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ORIGINAL ARTICLE

Demographics, presentation and symptoms of patients with Klippel-Feil syndrome: analysis of a global patient-reported registry

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Abstract

Introduction Klippel-Feil syndrome (KFS) occurs due to failure of vertebral segmentation during development. Minimal research has been done to understand the prevalence of associated symptoms. Here, we report one of the largest collections of KFS patient data.

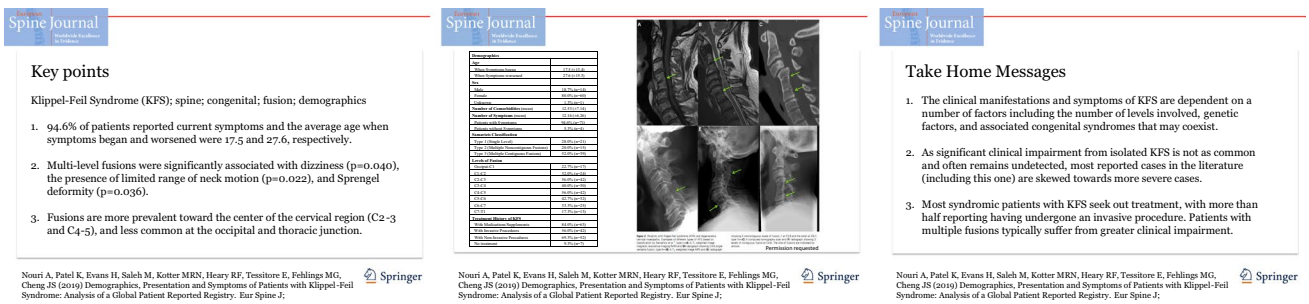
Methods Data were obtained from the CoRDS registry. Participants with cervical fusions were categorized into Type I, II, or III based on the Samartzis criteria. Symptoms and comorbidities were assessed against type and location of fusion.

Results Seventy-five patients (60F/14M/1 unknown) were identified and classified as: Type I, $n=21(28\%)$; Type II, $n=15(20\%)$; Type III, $n=39(52\%)$. Cervical fusion by level were: OC–C1, $n=17(22.7\%)$, C1–C2, $n=24(32\%)$; C2–C3, $n=42(56\%)$; C3–C4, $n=30(40\%)$; C4–C5, $n=42(56\%)$; C5–C6, $n=32(42.7\%)$; C6–C7, $n=25(33.3\%)$; C7–T1, $n=13(17.3\%)$. 94.6% of patients reported current symptoms and the average age when symptoms began and worsened were 17.5 ($\pm$ 13.4) and 27.6 ($\pm$ 15.3), respectively. Patients reported to have a high number of comorbidities including spinal, neurological and others, a high frequency of general symptoms (e.g., fatigue, dizziness) and chronic symptoms (limited range of neck motion [LROM], neck/spine muscles soreness). Sprengel deformity was reported in 26.7%. Most patients reported having received medication and invasive/non-invasive procedures. Multilevel fusions (Samartzis II/III) were significantly associated with dizziness ($p=0.040$), the presence of LROM ($p=0.022$), and Sprengel deformity ($p=0.036$).

Conclusion KFS is associated with a number of musculoskeletal and neurological symptoms. Fusions are more prevalent toward the center of the cervical region, and less common at the occipital/thoracic junction. Associated comorbidities including Sprengel deformity may be more common in KFS patients with multilevel cervical fusions.

Graphical abstract

These slides can be retrieved under Electronic Supplementary Material.



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Keywords Klippel-Feil syndrome · Pain · Clinical presentation · Demographics · Congenital · Cervical spine

Introduction

Klippel-Feil syndrome (KFS) is a clinical syndrome classically represented by the fusion of at least 1 pair of adjacent cervical vertebrae, often resulting in a shortened neck, lower hairline, and depending on the level of fusion, limitation in neck mobility [1–3]. However, this clinical triad has been reported to present in only an estimated 34–74% of patients [1]. It has been previously estimated that the prevalence of KFS is 0.71% using cadaver bones [4], and a more recently a study using cervical CT scans at an emergency department reported a prevalence of 0.58% [5], corroborating this earlier estimation.

The clinical impact of KFS can range from indolent, where patients are typically unaware of having a cervical fusion, to severe, where patients are typically identified at birth and have multiple levels of fusions and associated congenital anomalies in other body systems. Patients on the severe spectrum can suffer from neurological manifestations, but also may experience severe quality of life effects via a number of comorbidities, which may include musculoskeletal anomalies (e.g., Sprengel's deformity), and more rarely, visceral or otolaryngologic aberrations [6]. Contrarily, patients with isolated cervical fusion with or without their knowledge of it, may be predisposed to accelerated wear of adjacent cervical vertebrae and potentially may develop Degenerative Cervical Myelopathy (DCM) at a greater incidence than the general population [3, 7–9]. Indeed, it has been estimated that the relative risk of DCM development in KFS is 3.3 [3].

Unfortunately, most reports on KFS have been limited to case reports and series, typically describing patients with unique or more severe presentations, as significant clinical impairment from isolated KFS is not as common and is unlikely to merit publication. This has limited the ability to adequately describe the demographics and clinical symptoms most impactful to this population group. To address this knowledge gap, the present paper reports on patient-reported data derived from a rare disease registry put together by non-profit organizations.

Methods

Patient-reported data were derived from a single rare disease registry put together by two separate surveys from two different non-profit organizations which collected data on their members: (1) Sanford Health's CoRDS Registry, which specializes in collecting data from patients with rare conditions, (2) and Klippel-Feil syndrome freedom, which is an organization for providing information for patients and raising awareness of KFS. The data was obtained in January, 2018. Additionally, Sanford Health states in their survey that they regularly contact individuals in their registry for updates. Sanford Health works with patients, advocacy groups and researchers, and agglomerates the data in a rare disease registry. Patients and not doctors provide the responds to the data. Patients used their knowledge and therefore not all data points were filled out if patients did not know the answer to a specific question. Approval for use of the data was obtained from the respective organizations, and the data relayed to us for the purpose of this study were anonymized. The Klippel-Feil syndrome Freedom survey consisted of 115 questions split across several major topics: diagnosis, associated conditions, genetic testing, family history, children/pregnancy, general symptoms, spine/shoulder/head-related pain, pain management, demographics, and emotional impact. In total, 129 KFS patients completed the survey. The data was screened to include patients with cervical vertebral fusions. Participants were sorted into Classification Type I, II, or III based on the Samartzis criteria [1], Fig. 1. Chi-square tests and one-way ANOVA tests were done to determine the association between the severity of cervical fusion, as determined by the Samartzis classification, and other symptoms, with significance considered at $p < 0.05$ and trends considered at $p < 0.10$.

Results

There were 75 patients with fusions in the cervical spine that were included, while 54 patients were excluded for incomplete or duplicate data. The average age when symptoms associated with KFS began and worsened were 17.5 years (SD ± 13.4 years) and 27.6 years (SD ± 15.3 years), respectively (Table 1). A majority of patients were female (80%), and the sex of one patient was not identified. The average number of comorbidities was 12.53 ± 7.14, and the breakdown of specific conditions present is reported in Table 2. The average number of symptoms reported was 12.16 ± 6.26, with 94.6% patients reporting at least 1 symptom. The prevalence of general symptoms and chromic symptoms is presented in Table 3.

Based on the Samartzis classification, multiple contiguous (52%, Type III) was the most commonly reported, and followed by single level fusions (28%, Type I), and multiple noncontiguous fusion (20%, Type II). Levels of fusion most commonly involved C2–C3 and C4–5 (both 56%), and were followed by C5–6 (42.7%), C3–4 (40%), C6–7 (33.3%), and

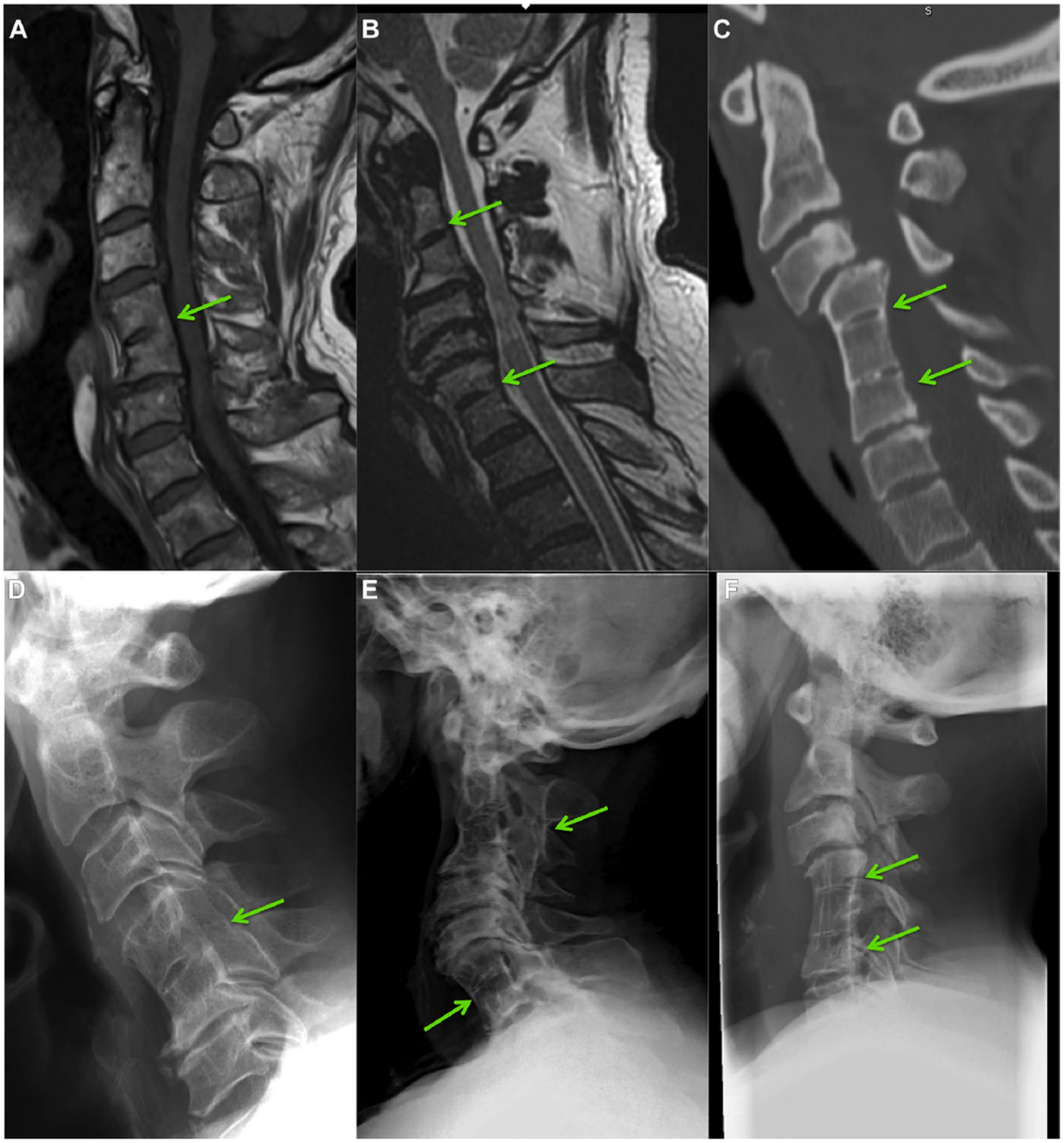

Fig. 1 The different types of KFS as seen on imaging: **a** and **d** (Type 1)—Single fusion between adjacent levels; **b** and **e** (Type 2)—Multilevel noncontiguous cervical fusions; **c** and **f** (Type 3) Multilevel contiguous cervical fusions. Adapted from: Nouri et al. (2017)

C1–2 (32%). Occiput–C1 fusion was the second least prevalent fusion (22.7%); however, it was still prevalent in nearly a quarter of patients. The least prevalent fusion was reported to be C7–T1 fusion.

Most patients sought out some kind of treatment (medical/supplement, invasive or non-invasive procedure), and only 9.3% of KFS patients reported no treatment. Medication/Supplementation (85%) and non-invasive treatment strategies (69.3%) were most commonly used; however, more than half (56%) of patients reported having had an invasive procedure as part of treatment.

Patients with multilevel fusions (Type II or III) were more likely to have a Sprengel Deformity ($p=0.036$) or missing rib ($p=0.046$), and have symptoms of dizziness ($p=0.04$) or limited range of motion in the spine ($p=0.022$) than patients with a single fusion level (Type I), Table 4. The prevalence of all other comorbidities or symptoms were not statistically significantly different between single or multiple levels of fusion. There was also no statistical difference between single and multiple level by sex ($p=0.652$).

An extensive list of reported symptoms and comorbidities is presented in "Appendix A".

Table 1 Patient characteristics and demographics

Demographics	
Age	
When symptoms began	17.5 (±13.4)
When symptoms worsened	27.6 (±15.3)
Sex	
Male	18.7% (*n* = 14)
Female	80.0% (*n* = 60)
Unknown	1.3% (*n* = 1)
Number of comorbidities (mean)	12.53 (±7.14)
Number of symptoms (mean)	12.16 (±6.26)
Patients with symptoms	94.6% (*n* = 71)
Patients without symptoms	5.3% (*n* = 4)
Samartzis classification	
Type 1 (single level)	28.0% (*n* = 21)
Type 2 (multiple noncontiguous fusions)	20.0% (*n* = 15)
Type 3 (multiple contiguous fusions)	52.0% (*n* = 39)
Levels of fusion	
Occiput-C1	22.7% (*n* = 17)
C1–C2	32.0% (*n* = 24)
C2–C3	56.0% (*n* = 42)
C3–C4	40.0% (*n* = 30)
C4–C5	56.0% (*n* = 42)
C5–C6	42.7% (*n* = 32)
C6–C7	33.3% (*n* = 25)
C7–T1	17.3% (*n* = 13)
Treatment history of KFS	
With medications/supplements	84.0% (*n* = 63)
With invasive procedures	56.0% (*n* = 42)
With non-invasive procedures	69.3% (*n* = 52)
No treatment	9.3% (*n* = 7)

Invasive procedures include surgery, Implanted pain device, Injections

Discussion

Patients with KFS captured by the CoRDS registry are likely to be individuals with a greater degree of severity as many patients with KFS remain undiagnosed. This reflects a similar trend within the reported academic literature, as most publications on KFS discuss patients that have likely been identified by clinical symptoms rather than by chance. In the present cohort only 28% were Type I, in other words, 72% of patients had multilevel fusions (Type II, 20%; Type III, 52%). Likewise, in the paper of 28 patients in which the KFS classification types were proposed [1], the prevalence for type I (25%) and multilevel fusions (Type II and II, 75%) were similar to our findings, but there were more Type II (50%) and less (25%) Type III types. In comparison, a recent study of CT scans obtained at an emergency department at a Level 1 trauma center, demonstrated that all 17 patients

Table 2 Prevalence of reported comorbidities

Spine	93.3% (*n* = 70)
Abnormal curvature	66.7% (*n* = 50)
Degenerative disk disease	53.3% (*n* = 40)
Osteoarthritis	50.7% (*n* = 38)
Herniated, slipped, bulging disks	45.3% (*n* = 34)
Instability	38.7% (*n* = 29)
Neurological	73.3% (*n* = 55)
Migraine	52% (*n* = 39)
Torticollis	24% (*n* = 18)
Dystonia (cervical)	13.3% (*n* = 10)
Cardiac	46.7% (*n* = 35)
Tachycardia	9.3% (*n* = 7)
Mitral valve prolapse	8% (*n* = 6)
Aortic valve stenosis/insufficiency/regurgitation	5.3% (*n* = 4)
Thoracic outlet syndrome	5.3% (*n* = 4)
Postural tachycardia	5.3% (*n* = 4)
Developmental	16.0% (*n* = 12)
Autism spectrum disorders	6.7% (*n* = 5)
Learning disability	4% (*n* = 3)
Intellectual disability	4% (*n* = 3)
ENT	61.3% (*n* = 46)
Hearing Loss	25.3% (*n* = 19)
TMJ	24% (*n* = 18)
Swallowing disorder	12% (*n* = 9)
Ophthalmology	72.0% (*n* = 54)
Reduced vision in one or both eyes	50.7% (*n* = 38)
Astigmatism	37.3% (*n* = 28)
Amblyopia or ptosis	10.7% (*n* = 8)
Gastrointestinal	60.0% (*n* = 45)
GERD	34.7% (*n* = 26)
Irritable bowel syndrome	25.3% (*n* = 19)
Gallbladder abnormalities	10.7% (*n* = 8)
Genitourinary	34.7% (*n* = 26)
Missing one or both kidneys	9.3% (*n* = 7)
Renal Fusion, horseshoe kidneys, or super kidney	8% (*n* = 6)
Urethra or ureter malformation/stenosis	5.3% (*n* = 4)
Abnormal renal rotation or placement	5.3% (*n* = 4)
Lower extremities	21.3% (*n* = 16)
Dysplasia of the knee	6.7% (*n* = 5)
Dysplasia of the hip bone	5.3% (*n* = 4)
Talipes equinovarus	1.3% (*n* = 1)
Upper extremities	60.0% (*n* = 45)
Sprengel deformity	26.7% (*n* = 20)
Thumb hypoplasia	10.7% (*n* = 8)
Congenital shoulder dislocation	6.7% (*n* = 5)
Connective tissue	13.3% (*n* = 10)
Ehlers-danlos syndrome	8% (*n* = 6)
Reproductive	46.7% (*n* = 35)
Abnormal reproductive organ rotation or placement	14.7% (*n* = 11)
Infertility	13.3% (*n* = 10)

Table 2 (continued)

Missing normal components of reproductive organs or entire organ	9.3% ($n=7$)
Pulmonary	41.3% ($n=31$)
Sleep apnea	25.3% ($n=19$)
Restrictive lung disease	9.3% ($n=7$)
Pulmonary airway malformation	1.3% ($n=1$)
Rheumatological	16.0% ($n=12$)
Ankylosing spondylitis	6.7% ($n=5$)
Juvenile rheumatoid arthritis	5.3% ($n=4$)
Rheumatoid arthritis	4% ($n=3$)

to put this in perspective [5, 10, 11]. On the contrary, Occiput–C1 and C7–T1 appear to be less common. Since patients with fusions at either the occipital or thoracic junction are expected to have greater disability, the finding that KFS mainly occurs toward the center of the cervical spine is likely to be positive. Patients with occipital fusions typically have significant impairment in their range of motion, as the craniocervical junction contributes to approximately 40–50% of neck flexion and rotation [12]. While, patients with fusions at the thoracic junction presumably would be predisposed to missing ribs, though this has not been clearly reported. Most patients in this cohort had multilevel fusions,

Table 3 Prevalence of reported symptoms

	Frequency
General symptoms	
Fatigue	76.0% ($n=57$)
Dizziness	61.3% ($n=46$)
Brain fog or memory loss	54.7% ($n=41$)
Balance problems	49.3% ($n=37$)
Fine motor control difficulties	37.3% ($n=28$)
Nausea	33.3% ($n=25$)
Bladder or bowel frequency	32.0% ($n=24$)
Gait disturbances	28.0% ($n=21$)
Bladder or bowel incontinence	20.0% ($n=15$)
Chronic symptoms	
Muscle tension and soreness in neck/shoulders/back	85.3% ($n=64$)
Limited range of motion in spine	82.7% ($n=62$)
Joint pain in neck and/or spine	78.7% ($n=59$)
Headaches, migraines, and/or head pain (including jaw/ears)	72.0% ($n=54$)
Joint popping/cracking in neck and/or spine	68.0% ($n=51$)
Muscle spasms in neck/shoulders/back	65.3% ($n=49$)
Nerve symptoms or neuropathy	58.7% ($n=44$)
Joint pain in hips/legs/feet	56.0% ($n=42$)
Joint popping/cracking in hips/legs/feet	44.0% ($n=33$)
Joint pain in arms or hands	40.0% ($n=30$)
Muscle tension in hips/legs/feet	36.0% ($n=27$)
Muscle spasms in hips/legs/feet	28.0% ($n=21$)
Joint popping in arms or hands	28.0% ($n=21$)
Muscle tension in arms or hands	29.3% ($n=22$)
Muscle spasms in arms or hands	21.3% ($n=16$)

identified in their review of 2917 patients had Type I KFS, and no patients were reported to have occipital–C1 or C7–T1 fusions [5]. This suggests that the findings in most studies and not just case series or reports are typically skewed toward patients with syndromic KFS.

It was observed in our cohort that the levels of fusions most commonly involved were toward the center of the cervical region (C2–C3 and C4–5) and less commonly at the cervical junctions. Other studies have shown variable types of level distribution and it is therefore difficult and it was found that they were more likely associated with Sprengel deformity, missing ribs and reduced range of motion compared to patients with single level fusions. The only symptom to be statistically worse in patients with multilevel fusions was dizziness. The prevalence of Sprengel deformity was 26.7% in our population, approximating the middle range of prevalence rates of 7–42.0% reported in previous studies [11]. Fusion between the occiput and C1, also referred to as occipitilization of the cervical vertebra was

Table 4 Comparison in the prevalence of associated comorbidities or symptoms in patients with single (Type I) versus multilevel fusions (Type II and III)

	Single level ($n=21$)	Multiple level ($n=54$)	p value
Associated comorbidities			0.264
Sprengel deformity	9.5% ($n=2$)	33.3% ($n=18$)	0.036
**Missing ribs	0.0% ($n=0$)	16.7% ($n=9$)	0.046
Instability	23.8% ($n=5$)	44.4% ($n=24$)	0.099
Tachycardia	19.0% ($n=4$)	5.6% ($n=3$)	0.071
Reduced vision in one or both eyes	66.7% ($n=14$)	44.4% ($n=24$)	0.084
Torticollis	9.5% ($n=2$)	29.6% ($n=16$)	0.067
Restrictive lung disease	19.0% ($n=4$)	5.6% ($n=3$)	0.071
*All other comorbidities were not statistically significantly different (> 0.05), or trending significance (0.10)			
General symptoms			0.827
Dizziness	42.8% ($n=9$)	68.5% ($n=37$)	0.04
Limited range of motion in spine	66.7% ($n=14$)	88.9% ($n=48$)	0.022
*All other symptoms were not statistically significantly different (> 0.05), or trending significance (0.10)			

*Chi Square Tests—only associations with $p<0.10$ are reported

**Missing ribs were erroneously labeled in the survey as missing cervical ribs

present in 22.7% of patients. Previous research has reported rates as high as 48.5% [13].

One of the key findings of the study was the prevalence of symptoms. These may also be related to existing comorbidities. Common symptoms included brain fog and fatigue; remarkably, nearly half of the patients complained of balance problems and 20% complained of incontinence. The latter two symptoms were potentially indicating previous or ongoing compression of neural elements.

Not surprisingly, the highest comorbidities reported were related to spine, with 93.3% of patients reporting additional spine anomalies, including abnormal curvature and degenerative disk disease. It has previously been suggested that patients with KFS are predisposed to accelerated degenerative disease [3, 7–9]. This is thought to occur due to increased wear placed upon disks to fused vertebral segments [14], potentially resulting in adjacent segment pathology. Ultimately, the ensuing degenerative changes and potential hypermobility that can occur in other cervical segments (typically in the upper cervical region) is believed to predispose patients with KFS to neurological injury from spinal cord or neural root compression. With regards to cervical curvature, while this is likely to represent mostly patients with kyphotic or hyperlordotic involvement, it has previously been reported that 5.4% of patients with cervical scoliosis have KFS [15]. This report indicated that half of the patients with cervical scoliosis had hemivertebrae fusions. It was also notable that, as with our cohort, the authors reported a high prevalence of females compared to males (71.4%, $n=20/28$).

The clinical manifestations and symptoms of KFS are dependent on a number of factors including the number of levels involved, genetic factors, and associated congenital syndromes that may coexist. Indeed, the list of conditions associated with congenital cervical fusion is quite extensive and ranges from more indolent conditions to severely disabling conditions like VACTERL deformities [16]. As a result, the presentation of patients can be quiet variable. Furthermore, it is challenging to interpret which symptoms are solely related to KFS, given the high number of comorbidities that present in symptomatic patients and the fact that most reports in the literature are skewed toward more severe cases. It is clear, however, from our report that most patients (> 90%) seek out treatment, with more than half (56%) reporting having undergone an invasive procedure.

Limitations

The nature of the data at our disposal resulted in both strengths and limitations, whose recognition are integral when interpreting our findings. While we had the opportunity to compare multiple variables, this also predisposes to the possibility for a Type I error. Therefore, further study is necessary to substantiate the significance of our findings. Further, patients included in the registry overly represented those with more severe KFS, which may be attributable to ascertainment bias. This bias is inherent to the fact many patients with "milder" KFS are unaware that they are afflicted. Lastly, but not least, a higher number of women were included than would have been expected based on previous epidemiological reports, and this may limit the generalizability of our findings. The reasons for this are not clear but may be partly due to the fact that individuals who

have engaged in KFS through social media were more commonly female.

Conclusion

The data reported herein likely represents a cohort of patients with KFS that is typically more severely impacted. In this group, it was found that most patients suffer from multiple additional comorbidities and symptoms. The data also indicates that multiple levels of fusion (Type II or III) may be associated with the occurrence of Sprengel Deformity, missing ribs, reduced neck mobility and symptoms of dizziness. Finally, it appears that the cervical levels typically involved in KFS tend to be toward the center of the cervical spine with C4–5 and C2–3 most commonly affected, whereas the occipital and thoracic junctions are less frequently affected.

Acknowledgement We wish to acknowledge Sanford Health (CoRDS Registry) and Klippel-Feil syndrome freedom, two non-profit organizations which collected the data used in the present study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Associated comorbidities

Associated spine abnormalities		
Abnormality	Frequency	Percent
Missing cervical ribs	9	12.0
Abnormal curvature	50	66.7
Missing spinous processes	6	8.0
Craniocervical junction abnormalities	11	14.7
Neuroenteric cyst	4	5.3
Degenerative disk disease	40	53.3
Osteoarthritis	38	50.7
Hemivertebrae	15	20.0
Sciatica	20	26.7
Herniated, slipped, bulging disks	34	45.3
Spina bifida	12	16.0
Instability	29	38.7

Associated neurological abnormalities		
Abnormality	Frequency	Percent
Chiari malformation	5	6.7
Basilar invagination	4	5.3
Tarlov cyst	1	1.3

Associated neurological abnormalities		
Abnormality	Frequency	Percent
Brainstem compression	4	5.3

Associated cardiac abnormalities		
Abnormality	Frequency	Percent
Pulmonary valve stenosis	0	0.0
Abnormal heart rotation	3	4.0
Tachycardia	7	9.3
Aortic valve stenosis/insufficiency/ regurgitation	4	5.3
Tetralogy of fallot	0	0.0
Atrial septal defect	3	4.0
Thoracic outlet syndrome	4	5.3
Mitral valve prolapse	6	8.0
Ventricular septal defects	2	2.7
Postural tachycardia	4	5.3

Associated developmental abnormalities		
Abnormality	Frequency	Percent
Learning disability	3	4.0
Autism spectrum disorders	5	6.7
Intellectual disability	3	4.0
Down syndrome	0	0.0

Associated ENT abnormalities		
Abnormality	Frequency	Percent
TMJ	18	24.0
Cleft or abnormal palate	7	9.3
Other ear abnormality	6	8.0
Deafness (completely) in one or both ears	3	4.0
Other nose abnormality	4	5.3
Goldenhar syndrome	0	0.0
Other throat, mouth, or jaw abnormality	0	0.0
Hearing loss	19	25.3
Swallowing disorder	9	12.0

Associated ophthalmologic abnormalities		
Abnormality	Frequency	Percent
Lateral rectus palsy	0	0.0
Amblyopia or ptosis	8	10.7
Nystagmus	1	1.3
Astigmatism	28	37.3
Reduced vision in one or both eyes	38	50.7
Blindness in one or both eyes	0	0.0
Strabismus	2	2.7
Coloboma	0	0.0
Duane syndrome	1	1.3

Associated GI abnormalities

Abnormality	Frequency	Percent
GERD	26	34.7
Abdominal wall closure defect	0	0.0
Inflammatory bowel disease	2	2.7
Gallbladder abnormalities	8	10.7
Irritable bowel syndrome	19	25.3
Gastric or stomach volvulus	0	0.0
Malrotation/duplication of bowel	0	0.0
Gastrointestinal atresia	0	0.0
Sphincter abnormalities	3	4.0
Gastroparesis	1	1.3

Associated GU abnormalities

Abnormality	Frequency	Percent
Neurogenic bladder	2	2.7
Abnormal renal rotation or placement	4	5.3
Urethra or ureter Malformation or stenosis	4	5.3
Horseshoe kidneys, renal fusion, or super kidney	6	8.0
Missing one or both kidneys	7	9.3

Associated lower extremity abnormalities

Abnormality	Frequency	Percent
Talipes equinovarus	1	1.3
Dysplasia of the knee	5	6.7
Tibial torsion	0	0.0
Dysplasia of the hip bone	4	5.3
Femoral torsion	0	0.0

Associated upper extremity abnormalities

Abnormality	Frequency	Percent
Syndactyly	1	1.3
Aplasia of the scapula	1	1.3
Thumb hypoplasia	8	10.7
Congenital shoulder dislocation	5	6.7
Upper extremity hypoplasia	1	1.3
Digital hypoplasia	1	1.3
Sprengel deformity	20	26.7

Associated connective tissue abnormalities

Abnormality	Frequency	Percent
Ehlers-Danlos	6	8.0

Associated neurological abnormalities

Abnormality	Frequency	Percent
Dysautonomia	1	1.3
Bell's palsy	2	2.7
Headache/migraine	39	52.0
Chronic fatigue syndrome	9	12.0
Mirror movements in hands	8	10.7

Associated neurological abnormalities

Abnormality	Frequency	Percent
Dystonia (cervical)	10	13.3
Torticollis	18	24.0
Dystonia (general)	4	5.3

Associated reproductive abnormalities

Abnormality	Frequency	Percent
Multiple components of reproductive organs	1	1.3
Abnormal reproductive organ rotation or placement	11	14.7
Infertility	10	13.3
Mayer-Rokitansky-Kuster-Hauser syndrome	2	2.7
Endometriosis	6	8.0
Missing normal components of reproductive organs or entire organ	7	9.3

Associated pulmonary abnormalities

Abnormality	Frequency	Percent
Restrictive lung disease	7	9.3
Pulmonary airway malformation	1	1.3
Sleep apnea	19	25.3
Pulmonary hypoplasia	0	0.0

Associated rheumatological abnormalities

Abnormality	Frequency	Percent
Rheumatoid arthritis	3	4.0
Ankylosing spondylitis	5	6.7
Juvenile RA	4	5.3

Associated spinal cord abnormalities

Abnormality	Frequency	Percent
Spina bifida (myelomeningocele or myelocele)	4	5.3
Caudal agenesis	1	1.3
Spina bifida occulta	10	13.3
Diastemyeloia	1	1.3
Syringomyelia/hydromelia	5	6.7
Intradural lipoma	0	0.0
Tethered cord syndrome	5	6.7
Lesion of white matter	2	2.7

Associated symptoms

General symptoms

Symptom	Frequency	Percent
Balance problems	37	49.3
Bladder or bowel frequency	24	32.0
Bladder or bowel incontinence	15	20.0

General symptoms		
Symptom	Frequency	Percent
Brain fog or memory loss	41	54.7
Dizziness	46	61.3
Fatigue	57	76.0
Fine motor control difficulties	28	37.3
Gait disturbances	21	28.0
Nausea	25	33.3
Chronic symptoms		
Symptoms	Frequency	Percent
Headaches, migraines, and/or head pain (including jaw/ears)	54	72.0
Muscle tension and soreness in neck/shoulders/back	64	85.3
Muscle spasms in neck/shoulders/back	49	65.3
Nerve symptoms or neuropathy	44	58.7
Limited range of motion in Spine	62	82.7
Joint pain in neck and/or spine	59	78.7
Joint popping/cracking in neck and/or spine	51	68.0
Joint pain in hips/legs/feet	42	56.0
Muscle tension in hips/legs/feet	27	36.0
Muscle spasms in hips/legs/feet	21	28.0
Joint popping/cracking in hips/legs/feet	33	44.0
Joint pain in arms or hands	30	40.0
Muscle tension in arms or hands	22	29.3
Muscle spasms in arms or hands	16	21.3
Joint popping in arms or hands	21	28.0

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