for particular age groups.
3. Furthermore, a large number of scales are invalid in most of the countries where they used, because they were not properly adapted to the circumstances of a foreign society, instead of being simply translated from the original language. No doubt, scale-based analysis is cheapest and convenient to patients but due to non-linearity in data, there should be another alternative for early detection.
4. Although there are several scales in the literature, most of them were developed for other diseases and then tested in PD.
5. Some of the scales need a lot of training before the application.
6. None of the scales is perfect, and it would probably be better to use combined scales even though we know that they overlap in some aspects.

Conclusions

PD is a non-preventable disorder that affects the quality of patient's life, but the cause behind this has nevertheless been revealed. Therefore, it is important to know the causes, manifestations, and treatment procedures of PD for better management. Many potential treatments for PD are being developed as a result of the emergence in experimental therapeutics and also there are many ways that can assist an affected person in a major way to meet the needs and survival. This review article offers original and applicable guidelines for PD researchers and practitioners on improving the biomarker for early detection based on the literature. During the review process, the 24 research articles were analyzed from a total of 451 articles. The chosen articles followed the inclusion–exclusion criteria. The article demonstrates the various diagnostic clinical scales of PD. These scales can help the patient for particular symptom diagnosis and all these have huge potential to find the PD on early stages and can also aid to reduce the burden of doctors, side-effects of medications, and patient's expenses in the treatment process.

Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 9 of 10

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Aggarwal *et al. Egypt J Neurol Psychiatry Neurosurg*   (2021) 57:174

Page 10 of 10

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