

ADDIS ABABA UNIVERSITY  
COLLEGE OF HEALTH SCIENCES  
SCHOOL OF MEDICINE,  
DEPARTMENT OF NEUROLOGY

ASSESSMENT OF SLEEP DISORDER PATTERN OF PATIENTS WITH PARKINSON DISEASE  
ATTENDING NEUROLOGY REFERRAL CLINIC IN TIKUR ANBESSA SPECIALIZED AND  
ZEWDITU MEMORIAL HOSPITALS, ADDIS ABABA, ETHIOPIA

*A Cross-sectional Point Prevalence Study*

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## List of Abbreviations

EDS	Excessive daytime sleepiness
ESS	Epworth sleepiness scale
HY scale	Hoehn and Yaher scale
MESS	Modified Epworth sleepiness scale
MSQ	Mayo Sleep Questionnaire
NMS	Non motor symptom
PD	Parkinson's disease
PDSS -2	Parkinson's disease sleep scale version two
PLMS	Periodic limb movements
PSG	Polysomnography
PSQI	Pittsburgh sleep quality index
RBD	Rapid Eye Movement (REM) sleep behavior disorder
RLS	Restless leg syndrome
SD	Standard deviation
SCOPA	Scale for outcomes in Parkinson's disease

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## Abstracts

**Background:** Parkinson's disease (PD) is progressive neurodegenerative disorder characterized by abnormal motor symptoms such as bradykinesia, tremor, rigidity, and postural instability. However, the nonmotor symptoms (NMS) of PD, including cognitive impairment, depression, psychosis, & sleep disorders are also important and could have greater significance for disability, decreased quality of life, and reduced lifespan of the patients. Sleep-related problems specific to PD may occur early and even predate the diagnosis of the disease but are generally more frequent and more severe in patients with advanced PD. Little is known about sleep disorder pattern in people with Parkinson's disease (PD) in Ethiopia and Africa.

**Objective:** To assess the prevalence of sleep disorder pattern and their associated predictors in PD patients in Tikur Anbessa Specialized Hospital and Zewditu Memorial Hospital, Addis Ababa, Ethiopia.

**Methods:** A cross-sectional follow up study was used to collect data on all 155 study respondents who visited the clinic over the four months of the study period. Data was collected using tool (standardized questionnaire) by trained neurology nurses and neurology residents. All the respondents were identified using a selection a criterion satisfying the required ethical clearance procedure was used including securing verbal consent before data collection. Then collected data was cleaned and analyzed using SPSS version 20 to determine the magnitude/prevalence of sleep disorder and regression with p-value to determine the associated factors that explained the dependent variable.

**Included:** All PD patients on follow up or diagnosed during a study period fulfilling the UK Brain Bank Criteria for idiopathic PD. **Exclusion criteria:** included the following: PD Patients with cognitive impairment who was unable to respond for the PDSS-2, PD Patients who didn't have willingness to give informed consent and PD patients out of the study period. The data included 155 PD patients. We used the PDSS-2 to collect sleep disorder Symptoms. Data were entered and analyzed by a computer software SPSS version 20. First bivariate analysis was done to identify those factors that determine the dependent variable then multivariate analysis and Chi-Squares were used to determine those factors that determine the their possible associated predicting factors.  $P$  values < 0.05 at confidence interval 95% were considered significant.

**Results:** Majority, 127 (81.9%) of the respondents were male. Almost all 140(90.6%) of the respondents getting up at night to pass urine at least one day per week and followed by 104(67%) who were unable to turn around while in bed in at least one day in a week. Patients reported problems on all items of sleep disorder, the least score being 4 and maximum score being 39 which indicates there was no patient without sleep disturbance pattern. The most striking point was 13.5% of patient had a score of more than 30. Over all 30.1% of patient slept well for less than 3 days per week. About one third of Parkinson disease (PD) patients (35%) Wake up early in the morning with painful posturing of limbs. Patient's age, marital status, employment status,

PD symptom duration, historical reportable sleep disturbance and disease severity were related to advanced sleep disturbance with p- value of 0.04, 0.02, 0.00, 0.01, 0.002 and 0.001 respectively.

**Conclusions:** Sleep disturbance symptoms on PD patients are prevalent in our study. When disaggregated, it increase with age ,higher disease severity, disease duration, being un married and un employed and presence of reportable previous sleep disturbance before PD symptoms. Considering the prominence of sleep disturbance in PD patients in this study, there warrants increase clinical awareness and efficacious therapies by neurology department on internal medicine and neurology residents as part of teaching and learning activities.

# CHAPTER ONE

## INTRODUCTION

### 1.1. Background

Parkinson's disease (PD) is progressive neurodegenerative disorder characterized by abnormal motor symptoms such as bradykinesia, tremor, rigidity, and postural instability. However, the nonmotor symptoms (NMS) of PD, including cognitive impairment, depression, anxiety, psychosis, sleep disorders, and autonomic dysfunction, are also important and could have greater significance for disability, decreased quality of life, and reduced lifespan of the patients.

The documentation of sleep-related problems associated with Parkinson's disease (PD) dates as far back as James Parkinson's original monograph about the disease. Sleep disturbances are present in approximately 38% to 98% of PD patients. Sleep-related problems specific to PD may occur early and even predate the diagnosis of the disease but are generally more frequent and more severe in patients with advanced PD. However, it is only recently that sleep disturbances related to PD have received much diagnostic and therapeutic attention, and there have been a large number of relevant reviews and research publications.

Sleep-related problems associated with Parkinson's disease can seriously compromise patients' quality of life and lead to impaired functioning in daily activities. Sleep disorders in patients with PD are common, and in spite of recognition in recent years, they remain under diagnosed and under-treated.

### 1.2. Statement of the problem

Patients with PD are at greater risk of developing sleep disturbance symptoms than the general population. Sleep disturbance symptoms as for other non-motor symptoms, are common and yet often under recognized feature of PD in clinical practice because of the absence of systematic or specific questioning by health care professionals.

Little is known about sleep disorder pattern in people with Parkinson's disease (PD) in Ethiopia, despite the large number of relevant reviews and research publications on sleep disorder pattern in people with PD elsewhere, where the problem has received much diagnostic and therapeutic attention. But as to our knowledge there are no English published data on sleep disorder pattern in people with PD, in Ethiopia or Africa. Even though the Sleep problems in PD merit particular attention as it is seen in other part of the world, it is under recognized and its assessment is not usually part of the routine evaluation of patients with PD in our setup.

### **1.3. Research objectives**

#### **1.3.1. General objective**

To determine the sleep disorder pattern in PD patients seen in the Outpatient Clinics of Tikur Anbessa specialized and Zewuditu Memorial Hospitals, Addis Ababa, Ethiopia; from July 2015 to Nov 2015.

#### **1.3.2. Specific objectives**

- To assess prevalence of sleep disorder pattern in PD patients.
- To determine the demographic factors associated with sleep disorder pattern in PD patients.
- To determine factors associated with sleep disorder pattern in PD patients.

### **1.4. Significance of the study**

Base on our literature review there are no English published data on sleep disorder pattern in Parkinson's disease patients in Ethiopia and Africa. Even if there are large number of relevant reviews and research publications on sleep disorder pattern in people with PD in other part of the world, where the problem receive much diagnostic and therapeutic attention. So our study tried to fill that gap.

## CHAPTER TWO

### LITERATURE REVIEW

#### Literature review

Parkinson's disease (PD) is a neurodegenerative disorder associated with a loss of dopamine-producing neurons in the substantia nigra pars compacta. The disease was described by James Parkinson in 1817, and his description remains remarkably accurate. The disease (PD) is characterized by abnormal motor symptoms such as bradykinesia, tremor, rigidity, and postural instability. Its prevalence is approximately 1% among those aged greater than 65yrs. The disease progresses relentlessly and ultimately major disability are due to motor symptoms, non motor symptoms and treatment complications (fluctuations and dyskinesias) .

Nonmotor symptoms of PD include; sleep disorders, cognitive impairment, depression, anxiety, psychosis and autonomic dysfunction. These can be as disabling as the much better studied motor symptoms. It could have greater significance for disability, decreased quality of life, and reduced lifespan of the patients. The documentation of sleep-related problems associated with Parkinson's disease (PD) dates as far back as James Parkinson's original monograph about the disease: 'His attendants observed, that of late the trembling would sometimes begin in his sleep, and increase until it awakened him: when he always was in a state of agitation and alarm. However, it is only recently that sleep disturbances related to PD have received much diagnostic and therapeutic attention. A particular reason for maintaining or improving the quality of sleep is the observation that sleep may temporarily improve the motor symptoms of PD.

A clinic-pathological study by the United Kingdom Brain Bank estimated that approximately 20% of PD patients actually present with NMS. Next to autonomic dysregulation, gastrointestinal and sensory symptoms, as well as neuropsychiatric alterations, sleep disturbances represent an important group of NMS. Disruptions of physiologic sleep are among the most common NMS, affecting up to two-thirds of PD patients , and can be either quantitative or qualitative in nature, often accompanied by severe effects upon social functioning. The non motor manifestations are frequently under recognized and undertreated by health care professionals (Aarsland et al, 2000; Findley et al, 2003; Karlsen et al, 1999). Shulman et al, 2002 found that symptoms of depression, anxiety, fatigue, and sleep disturbances were overlooked by physicians in more than 50% of neurological consultations for PD patients.

K. Ray Chaudhuri et al showed that Sleep disturbances were key aspect of the non-motor symptom complex of PD and affect health-related quality of life.

Among the nonmotor manifestations were numerous forms of alterations of physiologic sleep patterns that may present at different stages during the course of disease. These include changes

believed to be primarily related to the underlying neurodegenerative process of the disease as well as those brought about secondarily by pharmacologic treatment. The pathophysiology of sleep disturbance in PD is complex, largely unknown and multi factorial. The degeneration of central sleep regulation centers in the brainstem and thalamocortical pathways is implicated. Sleep disturbance may precede motor symptoms, and this probably reflects the degeneration of areas, such as the raphe nucleus (serotonin) and locus coeruleus (noradrenaline) .

Sleep problems can present at any stage during the course of disease and cause both nocturnal and diurnal changes to the physiologic sleep pattern. They can be either temporary, as exemplified by the somnolence reported by some during the beginning of dopamine agonist treatment, or chronic as in rapid eye movement (REM) sleep behavior disorder (RBD), which can persist for more than a decade before the first presentation of PD-specific symptoms. Broadly, sleep impairments in PD can be classified as: Firstly, a number of motor phenomena that are present in PD impact upon sleep, such as nocturnal akinesia, rigor, tremor, or early morning dystonia. Secondly, several specific sleep disorders are recognized in PD. These include rapid eye movement (REM) sleep behavior disorder (RBD), restless legs syndrome (RLS), insomnia, excessive daytime sleepiness (EDS), and sleep-related breathing disorders (SRBDs). Lastly, nearly all medications used to treat PD can potentially alter physiologic sleep patterns.

A community-based study reported 60% of patients with PD (144 of 239) with sleep problems, compared with 33% of healthy controls (33 of 100) with the same age and sex distribution. A recent study in 123 PD patients across all age groups and 96 age-matched controls using a newly validated non-motor questionnaire for PD (NMSQuest) reported that sleep problems such as restless legs syndrome (RLS), excessive day-time sleepiness and rapid eye movement (REM) behavior disorder (RBD) were highly significantly more common in PD patients compared with those in controls.

The prevalence of sleep disorders in Parkinson's disease (PD) was reportedly 40% to 90%. This has significant implications imposing a higher caregiver burden and impairing quality of life for both patients and their bed-partners. Sleep disturbances in PD may be grouped into four broad categories; insomnia, motor, urinary and neuropsychiatry problems.

Excessive day-time sleepiness (EDS), a common complaint of patients with PD, affects approximately 15.5% of these patients compared with only 1% of healthy age matched controls . A combination of the disease process, the effect of poor nocturnal sleep and anti-parkinsonian or other drugs may be causative. EDS manifests in many ways, and while some patients may feel sleepy and slowly drift off to sleep, others may have rapid-onset sleep without any preceding drowsiness resembling narcolepsy. Excessive day-time sleepiness can occur early in PD , may predate the diagnosis. Predictors of EDS in PD include increasing age, advanced disease, and higher dosages of dopaminergic medications. Dopamine agonists(DAs) in particular are a common cause of EDS in patients with PD (Frucht et al, 1999; Hauser et al, 2000. Gjerstad et

al.1995 followed 142 patients with PD for 4 years and found that the prevalence of EDS went from 7.7% to 29% as disease severity and duration increased.

Insomnia was found to be very common in PD and causes patients to be unable to fall asleep or maintain sleep. Causes for insomnia include depression, PD motor symptoms, and sleep/wake cycle abnormalities. Patients often develop a sleep pattern marked by excessive napping during the day and wakefulness at night. Insomnia probably represents the most common subjective complaint with regard to sleep in PD subjects. Both sleep onset insomnia and sleep-maintenance insomnia can arise. The first was believed to be associated with PD itself, while increased sleep fragmentation plays a significant role in the latter, occurring against the backdrop of nocturnal motor (e.g., akinesia/“off” state-related symptoms) and nonmotor (e.g., nocturia, psychotic symptoms, depression, specific sleep disorders) symptoms. Insomnia occurs in about 30% of patients with PD. The most common types of insomnia reported by patients with PD were sleep fragmentation and early awakenings, which were seen more frequently than in age-matched controls.

Hallucinations were reported in up to 40% of PD patients and were a major predictor for hospitalization and dependence. They had a disruptive effect on sleep, as they show a clear nocturnal preponderance and were mostly visual in nature. Risk factors intrinsic to the disease include cognitive impairment, dementia, age, disease duration and severity, depression, and co-occurrence of sleep disorders. Equally as significant, nearly all drugs used in treatment of PD were known to induce or worsen neuropsychiatric symptoms. Currently, no established standards on how to diagnose or quantify hallucinations in PD exist. Sleep disturbances themselves, in particular, REM sleep abnormalities, represent the strongest predictor for the occurrence of hallucinations. In an 8-year-long longitudinal evaluation of 80 PD subjects, RBD proved to be highly associated with visual hallucinations, and in a cross-sectional study of nearly 300 PD patients, hallucinations were almost three times more common if RBD was present. Interestingly, hallucinations in PD may reflect intrusions of dream content into wakefulness, possibly due to degeneration of brainstem areas specifically involved in REM sleep regulation.

Nightmares were reported in 30% of patients with PD and were correlated with disease severity and levodopa dose. Some patients with PD also manifest other parasomnias associated with dreams, such as vivid dreams, altered dream content, night terrors, RBD, and hallucinations.

RBD was first reported by Schenck *et al.* in 1986 . RBD is a parasomnia that has a population prevalence of 0.5% and characterised by the loss of the normal skeletal muscle atonia during REM sleep. During REM sleep, patients enact their dreams which can be vivid or unpleasant and partners report vocalizations (talking, shouting and vocal threats) and abnormal movements (arm/leg jerks, falling out of bed and violent assaults). Although clinical history may suggest a diagnosis, confirmation can be obtained by a single night of polysomnography with video telemetry demonstrating increased EMG activity during REM sleep. In a study using

polysomnographic recordings and a structured clinical interview, RBD was diagnosed in 11 of 33 consecutive patients with PD. Approximately one half of the RBD cases would not have been identified by the clinical interview alone. Although the pathological basis of RBD is unknown, speculation is that RBD is related to the degeneration of lower brainstem nuclei like the pedunculopontine and subcoeruleal nucleus.

RBD has received increasing attention since Shneck and colleagues reported that 38% of patients with RBD examined were diagnosed with PD 4 years after the onset of RBD. The median time interval between the diagnosis of RBD and PD was 13.0 years. Patients with RBD are predominantly male. Pacchetti et al. reported that the presence of RBD in patients with PD was associated with an approximate 3-fold increase in the risk of developing psychotic disorders. Arnulf et al. (31) suggested that hallucinations and delusions in non-demented patients with PD can result from abnormal REM sleep. This leads to an “acting out of dreams,” including sleep talking, shouting, and intense, sometimes violent, movements. Patients may inadvertently injure their bed partners by punching or choking them (Boeve et al, 2001). In a study of 19 patients with PD, 47% met the diagnostic criteria of RBD based on polysomnographic recordings, but only 33% of these cases were detected by a questionnaire.

Both drug-naïve and drug-treated PD patients may develop a syndrome of nocturnal restlessness resembling RLS and periodic leg movements (PLM) during sleep, whereas RLS has been reported to occur in PD at a rate twice the normal prevalence of RLS in general population. Restless legs syndrome occurs in approximately 20% of patients with PD (Ondo et al, 2001). The syndrome causes patients to experience an urge to move their legs, usually accompanied by uncomfortable leg sensations. It is typically worse during evening and night time hours and when patients are resting quietly. It is therefore often worse when patients lie down in bed to go to sleep. Unfortunately, many patients with restless legs syndrome find the sensations so uncomfortable that they walk around at night to relieve them.

The prevalence of RLS in patients with PD was between 0.5% and 20.8%, compared to 2.9% in controls. The observation that the onset of motor symptoms in PD often preceded the onset of RLS supports the hypothesis that PD may be one of the risk factors for RLS. However, still more than 50% patients have been reported to experience symptoms of RLS before the onset of PD. Both RLS, as defined by four essential diagnostic criteria set forth by the International RLS Study Group (IRLSSG): (1) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations, (2) onset or aggravation during periods of inactivity, (3) relief by movement, and (4) worsening in the evening or at night), and periodic limb movements in sleep (PLMS), which can be found in [90% of RLS patients, have been frequently described in PD.

Obstructive sleep apnea occurs in about 20% of patients with PD (Arnulf et al, 2002) and is defined by intermittently absent or reduced airflow during sleep despite respiratory effort. General population patients with sleep apnea are commonly obese and snore during sleep. However, patients may not give a history of snoring, and there was a suggestion that PD patients with sleep apnea need not be obese. Several studies had suggested an augmented frequency of SRBDs, particularly in the form of obstructive sleep apnea (OSA), although both mixed and central sleep apneas have also been described in patients with PD. PD patients with OSA primarily only experience mild to moderate OSA in comparison with idiopathic OSA syndrome. Heavy snoring, a feature characteristic of OSA, has been shown to correlate with EDS in both PD patients and controls alike.

Nocturia, another major nonmotor complaint reported by 62% of patients in the NMS Quest Study, may also lead to insomnia by increasing sleep fragmentation. Pathophysiologically, nocturia in PD is attributed to a combination of increased urine output at night and decreased bladder capacity. Nocturia and ‘off’-period-related urinary incontinence complicate sleep pattern in advanced disease. Eighty percent of patients with PD have two or more episodes of nocturia per night, and 33% urinate at least three times per night. The frequency of nocturia increases with PD severity.

Pain was reported in approximately 50% of patients with PD and was most commonly associated with foot dyskinesia. Because the pain is often linked to “off” states or insufficient doses of dopaminergic therapy, adjustment of PD medications may provide relief.

Polysomnography (PSG) studies had indicated that the latency to fall asleep, the frequency of awakenings, and the total number of hours spent sleeping increase with PD progression. Fragmented sleep, disturbance of sleep initiation, and daytime sleepiness are unmet needs for patients with PD. About 40% of patients with PD take sleeping pills, significantly more than are taken by elderly people without PD. Sleep fragmentation occurred about three times more frequently in patients with PD than in healthy controls (38.9% versus 12%). Comparison of polysomnographic sleep measures in 10 drug-free patients with PD and 10 age-matched healthy controls showed that patients with PD had significantly less total sleep time, less sleep period time, and reduced sleep efficiency. Patients with PD had more frequent awakenings and greater overall waking time than controls.

Evaluation of sleep in PD patients is important because sleep impairment has been widespread in this population and represents one of the major factors impacting quality of life throughout the course of disease. Addressing sleep disturbances and efficient clinical management of these symptoms are of great value to both patients and caregivers.

K R Chaudhuri et al tried to assess formal instruments available for quantifying the various aspects of nocturnal sleep problems in Parkinson's disease. They found out that Scales widely employed in clinical practice including the Epworth sleepiness scale (ESS) and the Pittsburgh sleep quality index (PSQI) did not systematically address and quantify the different aspects of sleep disturbance in Parkinson's disease. The unified Parkinson's disease rating scale (UPDRS) contains only one question related to sleep problems, and the newly validated Parkinson's disease quality of life scale (PDQ39) is also limited in terms of questions related to sleep. More recently, Marinus *et al.* have described the development of the SCOPA-SLEEP Scale. However, it does not address some problems specific to PD such as nocturnal hallucinations, pain, dystonia, tremor and nocturia. They showed that validated, simple to use, bedside clinical instrument to provide a semi quantitative assessment of the multi factorial nature of sleep problems in Parkinson's disease was PDSS-2. The PDSS-2 is scale addressing 15 commonly reported symptoms associated with sleep disturbance. Items of the PDSS address the following: overall quality of night's sleep (item 1); sleep onset and maintenance insomnia (items 2 and 3); nocturnal restlessness (items 4 and 5); nocturnal psychosis (items 6 and 7) nocturia (items 8); nocturnal motor symptoms (items 9–13); sleep refreshment (item 14); obstructive sleep apnea (item 15). This scale has been validated and employed extensively in a number of countries and was reported to exhibit high reliability. One multicenter study also found more severe nocturnal disturbances in patients with an advanced stage of PD, as measured by the PDSS, (Hoehn & Yahr (H&Y) stage IV) compared with those with early and moderate stages of the disease (H&Y I–III). These disturbances were associated with disease duration, depressive symptoms, and complications of dopaminergic treatments (such as dyskinesia and wearing-off symptoms). PDSS-2, a new version of PDSS, has been developed, and its total and three domain scores, including disturbed sleep, motor symptoms at night, and PD symptoms at night, have been shown to correlate with patients' quality of life, the Unified Parkinson's Disease Rating Scale (UPDRS) motor scores, and disease severity in different patterns. The PDSS-2, includes the screening of SAS, has been published with an excellent level of validity and reliability. Out of 19 scales that were rated, the PDSS emerged as the most comprehensive for appraisal of overall sleep impairment, as a screening tool, and as a measure of severity. Based on comparisons with polysomnography and other sleep questionnaires such as the Epworth Sleep scale, the PDSS appears to be a reliable tool to evaluate sleep characteristics in PD patients.

Elso Tinoco et al studied Sleep disorders on 90 PD patients using PDSS & found out that Sleep disorders are varied and frequent among patients with PD. A community based study in Norway by Elisabeth Svensson et al, on 176 consecutive PD outpatients studied on non-motor symptoms, including sleep problems. All participants responded to the Parkinson's disease Sleep Scale (PDSS), where an overall score below 82 or a score below 5 on a sub-item indicate possible sleep problem. Sleep problems were common among PD patients. While only 17% of the sample had an overall score below 82 on the PDSS, 70% of the patients had a score below 5 on one item.

There was no significant association between PD severity and any of the sleep items in the PDSS; whereas fatigue, mental health problems, and RLS were associated with PDSS score.

Lees and his colleagues have reported nocturnal disturbances in 215 of 220 PD patients, including nocturia (79%), difficulty turning over in bed (65%), painful muscle cramps (55%), nightmares (48%), limb or facial dystonia (34%), leg jerks (33%), and visual hallucinations (16%).

Thirty percent of patients with PD report improvements in their motor symptoms in the morning, before taking any medication. This phenomenon was referred to as “sleep benefit” . This benefit has also been reported after short naps. Thus, the mechanism by which sleep produces these benefits in motor symptoms remains unknown.

In Ethiopia and in Africa yet there was no published data on sleep disorder pattern in parkinsons disease, only few studies have been done on Parkinson’s disease. Hence this research assessed sleep disorder pattern in parkinsons disease in Ethiopian setup to help and improve care of patients.

## **CHAPTER THREE**

### **METHODOLOGY**

This chapter deals with the description of the research design, population and sample, research instruments, the procedure of data collection, and statistical methods.

#### **3.1. Methods and materials**

- ✓ **Study Area:** The study was hospital based study; it was conducted in Addis Ababa, the Ethiopian capital city, in two governmental referral hospitals; Tikur Anbessa Specialized Hospital and Zewditu Memorial Hospital, General Neurology Follow up clinic, department of Neurology, Addis Ababa University (AAU).

- ✓ On average 4-5PD patients are seen per each neurology referral clinic which is 2 days per week in each hospital. There are 8 neurology residents, 3 internal medicine residents and 6 nurses attending the clinics under supervision of seven neurologists.
- ✓ **Study Period:** Data were collected from July 1 to October 30, 2015.
- ✓ **Research Design:** Cross-sectional point prevalence study.

### 3.2. Population

- ✓ **Target Population:** All patients diagnosed with Parkinson's disease.
- ✓ **Source Population:** All patients diagnosed with PD and attended Neurology follow up clinics of Tikur Anbessa specialized & Zewuditu Memorial Hospitals from July 1 to Nov30, 2015.
- ✓ **Study Population:** All patients diagnosed with PD and attended outpatient Neurology follow up clinics of Tikur Anbessa specialized & Zewuditu Memorial Hospital from July 1 to Nov 30, 2015 and fulfilled inclusion criteria.

### 3.3. The study population

Since PD is a rare disease with estimated prevalence of 7 per 100,000 in Ethiopia (59), all patients fulfilling the inclusion criteria from July 1 to November, 30 2015 in the study area was included.

- ✓ **Inclusion criteria:**
  - Those PD Patients newly diagnosed & on treatment for PD
  - PD Patients whose Age  $\geq$  18 years old
  - PD Patients who had gave informed consent
- ✓ **Exclusion criteria:**
  - PD Patients with cognitive impairment who was unable to respond for the PDSS.
  - PD Patients who didn't had willingness to give informed consent.
  - PD patients out of the study period.
- ✓ During the study period there were 160 PD patients out of whom 5 patients excluded from the study 3 patient had cognitive impairment and 2 of the patients refused to accept consent.

### 3.4. Research variables

### 3.4.1. Dependent variables

Pattern of sleep disorders measured by:-

- Parkinson disease sleep scale version -2(PDSS-2) score
- Epworth sleep scale(ESS )score
- Mayo sleep questioner(MSQ) response

### 3.4.2. Independent variables

- Age
- Sex
- Marital status
- Ethnicity
- Religion
- Educational level
- Occupation status
- Co-morbid medical condition(s) and medications use
- Previous history of sleep disorder
- Duration of PD symptom
- Hoehn and Yahr stage of PD

### 3.5. Definition of important terms (Operational definition)

**Sleep:** - According to a simple behavioral definition, sleep is a reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment. Normal human sleep comprises two states—rapid eye movement (REM) and non-REM (NREM) sleep—that alternate cyclically across a sleep episode (61).

State characteristics : NREM sleep includes a variably synchronous cortical electroencephalogram (EEG; including sleep spindles, K-complexes, and slow waves) associated with low muscle tonus and minimal psychological activity; the REM sleep EEG is desynchronized, muscles are atonic, and dreaming is typical.

A nightly pattern of sleep in mature humans sleeping on a regular schedule includes several reliable characteristics: Sleep begins in NREM and progresses through deeper NREM stages (stages 2, 3, and 4 using the classic definition) before the first episode of REM sleep occurs approximately 80 to 100 minutes later. Thereafter, NREM sleep and REM sleep cycle with a period of approximately 90 minutes. NREM stages 3 and 4 concentrate in the early NREM cycles, and REM sleep episodes lengthen across the night (61).

**Insomnia:** - Is a persistent disorder that can make it hard to fall asleep, hard to stay asleep or both, despite the opportunity for adequate sleep.

**Obstructive sleep apnea:**-Is a sleep disorder manifested by Waking up at night due to snoring or difficulties with breathing.

**Nocturia:** - Defined as, getting up at night to pass urine .

**Hallucination:**-Seeing or hearing things that do not exist.

**Excessive daytime sleepiness (EDS):**-Feeling of tiredness and being sleepy after waking in the morning .

**Rapid eye movement behaviour disorder (RBD):**- Characterized by the loss of the normal skeletal muscle tone, atonia, during REM sleep. Patients enact their dreams which can be vivid or unpleasant and partners report vocalizations (talking, shouting and vocal threats) and abnormal movements (arm/leg jerks, falling out of bed and violent assaults) ([31](#)).

**Restless legs, periodic limb movements (RLS/PLM):**-

The syndrome causes patients to experience an urge to move their legs, usually accompanied by uncomfortable leg sensations. Defined by four essential diagnostic criteria set forth by the International RLS Study Group (IRLSSG):

- (1) An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations,
- (2) Onset or aggravation during periods of inactivity,
- (3) Relief by movement, and
- (4) Worsening in the evening or at night.

### **3.6. Data collection tool and procedure**

Data were collected by the principal investigator (PI) and the other senior neurology residents. Formal introduction were given to the senior neurology residents by the PI before data collection starts.

First, each PD patient was evaluated thoroughly and managed appropriately as part of the routine follow up, i.e., appropriate treatment was given (or continued if they are already on treatment) by the respective senior neurology residents. At the end of the routine follow up care, and before the actual data collection starts, a brief introduction of the study (the need to have this study, pros and cons, what to expect from this study, and the scope of this study) were given to each patient.

After one was sure that the patient understands all the information given above, and agrees to be involved in the study, then they were asked verbal consent. It was only then after that the actual

data collection started, provided that the patient agreed to participate in the study. Patients direct information were mainly taken into account but also files were checked for additional or some unclear delivered clinical information to supplement collected data.

### **3.7. Data collecting instrument**

- Parkinson disease sleep scale version- 2(PDSS-2) (56)
- The Epworth Sleepiness Scale (ESS)( from international movement disorder society)
- Mayo Sleep Questionnaire (MSQ)( from international movement disorder society)

Data was collected using a structured questionnaire in Amaharic. The PDSS-2, ESS and MSQ questionnaire was translated to Amharic and back translated to English to ensure quality of translation. Sleep disturbance pattern was evaluated using PDSS-2 which consists of 15 items that address factors of sleep quality, and frequency and severity of sleep-related problems that are known to be present in patients with PD. Each item was rated on a scale from 0-4.

Items of the PDSS address the following:

- Overall quality of night's sleep (item 1)
- Sleep onset and maintenance insomnia (items 2 and 3)
- Nocturnal restlessness (items 4 and 5)
- Nocturnal psychosis (items 6 and 7)
- Nocturia (items 8)
- Nocturnal motor symptoms (items 9–13)
- Sleep refreshment (item 14)
- Obstructive sleep apnea (item 15).

The Epworth Sleepiness Scale was used as a subjective measure of a patient's day time sleepiness. The test had a list of eight situations in which patients were rate to become sleepy on a scale of 0, no chance of dozing, to 3, high chance of dozing. Total score was based on a scale of 0 to 24. The scale estimates whether patients were experiencing excessive sleepiness that possibly requires medical attention. The eight component of ESS were sleepiness while: watching TV, sitting inactive in a public place (e.g., a theater or a meeting), as a passenger in a car for an hour without a break, lying down to rest in the afternoon when circumstances permit, sitting and talking to someone, sitting quietly after a lunch without alcohol, in a car while stopped for a few minutes in traffic.

Mayo Sleep Questionnaire was used to assess RBD contain a question which had five sub divisions to asses RBD from bed partner.

In our study, sleep disturbance were assessed in a cohort of patients with PD. Sleep disturbance were evaluated using those reliable instrument that has been independently validated, and found to be an acceptable, consistent, valid and precise scale in patients with Parkinson's disease.

### **3. 8. Ethical considerations**

A protocol approval was obtained from the ethical review Committee of the Department of Neurology and the Institutional Review Board (IRB) and Research and Publication Committee of the medical faculty of Addis Ababa University. Study subjects were provided informed verbal consent. Patients were received standard therapies for PD and co-morbid disorders regardless of whether they consent to study enrolment.

### **3.9. Data quality assurance, processing and analysis**

Data was cleaned and the presence of incomplete questionnaires was checked. Data was analyzed using SPSS version 20.0. Simple descriptive statistics were used to summarize the responses to each item and the total, and in particular to identify the maximum and minimum possible scores. Values beyond 3 SD (90%) from the mean were considered as outliers. Chi-square analysis between variables and Sleep disturbance pattern in PD patients were done. P-value of less than 0.05 was considered to be significant association.

### **3.10. Dissemination of the result**

The results of this study will be submitted to the Department of Neurology, Medical Faculty of Addis Ababa University and will be disclosed to the respective units of the Hospital, health professionals and authorities. We anticipate manuscript submission to a medical journal for publication.



## CHAPTER FOUR

### RESULTS

#### 4.1. Characteristics of the participants

A total of 155 respondents were included in this study; of these majority 127(81.9%) were males by gender, 89(57.4%) were in the age group 60 and above years with a mean age of 60years.

This study comprised 155 patients out of which 81.9% were men and 18.1% being women. Those patients age greater than 60 years were accounting 57.4%. The mean age being 60.45(12.3) years. The mean duration of symptom, duration since PD diagnosis and duration of PD treatment were 6.37, 4.90, 4.68yrs respectively. The mean duration of symptom, duration since PD diagnosis and duration of PD treatment in yrs were 6.37, 4.90, 4.68yrs respectively.

Out of the study populations 37 (23%) of respondents had previous history of reportable sleep problem namely insomnia (14 patients) and day time sleepiness (23 patients).

There were 5 and 10 PD patients with comorbid diabetes and hypertension on treatment respectively. And also twenty four percent of the study populations were using Artane.

Those PD patients with Hoen and Yahar stage I &II (53.6%), stage III (28.1%) and stage VI & V (18.3%). (Table 1)

**Table 1: Baseline characteristics of patients with parkinson disease attending neurology referral clinic in Tikur Anbessa specialized and Zewditu memorial hospitals, from July 1 to October 30, 2015.**

Character	Frequency	Percent (%)
Hospital		
Tikur Anbessa Hospital	135	87.1
Zewditu memorial	20	12.9
Gender		
Male	127	81.9
Female	28	18.1
Age groups		
<60 years	89	57.4
≥60 years	66	42.6
Mean/±SD	60.45/12.3	
Marital status		
Married	121	78.1
Widowed	19	12.3
Separated/divorced	9	5.8
Never married	6	3.6
Duration of PD symptom in years		

<5 years	85	54.8
>=5years	70	45.2
Duration of PD diagnosis in yrs		
<5 years	113	72.9
>=5years	42	27.1
Duration of PD treatment in yrs		
<5 years	118	76.1
>=5years	37	23.5
Educational status		
No formal education	48	31.2
Primary education	45	29.2
Secondary education	36	23.4
More than secondary education	25	16.2
Level of literacy		
Cannot read and write(no formal education)	38	79.2
Can read and write	10	20.8
Previous(before PD diagnosis) history of known sleep problem		
No	118	76.1
Yes	37	23.9
Types of previous sleep problem reported		
Day time sleepiness	23	14
Insomnia	14	9
Artane (Benzehexol) use		
No	117	75.5
Yes	38	24.5
Hoehn and Yahar staging		
Stage 1	30	19.6
Stage 1.5	7	4.6
Stage 2	23	15.0
Stage 2.5	22	14.4
Stage 3	43	28.1
Stage 4	23	15.0
Stage 5	5	3.3

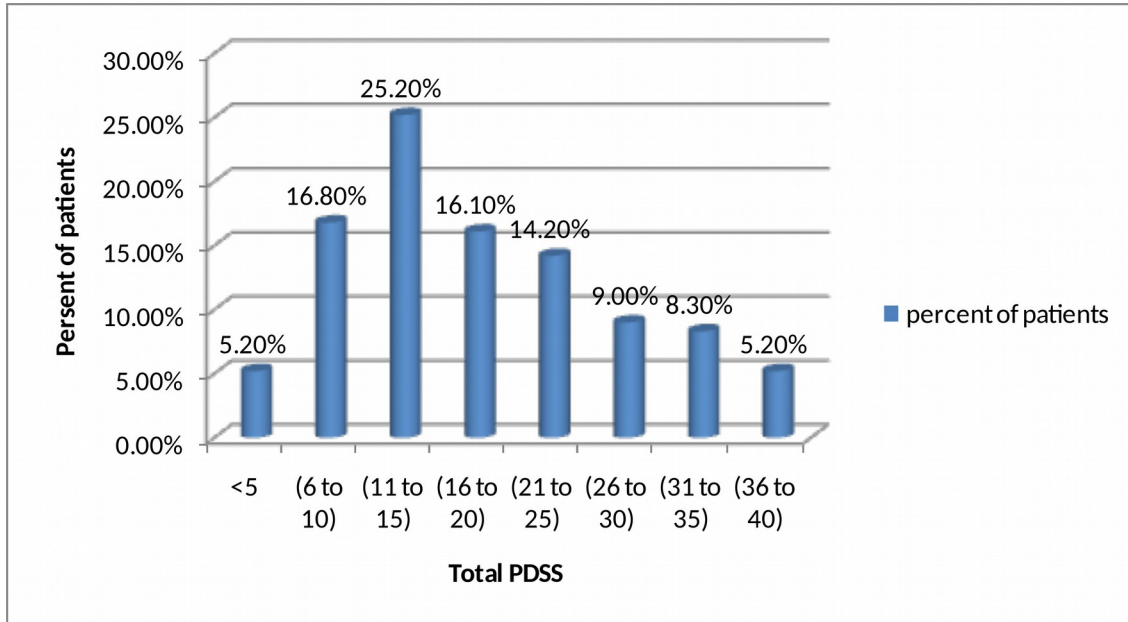
#### 4.2. All item scores based on PDSS-2 (0-60)

All Patients reported problems on all items of sleep disturbance, the least score being 4 and maximum score being 39 which indicates there was no patient without sleep disturbance pattern. Maximum score was for PDSS score 11 to 15 (25.2%) followed by 6 – 10(16.80%) and 16-20(16.10%). The most striking point was 13.5% of patient had a score of more than 30. Over all 30.1% of patient slept well for less than 3 days per week. This study also showed that 58.7% of patient got up at night to pass urine for more than 4 days per week. (Fig 1 & Table 2)

**Table 2: Prevalence of individual score of PDSS-2, of parkinson disease patients attending neurology referral clinic in Tikur Anbessa specialized and Zewditu memorial hospitals, from July 1 to October 30, 2015.**

Questions	Very often(This means 6 to 7 days a week) N (%)	Often(This means 4 to 5 days a week) N (%)	Sometimes( This means 2 to 3 days a week) N (%)	Occasionally (This means 1 day a week) N (%)	Never N (%)
1. Overall did you sleep well during the last week?	89(56.8)	19(12.6)	19(12.6)	23(14.8)	5(3.2)
2. Did you have difficulty falling asleep each night?	6(3.9)	16(10.6)	25(16.1)	36(23.5)	72(45.8)
3. Did you have difficulty staying asleep?	11(7.1)	19(12.8)	24(15.8)	32(20.6)	69(43.9)
4. Did you have restlessness of legs or arms at night or in the evening causing disruption of sleep?	4(2.6)	23(14.8)	14(9.4)	34(21.9)	80(51.3)
5. Was your sleep disturbed due to an urge to move your arms or legs?	5(3.4)	17(11.4)	20(12.9)	35(22.6)	78(49.7)
6. Did you suffer from distressing dreams at night?	12(7.7)	16(10.6)	28(18.4)	30(19.4)	69(43.9)
7. Do you suffer from distressing hallucinations at night (seeing or hearing things that you are told do not exist)?	4(2.6)	10(6.7)	14(9.4)	27(17.4)	100(63.9)
8. Do you get up at night to pass urine?	58(37.6)	33(21.3)	23(14.8)	26(16.8)	15(9.4)
9. Did you feel uncomfortable at night because you were unable to turn around in bed or move due to immobility?	11(7.4)	23(14.8)	24(15.5)	45(29.3)	52(32.9)
10. Did you feel pain in your arms or legs which wake you from sleep at night?	2(2.6)	14(9.0)	25(14.2)	36(24.5)	76(49.7)
11. Did you have painful muscle cramps in your arms or legs which wake you from sleep at night?	2(1.6)	14(9.0)	19(12.3)	48(31.3)	72(45.8)
12. Did you wake early in the morning with painful posturing of arms or legs?	4(2.6)	8(5.4)	17(11.4)	24(15.5)	102(65.1)
13. On waking did you experience tremor?	6(3.9)	20(12.9)	20(12.9)	44(28.7)	65(41.6)
14. Did you feel tired and sleepy after waking in the morning?	9(5.8)	17(11.3)	25(16.4)	40(25.8)	64(40.6)
15. Did you weak up at night due to snoring or difficulties with breathing?	9(5.8)	9(5.8)	13(8.7)	26(16.8)	97(62.9)

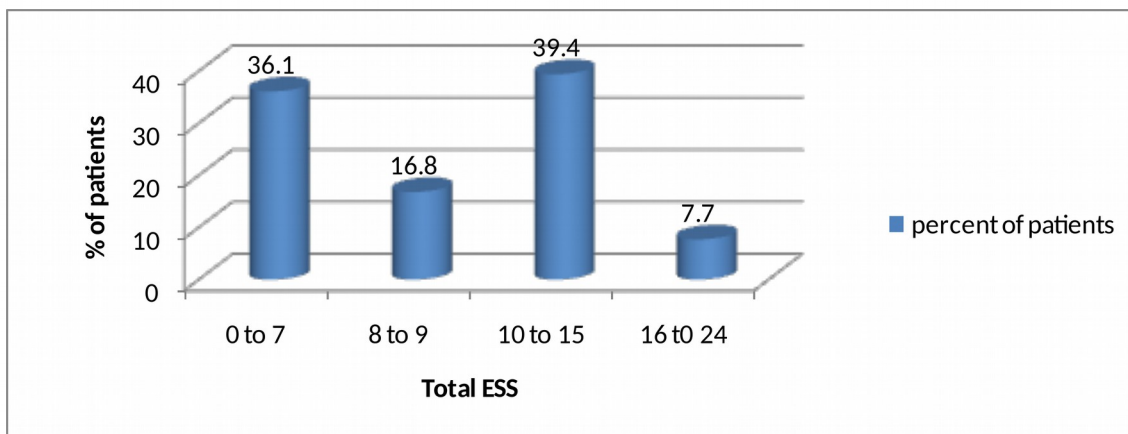
**Fig 1: Frequency distribution of total PDSS-2 score, of parkinson disease patients attending neurology referral clinic in Tikur Anbessa specialized and Zewditu memorial hospitals, from July 1 to October 30, 2015.**



**4.3. All item scores based on ESS (0-24)**

Except for five patients who had a score of zero which indicates no day time sleepiness, all the remaining patients had evidence of day time sleepiness of different degree. The most important finding was 47% of patient had excessive day time sleepiness which needs medical attention. (Fig 2)

**Fig 2: Frequency distribution of total ESS scores, of parkinson disease patients attending neurology referral clinic in Tikur Anbessa specialized and Zewditu memorial hospitals, from July 1 to October 30, 2015.**



#### **4.4. Gender influence**

Unfortunately it was difficult to see impact of gender on sleep disturbance pattern because most of the study population was male contributed 127(81.9%) and female being 28(18.1%). (Table 1)

#### **4.5. Influence of marriage**

This study showed that those patients who were never married and divorced had PDSS score of  $\geq 30$  than married patients (PDSS score of  $< 30$ ) which was statistically significant with P- value of 0.02 for confidence interval of 95%, Which imply that divorced and never married patients had higher sleep problem than married patients. (Table 3)

#### **4.6. Influence of employment status**

Our study also showed that unemployed PD patients had a higher PDSS score ( $\geq 30$ ) than employed patients who had PDSS score of ( $< 30$ ); which were statistically significant with P- value of 0.00 for confidence interval of 95 %.( Table 3)

#### **4.7. Influence of duration of PD symptom**

Thos PD patients with duration of symptom more than or equal to 5 years had higher PDSS score( $\geq 30$ ) than those patient with duration of PD symptom less than 5 years; which was statistically significant with P- value of 0.01 for confidence interval of 95%, which imply as the duration of PD symptom increase sleep disturbance pattern increase.(Table 3)

#### **4.8. Influence of historical sleep disturbance before PD symptom**

Thos patient who were having historical sleep disturbance before PD symptom had higher PDSS score ( $\geq 30$ ) than those patient with no prior history of sleep disturbance (PDSS score  $< 30$ ); which was statistically significant with P- value of 0.002 for confidence interval of 95%, Which indicates the presence of previous history of sleep disturbance had higher risk of having future sleep disturbance pattern. (Table 3)

**Table 3:- PDSS-2 score versus independent variables, of parkinson disease patients attending neurology referral clinic in Tikur Anbessa specialized and Zewditu memorial hospitals, from July 1 to October 30, 2015.**

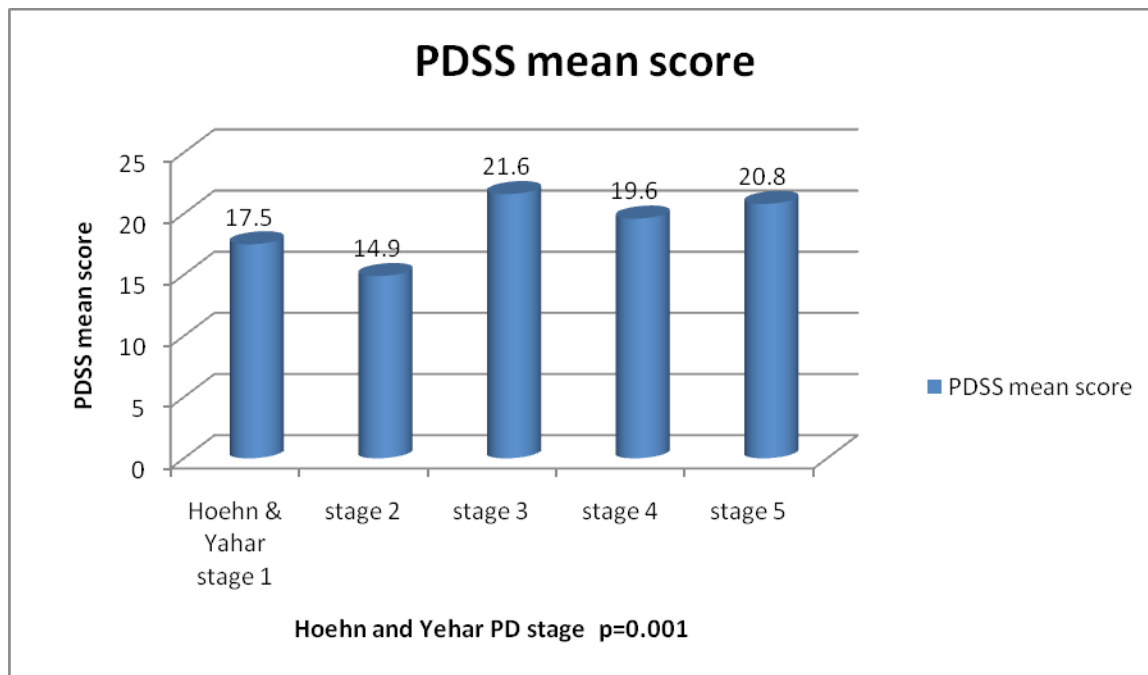
Variables	PDSS-2 total score N (%)		p-value	
	<30	≥30		
Gender				
	Female	24(18.0)	3(14.3)	0.47
	Male	109(82.0)	18(85.7)	
Age groups				
	<60 years	79(59.4)	9(42.9)	0.12
	≥60 years	54(40.6)	12(57.1)	
Marital status				
	Never married	5(3.8)	1(4.8)	<b>0.02</b>
	Married	104(78.2)	16(76.2)	
	Widowed	19(14.3)	--	
	Separated/divorced	5(3.8)	4(19.0)	
Duration of PD symptom in years				
	<5 years	78(58.6)	6(28.6)	<b>0.01</b>
	≥5 years	55(41.4)	15(71.4)	
Duration since PD diagnosed				
	<5 years	99(74.4)	13(61.9)	0.17
	≥5 years	34(25.6)	8(38.1)	
Duration of PD treatment				
	<5 years	102(76.7)	15(71.4)	0.38
	≥5 years	31(23.3)	6(28.6)	
Employment status				
	Employed	43(32.3)	--	<b>0.00</b>
	Unemployed	90(67.7)	21(100)	
Religion				
	Orthodox	104(78.2)	21(100)	0.06
	Muslim	23(17.3)	--	
	Other	6(4.5)	--	
Ethnicity				
	Amhara	73(54.9)	9(42.9)	<b>0.02</b>
	Oromo	26(19.5)	12(57.1)	
	Gurage	18(13.5)	--	
	Others	16(12.0)	--	
Educational status				
	No formal education	43(32.3)	5(25.0)	<b>0.03</b>
	Primary education	33(24.8)	11(55.0)	
	Secondary education	35(26.3)	1(5.0)	
	More than secondary education	22(16.5)	3(15.0)	
Hoehn and yahr				
	Stage 1	33(24.8)	4(19.0)	0.14
	Stage 2	44(33.1)	2(9.5)	
	Stage 3	34(25.6)	9(42.9)	
	Stage 4	18(13.5)	5(23.8)	
	Stage 5	4(3.0)	1(4.8)	

Artane use	Yes	32(24.1)	5(23.8)	0.61
	No	101(75.9)	16(76.2)	
Previous history of sleep disorder	Yes	26(19.7)	11(52.4)	<b>0.002</b>
	No	106(80.3)	10(47.6)	

#### 4.9. Influence of PD stage on PDSS-2 mean score

Those patients with higher Hoehn and Yahar stage had higher value of PDSS mean score which was statistically significant with p value of 0.001 for confidence interval of 95%. This indicates as disease severity increase there was higher rate of sleep disturbance pattern. (Fig 3)

**Fig 3: PDSS-2, mean score versus PD stage, of parkinson disease patients attending neurology referral clinic in Tikur Anbessa specialized and Zewditu memorial hospitals, from July 1 to October 30, 2015.**



#### 4.10. Age influence

Our study showed that those patients who are greater than or equal to 60 years of age had statistically significant day time sleepiness than those patient who were less than 60 yrs of age with p- value of 0.04 for confidence interval of 95%. Higher value of ESS score was for 10 to 15 score. (Table 3)

#### 4.11. Influence of PD stages on day time sleepiness

Our study also showed that as the PD stage advances the ESS score was higher which was statistically significant with P –value of 0.044 for confidence interval of 95%, which means higher level of sleepiness with the advance of PD stage. (Table 4)

**Table 4: ESS total score category versus independent variables, of parkinson disease patients attending neurology referral clinic in Tikur Anbessa specialized and Zewditu memorial hospitals, from July 1 to October 30, 2015.**

Variables	ESS total score N (%)				p-value
	0-7	8-9	10-15	16-24	
Gender					<b>0.002</b>
Female	8(29.6)	4(14.8)	8(29.6)	7(25.9)	
Male	47(37.0)	22(17.3)	53(41.7)	6(3.9)	
Age groups					<b>0.04</b>
<60 years	31(35.2)	21(23.9)	29(33.0)	7(8.0)	
≥60 years	24(36.4)	5(7.6)	32(48.5)	5(7.6)	
Marital status					0.26
Never married	1(16.7)	3(50.0)	2(33.3)	--	
Married	45(37.5)	20(16.7)	46(38.3)	9(7.5)	
Widowed	4(21.1)	2(10.5)	10(52.6)	3(15.8)	
Separated/divorced	5(55.6)	1(11.1)	3(33.3)	99	
Employment status					0.23
Employed	16(37.2)	11(25.6)	14(32.6)	2(4.7)	
Unemployed	39(35.1)	15(13.5)	47(42.3)	10(9.0)	
Religion					0.14
Orthodox	43(34.4)	25(20.0)	4(36.0)	12(9.6)	
Muslim	10(43.5)	1(4.3)	12(52.2)	--	
Other	2(33.3)	--	4(66.7)	--	
Ethnicity					0.53
Amhara	34(40.0)	14(16.5)	3(8.6)	6(7.1)	
Oromo	9(25.7)	9(25.7)	14(40.0)	3(8.6)	
Gurage	4(22.2)	2(11.1)	10(55.6)	2(11.1)	
Others	8(50.0)	1(6.2)	6(37.5)	1(6.2)	
Hoehn and yahr					<b>0.049</b>
Stage 1	18(48.6)	5(13.5)	13(35.1)	1(2.7)	
Stage 2	15(32.6)	9(19.6)	21(45.7)	1(2.2)	
Stage 3	16(37.2)	9(20.9)	14(32.6)	4(9.3)	
Stage 4	4(17.4)	3(13.0)	12(52.2)	4(17.4)	
Stage 5	2(40.0)	--	1(20.0)	2(40.0)	
Artane					<b>0.044</b>
Yes	19(51.4)	2(5.4)	13(35.1)	3(8.1)	
No	36(30.6)	24(20.5)	48(41.0)	9(7.7)	

## CHAPTER FIVE

### 5.1. Discussions of the main findings

This section discusses the major study findings in regard with the previous research findings reviewed in the literatures.

In our study there was no patient with PDSS-2 score of zero, which indicates that there was no PD patient without sleep disturbance if even if the degree varies, and 78% of patients in our study had a PDSS-2 score of more than ten, Which is comparable with the study done by Suzuki K et al which reported the prevalence of sleep disorder in PD patients as 40-90 % .

Our study showed that sleep onset insomnia  $\geq 2$  days/week was reported in 47 PD patients (30.3%) and sleep maintenance insomnia  $\geq 2$  days/week was reported in 54 PD patients (34.9%). Which is comparable with the study done by ; Kumar S et al which reported the prevalence of insomnia in PD patients were 30 %. Tandberg E et al also identified that the commonest type of insomnia in PD patients was sleep maintenance insomnia (sleep fragmentation) than sleep onset insomnia . This finding could be attributed to the prominence of motor symptom in our PD patients, which impair them to have non fragmented sleep.

In our study 55 PD patients (36.8%) reported hallucination in at least one day per week. Which is comparable with the study done by, Fenelon G et al which reported hallucination in PD patients 40 %.

Our study also showed 91 PD patients (58.7%) reported nocturia in at least 4 days per week. Which is comparable with the study done by Martine-Martin P et al; reported the prevalence of nocturia in PD patients 62%.

Charles H et al reported pain in 50% of PD patients . Our study also identified 77 PD patients (49.6%) reported pain at night which weak them up from their sleep, which is comparable with this study.

Claudi T et al an article on Parkinson disease sleep scale –validation of the revised version PDSS-2(56); total of 113 PD patients showed a mean (SD) total score of 16.5(+ 8.9) indicating mild to moderate sleep disturbance. Only 6.3% of patients had PDSS-2 score of more than 30(56). In our study those patient who had a PDSS-2 mean (SD) total score of 18.3(+ 9.1) and those PD patients with PDSS-2 score more than or equal to 30 were accounting for 23.3%.

A community based study done by Tandberg E et al showed that excessive day time sleepiness(EDS) was reported in 15.5% of PD patients. In our study based on ESS scale, EDS was seen in 74 PD patients (47.8%). Fabrbrini G et al also reported that EDS can occur in early PD, which was reviled in our study Hoehn and Yahar stage I(37.8%), stage II(47.8%), stage 3(41.9%). Charles H et al also identified that predictors of EDS were advanced disease stage

and age; which was reconfirmed in our study by those patient whose age  $\geq 60$  years had higher ESS score which was statistically significant with P value of 0.04 for confidence interval of 95%.

A multicentre study done in Japan by Suzuki K et al using PDSS tool found severe nocturnal disturbance seen in PD patient with advanced disease stage. Our study showed PD patients with advanced Hoehn and Yahr stage and longer duration of PD symptom ( $\geq 5$  years) were having higher PDSS score; which was statistically significant with P value of 0.001 and 0.01 respectively.

Arnulf I et al reported obstructive sleep apnea (OSA) in 20% of PD patients . Our study also revealed 57 PD patients (36.8%) reported OSA symptoms in at least one day per week. Hogl B et al identified that OSA was correlated with EDS(48), which was reconfirmed in our study. Those PD patients who reported OSA symptoms were having excessive day time sleepiness which was statistically significant with P value of 0.017 for confidence interval of 95%.

Our study also showed statistically significant association between marital status and PDSS total score; those patients who are divorced and never married had a PDSS total score higher than 30 than married PD patients with p value of 0.02. Which indicate that never married and divorced PD patients were at higher risk of developing advanced sleep disturbance pattern than married once, which was not seen in most studies. This finding may suggest being married has an advantage of having psychosocial support at home from bed partner, which might contribute for less sleep disturbance pattern than single and divorced PD patients.

In our study employment status had also statistically significant association (p value=0.00) with higher total PDSS score; which means those PD patients who were unemployed had a PDSS total score of  $>30$ . This indicates that unemployed PD patients were at higher risk of developing advanced sleep disturbance than employed once, which was not revealed in other study. This finding may support the fact that exercise has an impact on improvement of motor symptom of PD, which was one of the main contributors of sleep disturbance pattern in our study. That is may be why those patients who are employed have good sleep pattern than unemployed ones.

Our study also showed that previous history of reported sleep disturbance had statistically significant association (p value= 0.002) with higher PDSS score ( $\geq 30$ ). Which means those PD patients who had history of reportable sleep disturbance had higher likely hood of having advanced sleep disturbance than those PD patients with no previous history of reportable sleep disturbance, which was not addressed in other studies. This finding also supports the fact that sleep disturbance in PD may predate PD motor symptoms, which means PD patients may present with first symptom of sleep disturbance pattern.

## **5.2. Strength**

To assess sleep disturbance pattern we used a reliable instrument that has been independently validated, and found to be an acceptable, consistent, valid and precise scale in patients with Parkinson's disease.

To test for this scales we did also pre test on 20 PD patients 10 from each hospital and those patients were not included in the study.

Even if the estimated prevalence of PD patient were small we managed to get 155 PD patients, which was much higher than those studies done on PD previously.

## **5.3. The study limitations or weaknesses**

The data collected for this study was based on self-reported scale that was provided by patients targeted by the study. Therefore, there may be some potential reporting bias which may have occurred because of respondents' interpretation of the questions or desire to report their emotions in a certain way or simply because of inaccuracies of the responses.

Due to unavailability of polysomnography which is gold standard in assessment of sleep disturbance pattern we used simple validated clinical tool (PDSS-2).

Limitations of the PDSS tool, like any subjective semi quantitative scale which attempts to provide a holistic and clinical assessment of the complex etiology of sleep problems in Parkinson's disease. It is not validated against a gold standard measurement of sleep architecture such as polysomnography. However, complete validation of the PDSS might not be possible, as several of the 15 items have no gold standards that could be validated polysomnographically.

The other limitation on our study was we were planning to assess RBD using mayo sleep questioner which involve patients bed partner but there was only 15 patient who visited neurology referral clinic with their bed partner. So we couldn't able to determine RBD in our PD patients with mayo sleep questioner, even if PDSS-2 can asses some aspects of RBD.

## **5.4. Conclusion and recommendation**

### **Summary**

The general objective of this study was to determine the prevalence of sleep disturbance and their associated predicting factors in PD patients in Tikur Anbessa Specialized Hospital and Zewditu Memorial Hospital. Quantitative method was employed to answer the stated research questions.

Our study clearly showed that sleep disturbance in PD patients was comparably prevalent with international prevalence of sleep disturbance in PD patients.

This cross-sectional study also shows that more advanced sleep disturbance were associated with patient's age, marital status, employment status, PD symptom duration, historical reportable sleep disturbance and disease severity.

### **Conclusion**

Our study shows that patients with PD experience significantly more problems of sleep disturbance and virtually no sleep domain remains unaffected even if the degree of affection varies. We noticed that clinical symptoms of sleep disturbance were commonly encountered in our PD patients sample study.

The most often complained sleep disorder manifestations in our PD patients were getting up at night to pass urine at least one day per week (seen in 90.6% of PD patients) and unable to turn around in bed in at least one day per week (seen in 67.1% of PD patients); the least complained being waking up early in the morning with painful posturing of limbs (seen in 34.9% of PD patients).

In our study, the main predictors of sleep disturbance symptom in Parkinson's disease were patient's age, marital status, employment status, PD symptom duration, historical reportable sleep disturbance and disease severity.

### **5.6. Recommendations**

Based on the major findings of our study, the followings are recommended:

- ✓ While assessing PD patients, not only motor symptoms but also sleep disturbance symptoms should be assessed thoroughly as they also are prevalent.
- ✓ High index of suspicion should be on aged PD patients, never married and divorced PD patients as they have higher sleep disturbance pattern.
- ✓ To increase clinical awareness, among internal medicine and neurology residents, is important and may prevent under treatment of sleep disturbance Symptoms in our PD patients.
- ✓ Since nocturia and motor symptoms of PD contributed much for sleep disturbance symptoms in our PD patients, the focus of treatment should be on the treatment of those agents.
- ✓ Our study indicates the need for good randomized controlled studies to compare the presence of these symptoms in PD versus age matched non PD population.
- ✓ In general all stakeholders; neurology and internal medicine residents, neurologist, neurology department, Ethiopian PD society and federal ministry of health should contribute their share in addressing and treating sleep disturbance pattern in PD patients.

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# Appendices

## Study questionnaire *(English Version)*

This data collecting format is structured to be filled by the primary investigator and a trained nurse for a purpose of collecting data for the research to be done on Assessment of Sleep disorder pattern based on parkinson's disease sleep scale (PDSS-2) of patients with Parkinson disease attending neurology referral clinic in Tikur Anbessa specialized and Zewditu Memorial Hospitals, Addis Ababa, Ethiopia.

Instruction: Please put "✓" to indicate the answers on the appropriate boxes provided and answer specifically for the open ended questions accordingly.

### Part I. Demographic Data

1. Name of Hospital      a) Tikur Anbessa specialized            b) Zewditu Memorial
2. Code NO. ....
3. Handedness      Right            Left
4. Age (yrs) .....
5. Sex      Female            Male
6. Marital Status:  
a) Never married      b) Married            Living together            e)        
separated/divorced            d) Widowed
7. Duration of PD symptoms (yrs) -----
8. Duration since PD diagnosed (yrs) -----
9. Duration of PD treatment (mo/yrs) -----
10. Employment  
a) Employed            b) Unemployed
11. a) If employed specify the occupation  
a) Professional /technical /managerial            b) Clerical        
c) Sales and services            d) skilled manual        
e) Unskilled manual            f) Agriculture

g) Other  specify-----

b) If unemployed:-

a) Housewife  b) Retired

c) Out of job  d) other  specify-----

12. Religion

a) Orthodox  b) Muslim

c) Catholic  d) Protestant

e) Other  specify.....

13. Ethnicity

a) Oromo  b) Amhra  c) Tigrai

d) Guragie  e) Somali  f) Sidamo

g) Welaita  h) Other  Specify.....

14. Education

a) No formal education  b) Primary

c) Secondary  d) More than secondary

15. a) If no formal education ,then level of literacy

a) Can read and write  b) Can't read and write

16. Medication(s) taken/taking

16.1..... Dose ..... Frequency .....

16.2..... Dose ..... Frequency .....

16.3..... Dose ..... Frequency .....

16.4..... Dose ..... Frequency .....

17. Co-morbid medical condition(s) Yes  No

If yes,

17.1.....

17.2.....

17.3.....

17.4.....

16. Did you have consistent sleep schedule? Yes  No

17. Previous history of sleep disorder

a) Day time sleepness  b) Insomnia

c) Other  Specify.....

Part II: PDSS-2

Please rate the severity of the following based on your experiences: During the past week(7 days). Please make "✓" in the answer box.

Questions	Very often(This means 6 to 7 days a week)	Often(This means 4 to 5 days a week)	Sometimes(This means 2 to 3 days a week)	Occasionally(This means 1 day a week)	Never
1.Overall did you sleep well during the last week?	0 <input type="checkbox"/>	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>
2. Did you have difficulty falling asleep each night?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
3. Did you have difficulty staying asleep?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
4. Did you have restlessness of legs or arms at night or in the evening causing disruption of sleep?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
5. Was your sleep disturbed due to an urge to move your arms or legs?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
6. Did you suffer from distressing dreams at night?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
7. Do you suffer from distressing hallucinations at night (seeing or hearing things that you are told do not exist)?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
8. Do you get up at night to pass urine?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
9. Did you feel uncomfortable at night because you were unable to turn around in bed or move due to immobility?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>

10. Did you feel pain in your arms or legs which wake you from sleep at night?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
11. Did you have painful muscle cramps in your arms or legs which wake you from sleep at night?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
12. Did you wake early in the morning with painful posturing of arms or legs?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
13. On waking did you experience tremor?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
14. Did you feel tired and sleepy after waking in the morning?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
15. Did you weak up at night due to snoring or difficulties with breathing?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>

### Part III: The Epworth Sleepiness Scale

This tool assesses how likely are you to doze off or fall asleep in the following situations. You should rate your chances of dozing off, not just feeling tired.

Rate tendency to become sleepy on a scale of

- No chance of dozing = 0
- Slight chance of dozing = 1
- Moderate chance of dozing = 2
- High chance of dozing = 3

Situation	Chance of Dozing
Sitting and reading	
Watching TV	
Sitting inactive in a public place (e.g., a theater or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in traffic	

Total Score = \_\_\_\_\_

Interpretation:

0-7: It is unlikely that you are abnormally sleepy.

8-9: You have an average amount of daytime sleepiness.

10-15: You may be excessively sleepy depending on the situation. You may want to consider seeking medical attention.

16-24: You are excessively sleepy and should consider seeking medical attention.

## Part IV: Mayo Sleep Questionnaire

Do you live with the patient? Yes  No  (If No, end form here)

Do you sleep in the same room as the patient  Yes  No

If no, is it because of his/her sleep behaviors (i.e. snores too loud, acts out dreams, etc.)?   
Yes  No

Please mark "Yes" if the described event has occurred at least 3 times.

1. Have you ever seen the patient appear to "act out his/her dreams" while sleeping? (Punched or flailed arms in the air, shouted or screamed)

0 No

1 Yes

If Yes,

a. How many months or years has this been going on?

Year(s)

Months

b. Has the patient ever been injured from these behaviors (bruises, cuts, broken bones)?

No

Yes

c. Has a bed partner ever been injured from these behaviors (bruises, blows, pulled hair)?

No

- Yes
- No bed partner

d. Has the patient told you about dreams of being chased, attacked or that involve defending himself/herself?

- No
- Yes
- Never told you about dream

e. If the patient woke up and told you about a dream, did the details of the dream match the movements made while sleeping?

- No
- Yes
- Never told you about dreams

### Part V: Modified Hoehn and Yahr Staging

STAGE 0 = No signs of disease.

STAGE 1 = Unilateral disease.

STAGE 1.5 = Unilateral plus axial involvement.

STAGE 2 = Bilateral disease, without impairment of balance.

STAGE 2.5 = Mild bilateral disease, with recovery on pull test.

STAGE 3 = Mild to moderate bilateral disease; some postural instability; physically independent.

STAGE 4 = Severe disability; still able to walk or stand unassisted.

STAGE 5 = Wheelchair bound or bedridden unless aided.



13. መደበኛ ት/ት ካልተማረ ሀ)  መጻፍ እና ማንበብ የሚችል ለ)  መጻፍ እና ማንበብ የማይችል

14. እየወሰዱት ያለ ወይም የወሰዱት መድሃኒቶች

14.1.....መጠን.....በቀን ስንት ጊዜ.....

14.2 .....መጠን.....በቀን ስንት ጊዜ.....

14.3.....መጠን.....በቀን ስንት ጊዜ.....

14.4 .....መጠን.....በቀን ስንት ጊዜ.....

15. ሌላ የተወቀ በሽታ ዓይነቶች አሉት? አዎ  አይደለም

መልሱ አዎ ከሆነ ይዘርዘርቸው

15.1.....

15.2.....

15.3.....

15.4.....

16. ተመሳሳይ የሆነ የእንቅልፍ ፕሮግራም አለው? አዎ  አይደለም

17. ከዚህ በፊት የታወቀ የእንቅልፍ ችግር

ሀ/ ቀን እንቅልፍ ማብዛት ለ/ የእንቅልፍ እጦት ሐ. ሌሎች ይግለጹ.....

**ክፍል 2 ፤ PDSS (የ ፓርኪንሰን በሽታ የእንቅልፍ ችግሮች መለኪያ)**

የሚከተሉትን ጥያቄዎች ባለፈው አንድ ሳምንት (ሰባት ቀን) የክብደታቸውን መጠን ይግለጹ

መመሪያ፤ " -1 " ይህን ምልክት በተሰጠው ሳጥን ውስጥ ያስፍሩ

ጥያቄዎች	በጣም ሁል ጊዜ (ይህ ማለት በሳምንት 6-7 ጊዜ)	ሁልጊዜ (ይህ ማለት በሳምንት 4-5 ጊዜ)	አንዳንድ (ይህ ማለት በሳምንት 2-3 ጊዜ)	አልፎ አልፎ (አንድ ቀን)	በጭራሽ
1. በአጠቃላይ ባለፈው ሳምንት አጥጋቢ እንቅልፍ ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
2. እያንዳንዱ ለሌት እንቅልፍ እስከይዙት ተቸግረው ነበር?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>

3. ተኝተዉ የመቆየት ችግር (ቶሎ ቶሎ የመንቃት ችግር) ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
4. ማታ ማታ እግሮት እና ከቁጥጥሮት ዉጭ የመንቀስቀስ እንቅልፍ የመንሰት ችግር ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
5. እንቅልፍ የሚነሳ ከመጠን በላይ ያለፈ እጅትንና እግሮትን የማንቀሳቀስ ፍላጎት ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
6. ማታ ማታ በሚያስፈራ ህልም ተስቃይተው ያውቃሉ?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
ማ 7. ማታ ማታ በሚያስፈራ እይታ ወይም ድምፅ ይሰቃያሉ (በእውን የማይታይ ወይም የመይሰማ ነገር መስማት ወይም መመልከት)?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
8. ማታ ማታ ለሽንት ተነስተው ያውቃሉ?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
9. ማታ ማታ ሰውነቱ በመተሳሰር ምክንያት የሚይዘው ስሜቶች መሰማት አልጋላይ መንቀሳቀስ / መገላበጥ / ማቃት ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
10. ከእንቅልፍ የሚቀሰቅሱት የእጅ/የእግር ህመም / ስቃይ ስሜት ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
11. ከእንቅልፍ የሚቀሰቅሱት የእጅ / የእግር ህመም ያለዉ የጡንቻ መቆጥቆጥ ስሜት ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
12. ጧት ጧት እጅት/ እግርዎት ላይ ህመም ያለዉ መጣመም አጋጥሞት ከእንቅልፍ ተነስተው ያውቃሉ?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
13. ከእንቅልፍ ሲነሱ የሰዉነት መንቀጥቀጥ አጋጥሞት ያውቃል?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
14. ጧት ሲነሱ እንቅልፍ እንቅልፍ መለት ወይም ድካም ስሜት ነበረት?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>
15. ከእንቅልፍ የሚቀሰቅስ ማንከራፋት ወይም የመታፈን ስሜት ፍሮት ያውቃል?	4 <input type="checkbox"/>	3 <input type="checkbox"/>	2 <input type="checkbox"/>	1 <input type="checkbox"/>	0 <input type="checkbox"/>

### ክፍል 3 : “The Epworth Sleepiness Scale”

ይህ መጠይቅ እርሶ በሚከተሉት ሁኔታዎች ውስጥ ሆነው እንቅልፍ መምጣቱን የሚያስሰነው መመሪያ፤ ይህን መጠይቅ ሲመልሱ የድካም ስሜት ሳይሆን በእንቅልፍ መያዝን በተመለከተ ብቻ ነው የሚያዩት የሚከተሉትን መስፈሪያ ይጠቀሙ

- ምንም በእንቅልፍ ያለመያዝ **0**
- በትንሹ በእንቅልፍ መያዝ **1**
- በመጠኑ በእንቅልፍ መያዝ **2**
- በከፍተኛ መጠን የእንቅልፍ የመያዝ እድል **3**

ሁኔታ	በእንቅልፍ የመያዝ እድል
ቁጭ ብለው እና እያነበቡ	

ቴሌቪዥን እያዩ	
ህዝብ ባለበት ዝም ብለው ተቀምጠው (ቴያትር ቤት ወይም ስብሰባ)	
ያለምንም እረፍት ለ 1 ሰዓት መኪና ውስጥ እንደተሳፋሪ ሆነው	
ከሰዓት ሁኔታዎች ፈቅደው ጋደም ብለው እያረፉ	
ቁጭ ብለው ሰው እያናገሩ	
አልኮል ሳይጠቀሙ ከምሳ በኋላ ዝም ብለው ቁጭ እያሉ	
መኪና ውስጥ ለትንሽ ደቂቃ በትራፊክ ምክንያት ቆመው	

አጠቃላይ ውጤት = \_\_\_\_\_

**ክፍል 4: የማዮ እንቅልፍ መጠይቅ**

. ከታካሚው ጋር ይኖራሉ? አዎ አይደለም

መልሱ አይደለም ከሆነ የሚከተሉትን መጠይቆች ይለፉአቸው

. ከታካሚው ጋር እንድ ክፍል ይተኛሉ? አዎ አይደለም

መልሱ አይደለም ከሆነ ሲተኙ ታካሚው በሚያሳዩት ባህሪያት (ማንከራፋት ፣መጫህ የመሳሰሉት ነው? አዎ አይደለም

ለሚከተሉት መጠይቆች ድርጊቱ ከሶስትና ከዚያ በላይ ከሆነ አዎ የሚሉትን ይምረጡ

1. ታካሚውን እንቅልፍ ላይ ሆነው እንደእጃቸውን ማወራጨት መጫህ ማቃሰት እና የመሳሰሉትን እይተውባቸው ያውቃሉ?

0 አይደለም

1 አዎ

መልሱ አዎ ከሆነ

ሀ. ይህ ነገር ለስንት ወር ወይም ዓመት ነበር?

ለ. ታካሚው በዚህ ባህሪያቸው/ተግባራቸው (አጥንት መሰበር ፣መቆረጥ ሰውነታቸው የመንቀጥቀጥ ምልክት ማሳየት) እራሳቸውን ጎድተው ያውቃሉ?

 አይደለም አዎ

ሐ. ከታካሚው ጋር አብሮ የሚተኛ ሰው ተጎድቶ (እንደ ሰውነት ላይ የመቀጥቀጥ ፣መመታት፣ፀገር መነጨት የመሳሰሉት) ያውቃል?

 አይደለም አዎ ከታካሚው ጋር አብሮ የሚተኛ የለም (ተካሚ ብቻቸውን ነው የሚተኙት)

መ. ታካሚው ስለህልማቸው (ለምሳሌ መባረር ፣መመታት፣እና እራስን ከመመታት መከላከል) ነግረውት ያውቃሉ?

 አይደለም አዎ ስለህልማቸው ተናግረው አያውቁም

ሠ. ታካሚው ከእንቅልፋቸው ከነቁ በኋላ ስለ ህልማቸው ነግረውት ከሆነ ህልማቸውና በህልማቸው ያደረጉት እንቅስቃሴ አብሮ የሚሄድ ነው?

 አይደለም አዎ ስለ ህልማቸው ተናግረው አያውቁም