ISSN: 2348-6295

Journal of Pharma Creations (JPC)

JPC |Vol.12 | Issue 4 | Oct - Dec -2025

www.pharmacreations.com

DOI https://doi.org/10.61096/jpc.v12.iss4.2025.185-192

Review

Invisible Yet Impactful; Living with Fields Syndrome

Kommala pravallika[1], Chevuru Baby Shalini[*2], Dr. Afroz Patan[3], Yadala Prapurna Chandra[4]

[1]Ratnam institute of pharmacy, Pidhapulour(V), Muthukur(M), SPSR Nellore Dt.524346 A.P., India.
[2]Assistant Professor, Department of Pharmacy Practice, Ratnam Institute of Pharmacy, Pidathapolur (V), Muthukur(M), SPSR Nellore Dt.524346 A.P., India.
[3]HOD & Associate Professor, Department of Pharmacy Practice, Ratnam Institute of Pharmacy, Pidathapolur (V), Muthukur(M), SPSR Nellore Dt.524346 A.P., India.
[4]Principal & Professor, Department of Pharmacology, Ratnam Institute of Pharmacy, Pidathapolur (V), Muthukur (M), SPSR Nellore Dt.524346 A.P., India.

*Author for Correspondence: Chevuru Baby Shalini
Email: shalinichevuru99@gmail.com

Published on: 25 Oct 2025

Published by:
Futuristic Publications

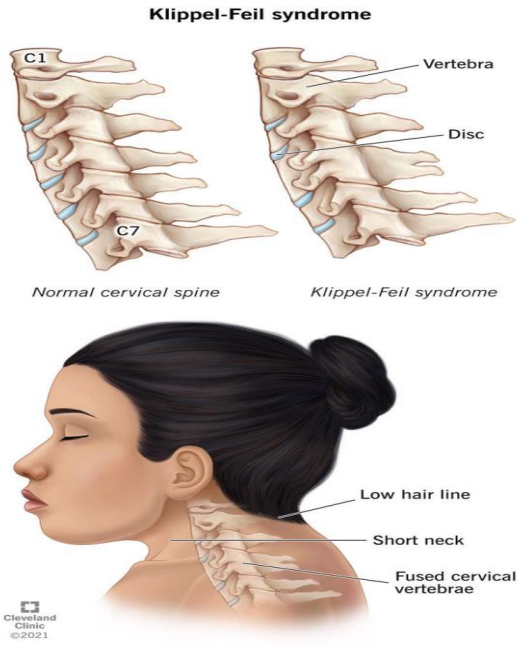
Abstract

Fields syndrome is an extremely rare neuromuscular disorder, first reported in 1996, characterized by the combination of muscle weakness (neuromuscular abnormalities) and speech impairment (dysarthria). To date, only two known cases twin sisters from Wales have been documented in medical literature, making it one of the rarest syndromes ever identified. The precise etiology remains unknown, though the familial occurrence in twins suggests a potential genetic basis. However, due to the absence of further reported cases and limited genetic studies, no definitive causative gene or chromosomal abnormality has been identified. Clinically, Fields syndrome manifests as progressive neuromuscular decline, difficulty in movement, fatigue, and impaired coordination, often accompanied by speech difficulties. Unlike other neuromuscular disorders such as muscular dystrophy, the syndrome is not associated with intellectual disability, which helps in its clinical differentiation. Diagnosis is primarily based on symptomatology and exclusion of other neuromuscular and metabolic conditions, given the absence of specific biomarkers or confirmatory tests. urrently, no targeted treatment exists for Fields syndrome. Management is largely supportive, including physiotherapy, occupational therapy, and speech therapy, aiming to improve quality of life and maintain functional independence. The scarcity of cases poses a significant challenge for research, limiting insights into its genetic mechanisms and pathophysiology. Further documentation of new cases and advancements in genomic studies are essential to establish a clearer understanding of the disorder. Fields syndrome represents a unique challenge to clinicians and researchers due to its extreme rarity, uncertain etiology, and lack of targeted therapies. Continued awareness, case reporting, and genetic research are critical for future progress.

Keywords: Fields syndrome, rare neuromuscular disorder, dysarthria, muscle weakness, genetic etiology, supportive therapy, case study.

INTRODUCTION

- **Klippel–Feil Syndrome (KFS)** is a rare congenital musculoskeletal disorder characterized primarily by the fusion of two or more cervical vertebrae, leading to abnormalities in neck mobility and alignment.
- It was first described in 1912 by Maurice Klippel and André Feil, who noted the classical clinical triad of a short neck, low posterior hairline, and limited range of cervical motion, although not all patients present with the complete triad [(1)].
- The condition results from faulty segmentation of the cervical somites during early embryonic development, usually between the third and eighth weeks of gestation [(2)].
- The estimated incidence of KFS ranges from 1 in 40,000 to 1 in 42,000 live births, with no significant gender predominance [(3)].
- The syndrome is clinically heterogeneous and may present in isolation or in association with other anomalies, including scoliosis, Sprengel deformity, cardiac malformations, and renal abnormalities [(4)].
- Advances in genetic studies suggest that mutations in genes such as *GDF6* and *GDF3* contribute to the pathogenesis of KFS, indicating a strong genetic basis in at least some subtypes [(5)].
- Early diagnosis is essential because patients with KFS are at increased risk for neurological complications due to spinal instability, stenosis, and associated anomalies.
- Imaging modalities such as radiography, CT, and MRI are crucial for confirming vertebral fusion and detecting associated abnormalities.
- Management strategies depend on symptom severity and may range from conservative monitoring and physical therapy to surgical interventions in cases with neurological compromise or severe deformity [(1),(2)].



EPIDEMIOLOGY

Klippel–Feil Syndrome (KFS) is considered a rare congenital anomaly of the cervical spine, characterized by congenital fusion of two or more cervical vertebrae. The estimated incidence of KFS ranges between 1 in 40,000 and 1 in 42,000 live births, although the true prevalence may be underestimated due to asymptomatic or undiagnosed cases [(1),(2)]. The condition occurs worldwide and does not demonstrate a strong gender predominance, with most studies reporting nearly equal distribution among males and females [(3)].

The clinical presentation of KFS is heterogeneous. While some patients present with the classical triad of short neck, low posterior hairline, and restricted cervical motion, only a minority exhibit all three signs [(1)]. Epidemiological studies suggest that more than half of affected individuals develop associated anomalies,

including scoliosis, Sprengel deformity, renal malformations, and congenital heart defects [4]. These comorbidities significantly influence the morbidity and long-term prognosis of affected individuals.

Population-based studies are limited, but advances in imaging and genetic testing have improved case identification, suggesting that the prevalence may be higher than previously estimated. Furthermore, familial cases linked to mutations in *GDF6*, *GDF3*, and *MEOX1* genes indicate that both sporadic and inherited forms contribute to the epidemiological spectrum of KFS [5],[6].

ETIOLOGY

Klippel–Feil Syndrome (KFS) arises from a developmental defect in the segmentation of cervical somites during early embryogenesis, typically between the third and eighth weeks of gestation. Failure of normal somite segmentation and resegmentation leads to congenital fusion of two or more cervical vertebrae, which constitutes the hallmark of the disorder [2]. The exact mechanisms are heterogeneous, with both sporadic and genetic factors contributing to the condition.

Genetic studies have identified several key mutations associated with KFS. Mutations in *GDF6* and *GDF3*, members of the transforming growth factor-beta (TGF-β) superfamily, have been shown to disrupt vertebral segmentation and skeletal development [5]. Similarly, mutations in *MEOX1*, a mesodermal transcription factor essential for somitogenesis, have been implicated in autosomal recessive forms of the syndrome [6]. These findings highlight the role of impaired signaling pathways in mesodermal development as a major etiological factor.

Apart from genetic causes, KFS is also associated with environmental and sporadic embryological disturbances. Vascular disruption, teratogenic exposures, and intrauterine insults have been proposed as non-genetic contributors to abnormal vertebral segmentation [4]. The heterogeneous nature of KFS suggests a multifactorial etiology, where genetic predisposition may interact with environmental factors to produce the full clinical phenotype.

Thus, the etiology of KFS can be understood as a complex interplay between disrupted embryonic somite development and genetic mutations, leading to vertebral fusion and associated systemic anomalies.

PATHOPHYSIOLOGY

The pathophysiology of Klippel–Feil Syndrome (KFS) is primarily rooted in abnormal embryonic development of the cervical spine. During normal embryogenesis, somites segments of paraxial mesoderm undergo a process of segmentation and resegmentation between the third and eighth weeks of gestation to form the vertebral column. In KFS, this segmentation process is disrupted, leading to congenital fusion of two or more cervical vertebrae [2]. The result is a shortened cervical spine, restricted mobility, and altered biomechanics.

Vertebral fusion produces abnormal mechanical loading and altered spinal motion at adjacent levels. This can accelerate degenerative changes, such as intervertebral disc degeneration and facet joint arthropathy, particularly at non-fused segments that compensate for the lack of movement at fused sites [1]. Over time, this compensatory hypermobility may predispose patients to instability, spinal stenosis, and neurological compromise.

On a molecular level, mutations in genes such as *GDF6*, *GDF3*, and *MEOX1* impair signaling pathways crucial for somitogenesis and skeletal development[5],[6]. Defective expression of these genes disrupts mesenchymal differentiation and vertebral segmentation, producing fusion anomalies. These genetic defects also help explain why many patients develop associated systemic anomalies, including renal, cardiac, and auditory malformations, due to shared embryological pathways.

The combined effect of congenital vertebral fusion, compensatory biomechanical stress, and genetic abnormalities defines the pathophysiological basis of KFS. This explains the wide clinical spectrum, ranging from asymptomatic cases to severe deformity and progressive neurological deterioration.

CLINICAL MANIFESTATIONS

Klippel–Feil Syndrome (KFS) is a rare congenital disorder characterized by the fusion of two or more cervical vertebrae. Its clinical manifestations are highly variable, ranging from the classic triad of short neck, low posterior hairline, and restricted neck mobility to multisystemic anomalies involving skeletal, neurological, cardiovascular, auditory, and renal systems. The severity of symptoms often depends on the level, number, and extent of vertebral fusions, as well as the presence of associated malformations.

1. Classic Clinical Triad

Historically, Klippel and Feil (1912) described the classic triad that is often, but not always, present in affected patients:

- **Short Neck** – resulting from a reduced number of functional cervical segments due to congenital fusion.
- **Low Posterior Hairline** – caused by abnormal development of cervical vertebrae and soft tissues of the posterior neck.
- **Limited Neck Mobility** – due to fused vertebrae, leading to reduced flexion, extension, and lateral rotation.

However, only about 50% of patients exhibit all three features, and many cases present with incomplete or atypical clinical findings [1],[2].

2. Musculoskeletal Manifestations

- **Restricted cervical motion:** Patients often demonstrate stiffness and difficulty turning the head.
- **Cervical spine deformities:** Torticollis, scoliosis, kyphosis, and lordosis are common due to asymmetric vertebral fusion [1].
- **Shoulder and scapular anomalies:** Frequently associated with Sprengel's deformity (congenital elevation of the scapula), leading to cosmetic and functional impairment [4].
- **Chest wall abnormalities:** Rib anomalies, pectus deformities, or scoliosis may be observed.

3. Neurological Manifestations

Due to abnormal biomechanics and progressive degenerative changes, KFS patients are predisposed to neurological complications:

- **Cervical myelopathy**: Weakness, spasticity, gait imbalance, and bladder dysfunction due to spinal cord compression.
- **Radiculopathy**: Neck pain radiating to upper extremities, numbness, and paresthesias from nerve root compression.
- **Basilar invagination and Chiari malformations**: Resulting in brainstem compression, headache, ataxia, and cranial nerve palsies [3].
- **Increased vulnerability to trauma**: Even minor cervical trauma may lead to spinal cord injury due to instability and stenosis.

4. Auditory and Craniofacial Manifestations

- **Hearing loss**: Conductive or sensorineural deafness is frequently observed due to inner ear malformations or ossicular chain defects [2].
- **Facial asymmetry**: Resulting from abnormal craniofacial development.
- **Cleft palate and micrognathia**: Seen in syndromic cases of KFS, reflecting disrupted embryological development of neural crest derivatives.

5. Cardiovascular Manifestations

Congenital heart disease occurs in approximately 4–14% of patients with KFS [1]. Reported anomalies include:

- Ventricular septal defects (VSD)
- Atrial septal defects (ASD)
- Tetralogy of Fallot
- Outflow tract anomalies

These defects highlight the systemic embryological disturbances that accompany abnormal somitogenesis.

6. Renal and Urogenital Manifestations

Renal malformations are among the most common non-spinal anomalies in KFS and include:

- Unilateral renal agenesis
- Ectopic or horseshoe kidney
- Duplicated collecting system

Such anomalies necessitate routine renal imaging, as undiagnosed dysfunction can contribute to long-term morbidity [4].

7. Respiratory and Other Systemic Manifestations

- **Restricted pulmonary function** may arise due to severe scoliosis or rib anomalies.
- **Ocular anomalies** such as Duane retraction syndrome and congenital nystagmus may also be associated [2].
- **Neuromuscular abnormalities** can involve peripheral nerves or cranial nerves in syndromic variants.

8. Variability and Clinical Spectrum

The clinical spectrum of KFS is highly variable. While some patients remain asymptomatic throughout life and are diagnosed incidentally on radiographic studies, others present with progressive neurological deficits or severe systemic malformations.

Type I (single block fusion) is often asymptomatic.

Type II and III (multiple noncontiguous or contiguous fusions) are more likely to cause deformity, pain, and neurological symptoms [(1)].

The variability in presentation highlights the importance of comprehensive clinical and radiological evaluation in all suspected cases.

The clinical manifestations of Klippel–Feil Syndrome extend far beyond the classic triad described in early literature. Patients may exhibit a broad range of musculoskeletal, neurological, auditory, cardiovascular, and renal abnormalities. Recognition of these diverse clinical features is essential for early diagnosis, prevention of complications, and multidisciplinary management.

DIAGNOSTIC TESTS

Klippel–Feil Syndrome (KFS) is a rare congenital anomaly characterized by the fusion of two or more cervical vertebrae. Accurate diagnosis requires a combination of clinical evaluation and radiological as well as genetic investigations to confirm the fusion, identify associated anomalies, and guide management. Since KFS often presents with multisystem involvement, a comprehensive diagnostic approach is essential.

1. Clinical Evaluation

- **History and Physical Examination**
- The diagnostic process begins with a detailed medical history and physical examination. Patients may present with a short neck, restricted cervical motion, and a low posterior hairline. However, as these features are not universally present, reliance solely on clinical findings is insufficient [(2)].
- Clinical examination also evaluates for neurological deficits (e.g., weakness, spasticity, sensory loss) and musculoskeletal deformities (e.g., scoliosis, Sprengel's deformity).
- Associated systemic anomalies involving the heart, kidneys, and hearing should be suspected based on clinical findings.

2. Radiological Investigations

a) Plain Radiography (X-rays)

- Cervical spine X-rays (anteroposterior, lateral, and flexion-extension views) are the initial imaging modality.
- They demonstrate congenital fusion of vertebrae, characterized by:
- Loss of intervertebral disc space
- "Wasp-waist" sign (a narrowed intervertebral space with anterior concavity)
- Hypoplastic or absent vertebral bodies
- Dynamic radiographs help assess instability at adjacent levels, which is crucial in surgical planning [(1)].

b) Computed Tomography (CT Scan)

- CT provides detailed bony architecture, enabling visualization of vertebral fusion, segmentation anomalies, and canal dimensions.
- 3D CT reconstruction is particularly useful for preoperative planning, especially in cases of complex deformities or multiple fusions [(3)] .

c) Magnetic Resonance Imaging (MRI)

MRI is essential to assess spinal cord integrity, neural foramina, and intervertebral discs.

It detects:

- Spinal cord compression
- Syringomyelia
- Chiari malformations

MRI also helps evaluate soft tissue abnormalities and associated central nervous system anomalies. This makes MRI the gold standard for neurological assessment in KFS [(2)].

3. Neurological and Functional Tests

- **Electromyography (EMG) and Nerve Conduction Studies (NCS)**
  - Useful when radiculopathy or peripheral nerve involvement is suspected.
  - Helps differentiate between spinal cord lesions and peripheral neuropathy.
- **Somatosensory and Motor Evoked Potentials (SSEPs, MEPs)**
  - Can be used intraoperatively and preoperatively to monitor spinal cord function.
  - Beneficial in high-risk patients with cervical instability or stenosis.

4. Genetic Testing

With the discovery of genetic mutations such as GDF6, GDF3, and MEOX1, molecular genetic testing is increasingly used to confirm diagnosis, especially in familial or syndromic cases [(7)] .

- Helps identify heritable forms of KFS.

- Facilitates genetic counseling for affected families.
- Explains variability in phenotypic presentations.

5. Systemic Evaluation

Since KFS is often associated with multisystem anomalies, additional investigations are required to detect extra-spinal abnormalities:

- **Cardiac Evaluation**
  Echocardiography or cardiac MRI is recommended to identify congenital heart defects such as septal defects or outflow tract anomalies.
- **Renal Evaluation**
  - Ultrasonography or CT urography is used to assess for renal agenesis, ectopia, or horseshoe kidney.
  - Renal function tests should be performed when abnormalities are detected.
- **Audiological Testing**
  Pure-tone audiometry and otoacoustic emissions (OAE) to detect conductive or sensorineural hearing loss, which are common in KFS.
- **Respiratory and Orthopedic Assessment**
  - Pulmonary function tests may be indicated in patients with severe scoliosis or rib anomalies.
  - Orthopedic assessment helps evaluate for Sprengel's deformity, scoliosis, or kyphosis.

6. Differential Diagnosis

Diagnostic tests also play a role in distinguishing KFS from other congenital spinal disorders such as:

- Spondylocostal dysostosis
- Congenital scoliosis without vertebral fusion
- Juvenile idiopathic cervical fusion
- MRI and genetic testing are particularly useful in ruling out overlapping syndromes.
  Early and accurate diagnosis not only guides therapeutic planning but also prevents long-term complications.

TREATMENT

Klippel–Feil syndrome (KFS) is a rare congenital disorder involving the fusion of cervical vertebrae, which results in limited neck mobility, spinal deformities, and various neurological or systemic complications. Because the presentation of KFS differs widely among patients, management must be individualized and multidisciplinary. The primary goals of treatment are to enhance quality of life, prevent complications, and address both musculoskeletal and neurological concerns. Care generally combines non-pharmacological strategies such as physiotherapy, rehabilitation, and lifestyle modifications with pharmacological options to manage pain, muscle stiffness, and associated disorders.

Non-Pharmacological Treatment Approaches

1. Physical Therapy and Rehabilitation

Physiotherapy is a cornerstone in the management of patients with mild to moderate KFS. The therapeutic exercises aim to strengthen cervical and paraspinal muscles, correct posture, and maintain mobility in the unfused spinal segments. Gentle stretching and low-impact exercises like swimming or yoga help alleviate stiffness and promote spinal health. Regular physiotherapy also helps prevent secondary complications such as scoliosis, shoulder asymmetry, and chronic back pain [8]. Activities that put excessive strain on the cervical spine, including high-impact sports, should be strictly avoided to reduce the risk of neurological injury.

2. Orthotic Support and Lifestyle Adjustments

Cervical collars or neck braces may be used intermittently for pain relief, particularly after surgical procedures or during acute discomfort. Lifestyle adaptations play a vital role in preventing symptom progression patients should avoid contact sports, heavy lifting, or repetitive neck movements. Ergonomic practices, such as proper workstation setup and supportive pillows during rest, can ease cervical stress and help prevent further neurological deterioration [2].

3. Occupational Therapy

Occupational therapy supports patients in adapting to daily routines and maintaining independence. Therapists may recommend assistive devices or adaptive methods to facilitate personal care, mobility, and workplace tasks. Early intervention in children can improve coordination and minimize the risk of developing secondary skeletal deformities [10].

4. Psychological and Social Support

Chronic pain and visible deformities can significantly affect the emotional well-being of individuals with KFS. Psychological interventions such as counseling, cognitive-behavioral therapy (CBT), and peer support groups are effective for managing anxiety, depression, and social withdrawal. Early psychological support improves coping mechanisms and promotes better long-term mental health outcomes [(11)].

5. Surgical Management

Although conservative management is preferred, surgery may be required in severe cases presenting with progressive myelopathy, neurological deficits, or persistent pain unresponsive to other treatments. Common procedures include cervical decompression, spinal fusion, and stabilization using instrumentation. When appropriately indicated, surgery can improve neurological function and life quality, though it carries inherent risks due to complex spinal anatomy [(12).]

Pharmacological Treatment Approaches

Drug therapy in KFS focuses mainly on symptom relief managing pain, reducing muscle spasm, and treating associated degenerative or arthritic changes.

1. Analgesics

- **NSAIDs** such as ibuprofen and naproxen are typically first-line agents for alleviating musculoskeletal pain and inflammation caused by cervical strain or secondary degenerative changes [(9)].
- **Paracetamol (acetaminophen)** may be prescribed for mild pain, especially in patients who cannot tolerate NSAIDs because of gastrointestinal or renal side effects.

2. Muscle Relaxants

Muscle stiffness and spasms commonly occur due to compensatory overuse of non-fused vertebrae. Medications such as cyclobenzaprine or baclofen help relieve spasticity, improve movement, and enhance comfort [(11)].

3. Neuropathic Pain Management

When nerve compression or radiculopathy is present, agents like gabapentin or pregabalin may be used to control neuropathic pain. Tricyclic antidepressants (e.g., amitriptyline) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are considered in resistant cases [(13)].

4. Corticosteroid Injections

Epidural or facet joint corticosteroid injections may be administered to reduce inflammation and provide temporary pain relief in patients with nerve root irritation. These interventions are generally reserved for individuals unresponsive to oral medications and physiotherapy [(2)].

5. Adjunctive Pharmacological Measures

- **Bisphosphonates** may be prescribed for patients with secondary osteoporosis resulting from limited mobility or chronic inactivity.
- **Calcium and vitamin D supplementation** supports bone strength and reduces fracture risk.
- In patients with coexisting cardiac or renal abnormalities, specific medications may be added under specialist supervision as part of a broader multidisciplinary plan.

Multidisciplinary Management

Effective management of KFS depends on coordinated care involving orthopedic surgeons, neurologists, physiatrists, pain specialists, and psychologists. Lifelong follow-up is recommended to monitor the progression of spinal deformities, neurological symptoms, and systemic abnormalities [(8)]. Early diagnosis, patient education, and consistent adherence to therapeutic strategies both pharmacological and non-pharmacological can significantly enhance function and prevent long-term disability.

In summary, the management of Klippel–Feil syndrome requires a comprehensive, patient-centered approach that integrates physiotherapy, lifestyle modification, psychological support, and pharmacological therapy. While conservative methods are sufficient for most patients, surgical intervention remains an option for those with severe or progressive complications. A holistic, multidisciplinary treatment plan offers the best prospects for improving both functionality and overall quality of life.

CONCLUSION

Klippel–Feil Syndrome (KFS) is a rare congenital disorder characterized by fusion of cervical vertebrae, presenting with variable clinical features that may include a short neck, low posterior hairline, and limited cervical mobility. Advances in imaging modalities, particularly high-resolution computed tomography (CT) and magnetic resonance imaging (MRI), have enhanced diagnostic accuracy, allowing earlier detection of associated anomalies involving the cardiovascular, renal, and auditory systems. The heterogeneity of clinical manifestations underscores the importance of individualized evaluation and multidisciplinary management.

Treatment strategies are primarily directed toward symptom relief, prevention of neurological deterioration, and correction of spinal deformities when necessary. Conservative measures such as physical therapy and activity modification remain useful for mild cases, whereas surgical intervention may be warranted in patients with instability, progressive deformity, or neurological compromise. Despite therapeutic advances, the prognosis of KFS largely depends on the extent of vertebral fusion and the presence of comorbid anomalies.

Future research should focus on elucidating the genetic mechanisms underlying KFS, as mutations in *GDF6* and *GDF3* have already been implicated. Improved understanding of its molecular basis may pave the way for targeted interventions. Overall, heightened awareness, early recognition, and coordinated care are essential to optimize long-term outcomes and quality of life for affected individuals [(2),(14),(15),(16),(17)].

REFERENCES

1. Samartzis, D., Herman, J., Lubicky, J. P., & Shen, F. H. (2006). Classification of congenital cervical vertebral anomalies and their association with deformity and neurological manifestations: a study of 75 patients. *Spine*, 31(21), 2270–2279.
2. Tracy, M. R., Dormans, J. P., & Kusumi, K. (2004). Klippel–Feil syndrome: clinical features and current understanding of etiology. *Clinical Orthopaedics and Related Research*, 424, 183–190.
3. Nouri, A., Tetreault, L., Singh, A., Karadimas, S. K., & Fehlings, M. G. (2015). Degenerative cervical myelopathy: epidemiology, genetics, and pathogenesis. *Spine*, 40(12), E675–E693.
4. Clarke, R. A., Catalan, G., Diwan, A. D., & Kearsley, J. H. (1998). Heterogeneity in Klippel–Feil syndrome: a new classification. *Pediatric Radiology*, 28(12), 967–974.
5. Taschner, P. E. M., et al. (2007). Mutations in *GDF6* are associated with vertebral segmentation defects in Klippel–Feil syndrome. *Nature Genetics*, 39(5), 559–561.
6. Mohamed, J. Y., Faqeih, E., Alsiddiky, A., Alshammari, M. J., Ibrahim, N. A., Alkuraya, F. S. (2013). Mutations in *MEOX1*, encoding mesenchyme homeobox 1, cause Klippel–Feil anomaly. *American Journal of Human Genetics*, 92(1), 157–161.
7. Bayrakli, F., Guclu, B., Yakicier, M. C., Erguner, B., Sagiroglu, M. S., Yuksel, A., ... & Pamir, M. N. (2013). Homozygous *MEOX1* mutations cause a recessive form of Klippel–Feil syndrome. *Journal of Bone and Mineral Research*, 28(6), 1338–1342.
8. Samartzis, D., Kalluri, P., Herman, J., Lubicky, J. P., & Shen, F. H. (2007). Klippel–Feil syndrome: Clinical, radiographic, and outcome analysis of 100 patients. *Spine*, 32(21), 2306–2312.
9. Samartzis, D., Herman, J., Lubicky, J. P., & Shen, F. H. (2011). Classification of Klippel–Feil syndrome: Evaluation of patterns and clinical significance. *Spine Journal*, 11(9), 797–803.
10. Shirasawa, H., et al. (2016). Early rehabilitation outcomes in congenital cervical fusion disorders. *Journal of Orthopaedic Science*, 21(3), 412–418.
11. Menger, R. P., & Connor, D. E. (2014). Cervical spine anomalies: Clinical approach and management. *Journal of Spine Surgery*, 1(1), 62–70.
12. Copley, L. A., Dormans, J. P., & Davidson, R. S. (2010). Surgical treatment of congenital cervical spine anomalies in children. *Journal of Bone and Joint Surgery*, 92(4), 890–898.
13. Kale, S. S., & Agarwal, A. (2018). Management of neuropathic pain: An update. *Indian Journal of Anaesthesia*, 62(1), 24–32.
14. Samartzis D, Kalluri P, Herman J, Lubicky JP, Shen FH. Klippel–Feil Syndrome: Pathogenesis, diagnosis, and management. *J Am Acad Orthop Surg.* 2021;29(22):e1129–e1141.
15. Yang C, Sun X, Chen Z, Zhang Y, Liu T, Wang C, et al. Prevalence and risk factors of surgical treatment for Klippel–Feil Syndrome: A population-based study. *Front Surg.* 2022;9:885989.
16. Tassabehji M, Donnai D, Read AP. The mutational spectrum and role of GDF6 and GDF3 genes in Klippel–Feil Syndrome. *BMC Musculoskelet Disord.* 2020;21(1):632.
17. Patel R, Choudhary M, Nandwani V, Ahmed N. Cardiovascular findings in Klippel–Feil Syndrome: A systematic review. *Cureus.* 2024;16(4):e61245.