Troia Med J 2026;7(2):99-107
DOI: 10.55665/troiamedj.1797107

REVIEW

Klippel-Feil syndrome: rare clinical associations and significance

Süleyman AKILLI[1], Ozan IŞIK[2]

[1] *Deparment of Neurosurgery, Adnan Menderes University Medicine Faculty, Aydın, Türkiye*
[2] *Department of Neurosurgery, Denizli Servergazi State Hospital, Denizli, Türkiye*

ABSTRACT
Klippel–Feil syndrome (KFS) is a rare congenital disorder characterized by fusion of cervical vertebrae and accompanied by a wide spectrum of systemic anomalies. This narrative review summarizes current knowledge on the genetic basis, clinical spectrum, and rare associations of KFS with implications for multidisciplinary care. Recent genetic studies have identified variants in several developmental pathways, suggesting an emerging concept of oligogenic inheritance and variable expressivity. Clinically, beside the classic triad of short neck, low posterior hairline, and restricted cervical motion, patients may present with scoliosis, Sprengel deformity, craniovertebral junction abnormalities, split cord malformations, posterior fossa lesions, and genitourinary and cardiovascular anomalies. Otologic involvement, including conductive or sensorineural hearing loss and cochlear implant challenges, further complicates management. Awareness of potential difficult airway and spinal cord vulnerability is crucial for anesthesiologists and surgeons. Early recognition, systematic screening for associated anomalies, and coordinated follow-up are essential to prevent complications and optimize long-term outcomes. We narratively reviewed recent clinical, radiologic, and genetic literature to contextualize reported prevalences and rare associations.
Keywords: Klippel-Feil syndrome, congenital abnormalities, spinal diseases

ÖZET

Klippel-Feil sendromu: nadir klinik ilişkiler ve önemi
Klippel–Feil sendromu (KFS), servikal vertebraların konjenital füzyonu ile karakterize, çok sayıda sistemik anomali ile birlikte görülebilen nadir bir gelişimsel bozukluktur. Bu derlemede, KFS'nin genetik altyapısı, klinik özellikleri ve nadir eşlik eden durumları güncel literatür ışığında ele alınmakta; multidisipliner yaklaşımın önemi vurgulanmaktadır. Son yapılan genetik çalışmalar, birden fazla gelişimsel yolakta saptanan varyantları ortaya koymuş olup, tek genli bir mekanizmadan ziyade değişken ekspresyonla seyreden, ortaya çıkmakta olan oligenik bir katkıya işaret etmektedir. Klinik olarak, kısa boyun, düşük posterior saç çizgisi ve servikal hareket kısıtlılığından oluşan klasik triada ek olarak; skolyoz, Sprengel deformitesi, kraniovertebral bileşke anomalileri, split kord malformasyonları, posterior fossa patolojileri ile genitoüriner ve kardiyovasküler anomaliler eşlik edebilir. Ayrıca iletim tipi veya sensörinöral işitme kaybı gibi otolojik tutulumlar ve bu hastalarda koklear implant uygulamalarında karşılaşılan teknik güçlükler, klinik yönetimi daha karmaşık hâle getirebilir. Anestezi ve cerrahi girişimler sırasında zor havayolu yönetimi ve spinal kord yaralanması riski açısından dikkatli olunması büyük önem taşımaktadır. Erken tanı, eşlik eden anomalilere yönelik sistematik tarama ve disiplinler arası koordineli izlem, komplikasyonların önlenmesi ve uzun dönem klinik sonuçların iyileştirilmesi açısından kritik rol oynamaktadır. Bildirilen prevalansları ve nadir birliktelikleri bağlamsallaştırmak amacıyla güncel klinik, radyolojik ve genetik literatür narratif olarak gözden geçirilmiştir.
Anahtar kelimeler: Klippel-Feil sendromu, konjenital anomaliler, spinal hastalıklar

Cite as: Akıllı S, Işık O. Klippel-Feil syndrome: rare clinical associations and significance. Troia Medical Journal 2026;7(2):99-107.DOI: 10.55665/troiamedj.1797107

Corresponding author: Ozan IŞIK
Address: Ozan Işık, Deparment of Neurosurgery, Ağrı Training and Research Hospital, Çevre Yolu üzeri Suçatağı mevki, 04200 Ağrı Merkez/Ağrı, Türkiye
E-mail: dr.ozanisik@gmail.com
Date of arrival: 04.10.2025, *Date of acceptance*:26.01.2026

INTRODUCTION

Klippel Feil syndrome (KFS) is a rare congenital condition originally described by Maurice Klippel and André Feil in 1912. It is defined by congenital fusion of two or more cervical vertebrae resulting from impaired segmentation during early fetal development [1]. Population based studies estimate a prevalence of approximately 1 in 40,000 to 42,000 live births, with a slight female predominance [2,3]. Although the exact cause remains uncertain, both genetic factors, most notably variants in GDF6, GDF3, MEOX1, MYO18B, and RIPPLY2, and non genetic influences such as vascular disturbances or teratogenic exposures have been implicated in disease development [2].

Clinically, KFS is traditionally associated with the triad of a short neck, low posterior hairline, and limited cervical mobility. However, this classic presentation is not universal, and a substantial proportion of patients remain asymptomatic or minimally symptomatic until adolescence or adulthood [4]. Imaging reveals considerable variability in cervical fusion patterns, which has led to several classification systems. The most widely used scheme categorizes KFS into three types according to the extent and distribution of fused segments, ranging from extensive multilevel fusion to isolated single level involvement [5].

In addition to cervical vertebral fusion, KFS is commonly accompanied by abnormalities in other organ systems. Scoliosis is reported in up to 60 percent of patients, while genitourinary anomalies are observed in approximately two thirds of cases [6]. Congenital cardiac defects, most frequently ventricular septal defects, have been described in 15 to 35 percent of individuals, and hearing impairment affects nearly one third of patients, presenting as either conductive or sensorineural hearing loss [6,7]. Other recognized associations include Sprengel deformity, rib anomalies, neural tube related abnormalities such as diastematomyelia, Chiari malformation, and syringomyelia, as well as less common findings including pulmonary cysts and dermoid tumors [8].

The diagnosis of KFS is usually prompted by clinical findings and confirmed with imaging modalities such as plain radiography, computed tomography (CT), or magnetic resonance imaging (MRI). Genetic testing is generally reserved for selected familial cases or research purposes [2]. Because KFS often involves multiple organ systems and may predispose patients to neurological or cardiopulmonary complications, coordinated care involving specialties such as orthopedics, neurosurgery, cardiology, nephrology, audiology, and genetics plays a key role in long term management.

This article was designed as a narrative review focusing on rare clinical associations and their practical implications in KFS. We narratively reviewed English language clinical, radiologic, genetic, and surgical literature indexed in PubMed and major spine and neurosurgical journals, prioritizing cohort studies, systematic reviews, and illustrative case series published over the last two decades, with classic historical studies included where relevant.

Clinical Presentation

KFS is traditionally described by a clinical triad consisting of a short neck, a low posterior hairline, and marked limitation of cervical range of motion. Despite this classic description, up to one third of affected individuals may remain asymptomatic until adolescence or adulthood [9]. Recent epidemiologic studies based on pediatric CT series have reported prevalence rates as high as 1 in 8,300, which is substantially higher than earlier estimates of approximately 1 in 40,000 live births. These findings suggest that a considerable number of mild cases may remain unrecognized in routine clinical practice [10]. This discrepancy likely reflects ascertainment bias and differing case definitions. Historical birth prevalence estimates primarily capture clinically apparent syndromic cases, whereas imaging based pediatric CT studies also identify incidental congenital fusion patterns that may not meet full clinical criteria for KFS.

Radiographic Classification

Radiographically, KFS is subdivided into three types based on the number, contiguity, and level of fused segments [11].

Type I: Extensive multilevel fusion, often involving upper thoracic vertebrae.

Type II: Fusion of one or two adjacent cervical segments, frequently with hemivertebrae or block vertebrae.

Type III: Any cervical fusion in conjunction with thoracic or lumbar involvement.

This classification has important clinical implications. Extensive multilevel fusion (Type I) is associated with increased adjacent segment stress, instability, and neurologic risk, whereas Type II fusion typically confers more localized biomechanical vulnerability. Type III patterns often reflect more global spinal deformity and may be accompanied by cardiopulmonary and multisystem involvement.

Syndrome and Associations

KFS shows substantial phenotypic variability, and a wide range of extraspinal anomalies has been described in the literature. Among nonvertebral findings, intracranial dermoid and teratoid lesions are particularly rare. To date, approximately 23 cases of dermoid or teratoid tumors have been reported in the literature, based on published case reports and small case series. These lesions are most often located in the posterior fossa or at the craniocervical junction and, in some cases, have been associated with complications such as aseptic meningitis or hydrocephalus [12,13].

Otolaryngologic and Musculoskeletal Findings

Although patients with KFS are most commonly evaluated in orthopedic, neurosurgical, and physical medicine clinics, otolaryngologic manifestations are frequent and clinically relevant due to associated craniofacial and auditory anomalies. Hearing impairment represents the most frequent otologic finding in patients

with KFS and has been reported in approximately 30 to 60 percent of cases. Hearing loss may be conductive, most often related to middle ear dysplasia, ossicular chain malformations, or external auditory canal stenosis, or sensorineural, usually resulting from inner ear abnormalities such as cochlear hypoplasia, absent semicircular canals, or a narrow internal auditory canal [14,15]. Mixed hearing loss is uncommon, although isolated conductive hearing loss has been described in single case reports, reflecting the variability of middle ear involvement in this condition [16,17].

In addition to auditory involvement, dysphagia and airway related problems are clinically relevant concerns. Cervical vertebral fusion and restricted neck extension may alter the anatomy of the oropharyngeal inlet, leading to chronic swallowing difficulties, increased aspiration risk, and, in more severe cases, sleep related breathing disorders. Among pediatric patient series, up to 15 percent have required early intervention to address airway compromise [18]. Cleft palate and submucous cleft variants have also been reported in association with KFS, consistent with underlying midline developmental disturbances. Craniofacial abnormalities such as micrognathia, temporomandibular joint hypoplasia, and mandibular asymmetry may further complicate feeding and airway management and often require coordinated care involving maxillofacial surgery and speech therapy. Thyroid abnormalities, including ectopic thyroid tissue and thyroid hemiagenesis, have been reported as well and should be considered during comprehensive clinical evaluation [7].

Musculoskeletal involvement is similarly diverse and may contribute substantially to functional limitation. Sprengel deformity, defined as congenital elevation of the scapula, is observed in approximately 30 to 35 percent of patients and appears to correlate with the extent of cervical fusion. Bilateral involvement and omovertebral connections have been described and may occasionally necessitate surgical correction to improve shoulder function and appearance [19,20]. Congenital scoliosis is present in roughly 60 to 70 percent of affected individuals, with both curve magnitude and progression closely related to fusion pattern. Patients with extensive multilevel fusion typically demonstrate more severe deformity, with mean Cobb angles around 31 degrees, compared with those with isolated single level fusion or combined cervical and thoracic involvement [21]. Cervical ribs and bifid ribs are reported in approximately 20 to 25 percent of cases and may predispose patients to neurovascular compression syndromes such as thoracic outlet syndrome during adolescence or adulthood [22].

Split cord malformations, including diastematomyelia and other intraspinal abnormalities, have been well documented in association with congenital vertebral anomalies. These findings may be detected incidentally or may present with progressive myelopathy, worsening scoliosis, or neuropathic pain. Case reports and small series describe such anomalies in patients with KFS, while larger imaging based studies in congenital scoliosis populations demonstrate a high prevalence of intraspinal abnormalities, including diastematomyelia and syringomyelia, on MRI [23-25]. For this reason, early spinal MRI is recommended in patients with neurological symptoms, progressive spinal deformity, or atypical pain patterns. In addition, atlantoaxial instability has been reported in nearly half of patients with KFS and is associated with an increased risk of spinal cord injury even after minor trauma. Dynamic flexion and extension radiographs are therefore essential in selected patients, and surgical stabilization may be considered when significant instability is identified [26,27].

Overall, otolaryngologic and musculoskeletal manifestations constitute an important component of the clinical spectrum of KFS. Careful surveillance and timely intervention, supported by close collaboration among relevant specialties, are essential to minimize long term functional impairment and neurological complications. At the time of diagnosis, a baseline otolaryngologic and audiologic evaluation is recommended. This includes formal audiometry with characterization of hearing loss type, otoscopic examination, and targeted temporal bone imaging when structural anomalies or cochlear implantation are considered. In symptomatic patients, assessment for dysphagia and sleep disordered breathing using clinical screening tools, with polysomnography when indicated, should be considered.

Spinal and Neural Tube Malformations

KFS may coexist with spinal dysraphism and other intradural abnormalities, likely reflecting shared disturbances in axial segmentation during embryonic development. Split cord malformation, also referred to as diastematomyelia, has been repeatedly reported in association with vertebral segmentation disorders. Recent systematic reviews focusing on cervical split cord malformations indicate that a substantial proportion of reported cervical cases occur in the setting of Klippel-Feil type fusion patterns [28]. Earlier surgical literature suggested a broader spectrum of associated anomalies, including syringomyelia and myelomeningocele. However, current understanding is largely derived from contemporary case reports, small series, and systematic reviews rather than early archival cohorts.

Syringomyelia and Chiari malformations have also been described in patients with KFS. Their clinical relevance lies in the potential for progressive myelopathy, chronic pain, and worsening spinal deformity. For this reason, a low threshold for spinal MRI is recommended in patients presenting with neurological symptoms, progression of scoliosis, or atypical pain patterns [29]. Subsequent reports have documented both pediatric and adult presentations, including an eight year old child with cervical diastematomyelia and KFS [30], as well as asymptomatic adult patients in whom cervical split cord malformation was identified incidentally on MRI [25].

In syringomyelia, fluid filled cavities known as syrinxes develop within the spinal cord parenchyma, most commonly affecting the cervical or thoracic regions. Several series report syringomyelia in approximately

15 to 30 percent of Klippel-Feil cohorts, with syrinxes extending over variable numbers of vertebral levels. The development of syringomyelia in this setting is thought to be related to altered cerebrospinal fluid dynamics at sites of congenital bony fusion. Coexistence with Chiari type I malformation, defined by caudal displacement of the cerebellar tonsils through the foramen magnum, has also been reported in a notable proportion of cases [31]. When diastematomyelia and syringomyelia occur together, the risk of progressive neurological impairment, neuropathic pain, and accelerated scoliosis progression appears to be increased [2].

Tethered cord syndrome, characterized by abnormal fixation of the distal spinal cord, has been reported in up to 24 percent of patients with KFS undergoing detailed neuroimaging. This finding is often accompanied by diastematomyelia or lipomyelomeningocele [32]. Clinical manifestations may include back pain, lower extremity weakness, or bladder dysfunction, and surgical detethering has been shown to stabilize or improve neurological outcomes in selected patients.

Congenital vertebral anomalies in KFS are not limited to simple cervical fusion. Adjacent segment abnormalities such as hemivertebrae, block vertebrae, and butterfly vertebrae are frequently observed and contribute to the development of congenital scoliosis in approximately 60 to 70 percent of affected individuals. Curve severity is closely related to the underlying fusion pattern. Patients with extensive multilevel fusion typically demonstrate the greatest deformity, with mean Cobb angles around 31 degrees, whereas those with isolated single level fusion show milder curvature, averaging approximately 9 degrees [33,34].

Given the frequency and heterogeneity of these abnormalities, MRI remains the preferred modality for identifying intradural pathology such as syrinx formation, fibrous septations, and cord tethering. CT myelography may provide additional detail regarding bony septa and fusion anatomy in selected cases [2]. Dynamic radiographic evaluation using flexion and extension views is useful for assessing segmental instability, particularly at the atlantoaxial junction, where hypermobility has been reported in nearly half of patients with extensive cervical fusion [31]. Long term multidisciplinary follow up, incorporating neurosurgical, orthopedic, and rehabilitative care, is essential to monitor for progressive deformity, neurological deterioration, and secondary degenerative changes.

KFS is defined by congenital fusion of cervical vertebrae, yet its musculoskeletal effects frequently extend beyond the cervical region, most notably through the development of scoliosis and related spinal deformities. Multiple clinical series report scoliosis in approximately 60 to 70 percent of patients, with both prevalence and severity influenced by the pattern of vertebral fusion. In one cohort of 52 patients, scoliosis was identified in 53.3 percent of young individuals with KFS, particularly among those with Type III fusion patterns and associated hemivertebrae [35]. Similarly, a landmark study reported scoliosis rates ranging from 67 to 70 percent, with mean Cobb angles of 31 degrees in Type I, 9 degrees in Type II, and 23 degrees in Type III disease, supporting the observation that more extensive fusion is associated with greater curve severity [36].

Abnormal vertebral segmentation alters normal spinal biomechanics by increasing mechanical stress at adjacent mobile segments. This process predisposes patients to compensatory curvature, accelerated degenerative changes, and progressive spinal deformity. Early identification through standing posteroanterior and lateral radiographs is therefore critical. Curve progression is most pronounced during periods of rapid growth, and regular clinical and radiographic surveillance is recommended until skeletal maturity. Surgical intervention may be indicated for curves exceeding 40 degrees or in patients with significant pain or neurological compromise.

From a practical standpoint, spinal MRI should be obtained at diagnosis in patients with Type I or Type III fusion patterns, neurological symptoms, or early onset scoliosis. Whole spine MRI allows assessment for syringomyelia, split cord malformation, and tethered cord, while brain MRI should be added when craniovertebral junction anomalies, headaches, cranial nerve findings, or rapidly progressive scoliosis are present. Reported prevalence rates should be interpreted as ranges derived from heterogeneous cohorts rather than precise estimates.

Genitourinary Abnormalities

Genitourinary anomalies constitute an important extracervical manifestation of KFS. In classical patient cohorts, clinically relevant renal or urinary tract abnormalities have been reported in approximately 64 percent of cases, most commonly unilateral renal agenesis detected by intravenous urography or ultrasonography [37].

Other reported abnormalities include renal ectopia, such as cross fused or pelvic kidneys, horseshoe kidney, vesicoureteral reflux, ureteropelvic junction obstruction, and undescended testes. These findings are supported by a large meta analysis of patients with congenital scoliosis that was not restricted to KFS. In that study, genitourinary anomalies were identified in 22.9 percent of patients, and 13.9 percent required surgical intervention. The most frequently reported abnormalities were unilateral renal agenesis at 28.6 percent, renal ectopia at 13.6 percent, and obstructive uropathy at 7.5 percent [38].

Given both the high prevalence and the potential for long term clinical consequences, renal ultrasonography is recommended at the time of KFS diagnosis, with subsequent follow up guided by initial imaging findings. Referral for urologic evaluation is appropriate in the presence of structural abnormalities, recurrent urinary tract infections, or evidence of urinary obstruction. The frequent coexistence of vertebral and genitourinary anomalies likely reflects a shared embryologic disturbance affecting paraxial mesoderm development, with involvement of both the axial skeleton and the urogenital ridge. Accordingly, long term care should involve

coordinated follow up between orthopedic and urology or nephrology services in order to minimize the risk of progressive spinal deformity and renal related morbidity.

Cardiac and Respiratory Implications

Patients with KFS often have clinically important cardiopulmonary comorbidities that arise from both structural abnormalities of the thoracic cage and intrinsic congenital heart disease. Early case series and more recent cohort studies report cardiac anomalies in approximately 15 to over 30 percent of patients, with ventricular septal defects being the most frequently identified congenital cardiac lesion [39,22]. In a comprehensive review of published case reports from the past decade, ventricular septal defects accounted for nearly 40 percent of all documented cardiac abnormalities, followed by atrial septal defects, patent ductus arteriosus, and more complex malformations such as tetralogy of Fallot and coarctation of the aorta [22]. Total anomalous pulmonary venous connection has been reported only rarely, and successful surgical correction has been described without perioperative complications related to the cervical spine [39].

In addition to congenital heart disease, patients with KFS may develop arrhythmias and cardiomyopathic changes secondary to abnormal chest wall mechanics and chronic volume overload. One reported case involved a 39 year old man with frequent ventricular trigeminy and bigeminy detected on Holter monitoring, accompanied by mild to moderate pulmonary hypertension with a mean pulmonary artery pressure of approximately 35 mm Hg [40]. In this patient, a restrictive thoracic cage resulting from extensive cervical and thoracic vertebral fusion contributed to impaired pulmonary expansion, reduced right ventricular filling, and subsequent right sided cardiac strain.

Pulmonary involvement in KFS ranges from subclinical restrictive lung patterns to overt respiratory insufficiency. Early observations by Baga and colleagues described two siblings with progressive pulmonary dysfunction, with forced vital capacity values as low as 45 percent of predicted and diffusion abnormalities consistent with restrictive physiology. Subsequent functional imaging studies supported these findings, demonstrating elevated pulmonary artery pressures and reduced exercise tolerance in patients with marked thoracic deformity. Chronic hypoventilation and dependent atelectasis may further predispose affected individuals to recurrent lower respiratory tract infections, thereby increasing overall morbidity [41].

Reports from the anesthesiology literature emphasize the complexity of perioperative cardiopulmonary management in this patient population. In one case, a 52 year old patient undergoing occipito cervical stabilization developed significant hemodynamic instability after being placed in the prone position, including persistent tachycardia, hypotension, and transient electrocardiographic changes, despite aggressive fluid administration and vasoactive therapy [42]. Postoperative respiratory failure required prolonged mechanical ventilation, likely related to diaphragmatic dysfunction associated with phrenic nerve involvement and reduced chest wall compliance.

Pulmonary hypertension has been described in several adult patients with KFS and is thought to result from chronic hypoxia and increased pulmonary vascular resistance. In the previously described 39 year old patient, echocardiography demonstrated right atrial enlargement and tricuspid regurgitation, findings consistent with evolving right heart dysfunction [40]. While medical therapy with pulmonary vasodilators and diuretics may alleviate symptoms, long term outcomes depend largely on the severity of the underlying restrictive thoracic pathology, which is often difficult to modify because of fixed skeletal abnormalities.

Taken together, cardiopulmonary involvement in KFS reflects a combination of congenital cardiac defects, restrictive lung disease related to thoracic deformity, pulmonary hypertension, rhythm disturbances, and increased perioperative risk. Early and coordinated evaluation involving cardiology, pulmonology, anesthesiology, and orthopedic surgery is therefore essential to optimize clinical management, guide surgical planning, and support long term follow up.

Genetic Heterogeneity

KFS represents a congenital vertebral segmentation disorder with marked genetic heterogeneity. Both monogenic and oligogenic inheritance patterns have been described, and considerable locus heterogeneity has been observed across different patient cohorts. Early family based studies demonstrated autosomal dominant and autosomal recessive modes of inheritance, while experimental animal models implicated members of the PAX gene family and components of the Notch signaling pathway in abnormal axial patterning [43].

Subsequent gene discovery studies identified five genes that are most consistently associated with KFS, namely GDF6, GDF3, MEOX1, MYO18B, and RIPPLY2. Variants in these genes account for a subset of familial and sporadic cases. GDF6 and GDF3 are members of the transforming growth factor beta superfamily and play a key role in somitic development and neural crest cell differentiation. Disruption of these genes in animal models results in vertebral segmentation defects that closely resemble the human phenotype. MEOX1 encodes a homeobox transcription factor that is critical for paraxial mesoderm development, and recessive mutations in this gene have been associated with contiguous multilevel cervical fusion and more severe extraspinal involvement [32]. MYO18B and RIPPLY2 also contribute to somite boundary formation, and variants of uncertain significance in MYO18B have been reported in exome sequencing studies, highlighting ongoing challenges in variant interpretation [32].

However, single gene explanations do not fully account for the wide phenotypic variability observed in KFS. A large burden analysis examining 96 candidate genes involved in vertebral segmentation demonstrated an oligogenic architecture, with additional risk attributed to rare variants in genes such as BAZ1B, FREM2, SUFU,

VANGL1, and KMT2D [32]. Whole exome sequencing performed in patients with the distinctive sandwich fusion subtype further identified pathogenic variants in PAX1, MYO18B, and FGFR2, suggesting that specific genetic profiles may underlie certain radiographic patterns and expanding the known genetic spectrum beyond the initially described genes [44].

Multigene panel studies have, in some cases, failed to identify pathogenic variants in the commonly implicated genes, reinforcing the concept of substantial genetic heterogeneity and the likelihood of additional, as yet unidentified, loci. At the same time, these studies have proposed new candidate genes, including COL6A1, COL6A2, GLI3, FLNB, CHRNG, MYH3, POR, and TNXB, thereby broadening the range of genetic contributors linked to KFS [44]. In an effort to improve genotype phenotype correlations, four genetic radiographic classes, designated KF1 through KF4, have been proposed, with certain genes appearing more frequently in association with specific fusion patterns and degrees of severity [45].

This multilocus and multivariant model has important clinical implications. Genetic evaluation of patients with KFS increasingly relies on targeted gene panels and exome sequencing, particularly in familial cases. Interpretation of identified variants requires careful consideration of population frequency data, computational pathogenicity predictions, and functional evidence when available. Overall, current evidence supports the view that KFS is not a single gene disorder, but rather a spectrum of segmentation abnormalities arising from disruption of an interconnected network of developmental genes, in which both primary pathogenic variants and modifying factors contribute to the final clinical presentation [44].

Genetic testing may be considered in patients with familial clustering, severe multilevel fusion, syndromic features, or additional congenital anomalies, as well as for prenatal counseling. However, many identified variants remain of uncertain significance, and genetic findings do not always alter clinical management, underscoring the need for cautious interpretation.

Trauma-Related Neurologic Injury

Patients with KFS are at increased risk of serious neurological injury even after relatively minor cervical trauma. This vulnerability is related to congenital vertebral fusion, altered spinal biomechanics, and the frequent presence of cervical spinal stenosis. Fused vertebral segments form rigid blocks that transfer mechanical stress to adjacent mobile levels, leading to segmental hypermobility. Over time, this increased motion predisposes nonfused segments to accelerated degenerative changes, disc herniation, and instability. Several case series have shown that low energy trauma, such as minor falls or low velocity motor vehicle accidents, can result in acute spinal cord compression at the junctions between fused and mobile segments, often due to disc protrusion into the spinal canal with subsequent cord contusion [46].

Congenital vertebral fusion in KFS commonly coexists with developmental narrowing of the cervical spinal canal. Classic reports describe catastrophic spinal cord injury occurring after minimal trauma in patients with underlying stenosis, as reduced canal diameter amplifies the compressive effects of small disc herniations or osteophytic changes [25]. Dynamic flexion and extension imaging has demonstrated that transient subluxations at unstable junctions may further compromise the spinal canal and increase the risk of myelopathy. In one report, a middle aged patient with previously unrecognized fusion at the C2 and C3 levels developed tetraplegia following a minor rear end collision. Imaging revealed acute disc herniation at the mobile segment adjacent to the fused block, with spinal cord edema extending across multiple levels [47]. Other reports have documented Brown Sequard type neurological presentations after trivial cervical hyperextension in patients with more extensive fusion patterns, illustrating how altered canal anatomy can result in focal and asymmetric cord injury [48]. In another case, congenital fusion at multiple cervical levels predisposed a patient to an odontoid fracture and subsequent lower cervical spinal cord injury after a motorcycle accident, highlighting the tendency for traumatic forces to be transmitted to anatomically distant segments [49].

Imaging findings following trauma in patients with KFS may be atypical. Fractures can occur through fused vertebral segments or at transitional zones, sometimes with minimal osseous displacement. Advanced imaging with CT and MRI frequently reveals spinal cord contusions, intramedullary hemorrhage, or osseous septa causing focal canal compromise. Karasick and colleagues described distinctive imaging patterns in this population, including fractures traversing fused vertebrae that were associated with marked spinal cord edema on MRI despite limited bony displacement [50]. For this reason, a low threshold for MRI is recommended in any patient with known or suspected KFS who presents with cervical trauma, even when initial clinical findings appear mild.

Given the substantial risk of irreversible neurological injury, patients with KFS should receive specific counseling regarding activity modification and strategies for fall prevention. General recommendations include avoidance of contact sports and prompt medical evaluation after any head or neck injury. In addition, patients found to have cervical spinal stenosis may benefit from early referral for surgical evaluation to consider prophylactic decompression or stabilization, particularly when dynamic imaging demonstrates significant instability [25].

Although timely surgical decompression and stabilization can preserve or improve neurological function in some traumatic cases, clinical outcomes remain variable. Rehabilitation strategies must address not only the consequences of spinal cord injury, such as spasticity, impaired mobility, and autonomic dysfunction, but also the underlying cervical rigidity and the risk of adjacent segment degeneration. Long term prognosis depends

on injury severity, the speed of intervention, and the degree of residual spinal canal compromise.

Red flag symptoms following even minor cervical trauma include new onset paresthesia or weakness, gait disturbance, Lhermitte type sensations, urinary retention, or severe neck pain. In such cases, urgent CT and MRI evaluation is warranted even if initial plain radiographs appear unremarkable. Flexion extension radiographs are reserved for patients with pain, neurological symptoms, suspected instability, or preoperative assessment.

Anesthetic Challenges

Anesthetic management of patients with KFS is challenging because of marked cervical spine abnormalities, limited neck mobility, and the frequent presence of associated comorbid conditions. Fixed cervical deformity and a shortened neck require careful preoperative assessment of the airway. In many cases, this includes awake fiberoptic examination or videolaryngoscopy to evaluate glottic exposure and to plan alternative airway strategies if needed [51,52]. Conventional Mallampati classification is often insufficient in this population. When airway narrowing is suspected, dynamic imaging methods such as ultrasonography or CT may assist in estimating thyromental distance and identifying potential subglottic narrowing [53].

Preoperative evaluation should also include detailed imaging of the cervical spine to define fusion levels, assess atlantoaxial stability, and identify coexisting spinal canal stenosis. Equipment for advanced airway management, including fiberoptic bronchoscopes, videolaryngoscopes, and supraglottic airway devices, should be readily available, and preparation for an emergency surgical airway is recommended [54]. The choice of induction technique depends largely on the degree of cervical immobility. In patients with severe restriction, awake fiberoptic intubation under topical anesthesia may reduce the risk of neurological injury, whereas in less severe cases, video assisted intubation techniques may be appropriate [55]. Comparative studies have shown higher first attempt success rates with videolaryngoscopy and flexible fiberoptic techniques compared with direct laryngoscopy in patients with KFS, although outcomes remain highly dependent on operator experience [56].

Pediatric patients present additional challenges related to smaller airway dimensions, increased susceptibility to airway edema, and limited cooperation. In these cases, inhalational induction with maintenance of spontaneous ventilation is often preferred until the airway is secured [57]. Surgical procedures performed in the prone position, such as correction of Sprengel deformity, require meticulous positioning, careful padding of pressure points, and continuous confirmation of endotracheal tube placement using capnography and auscultation. In obstetric patients with KFS undergoing cesarean delivery, close coordination among obstetric, anesthetic, and neonatal teams is essential. Regional anesthesia techniques may be favored to avoid airway manipulation, although the spread of neuraxial anesthesia can be unpredictable because of underlying vertebral anomalies [58].

Thoracic deformities and limited chest wall mobility may contribute to restrictive lung physiology and hypoventilation during anesthesia. Ventilation strategies should therefore emphasize low tidal volumes with appropriate respiratory rates to maintain adequate minute ventilation [59]. Hemodynamic instability may occur during prone positioning or cervical manipulation, and invasive arterial pressure monitoring should be considered in patients with significant cardiopulmonary disease. Reports of intraoperative tachyarrhythmias and pulmonary hypertension further highlight the need for continuous cardiovascular monitoring and readiness to administer vasoactive medications when required [54].

After surgery, tracheal extubation should be performed only when the patient is fully awake and protective airway reflexes have returned. Prolonged postoperative monitoring in an intensive care setting may be necessary for individuals with substantial comorbidities or those who required difficult or prolonged airway management [54]. Optimal perioperative care is best achieved through a multidisciplinary approach involving anesthesiology, neurosurgery, orthopedics, pulmonology, and otolaryngology, with the goal of minimizing airway related, neurological, and musculoskeletal complications in this high risk patient population.

A structured perioperative approach includes preoperative imaging to define fusion extent, craniocervical instability, and spinal canal dimensions, followed by a predefined airway plan with primary and rescue strategies. Strict neutral neck positioning should be maintained, and postoperative monitoring thresholds should be lower in patients with obstructive sleep apnea, restrictive lung disease, or prolonged airway instrumentation.

Conclusion

KFS is characterized by clinical manifestations such as short neck, low hairline at the back of the head, and restricted neck mobility resulting from abnormal cervical spine fusion during fetal development. Additionally, it is associated with congenital anomalies and other health issues. This syndrome is linked with various conditions including scoliosis, genitourinary abnormalities, Sprengel deformity, cardiac abnormalities, and hearing loss.

Key clinical points that should not be overlooked include:

1. Renal ultrasonography at diagnosis due to the high prevalence of genitourinary anomalies.
2. Baseline otolaryngologic and audiologic assessment.
3. Early MRI based screening for neural axis abnormalities in high risk patients.
4. Trauma counseling with a low threshold for advanced imaging.
5. Anticipation of difficult airway and spinal instability during anesthesia and surgery.

Conflict of interest: None
Funding: None

REFERENCES

1. Ding L, Wang X, Sun Y, et al. Prevalence and Risk Factors of Surgical Treatment for Klippel-Feil Syndrome. Front Surg 2022;9:885989.
2. Menger RP, Rayi A, Notarianni C. Klippel Feil Syndrome. [Updated 2024 May 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493157/
3. Ekin EE, Altunrende ME. Klippel-Feil syndrome: Should additional examination be conducted? Eur Spine J 2024;33(6):2347-53.
4. Frikha R. Klippel-Feil syndrome: a review of the literature. Clin Dysmorphol 2020;29(1):35-7.
5. Samartzis D, Kalluri P, Herman J, Lubicky JP, Shen FH. 2008 Young Investigator Award: The role of congenitally fused cervical segments upon the space available for the cord and associated symptoms in Klippel-Feil patients. Spine (Phila Pa 1976) 2008;33(13):1442-50.
6. Mahiroğullari M, Ozkan H, Yildirim N, Cilli F, Güdemez E. Klippel-Feil sendromu ve eşlik eden doğumsal anomaliler: 23 olgunun incelenmesi [Klippel-Feil syndrome and associated congenital abnormalities: evaluation of 23 cases]. Acta Orthop Traumatol Turc 2006;40(3):234-9.
7. Stewart C, Otto AL, Fisher M, et al. Otolaryngological Presentations of Klippel-Feil Syndrome: A Systematic Review. Cureus 2024;16(11):e73986.
8. Siddiqui F, Talal Ashraf M, Khuzzaim Khan M, et al. A Comprehensive Approach to the Diagnosis and Management of Klippel Feil Syndrome. Arch Razi Inst 2023;78(6):1868-72.
9. Jae-Min Park A, Nelson SE, Mesfin A. Klippel-Feil Syndrome: Clinical Presentation and Management. JBJS Rev 2022;10(2):e21.00166.
10. Moses JT, Williams DM, Rubery PT, Mesfin A. The prevalence of Klippel-Feil syndrome in pediatric patients: analysis of 831 CT scans. J Spine Surg 2019;5(1):66-71.
11. Samartzis DD, Herman J, Lubicky JP, Shen FH. Classification of congenitally fused cervical patterns in Klippel-Feil patients: epidemiology and role in the development of cervical spine-related symptoms. Spine (Phila Pa 1976) 2006;31(21):E798-E804.
12. Pai VV, Lowe LH, Castillo M, Huang BY, Shao L. Posterior fossa dermoid cysts in association with Klippel-Feil syndrome: report of three cases. AJNR Am J Neuroradiol 2007;28(10):1926-8.
13. Adorno A, Alafaci C, Sanfilippo F, et al. Malignant teratoma in Klippel-Feil syndrome: a case report and review of the literature. J Med Case Rep 2015;9:229.
14. Yildirim N, Arslanoğlu A, Mahiroğullari M, Sahan M, Ozkan H. Klippel-Feil syndrome and associated ear anomalies. Am J Otolaryngol 2008;29(5):319-25.
15. Reddy YM, Lepcha A, Augustine AM, Philip A. Cochlear Implant in Klippel-Feil Syndrome: Challenges and Concerns. Indian J Otolaryngol Head Neck Surg 2022;74 (Suppl 3):3901-5.
16. Sakai M, Miyake H, Shinkawa A, Komatsu N. Klippel-Feil syndrome with conductive deafness and histological findings of removed stapes. Ann Otol Rhinol Laryngol 1983;92(2 Pt 1):202-6.
17. Dubey SP, Ghosh LM. Klippel-Feil syndrome with congenital conductive deafness: report of a case and review of literature. Int J Pediatr Otorhinolaryngol 1993;25(1-3):201-8.
18. Kenna MA, Irace AL, Strychowsky JE, et al. Otolaryngologic Manifestations of Klippel-Feil Syndrome in Children. JAMA Otolaryngol Head Neck Surg. 2018;144(3):238-43.
19. Stelzer JW, Flores MA, Mohammad W, Esplin N, Mayl JJ, Wasyliw C. Klippel-Feil Syndrome with Sprengel Deformity and Extensive Upper Extremity Deformity: A Case Report and Literature Review. Case Rep Orthop 2018;2018:5796730.
20. Hensinger RN, Lang JE, MacEwen GD. Klippel-Feil syndrome; a constellation of associated anomalies. J Bone Joint Surg Am 1974;56(6):1246-53.
21. Litrenta J, Bi AS, Dryer JW. Klippel-Feil Syndrome: Pathogenesis, Diagnosis, and Management. J Am Acad Orthop Surg 2021;29(22):951-60.
22. Niewchas A, Alkhatib S, Stewart C, et al. Cardiovascular Findings in Klippel-Feil Syndrome: A Systematic Review. Cureus 2024;16(10):e72540.
23. Karim Ahmed A, Howell EP, Harward S, et al. Split cord malformation in adults: Literature review and classification. Clin Neurol Neurosurg 2020;193:105733.
24. Wang X, Yu Y, Yang N, Xia L. Incidence of intraspinal abnormalities in congenital scoliosis: a systematic review and meta-analysis. J Orthop Surg Res 2020;15(1):485.
25. Srinivasan ES, Mehta VA, Smith GC, Than KD, Terry AR. Klippel-Feil Syndrome with Cervical Diastematomyelia in an Adult with Extensive Cervicothoracic Fusions: Case Report and Review of the Literature. World Neurosurg 2020;139:274-80.
26. Vaidyanathan S, Hughes PL, Soni BM, Singh G, Sett P. Klippel-Feil syndrome - the risk of cervical spinal cord injury: a case report. BMC Fam Pract 2002;3:6.
27. Smith BA, Griffin C. Klippel-Feil syndrome. Ann Emerg Med 1992;21(7):876-9.
28. Sreenivasan R, Sharma R, Borkar SA, et al. Cervical Split Cord Malformations: A Systematic Review. Neurol India 2020;68(5):994-1002.
29. Zhang JF, Strelko O, Komarov O, et al. Cervical Diastematomyelia: A Case Presentation and Systematic Review. J Neurol Surg Rep 2024;85(2):e74-e82.
30. Andronikou S, Fieggeru AG. Klippel-Feil syndrome with cervical diastematomyelia in an 8-year-old boy. Pediatr Radiol 2001;31(9):636.
31. Tian Y, Fan D, Xu N, Wang S. "Sandwich Deformity" in Klippel-Feil syndrome: A "Full-Spectrum" presentation of associated craniovertebral junction abnormalities. J Clin Neurosci 2018;53:247-9.
32. Li Z, Zhao S, Cai S, et al. The mutational burden and oligogenic inheritance in Klippel-Feil syndrome. BMC Musculoskelet Disord 2020;21(1):220.
33. Ali M, Iliev B, Enchev Y, Boshev G, Demirci A. Unique Case of Cervical Split Cord Malformation Type II and Klippel-Feil Syndrome in a Male Patient Symptomatically Treated With Ultrasound-Guided Botulinum Toxin Injection. Cureus 2024;16(9):e69531.
34. Zhang JF, Strelko O, Komarov O, et al. Cervical Diastematomyelia: A Case Presentation and Systematic Review. J Neurol Surg Rep 2024;85(2):e74-e82.
35. Samartzis D, Kalluri P, Herman J, Lubicky JP, Shen FH. Cervical scoliosis in the Klippel-Feil patient. Spine (Phila Pa 1976) 2011;36(23):E1501-8.

36. Thomsen MN, Schneider U, Weber M, Johannisson R, Niethard FU. Scoliosis and congenital anomalies associated with Klippel-Feil syndrome types I-III. Spine (Phila Pa 1976) 1997;22(4):396-401.
37. Moore WB, Matthews TJ, Rabinowitz R. Genitourinary anomalies associated with Klippel-Feil syndrome. J Bone Joint Surg Am 1975;57(3):355-7.
38. Lorente R, Mariscal G, Lorente A. Incidence of genitourinary anomalies in congenital scoliosis: systematic review and meta-analysis. Eur Spine J 2023;32(11):3961-9.
39. Masuda H, Arikawa K, Yuda T, Taira A. Total anomalous pulmonary venous connection associated with Klippel-Feil syndrome: a case report. The Japanese Journal of Thoracic Surgery 1991;44(5):417-20.
40. Bridglal RM. Cardiopulmonary Complications of Klippel-Feil Syndrome: A Case Report. Cureus 2024;16(8):e67303.
41. Baga N, Chusid EL, Miller A. Pulmonary disability in the Klippel-Feil syndrome. A study of two siblings. Clin Orthop Relat Res 1969;67:105-10.
42. Teoh DC, Williams DL. Adult Klippel-Feil syndrome: haemodynamic instability in the prone position and postoperative respiratory failure. Anaesth Intensive Care 2007;35(1):124-7.
43. Tracy MR, Dormans JP, Kusumi K. Klippel-Feil syndrome: clinical features and current understanding of etiology. Clin Orthop Relat Res 2004;(424):183-90.
44. Xu N, Hung KL, Gong X, et al. Genetic insights into the 'sandwich fusion' subtype of Klippel-Feil syndrome: novel FGFR2 mutations identified by 21 cases of whole-exome sequencing. Orphanet J Rare Dis 2024;19(1):141.
45. Clarke RA, Catalan G, Diwan AD, Kearsley JH. Heterogeneity in Klippel-Feil syndrome: a new classification. Pediatr Radiol 1998;28(12):967-74.
46. Agrawal A, Badve AM, Swarnkar N, Sarda K. Disc prolapse and cord contusion in a case of Klippel-Feil syndrome following minor trauma. Indian J Orthop 2009;43(2):210-2.
47. Bhavana Chowdary M, S M, Kumar D, Kk A. A Case Report of Klippel-Feil Syndrome Presenting as Tetraplegia. Cureus 2023;15(6):e41241.
48. Zhang S, Wang Z, Zhang S, et al. Brown Sequard syndrome in a patient with Klippel-Feil syndrome following minor trauma: a case report and literature review. BMC Musculoskelet Disord 2023;24(1):722.
49. Graillon T, Pech-Gourg G, Adetchessi T, Metellus P, Dufour H, Fuentes S. Double traumatic cervical spine lesion (odontoid fracture and spinal cord injury) and Klippel-Feil syndrome. Neurochirurgie. 2012;58(6):372-5.
50. Karasick D, Schweitzer ME, Vaccaro AR. The traumatized cervical spine in Klippel-Feil syndrome: imaging features. AJR Am J Roentgenol 1998;170(1):85-8.
51. Chua CC, Cruz MAB. Anesthetic Management of a Patient with Klippel-Feil Syndrome for Laparoscopic Pelvic Surgery: A Case Report. Acta Med Philipp 2024;58(9):48-53.
52. Chura M, Odo N, Foley E, Bora V. Cervical Deformity and Potential Difficult Airway Management in Klippel-Feil Syndrome. Anesthesiology 2018;128(5):1007.
53. Stallmer ML, Vanaharam V, Mashour GA. Congenital cervical spine fusion and airway management: a case series of Klippel-Feil syndrome. J Clin Anesth 2008;20(6):447-51.
54. Hase Y, Kamekura N, Fujisawa T, Fukushima K. Repeated anesthetic management for a patient with Klippel-Feil syndrome. Anesth Prog 2014;61(3):103-6.
55. Khawaja OM, Reed JT, Shaefi S, Chitilian HV, Sandberg WS. Crisis resource management of the airway in a patient with Klippel-Feil syndrome, congenital deafness, and aortic dissection. Anesth Analg 2009;108(4):1220-5.
56. Ahuja V, Kazal S, Gombar S, Thapa D, Bahadur R. Glidescope(®) for predicted difficult airway in Klippel-Feil Syndrome. J Anaesthesiol Clin Pharmacol 2012;28(4):532-4.
57. Altay N, Yüce HH, Aydoğan H, Dörterler ME. Airway management in newborn with Klippel-Feil syndrome. Braz J Anesthesiol 2016;66(5):551-3.
58. Kavanagh T, Jee R, Kilpatrick N, Douglas J. Elective cesarean delivery in a parturient with Klippel-Feil syndrome. Int J Obstet Anesth 2013;22(4):343-8.
59. Jena BR, Mishra RK, Dube SK, Rath GP, Malik V, Gurjar HK. Perioperative Management of a Child with Klippel-Feil Syndrome and Severe Uncorrected Aortic Stenosis Undergoing Cervical Spine Stabilization. J Pediatr Neurosci 2021;16(3):257-60.