

Wolf–Hirschhorn Syndrome: A Comprehensive Review of Clinical Features, Developmental Outcomes, Functional Abilities and Family Caregiving Challenges in Indian Families

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Abstract - Wolf–Hirschhorn syndrome (WHS) is a rare chromosomal disorder caused predominantly by deletion of the distal short arm of chromosome 4, particularly the 4p16.3 region. The syndrome is characterized by a recognizable craniofacial phenotype, prenatal and postnatal growth restriction, developmental delay or intellectual disability, hypotonia, epilepsy and a variable spectrum of congenital abnormalities. The clinical presentation is highly heterogeneous and is influenced, among other factors, by the size and genomic content of the deletion and by additional chromosomal abnormalities. Although advances in cytogenetic and molecular diagnostic techniques have improved recognition of WHS, affected children and their families frequently require lifelong multidisciplinary medical, developmental and social support.

This review summarizes published evidence concerning the genetic basis, clinical manifestations, neurodevelopmental outcomes, communication, motor development, functional abilities, associated medical conditions and long-term care requirements of individuals with WHS. Particular attention is given to the available evidence concerning Indian patients and families. Published Indian reports include individual cases, a four-patient case series and a large Indian pedigree with a complex chromosome 4p/3p rearrangement. These reports demonstrate the phenotypic and genetic heterogeneity of WHS in the Indian population, while also illustrating the importance of molecular cytogenetic investigation and parental chromosomal assessment.

The review further considers family caregiving challenges, including dependence in activities of daily living, communication difficulties, recurrent medical needs, rehabilitation requirements, educational limitations, psychosocial burden and the need for continuing family support. International caregiver studies indicate substantial effects on family quality of life, emotional well-being, time availability and social support. However, WHS-specific caregiver research from India remains very limited. Therefore, conclusions concerning Indian families should be interpreted

cautiously and should not be generalized beyond the available evidence. Future Indian research should systematically investigate developmental trajectories, functional independence, caregiver burden, access to rehabilitation, socioeconomic consequences and long-term outcomes using multicentre and family-centred approaches.

Keywords: Wolf-Hirschhorn syndrome; 4p deletion; chromosome 4; developmental delay; intellectual disability; epilepsy; motor development; communication; functional ability; caregivers; family quality of life; India; rare disease.

1. INTRODUCTION

Wolf–Hirschhorn syndrome (WHS), also known as 4p deletion syndrome, is a rare chromosomal disorder resulting primarily from deletion of genetic material from the short arm of chromosome 4. It is recognized as a contiguous gene deletion syndrome with considerable variation in clinical severity. The syndrome was originally described in the early 1960s and subsequently became recognized by its characteristic combination of craniofacial appearance, growth deficiency, developmental impairment, hypotonia, seizures and multiple congenital anomalies.

The estimated frequency has traditionally been reported in the range of approximately 1 in 20,000–50,000 births, although the true prevalence may be difficult to determine because mild or atypical cases can remain undiagnosed. A female predominance has also been described in published cohorts.

WHS is clinically important not only because of its genetic and medical manifestations but also because of its profound effects on development and family life. Children may experience severe limitations in motor development, communication, feeding, learning and independence. Some individuals acquire walking with or without assistance, whereas others remain dependent for mobility and personal care. Communication abilities

range from limited verbal language to predominantly non-verbal communication.

Sequences extend beyond the affected individual. Parents and other family members may provide continuous assistance with feeding, mobility, medication, hygiene, communication and medical appointments.

For Indian families, these challenges may occur within a healthcare and rehabilitation environment characterized by unequal access to specialist genetic diagnosis, rehabilitation, speech and communication services and long-term disability support. However, WHS-specific family research from India remains scarce. Consequently, the purpose of this review is not to claim that the experiences of a small number of Indian families represent all Indian families, but rather to bring together the available evidence and identify important gaps for future research.

2. Body of Paper

Genetic Basis of Wolf–Hirschhorn Syndrome

WHS results from deletion of genetic material from the distal portion of chromosome 4p, with the critical region located at 4p16.3. The syndrome is therefore commonly referred to as 4p deletion syndrome.

The extent of the deletion varies substantially between individuals. Some deletions are large and readily detectable by conventional cytogenetic methods, whereas smaller deletions may require molecular cytogenetic techniques. The clinical phenotype can also vary according to deletion size and the specific genomic regions involved.

The Wolf–Hirschhorn syndrome critical region contains several genes implicated in the phenotype. Studies of genotype–phenotype relationships have suggested contributions from genes including WHSC1 and LETM1, although deletion of these genes alone does not explain the complete WHS phenotype. Research indicates that loss of additional genomic material is important for expression of characteristic features such as seizures and the typical craniofacial phenotype.

Consequently, WHS should not be considered a disorder caused by a single gene mutation. Rather, it is a genomic disorder involving loss of a chromosomal segment containing multiple genes.

Types of chromosomal abnormalities

The most common mechanism is a terminal deletion of 4p. However, other chromosomal mechanisms can occur, including:

- terminal deletions
- interstitial deletions
- ring chromosome 4

- unbalanced translocations
- complex chromosomal rearrangements
- deletions associated with additional chromosomal gains or losses.

The presence of an unbalanced translocation has important implications for genetic counselling because one of the parents may carry a balanced rearrangement without obvious clinical manifestations.

Diagnosis

Diagnosis is based on recognition of the characteristic phenotype combined with cytogenetic or molecular confirmation. Traditional karyotyping can identify relatively large deletions. However, smaller deletions may be missed using conventional cytogenetics. In an Indian case series of four children, one patient was diagnosed by karyotyping whereas three were diagnosed using multiplex ligation-dependent probe amplification (MLPA). The authors emphasized the importance of molecular cytogenetic testing and recommended parental karyotyping in children diagnosed with WHS.

Potential diagnostic approaches include:

1. Conventional karyotyping
2. Fluorescence in situ hybridization (FISH)
3. MLPA
4. Chromosomal microarray
5. Array comparative genomic hybridization
6. Other genomic technologies when clinically indicated.

The choice of testing depends on clinical presentation, available facilities and the suspected chromosomal abnormality.

Major Clinical Features

WHS has a broad clinical spectrum. Nevertheless, several manifestations occur sufficiently frequently to constitute the characteristic clinical profile.

Craniofacial characteristics

The classical facial appearance has historically been described as resembling a "Greek warrior helmet."

Characteristic findings may include:

- high forehead
- prominent glabella
- hypertelorism
- broad or prominent nasal bridge
- large or protruding eyes
- epicanthal folds
- short philtrum
- downturned corners of the mouth
- micrognathia
- distinctive facial proportions

The facial phenotype can become less pronounced with age and may be influenced by deletion size.

The facial appearance is useful diagnostically but should not be considered sufficient for diagnosis because atypical presentations occur.

Growth Restriction and Nutritional Problems

Growth impairment is one of the major features of WHS.

Prenatal growth restriction may be followed by:

- low birth weight
- short stature
- poor weight gain
- feeding difficulties
- failure to thrive
- reduced muscle mass
- nutritional deficiencies

An analysis of 87 individuals reported prenatal growth deficiency in approximately 80% of patients, together with short stature and slow weight gain.

Feeding problems may result from a combination of hypotonia, oral-motor dysfunction, swallowing difficulties and structural abnormalities.

Long-term nutritional management can therefore become an important component of family caregiving.

Neurological Manifestations and Epilepsy

Epilepsy is one of the most significant neurological manifestations of WHS.

A review of clinical and epilepsy characteristics reported that seizures occur in more than 90% of affected individuals in the literature reviewed, with onset frequently during the first three years of life and a peak during infancy. Generalized tonic-clonic seizures are commonly described, although several seizure types may occur.

More recent cohort evidence continues to demonstrate a high epilepsy burden. A 2025 study involving 140 individuals from Spain and Latin America reported epilepsy in 92% of participants and found that more severe epilepsy was associated with larger deletions and poorer developmental outcomes.

Seizure management can create considerable demands for families because caregivers may need to:

- recognize seizure activity
- administer antiseizure medication
- attend repeated neurological consultations
- monitor medication effects
- respond to emergency episodes
- manage seizure-related restrictions and safety concerns.

The early age of seizure onset means that epilepsy may affect family life from infancy.

Developmental and Intellectual Outcomes

Global developmental delay is a central feature of WHS.

The degree of developmental impairment varies, but delays may involve:

- gross motor development
- fine motor development
- cognition
- adaptive functioning
- communication
- social development
- self-care

In the large natural-history cohort of 87 patients, global developmental delay of varying severity was reported in all patients. Importantly, developmental progress does not necessarily stop completely. Longitudinal studies have documented gradual developmental gains over time, although many individuals continue to have substantial functional limitations.

This distinction is important for counselling families. Severe developmental disability should not automatically be interpreted as complete absence of developmental potential.

Motor Development and Mobility

Hypotonia is extremely common in WHS and contributes to delayed motor development.

Motor milestones such as:

- head control
- rolling
- sitting
- crawling
- standing
- walking

may occur considerably later than expected.

The natural-history study of 87 individuals found that almost half were able to walk independently or with support. Another study involving 27 families found that approximately one-third of affected individuals could walk independently, illustrating the variability of functional outcomes.

Therefore, walking ability should not be predicted solely from diagnosis. Individual assessment and longitudinal observation are essential.

Some individuals may require:

- physiotherapy
- orthoses
- walking aids
- supported standing
- wheelchair mobility
- full assistance with transfers

Speech, Language and Communication

Communication impairment is one of the most significant long-term challenges associated with WHS.

Many individuals develop very limited speech or remain non-verbal. Receptive language may exceed expressive language, allowing some individuals to understand simple instructions despite limited ability to communicate verbally.

A study examining communicative and functional abilities in 11 individuals with WHS found substantial impairment across communication, cognition, feeding and personal autonomy, with considerable variation between individuals.

However, communication outcomes are not uniformly severe. Earlier case evidence demonstrated that an individual with a relatively small deletion developed considerable speech and language abilities. This supports the importance of considering genotype–phenotype variability.

A 2025 report examining clinical features, behaviour and language in a female with WHS across childhood and adolescence again emphasized substantial language and behavioural impairment despite long-term intervention.

Communication interventions

Interventions may include:

- speech and language therapy
- picture communication
- gestures
- communication boards
- object-based communication
- augmentative and alternative communication (AAC)
- eye-gaze systems
- caregiver-mediated communication strategies

For a non-verbal individual, the objective should not simply be speech production. Functional communication and the ability to express needs, discomfort, preferences and emotions are equally important.

Feeding and Swallowing Difficulties

Feeding problems are common in individuals with severe developmental impairment.

Potential difficulties include:

- poor sucking
- prolonged feeding
- chewing difficulties
- dysphagia
- aspiration risk
- oral-motor dysfunction
- food selectivity
- inadequate caloric intake

Feeding difficulties can substantially increase caregiver workload because meals may require extended periods and close supervision.

Individuals with severe feeding impairment may require evaluation by:

- paediatricians
- speech and swallowing specialists
- dietitians
- occupational therapists
- gastroenterology specialists

Congenital and Associated Medical Abnormalities

WHS is a multisystem disorder.

Reported associated abnormalities include:

Cardiovascular

- congenital heart defects
- septal defects
- pulmonary stenosis and other structural abnormalities

Neurological

- seizures
- abnormal EEG
- structural brain abnormalities
- hypotonia
- developmental disability

Skeletal

- skeletal anomalies
- foot abnormalities
- scoliosis or other musculoskeletal problems.

Hearing and vision

- hearing impairment
- ocular abnormalities
- refractive problems
- structural eye abnormalities.

Dental and oral

- abnormal tooth development
- missing teeth
- cleft lip/palate in some individuals
- feeding-related oral-motor difficulties

Genitourinary

Renal and genital abnormalities have also been described, particularly in individuals with larger or more complex chromosomal abnormalities.

The large natural-history study reported skeletal anomalies in approximately 60%, heart lesions in approximately 50%, abnormal tooth development in approximately 50%, hearing loss in approximately 40% and structural CNS abnormalities in approximately 80% of its cohort.

These figures originate from a historical cohort and should not automatically be interpreted as prevalence estimates for contemporary Indian populations.

Behavioural and Social Characteristics

Behavioural development in WHS is complex.

Some individuals may exhibit:

- repetitive behaviours
- stereotypes
- social communication difficulties
- behavioural rigidity
- sensory sensitivities
- features resembling autism spectrum disorder

However, behavioural manifestations vary considerably between individuals.

A 2025 case report documented autism-spectrum features during childhood together with substantial language and behavioural impairment.

Because communication limitations can sometimes appear as behavioural problems, assessment should consider whether the individual has an adequate method for expressing pain, hunger, discomfort, fear or preferences.

Functional Abilities and Activities of Daily Living

Functional ability is one of the most important aspects of long-term WHS outcomes.

Important areas include:

Functional domain Possible WHS-related difficulty
Mobility Delayed or absent independent walking
Transfers Need for caregiver assistance
Feeding Prolonged or assisted feeding
Dressing Partial or complete dependence
Bathing Often requires assistance
Toileting Delayed acquisition or lifelong assistance
Communication Limited verbal or non-verbal communication
Medication Caregiver-dependent
Safety Continuous supervision may be required
Education Need for individualized/special education
Social participation Limited by mobility and communication barriers

A study of adults with WHS found that among 12 caregivers who completed an activities-of-daily-living assessment, two individuals were partly independent whereas ten required total care.

This finding highlights the importance of considering WHS as a lifelong developmental condition rather than focusing exclusively on childhood medical manifestations.

Transition from Childhood to Adolescence and Adulthood

Long-term outcomes have historically been understudied.

There is evidence that individuals with WHS can survive into adulthood, but published information regarding adult health and independence remains limited. A natural-history study specifically addressing adults noted that long-term survival and adult functional outcomes had been poorly characterized in earlier literature.

The transition to adolescence and adulthood raises additional issues:

- continuation of medical care
- transition from paediatric to adult healthcare
- puberty and reproductive health
- mobility
- communication
- vocational or day-program opportunities
- social participation
- supported decision-making
- long-term accommodation
- caregiver succession and
- future planning

For families, one of the most difficult questions may be:

“Who will care for my child when I am no longer able to provide the same level of care?”

This issue deserves substantially greater research attention.

Family Caregiving Challenges

WHS is not only a medical diagnosis; it is a lifelong family experience.

Caregiving responsibilities may include:

- daily personal care
- feeding
- medication administration
- physiotherapy
- speech therapy
- seizure monitoring
- specialist consultations
- educational support
- communication assistance
- behavioural support
- continuous supervision

The intensity of care can increase substantially when the affected individual has severe motor and communication impairment.

A WHS-specific study involving 22 Spanish caregivers found that clinical characteristics of affected individuals were related to parental quality of life and emphasized the importance of psychosocial support and social networks.

A subsequent family quality-of-life study reported that emotional well-being was particularly affected and identified stress relief and availability of time as important concerns. These findings provide evidence for

the broader caregiving burden associated with WHS, although they should not be assumed to represent Indian families directly.

Psychological and Emotional Challenges for Parents

Parents may experience a wide range of emotions following diagnosis and during long-term caregiving.

Potential challenges include:

- uncertainty about prognosis
- concern about developmental progress
- fear regarding seizures and medical complications
- grief associated with unmet developmental expectations
- anxiety about future independence
- social isolation
- exhaustion
- financial stress
- difficulty balancing employment and caregiving
- concern regarding future care after parental aging

However, families should not be characterized only in terms of burden. Parents may also develop:

- strong advocacy skills
- extensive knowledge of their child's medical needs
- improved coping strategies
- close family relationships
- resilience
- increased awareness of disability rights
- active participation in rehabilitation and education

Research on WHS caregivers has specifically suggested that problem-focused coping and social support may be associated with better psychological and social quality of life.

Wolf–Hirschhorn Syndrome in Indian Families

The Indian literature on WHS remains limited compared with the international literature.

Nevertheless, several important publications demonstrate that WHS occurs in Indian patients and that the underlying genetic mechanisms can be diverse.

Indian case report

A 2012 Indian report described a patient with a terminal chromosome 4p deletion detected through GTG-banded cytogenetic analysis. The patient displayed characteristic clinical manifestations including craniofacial abnormalities and congenital anomalies.

Indian case series

Chaudhry and colleagues reported four Indian patients with WHS in 2020. One case was detected by conventional karyotyping, whereas three were identified

using MLPA. The authors emphasized that conventional cytogenetics may not identify all patients and recommended molecular cytogenetic investigation and parental karyotyping.

This study is particularly valuable for the Indian context because it demonstrates both clinical heterogeneity and differences in diagnostic detectability.

Large Indian pedigree

An especially important report described a five-generation Indian family involving ten affected individuals with a complex rearrangement involving chromosomes 4p16.1 and 3p26.3.

Three individuals with 4p16.1 deletion and 3p26.3 duplication showed a typical WHS phenotype, whereas other family members carrying different chromosomal changes displayed different clinical presentations.

This family illustrates an important principle:

Chromosomal architecture and the precise genomic imbalance can substantially influence clinical presentation.

It also demonstrates why parental and family chromosomal studies can be important in apparently familial cases.

Challenges Specific to the Indian Context

Although WHS-specific Indian caregiver studies are scarce, several areas warrant particular attention in future Indian research.

Access to genetic diagnosis

Specialized genetic testing may not be equally available to all families.

Potential barriers include:

- geographical distance from genetic centres
- cost
- limited awareness
- delayed referral
- availability of molecular testing
- interpretation of complex chromosomal findings
- limited access to genetic counselling

The Indian WHS case series demonstrates that molecular testing can identify deletions that may not be readily detected through conventional cytogenetics.

Rehabilitation services

Long-term rehabilitation may involve:

- physiotherapy;
- occupational therapy;
- speech therapy;
- feeding therapy;
- special education;
- behavioural intervention; and
- assistive technology.

For families living away from major cities, repeated access to these services can be difficult.

Financial burden

The financial consequences may involve:

- genetic testing
- hospitalization
- medications
- therapy
- assistive devices
- special education
- nutritional support
- loss of parental working time

However, specific WHS-related financial burden data for Indian families are currently insufficient, and future studies should measure these outcomes rather than assuming their magnitude.

Education and Social Participation

Educational needs vary according to developmental and functional abilities.

Potential educational approaches include:

- individualized education plans
- special education
- sensory-based learning
- structured routines
- visual supports
- augmentative communication
- occupational therapy
- functional life-skills training

For individuals with severe intellectual and motor impairment, educational goals may appropriately emphasize:

- communication
- self-care
- mobility
- social interaction
- sensory engagement
- choice-making
- safety
- quality of life

Educational success should therefore not be measured solely by conventional academic achievement.

Importance of Multidisciplinary Care

The multisystem nature of WHS requires coordinated care.

A multidisciplinary team may include:

Medical specialists

- paediatrician
- clinical geneticist
- neurologist
- cardiologist

- nephrologist when indicated
- ophthalmologist
- ENT/audiologist
- dentist

Developmental and rehabilitation professionals

- physiotherapist
- occupational therapist
- speech-language therapist
- psychologist
- special educator
- dietitian

Family and social support

- genetic counsellor
- social worker
- disability-support organizations
- parent support groups

The objective should be a coordinated, family-centred plan rather than isolated management of individual symptoms.

Genetic Counselling

Genetic counselling is particularly important because the recurrence risk depends on the mechanism of the chromosomal abnormality.

Many WHS cases result from de novo chromosomal deletions. However, an unbalanced rearrangement may occasionally result from a parental balanced chromosomal rearrangement. Therefore, parental chromosome analysis may be recommended following diagnosis. This was specifically emphasized in the Indian four-patient case series.

Families should receive individualized counselling rather than relying on a generalized recurrence estimate.

Family-Centred Care

A family-centred approach recognizes that parents are not merely caregivers but important members of the clinical team.

Parents frequently know:

- the individual's baseline behaviour
- seizure pattern
- preferred communication method
- feeding tolerance
- sleep pattern
- signs of discomfort
- mobility abilities
- responses to interventions

Healthcare professionals should therefore encourage structured communication with families.

Family-centred care should include:

1. clear explanation of diagnosis
2. realistic developmental counselling
3. access to rehabilitation

4. caregiver education
5. psychosocial support
6. emergency planning
7. transition planning
8. long-term follow-up

Current Evidence Gaps

Several important gaps are evident in the literature.

Gap 1: Limited Indian epidemiological data

Reliable population-level prevalence estimates for WHS in India are lacking.

Gap 2: Limited longitudinal Indian studies

Most Indian publications are case reports or small case series.

Gap 3: Limited caregiver research

There is insufficient WHS-specific research examining:

- caregiver burden
- parental stress
- family quality of life
- financial consequences
- employment effects
- sibling experiences
- social participation
- future-care planning

Gap 4: Limited adult Indian data

Long-term outcomes after childhood remain poorly documented.

Gap 5: Limited functional-outcome research

There is a need for standardized assessment of:

- mobility
- communication
- activities of daily living
- feeding
- self-care
- adaptive behaviour

Gap 6: Limited intervention research

Evidence regarding the effectiveness of specific rehabilitation strategies remains limited.

Proposed Research Framework for Indian WHS Studies

Future Indian research could use a multicentre observational design.

Participant characteristics

- confirmed WHS diagnosis
- age
- sex
- geographic location
- genetic abnormality
- deletion size where available

Clinical variables

- seizures
- cardiac abnormalities
- renal abnormalities

- hearing
- vision
- feeding
- growth
- hypotonia
- Developmental variables
- sitting
- standing
- walking
- speech
- communication
- cognition
- adaptive functioning

Functional variables

- feeding independence
- toileting
- dressing
- mobility
- communication
- medication dependence

Family variables

- caregiver age
- caregiver relationship
- employment
- education
- family size
- access to therapy
- transportation
- financial burden
- social support
- caregiver quality of life

Such a framework would provide considerably stronger evidence concerning the Indian WHS population than isolated case reports.

3. Discussion

The available literature demonstrates that WHS is a clinically heterogeneous chromosomal disorder with substantial effects on growth, neurological function, development, communication and independence. The 87-patient natural-history study established many of the classical clinical characteristics, including growth restriction, seizures, hypotonia, developmental delay, skeletal and cardiac abnormalities, hearing impairment and structural CNS abnormalities. More recent literature has continued to emphasize the importance of epilepsy, communication impairment and long-term functional dependence. The 2025 epilepsy cohort involving 140 individuals further illustrates the continuing clinical importance of seizures and their relationship with

developmental outcomes. At the same time, WHS should not be interpreted as a uniform phenotype. The degree of chromosomal deletion, additional chromosomal changes and individual biological variability contribute to differences in clinical presentation. The Indian evidence is particularly valuable in demonstrating this heterogeneity. The four-patient Indian case series and the large Indian pedigree show that molecular characterization is important and that conventional cytogenetics alone may not adequately characterize all cases. Functional outcomes are equally important. Studies demonstrate that some individuals achieve independent or supported walking, whereas others require extensive assistance. Communication abilities similarly vary from limited verbal communication to substantial language impairment. For families, the consequences can be lifelong. Caregivers may need to provide assistance with almost every aspect of daily life. International WHS-specific studies have demonstrated effects on family quality of life, emotional well-being, time availability and psychosocial functioning.

However, there is an important evidence limitation: most caregiver studies have been conducted outside India. Therefore, the Indian context should be viewed as an important research area rather than an area in which conclusions are already firmly established.

Implications for Indian Healthcare and Rehabilitation

The available evidence supports several priorities for India.

Earlier diagnosis

Clinicians should consider WHS when children present with the characteristic combination of:

- growth restriction
- distinctive facial phenotype
- hypotonia
- developmental delay
- seizures
- congenital abnormalities

Improved access to molecular diagnosis

Where clinically appropriate, molecular cytogenetic techniques can complement conventional karyotyping.

Long-term developmental monitoring

Assessment should continue beyond infancy and early childhood.

Family-centred rehabilitation

Therapy goals should be individualized according to functional needs rather than solely age-based developmental expectations.

Communication support

Non-verbal individuals should be provided with appropriate alternative communication methods.

Caregiver support

Parents require information, psychosocial support, respite opportunities and access to disability-related resources.

Transition planning

Families should receive support for adolescence and adulthood rather than focusing exclusively on early childhood.

Future Directions

Future WHS research in India should move beyond isolated clinical descriptions toward systematic longitudinal studies.

Priority areas include:

1. Establishment of Indian WHS registries.
2. Multicentre clinical characterization.
3. Genotype–phenotype correlation studies.
4. Longitudinal developmental follow-up.
5. Standardized functional assessment.
6. Caregiver quality-of-life studies.
7. Economic burden assessment.
8. Research on communication and AAC.
9. Adult outcome studies.
10. Development of Indian family-support networks.
11. Evaluation of rehabilitation interventions.
12. Studies of access to genetic counselling and molecular diagnosis.

Particular attention should be given to families caring for adolescents and adults with severe functional dependence because the long-term care requirements may differ substantially from those of young children.

Limitations of the Present Review

This review has several limitations.

First, WHS is a rare disorder, and much of the available evidence consists of case reports, small cohorts and retrospective studies.

Second, clinical studies differ in diagnostic methods, age distributions, deletion sizes and outcome measurements.

Third, much of the evidence concerning family quality of life and caregiver burden comes from non-Indian populations.

Fourth, Indian evidence remains relatively sparse. Therefore, the phrase "Indian families" in the title should be understood as an emphasis on the Indian evidence gap and context rather than a claim that a representative national sample has been studied.

Finally, historical studies may report prevalence estimates that differ from those found in modern molecularly diagnosed populations.

4. Conclusion

Wolf-Hirschhorn syndrome is a rare and highly heterogeneous chromosomal disorder with multisystem medical manifestations and substantial developmental and functional consequences. Growth restriction, hypotonia, developmental delay, intellectual disability, epilepsy, communication impairment and congenital abnormalities constitute important components of the clinical spectrum.

The available literature demonstrates that developmental and functional outcomes vary considerably. Some individuals acquire independent or assisted walking and develop useful communication, whereas others remain profoundly dependent for mobility, communication and activities of daily living. Consequently, individualized developmental assessment and long-term rehabilitation are essential.

For families, WHS represents a lifelong caregiving journey. Medical management, therapy, education, communication support and assistance with daily activities may continue throughout childhood and adulthood. International evidence demonstrates meaningful effects on family quality of life, emotional well-being and time availability.

Indian evidence, although limited, confirms the presence of WHS and demonstrates substantial genetic and phenotypic heterogeneity. Indian reports also highlight the importance of molecular cytogenetic diagnosis and parental chromosomal evaluation. However, systematic research concerning Indian families-particularly caregiver burden, financial consequences, rehabilitation access, functional independence and adult outcomes is still insufficient.

Future Indian studies should therefore adopt family-centred, multidisciplinary and longitudinal approaches. Establishment of national or multicentre WHS registries, standardized functional assessments and caregiver-focused research could substantially improve understanding of the syndrome and help develop more appropriate clinical, rehabilitation and social-support strategies for affected individuals and their families.

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