

Epidemiologic Disparities and Challenges in Non-parkinsonian Tremor Disorders Research: A Scoping Review Emphasizing the Indian Context

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Abstract

Non-parkinsonian tremors represent a heterogeneous spectrum of movement disorders where knowledge gaps persist regarding epidemiology, pathophysiology, and clinical burden. This scoping review aimed to systematically consolidate literature on these disorders in India across the domains of prevalence, biological mechanisms, psychiatric comorbidity, disability impact, and quality of life. A systematic search was undertaken across databases to identify studies on non-parkinsonian tremors in India. Extracted data were synthesized descriptively under themes spanning reported prevalence estimates and variability, proposed biological processes, psychiatric symptom rates, stigma perceptions, and quality-of-life deficits. Methodological appraisal was undertaken. Twenty-nine studies reported prevalence estimates displaying wide variability from 0.09% to 22% for essential tremor, partly attributable to definitional inconsistencies. Proposed pathologic processes centered on cerebellar dysfunction, neurotransmitter disturbances, and genetic risks. Nine studies revealed variable anxiety (6.8%–90%) and depression (3.4%–60%) rates among essential tremor patients, while two indicated perceived stigma. Five studies unanimously concurred significant quality of life impairment in essential tremors. Evidence of dystonic tremor, functional tremor, and other tremors was limited. This review exposed critical knowledge gaps and methodological limitations, while systematically evaluating the Indian literature on non-parkinsonian tremors concerning epidemiology, mechanisms, and clinical burden. Large-scale collaborative research applying standardized diagnostic criteria is imperative to determine contemporary prevalence statistics and comprehensively characterize the multifaceted disability footprint to inform patient-centric models optimizing diagnosis and holistic care.

Keywords: Epidemiology, essential tremor, non-parkinsonian tremor, pathogenesis, prevalence

INTRODUCTION

Tremor disorders constitute common movement disorders, encompassing a heterogeneous spectrum of conditions including essential tremor (ET) and other entities.^[1] The nomenclature surrounding tremors has been controversial, with variability in the terms applied to describe these hyperkinetic movement disorder subtypes beyond classic Parkinsonian tremors. ET represents the most commonly employed umbrella categorization. However, even the ET terminology encompasses heterogeneous phenotypic manifestations ranging from pure motor tremors to tremors associated with subtle cognitive or psychiatric disturbances or subtle imbalance or posturing of fingers.^[3] Terms such as “dystonic tremor” or “essential tremor plus” intrinsically incorporate assumptions regarding underlying pathogenesis that remain incompletely deciphered. Besides ET, ET plus, and dystonic tremors, other tremor disorders with separate pathogenesis and localization include functional tremor, orthostatic tremor, cerebellar tremor, and neuropathic tremor. The epidemiology and intricate biological basis underpinning even the most prevalent non-parkinsonian tremor disorder, ET, remain incompletely deciphered. Reported prevalence proportions for ET alone display over 10-fold variability globally, underscoring knowledge gaps.^[2] In the specific Indian context, contemporary statistics on occurrence rates and diagnostic

precision are particularly sparse across both ET and other less-common non-parkinsonian tremor disorders. In addition, gaps exist concerning accurately determining occurrence rates by applying consistent contemporary diagnostic criteria and assessment tools. Resultant deficiencies contribute to the wide variability in reported ET prevalence estimates. Therefore, for this review, the use of the broader designation “non-parkinsonian tremor” serves a pragmatic purpose in lumpingly capturing the overarching spectrum encompassing ETs and similar manifestations. This approach aligns with the research priority of first accurately characterizing the epidemiologic, clinical, and biological heterogeneity within the collective group before reliably splitting distinct phenotypes.

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Submitted: 15-Jan-2024 **Revised:** 25-Mar-2024 **Accepted:** 08-Apr-2024
Published: 27-Apr-2024

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DOI: 10.4103/aian.aian_36_24

Besides definitional challenges, gaps persist regarding the meticulous elucidation of the amalgamation of processes extending from neural circuitry disturbances to genetic risks potentially contributing to tremor genesis.^[4-7] Proposed contributory processes implicate cerebellar neurodegeneration and aberrant oscillations,^[4,7] neurotransmitter disturbances,^[7] and certain genetic susceptibility polymorphisms.^[5,6] Recent evidence also suggests a potential autoimmune basis in an ET subset.^[8] Despite research advances, intricate pathologic mechanisms underlying ET and rarer non-parkinsonian tremors remain partially elucidated. This hinders the development of targeted therapies. The advancements in targeted therapies warrant the precise unravelment of these intricacies.

In addition, substantial lacunae remain concerning systematic assessments of the psychiatric comorbidity, disability, stigma, and quality-of-life burdens imposed by these chronic, relatively incurable conditions. The associated humanistic, societal, and economic costs underscore the necessity for consolidated evaluation frameworks.

In summary, non-parkinsonian tremors encompass a heterogeneous spectrum of movement disorders where substantial research gaps persist concerning unraveling epidemiology, pathologic underpinnings, and clinical burden. This scoping review aims to systematically aggregate current insights in the Indian setting across these disorders to spotlight knowledge deficits and inform future research priorities for optimizing patient care.

The key objectives include the following:

1. Elucidating occurrence rates, variability in diagnostic criteria, and distributions across Indian subpopulations;
2. Appraising proposed biological mechanisms linked to non-parkinsonian tremor subtypes;
3. Estimating the psychiatric comorbidity, specifically anxiety and depression; and
4. Evaluating perceived stigma or embarrassment faced by patients and quality-of-life impact.

The primary target population includes Indian patients with non-parkinsonian tremor disorders. We compare the data from India on the outcomes of interest with the global datasets. The outcomes of interest span reported prevalence estimates, proposed pathologic processes, standardized assessments of psychiatric symptoms (anxiety, depression), quality-of-life measures, and stigma perceptions.

METHODS

This scoping review was conducted based on the methodological framework for scoping reviews outlined by Arksey and O'Malley^[9] and followed the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement.^[10]

Search strategy

A systematic search was undertaken across PubMed, Embase, Web of Science, and Cochrane Library databases from inception

to July 2023 to identify studies related to non-parkinsonian tremor disorders in the Indian context. The search syntax combined Medical Subject Headings and keywords representing concepts related to non-parkinsonian tremors (e.g., “essential tremor,” “dystonic tremor”), epidemiologic metrics (e.g., “prevalence,” “incidence”), psychiatric outcomes (e.g., “anxiety disorders,” “depression”), disability and quality-of-life impacts (e.g., “quality of life”) along with a country limitation for India separately to include all studies reported from India. Limits were applied to restrict retrieved records to the English language and studies only about human subjects, and exclude editorials, letters, conference abstracts, and case reports. Supplementary hand searches of reference lists of eligible full-text articles were also conducted. References were collated using Zotero reference management software,^[11] and Rayyan systematic review web application was utilized to track study screening and selection.^[12]

The literature searches across all databases were initially conducted in July 2023. After finishing the preliminary research synthesis, the searches were rerun from August 2023 to December 2023 to capture more recently published studies to be considered for the review until journal submission and relevant new information was added appropriately. The full search strategies for all databases are presented in supplementary document Appendix 1.

Terminology standardization

The broad umbrella term “non-parkinsonian tremors” was applied to collectively encompass ETs and other tremor disorders, excluding parkinsonian tremors. For terminology standardization, the broad umbrella term “non-parkinsonian tremors” was aligned with the 2017 International Parkinsonism and Movement Disorder Society consensus criteria for tremor classification.^[1] The label “essential tremor” was only used where this specific clinical phenotype was examined. These standardizations in terminology were maintained throughout.

Eligibility criteria

Studies were considered eligible for inclusion if they reported original data on prevalence estimates, proposed biological mechanisms, assessed psychiatric comorbidities, or evaluated quality-of-life impacts specifically among patients with non-parkinsonian tremor disorders. Reviews, viewpoints, conference abstracts, case reports, non-English language publications, and studies that focused solely on parkinsonian tremors, treatment efficacy without any prevalence, mechanistic or clinical data were excluded.

Study selection

Initial screening of titles and abstracts against the predefined eligibility criteria was undertaken independently by two reviewers (SD and SU) to identify publications warranting full-text review. Any disagreements regarding study inclusion were resolved by discussion and consensus between the two reviewers.

Data extraction

Relevant data from included studies were extracted by the two independent reviewers using a standardized form capturing

details on study design, population characteristics, diagnostic criteria used for ascertainment of tremor cases, assessment tools or techniques implemented, key metrics reported, such as prevalence estimates, or outcomes evaluated, including proposed biological processes or results of psychiatric and functional burden assessments. Any disagreements during the data extraction process were harmonized via deliberative consensus.

Data synthesis

The evidence gleaned from full-text articles was synthesized descriptively under distinct themes spanning tremor prevalence, diagnostic criteria variability, postulated pathophysiologic mechanisms for specific tremor disorders, prevalence of psychiatric comorbidities, perceived stigma/embarrassment evaluations, and quality-of-life assessments. Summary tables were made to succinctly present key data points on prevalence estimates across studies and proposed tremorgenic biological processes involving genetic risks and neurotransmitter disturbances. Variability associated with diagnostic criteria and resultant impacts on reported occurrence rates were noted. The burden of psychiatric symptoms and quality-of-life deficits in the context of ETs were summarized from studies incorporating standardized instruments.

Quality appraisal

The full text of studies passing preliminary abstract screening was retrieved and examined independently by the two reviewers. Those conforming to eligibility criteria were included in the qualitative synthesis. The methodological quality and potential risk of bias associated with included studies were evaluated by validated tools. The 16-item Appraisal Tool for Cross-Sectional Studies (AXIS) was applied to critically appraise quantitative biases in cross-sectional surveys related to sample selection and size, measurement biases in exposure and outcome evaluation, nonresponse rates, and statistical analysis techniques.^[13] The Newcastle–Ottawa scale was employed to assess the risk of bias in case–control or cohort studies across domains of sample selection, comparability of groups, and adequacy of outcomes, with higher scores indicating a lower risk of bias.^[14]

The study screening and selection process is methodically documented using a Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flowchart [see Figure 1].

RESULTS

The systematic search yielded 1699 records, which were reduced to 1270 after removing duplicates. Screening titles and abstracts excluded 1102 records, leaving 168 articles for full-text review. Finally, 60 studies met the eligibility criteria and were included [see Figure 1].

Findings were categorized under prevalence statistics (29 studies),^[15-23] proposed pathophysiologic mechanisms (15 studies),^[4-7,24-30] assessments of psychiatric comorbidities (nine studies),^[31-40] the stigma associated

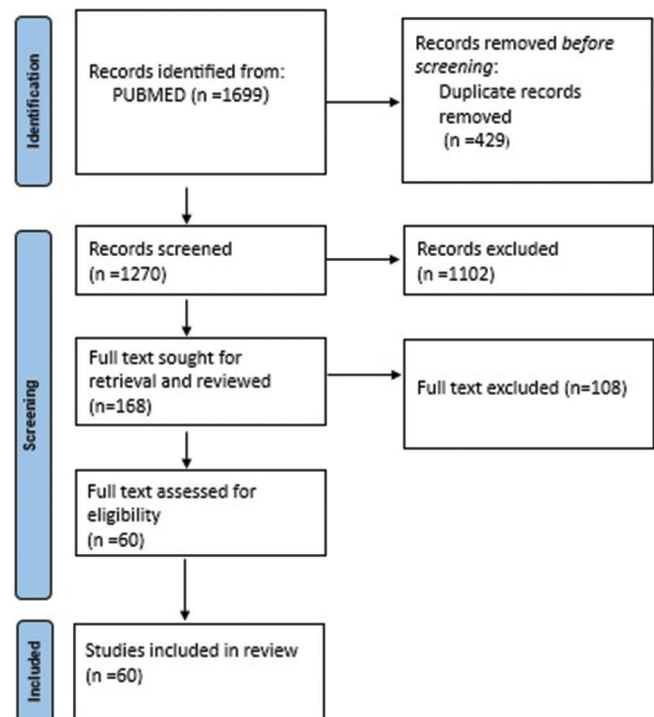


Figure 1: PRISMA flowchart depicting the study screening and selection process

with tremor disorder (two studies),^[41,42] and evaluations of quality-of-life impact (five studies).^[36,43-46]

Prevalence estimates and diagnostic criteria

Of the 29 studies that focused on prevalence, four were Indian population-based studies, three were Indian hospital-based studies, one was an elderly home-based study from India, and 20 were global datasets.^[15-19,20,21,23]

Seven studies utilized formal diagnostic criteria defined by the Movement Disorder Society (MDS) for assigning tremor subtypes.^[17-19,23] While some specifically estimated ET prevalence, others quantified overall tremor rates without distinguishing between ET and other non-parkinsonian tremors.

Reported prevalence proportions displayed wide variability, ranging from 0.09% for ET in an Indian rural population^[17] to 8.8% in a large nursing home elderly population in New York City [Table 1]. Indian data underrepresented less-prevalent non-ET disorders. Studies applying updated MDS criteria for ET classification demonstrated higher prevalence estimates between 1.2% and 5.5% compared to those using nonstandardized case definitions. There are four studies in literature for tremor prevalence in dystonia, and it ranges from 16.78% to 55.39%. One cross-sectional study from India reported that 45.55% of patients with dystonia had tremors. Two studies on functional tremor prevalence reported its prevalence to range from 1.66% to 22.7%. There is a scarcity of studies specifically assessing the prevalence or incidence of other tremor disorders like dystonic tremors, functional tremors,

Table 1: Reported prevalence estimates for ETs and non-parkinsonian tremors^a

Study	Population/sample	Diagnostic criteria	Prevalence	Reference
ET				
Das <i>et al.</i> , 2009	Indian population	Clinical diagnosis	ET: 0.39%	15
Bharucha <i>et al.</i> , 1988	Indian Parsi population	Clinical diagnosis	ET: 46.3 per 1000	16
Chin <i>et al.</i> , 2021	Indian rural population	Clinical diagnosis using MDS 2017 classification	ET: 0.09%	17
Benito-León <i>et al.</i> , 2003	Spanish elderly cohort	Clinical diagnosis	ET: 4.8%	#R13
Okubadejo <i>et al.</i> , 2006	Nigerian population, urban	Clinical diagnosis	ET: 1.2%	#R17
Seijo-Martínez <i>et al.</i> , 2013	Spanish elderly population-based door-to-door survey	Clinical diagnosis	ET: 8.63%	#R18
Eliassen <i>et al.</i> , 2019	Population-based study in Faroe Island	Clinical diagnosis	ET: 2.9%	#R12
Tan, 2005	Population-based study in Singapore	Clinical diagnosis	ET: 0.3%	#R11
Mancini, 2007	Population-based study in Italy	Clinical diagnosis	ET: 0.8%	#R8
Glik, 2008	Population-based study in Israel	Clinical diagnosis	ET: 0.8%	#R7
Sur, 2008	Population-based study in Turkey	Clinical diagnosis	ET: 3.1%	#R9
Dogu, 2003	Population-based study, Turkey	Clinical diagnosis	ET: 4.0%	#R10
Non-parkinsonian tremor (overall tremors)				
Shukla, 2004	Indian hospital-based study	Clinical diagnosis	Overall tremor: 12.74%	19
Prashanth <i>et al.</i> , 2021	Indian hospital-based study	Clinical diagnosis	Overall tremor: 7.7%	18
Muthane, 2006	Indian elderly home-based study	Clinical diagnosis	Overall tremor: 4.5%	23
Tse, 2008	Elderly home-based study in New York City	Clinical diagnosis	Overall tremor: 11.8% ET: 8.8%	#R16
Wenning, 2015	Italian Bruneck study cohort	Clinical diagnosis	Overall tremor: 14.5%	#R15
Fahn and Jankovic, 2009	Hospital clinic based in USA	Clinical diagnosis	Overall tremor: 15.8%	#R14
Chowdhury <i>et al.</i> , 2006	Indian urban hospital-based study	Clinical diagnosis	Overall tremor: 1.08%	20
Das <i>et al.</i> , 2006	Indian population based, urban	Standard questionnaire	Overall tremor: 14.1 per 1000	21
Pandey <i>et al.</i> , 2023	Indian hospital based, urban	Clinical diagnosis, MDS 2017 classification	Did not assess overall tremor prevalence, assessed percentage of different tremor subtypes	47
Tremor prevalence in patients with dystonia				
Pandey <i>et al.</i> , 2017	Hospital-based cross-sectional study in India	Clinical diagnosis plus surface EMG	Tremor prevalence in dystonia: 45.55%	#R1
Gigante <i>et al.</i> , 2016	Cross-sectional hospital-based study in Italy	Clinical diagnosis	Tremor prevalence in dystonia: 34%	#R2
Erro <i>et al.</i> , 2014	Cross-sectional, movement disorder clinic-based study	Clinical diagnosis	Tremor prevalence in dystonia: 55.39%	#R3
Defazio <i>et al.</i> , 2013	Cross-sectional study, movement disorder clinic based in Italy	Clinical diagnosis	Tremor prevalence in dystonia: 16.78%	#R4
Rudzinska and Krawczyk, 2013	Case-control study, Poland	Clinical diagnosis	Tremor prevalence in dystonia: 50%	#R5
Functional tremors (no study from India assessed prevalence)				
Tinazzi <i>et al.</i> , 2021	Retrospective data review of patients attending Italian movement disorder clinic	Clinical diagnosis	Functional tremor: 22.7%	#R20
Factor <i>et al.</i> , 1995	Retrospective data review	Clinical diagnosis	Functional tremor: 50%	#R21

^aAdditional references (#R) are added as a document in online-only supplement appendix, along with detailed search strategies EMG=electromyography, ET=Essential tremor, MDS=Movement Disorder Society

orthostatic tremors, neuropathic tremors, or cerebellar tremors, either in the community or in clinic or hospital. Recently, a registry-based study conducted in a tertiary care hospital's movement disorder clinic in India classified non-parkinsonian tremor disorder based on MDS tremor classification and it showed that dystonic tremor was more common than ET and ET plus disorders.^[47] In this study, among 475 patients

with non-parkinsonian tremors, 158 (33.26%) had dystonic tremors, 64 (13.47%) had ET, 68 (14.31%) had ET plus, and 124 (26.1%) had secondary (acquired) causes. A retrospective analysis of 335 ET patients in Thailand revealed that using the new MDS criteria resulted in 104 cases of ET plus, compared to 117 with the traditional ET diagnosis; the remaining cases were classified as indeterminate tremor or isolated focal

tremor.^[40] ET plus was linked to late-onset tremors and higher rates of anxiety (6.7%) and depression (10.6%), with poorer treatment responses compared to traditional ET (anxiety: 6.8%, depression: 3.4%). Similarly, a Chinese study reclassified 280 ET syndrome cases, identifying 117 as ET plus, 121 as traditional ET, and the rest as indeterminate tremors or isolated focal tremors. The updated diagnostic algorithms revealed higher psychiatric and cognitive comorbidities in the ET plus group.^[38]

Pathophysiologic mechanisms

Proposed mechanisms centered on cerebellar hyperactivation,^[4,24] neurotransmitter disturbances, and mutations affecting cerebellar neurodegeneration in ET risk genes^[4-7] [Table 2]. These implicate aberrant cerebello-thalamo-cortical circuit dysfunction, neurotransmission abnormalities, and genetic variabilities in likely ET pathogenesis. Evidence on rarer disorders was limited, but suggested cerebellar^[25,26] and basal ganglia involvement in dystonic tremor while proposing a central generator for orthostatic tremor.^[27] A summary of other proposed non-parkinsonian tremor disorders is presented in the table.

Psychiatric comorbidity

Nine studies examined psychiatric comorbidity in ET, revealing variable anxiety (6.8%–90%) and depression (3.4%–60%) rates [Table 3]. Both motor severity and disability displayed positive correlations. Population-based studies tended toward lower comorbidities relative to clinic-based data. In addition, two studies showed that

ET plus has higher prevalence of anxiety and depression compared to ET. Evidence regarding non-ET tremors was scarce^[32-40] [see Table 3].

Stigma in tremor disorders (*n* = 2)

Evidence on stigma exclusively among patients with ET or other non-parkinsonian tremor disorders was scarce. One study indicated that psychosocial factors like social anxiety and negative self-concepts may contribute to greater perceived disability compared to actual motor impairment in ET.^[41] Assessments of stigma dimensions revealed that ET patients frequently conceal their diagnosis and feel uncomfortable in social situations due to their tremors.^[42] However, no studies have comprehensively evaluated various dimensions of stigma and associated determinants, specifically among Indian patients with tremor disorders.

Quality-of-life impact

Five studies unanimously reported pervasive quality-of-life deficits across domains among ET patients [Table 4].^[32,36,43-46] Greater tremor severity and psychiatric symptoms are strongly associated with poorer quality of life. No assessments of the quality of life in non-ET tremors existed.

Methodological quality appraisal

The methodological quality and potential risk of bias were appraised using validated tools for cross-sectional surveys (AXIS) and case-control or cohort studies (Newcastle-Ottawa scale).^[13,14] Identified limitations encompassed unclear sampling methods, participation bias, limited generalizability to the source population, and inconsistent diagnostic criteria, which precluded drawing causal inferences and warranted caution in interpreting reported prevalence estimates or comorbidity rates [see Table 5].

Table 2: Proposed pathologic mechanisms for ET and other non-parkinsonian tremors^a

Tremor type	Proposed pathophysiologic mechanism
ET	<ol style="list-style-type: none"> 1. Cerebellar dysfunction- Functional neuroimaging shows cerebellar hypermetabolism and activation in ET patients^[4,24,26] 2. Neurotransmission abnormalities- Reduced GABA, altered glutamatergic levels^[5] 3. Genetic factors- mutation in <i>LINGO1</i>, <i>SLC1A2</i>, and other genes linked to Purkinje cell survival, which increase ET risk^[6]
Dystonic tremor	<ol style="list-style-type: none"> 1. Cerebellar decoupling hypothesis^[25] 2. Basal ganglia oscillation hypothesis (#R23)
Orthostatic tremor	<ol style="list-style-type: none"> 1. Central generator in the cerebellum and the brainstem 2. Abnormal connectivity in the frontoparietal network and the executive network^[27]
Functional tremor	Still unclear, but the proposed mechanism is involvement of the limbic system (amygdala) ^[28]
Cerebellar tremor	Lesion in Guillain Mollaret triangle ^[29]
Holmes tremor	Involvement of multiple circuits such as red nucleus, globus pallidus interna, thalamus, cerebellum, and pontomedullary junction ^[7]
Neuropathic tremor	Damage to peripheral nerves, disrupting normal sensory feedback and motor control ^[30]

^aAdditional references (#R) are added as a document in online-only supplement appendix, along with detailed search strategies. ET=Essential tremor, GABA=Gamma-aminobutyric acid

DISCUSSION

In this scoping review, we systematically consolidated and synthesized literature that focused on non-parkinsonian tremor disorders in the Indian context. The study addressed objectives spanning four core domains – elucidating prevalence statistics, proposed biological underpinnings, psychiatric comorbidity burden, and assessments of disability impact.

The review revealed substantial heterogeneity in reported Indian prevalence estimates for ET, ranging from 0.09% to 22% across studies.^[17] Relative to global data, Indian statistics tended to demonstrate overall lower ET rates, except in isolated communities. Besides definitional variability in earlier studies, the predominant reliance on older assessment frameworks rather than current consensus diagnostic recommendations likely contributed to the wide variability in apparent prevalence rates. The notable divergence in reported prevalence rates underscores the need for contemporary epidemiologic studies employing consistent, standardized diagnostic criteria to ascertain precise prevalence. As evidenced by recent Asian studies, the application of revised tremor classification systems reveals a greater prevalence of ET plus relative to conventionally defined ET

Table 3: Reported rates of psychiatric comorbidities among patients with ET

Study	Population/sample	Assessment method	Anxiety	Depression	Reference number
Lorenz <i>et al.</i>	German tertiary hospital	SF36, EPQ-R, MCS	63%	60%	32
Chandran and Pal	Indian tertiary hospital	Multiple scales	62%	60%	33
Dai <i>et al.</i>	USA	NA	27.73%	25.61%	34
Sengul <i>et al.</i>	Turkey	BAI, BDI	71.1%	35.5%	35
Louis <i>et al.</i>	USA	CSED	-	48.5%	36
Huang <i>et al.</i>	China	HDRS, HARS	63.3%	54.3%	37
Acar and Acar <i>et al.</i>	Turkey	HARS	90%	-	39
Lolekha <i>et al.</i>	Thailand	Not specified	6.8%	3.4%	40
ET plus					
Lolekha <i>et al.</i>	Thailand	Not specified	6.7%	10.6%	40
Haug <i>et al.</i>	Chinese	HARS, HDRS	70.9%	66.7%	38

BAI=Beck Anxiety Inventory scale, BDI=Beck Depression Inventory scale, CSED=Center for Epidemiological Studies Depression scale, EPQ-R=Eysenck Personality Questionnaire, ET=essential tremor, HARS=Hamilton Anxiety Rating Scale, HDRS=Hamilton Depression Rating Scale, MCS=mental component score, SF36=short form 36-item health survey

Table 4: Studies assessing the impact on quality of life in ET

Author	Year	Scale/instrument used	Key finding on QOL	Reference number
Troster <i>et al.</i>	2002	QUSET, Beck Anxiety Inventory, Beck Depression Inventory	Impaired self-esteem, lower life satisfaction	43
Lorenz <i>et al.</i>	2006	SF36, EPQ-R, MCS	Reduced physical/mental QOL	32
Chandran and Pal	2012	QEUST	Anxiety/depression associated with worse QOL	44
Louis <i>et al.</i>	2015	QUEST	Severe tremor related to social isolation	45
Louis <i>et al.</i>	2012	QUEST	Depressive symptoms associated with worse QOL	36
Peng <i>et al.</i>	2020	QUEST	ET with head tremor had poor QOL	46

EPQ-R=Eysenck Personality Questionnaire, ET=essential tremor, MCS=mental component score, QOL=quality of life, QUEST=quality of life in essential tremor patient questionnaire, SF36=short form 36-item health survey

cases.^[48,49] The ET plus subtype demonstrates distinct features of later-onset, exaggerated upper limb tremors, heightened psychiatric burdens, and poorer therapeutic responses that warrant dedicated focus, given their disproportionate disability footprint. A similar finding was observed in a study which demonstrated that nearly half of ET patients were reclassified into the ET plus category following adherence to the new consensus MDS tremor classification.^[49] An additional study showed that questionable dystonia was the most common soft sign in 45 ET plus patients.^[3] However, these studies were cross-sectional studies, not reporting the prevalence of different tremor disorders in the clinic. In this context, adhering to the recent standardized consensus classification system, the 2017 International Parkinsonism and Movement Disorder Society diagnostic criteria are pivotal for future epidemiologic studies to rectify this knowledge gap.^[1] For instance, the Italian Tremor Network demonstrated that recalibrating ET diagnoses using the updated MDS criteria revealed a notably higher prevalence of “essential tremor plus” motor and nonmotor subtypes compared to traditional ET classifications.^[48] The integration of such contemporary diagnostic frameworks will enable more accurate ascertainment and subclassification of cases in future prevalence statistics and clinical characterizations.

Proposed pathologic processes centered around cerebellar neurodegeneration and aberrant connectivity changes.^[4]

Advances have also been made in deciphering the roles of neurotransmitter disturbances^[5] and susceptibility genetic polymorphisms.^[6] However, sizable gaps persist concerning accurately characterizing the intricate tremorogenic mechanisms extending beyond glutamatergic and GABAergic signaling, unraveling complex inheritance patterns, and translating insights into targeted interventions.^[4-7] Elucidating the interplay between cerebellar hyperactivation and diverse neurotransmitter pathways coupled with an in-depth exploration of the genetic landscape emerges as a promising target for guiding discovery endeavors focused on precision therapies.^[4-7] Therapies modulating glutamatergic signaling may offer hope, but warrant further investigation and validation.

The review revealed a lack of studies on perceived stigma, embarrassment, and the resulting social isolation burden imposed by these chronic disorders within the cultural milieu of India. The limited evidence gleaned indicates that psychosocial factors like social anxiety and negative self-concepts may promote greater perceived disability in ET patients. A dedicated scale, the ET stigma scale, has been recently proposed to study stigma in patients with tremor disorders.^[50] Assessing the impact of these issues is pivotal to informing patient advocacy and policy efforts supporting individuals living with these chronic movement disorders.

Table 5: Methodological quality assessment of included studies using AXIS and NOS

Author	Year of study	Design	Quality tool	Quality score	Remarks
Louis <i>et al.</i>	2013	Cross-sectional survey	AXIS	Moderate	Unclear sampling method
Dogu <i>et al.</i>	2003	Cross-sectional survey	AXIS	Moderate	Unclear sampling method
Chandran and Pal	2012	Cross-sectional analysis	AXIS	Moderate	Convenient sampling Information of nonrespondents not available
Huang <i>et al.</i>	2019	Cross-sectional analysis	AXIS	Moderate	Limitation not described
Peng <i>et al.</i>	2020	Case-control	NOS	5/9	Inadequate definition of control
Sengul <i>et al.</i>	2014	Case-control	NOS	7/9	The nonresponse rate is not described and the hospital control not detailed
Acar and Acar <i>et al.</i>	2019	Case-control	NOS	4/9	Inadequate definition of control
Dai <i>et al.</i>	2022	Retrospective cohort	NOS	6/9	No comparison group
Lorenz <i>et al.</i>	2006	Case-control	NOS	4/9	Inadequate definition of controls
Louis <i>et al.</i>	2015	Cross-sectional survey	AXIS	Moderate	Sampling methods unclear
Benito-Leon <i>et al.</i>	2013	Cross-sectional survey	AXIS	Moderate	Sampling methods unclear
Das <i>et al.</i>	2009	Cross-sectional survey	AXIS	Moderate	Independent criteria used
Bharucha <i>et al.</i>	1988	Cross-sectional survey	AXIS	Moderate	Independent criteria used; limitation of study not properly defined
Chin <i>et al.</i>	2019	Cross-sectional survey	AXIS	Moderate	Limitation of study not discussed
Okubadejo <i>et al.</i>	2006	Cross-sectional survey	AXIS	Moderate	Nonresponder not described
Seijo-Martínez <i>et al.</i>	2013	Cross-sectional survey	AXIS	Moderate	Participation bias
Eliassen <i>et al.</i>	2019	Cross-sectional survey	AXIS	Moderate	Unclear sampling method, participation bias
Fahn and Jankovic	2009	Cross sectional	AXIS	Moderate	Duration of study not determined
TSE	2008	Cross-sectional survey	AXIS	Moderate	Unclear sampling method
Wenning	2005	Prospective	NOS	6/9	No comparison group
Shukla	2004	Prospective cross sectional	AXIS	Moderate	Limitation of study not discussed
Prashanth <i>et al.</i>	2021	Retrospective cross-sectional	AXIS	Moderate	Nonresponders not described and limitations are not discussed appropriately
Regragui <i>et al.</i>	2014	Cross sectional	AXIS	Moderate	Unclear sampling method
Dogu <i>et al.</i>	2003	Cross sectional	AXIS	Moderate	Nonresponder not described
Tan <i>et al.</i>	2005	Cross sectional	AXIS	Moderate	Nonresponder not described
Glik <i>et al.</i>	2009	Cross sectional	AXIS	Moderate	Limitation of study not discussed
Pandey <i>et al.</i>	2017	Cross sectional	AXIS	Moderate	Nonresponder not described
Gigante <i>et al.</i>	2016	Cross sectional	AXIS	Moderate	Selection bias and nonresponders not described
Erro <i>et al.</i>	2014	Cross sectional	AXIS	Moderate	Nonresponder not described
Defazio <i>et al.</i>	2013	Cross sectional	AXIS	Moderate	Selection bias and nonresponders not described
Pandey and Koul	2017	Cross sectional	AXIS	Moderate	Limitation not described
Pandey <i>et al.</i>	2023	Registry	AXIS	Moderate	Referral bias, multiple raters, without assessment of inter-rater agreement

AXIS=Appraisal Tool for Cross-Sectional Studies, NOS=Newcastle-Ottawa scale

Regarding the psychiatric burden, variable anxiety and depression rates were reported among ET patients.^[31-40] Both motor severity and disability displayed positive correlations. Nonetheless, substantial gaps exist concerning standardized assessments and population-representative contemporary data from India. Available studies unanimously concur on the adverse impact of ET on quality of life spanning physical, social, emotional, and functional spheres. Disease severity and psychiatric comorbidity are consistently associated with profound deficits. However, significant gaps were evident in contemporary data from the broader Indian setting capturing patient-centered perspectives.

RESEARCH AND PRACTICE IMPLICATIONS

The review spotlights imperative next steps encompassing large-scale collaborative studies underpinned by updated diagnostic criteria to address the exposed deficiencies in

contemporary prevalence statistics. Furthermore, systematically evaluating disability burden through consolidated frameworks emerges as pivotal to accurately characterize the psychiatric, stigma, quality-of-life, and economic impacts imposed by these disorders. Similarly, routine screening for comorbidities and multidisciplinary management spanning pharmacologic, psychosocial, and rehabilitation approaches in line with national or global collaborative efforts can pave the way for integrated models of care. The resultant insights can pave the way for optimized diagnostic algorithms, personalized interventions, and elevated models of holistic care, while also informing patient advocacy efforts and health policies supporting individuals living with tremor disorders.

Limitations

This scoping review has certain limitations worth acknowledging. The exclusion of non-English language

publications may have contributed to language bias. The predominant focus on ET within the broader realm of non-parkinsonian tremors constrained perspectives on other tremor disorders. The variable methodological quality of included observational studies posed challenges for evidence interpretation. The cross-sectional or retrospective nature of studies also precluded causal inferences. The lack of experimental research on proposed biological mechanisms limited mechanistic insights into observational associations. However, these limitations underscore the need to address the exposed gaps through methodologically robust frameworks.

CONCLUSIONS

In summary, while exposing critical knowledge gaps, this scoping review offers systematic perspectives into non-parkinsonian tremor disorders, encompassing the Indian context, across the domains of epidemiology, biological underpinnings, and clinical burden.

The key implications spotlighted by this review are as follows:

1. The need for large-scale collaborative studies underpinned by standardized diagnostic criteria to accurately determine contemporary prevalence statistics through methodologically robust frameworks
2. Consolidated assessments through validated frameworks are imperative to systematically characterize the multifactorial clinical burden spanning motor, psychiatric, and psychosocial spheres imposed by these chronic disorders in the cultural context of Indian patients and they emerge as a pivotal research priority.

The resultant insights may pave the way for optimized diagnostic paradigms, precisely targeted interventions, and elevated models of holistic care against the uniquely Indian backdrop.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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APPENDIX 1: SEARCH STRATEGIES

Comprehensive literature searches were conducted in July 2023 and updated from August 2023 to December 2023 across the following databases: PubMed, Embase, Web of Science and Cochrane Library. No date or language restrictions were applied. The search strategies utilized a combination of Medical Subject Headings (MeSH) and keywords representing the broad concepts of:

1. Non-parkinsonian tremor disorders
2. Epidemiological metrics
3. India

The search syntax combined terms denoting tremor categorizations beyond Parkinsonian tremors encompassing phenomenological descriptors or putative anatomical localizations. This was coupled with various epidemiological metrics and indicators along with terms related to India.

In PubMed and Embase, search builders and filters were applied to restrict records to English language, and human studies and exclude editorials, letters, conference abstracts and case reports. In other databases, field tags and string-based restrictions served the same purpose.

The PubMed search strategy utilized:

("Essential Tremor"[Mesh]) OR (Essential[title/abstract] OR Idiopathic[title/abstract] OR Benign[title/abstract]) AND Tremor*[title/abstract] OR ("Tremor/classification"[Mesh]) OR ("Tremor/diagnosis"[Mesh]) OR ("Tremor/epidemiology"[Mesh]) OR (Non-parkinsonian[title/abstract] OR Dystonic[title/abstract] OR Postural[title/abstract] OR Task-specific[title/abstract] OR Primary writing[title/abstract] OR Cerebellar[title/abstract] OR Functional[title/abstract] OR Orthostatic[title/abstract] AND (Tremor*[title/abstract]) AND ("Prevalence"[Mesh]) OR "Incidence"[Mesh] OR (Epidemiology*[title/abstract] OR Occurrence*[title/abstract] OR Prevalence*[title/abstract]) AND (("India"[Mesh]) OR (India*[title/abstract]))

The Embase search strategy used:

('essential tremor'/exp OR (((essential OR idiopathic OR benign) NEXT/1 tremor):ti, ab) OR 'tremor'/exp OR 'tremor classification'/exp OR 'tremor diagnosis'/exp OR 'tremor epidemiology'/exp OR (((non NEXT/1 parkinsonian) OR dystonic OR postural OR task NEXT/1 specific OR 'primary writing' OR cerebellar OR orthostatic) NEXT/1 tremor):ti, ab) AND ('prevalence'/exp OR 'incidence'/exp OR epidemiology*:ti,ab OR occurrence*:ti,ab OR prevalence*:ti,ab) AND (india/exp OR india*:ti, ab)

The Web of Science strategy utilized:

TS=(((("Essential Tremor") OR ((Essential OR Idiopathic OR Benign) NEAR/1 Tremor*)) OR ((Non-parkinsonian OR Dystonic OR Postural OR "Task-specific" OR "Primary writing" OR Cerebellar OR Orthostatic) NEAR/1 Tremor*)) AND TS=(Prevalence* OR Incidence OR Occurrence* OR Epidemiology*) AND TS=(India*)

The Cochrane Library search used:

("Essential Tremor") OR (Essential OR Idiopathic OR Benign) OR (Non-parkinsonian OR Dystonic OR Postural OR "Task-specific" OR "Primary writing" OR Cerebellar OR Orthostatic) NEAR/1 Tremor):ti, ab AND ((Prevalence* OR Incidence OR Occurrence* OR Epidemiology*):ti,ab AND ((India*)):ti, ab

These databases were also searched for specific types of studies using the following associated search terms with tremors: "Psychiatric co-morbidities", "Anxiety", "Depression", "Quality of life" and "Hospital-based/ clinic-based studies" to get relevant studies assessing these aspects.

The literature searches across all databases were initially executed in July 2023. After finishing the preliminary research synthesis, the searches were re-run from August 2023 to December 2023 to capture more recently published studies to be considered for the review up until journal submission. The information derived from the few newer studies was added appropriately at relevant places in the manuscript.

Additional References used in the manuscript: [as the AIAN journal format only allows 50 references]: [cited as #R1-#R23 in tables]

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