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The Clinical Characteristics and Surgical Outcomes of Spine Deformity in Pediatric Patients with Prader-Willi Syndrome

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Abstract

Background: Prader-Willi syndrome (PWS) requires early recognition and surgical intervention due to its complicated clinical characteristics and frequent association with progressive spine deformity. The purpose of the study is to investigate the clinical characteristics and surgical outcomes of spine deformity for PWS patients.

Methods: We retrospectively analyzed 12 PWS patients (mean age: 13) with severe kyphoscoliosis who underwent spinal correction surgery between 2013 and 2022 with at least 2-years follow-up (mean duration: 3.2 years) evaluating demographic characteristics, curve patterns, surgical strategies and complications.

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Results: All the patients had scoliosis (mean thoracic Cobb angle: 78.5° ± 15.6°, mean lumbar Cobb angle: 62.6° ± 31.6°), with 41.7% exhibiting concurrent kyphosis (mean kyphotic angle: 83.6° ± 11.2°). The thoracolumbar double curves (50%) and atypical long thoracic curves (25%) were predominant patterns. The mean thoracic and lumbar flexibility were 37.9% and 52.3% respectively. Nine patients received spinal fusion surgery and three patients received growing rod surgery. The average of fused segments was 13.5 ± 1.3, and distal fusion predominantly stopped at stable vertebra (SV) (75%). The mean thoracic curve correction rate was 60.2% ± 20.4% immediately post-operation and mean correction loss rate of 9.9% ± 11.1% at the last follow-up. The mean lumbar curve correction rate was 71.8% ± 17.9% immediately post-operation and mean correction loss rate of 18.7% ± 24.9% at the last follow-up. Complications occurred in 41.7% of patients, including surgical site infections (SSI) (25%), neurological deficits (8.3%) and excessive bleeding (8.3%).

Conclusion: Scoliosis in PWS patients predominantly manifests as thoracolumbar double curves or atypical long thoracic curves, frequently accompanied by kyphosis, while demonstrating relative good flexibility. Posterior spinal fusion extending to the SV improved good correction outcomes. Surgical challenges included excessive bleeding, SSI and neurological deficits. These findings emphasize the necessity of individualized surgical strategies to optimize outcomes in this high-risk population.

Keywords *Prader-Willi syndrome, scoliosis, clinical characteristics, surgical outcomes*

1. Background

Prader-Willi syndrome (PWS), alternatively termed hypotonia-intellectual disability-hypogonadism-obesity syndrome, is a complex multisystem disorder arising from genomic imprinting abnormalities that contravene Mendelian inheritance patterns [1]. Epidemiological studies estimate its prevalence between 1/10,000 and 1/30,000 live births, with an average mortality rate of 3% across all age groups [2, 3]. The syndrome manifests distinctive clinical features: neonates typically present with severe hypotonia, diminished sucking reflex, and feeding difficulties, while childhood progression is characterized by pathological obesity, hypothalamic-derived hypogonadism, and behavioral abnormalities. Characteristic craniofacial dysmorphism (almond-shaped eyes, narrow forehead, thin upper lip) is frequently observed, accompanied by multiorgan complications including growth hormone deficiency, adrenal insufficiency, thyroid dysfunction, glucose metabolism disorders (impaired glucose tolerance and type 2 diabetes), sleep-disordered breathing, gastrointestinal dysmotility, coagulation abnormalities, and periodontal disease [4-6].

Spinal deformities represent prevalent musculoskeletal complications in PWS patients, with reported incidence rates ranging from 45% to 86% [7]. Scoliosis and kyphosis constitute the most frequent spinal pathologies [8]. A retrospective analysis by Wijngaarden *et al.* involving 96 pediatric PWS cases revealed a scoliosis prevalence of 37.5% (36/96). Contrastingly, Nakamura *et al.* documented a 30% scoliosis rate (58/193) in their PWS cohort [9]. Notably, the relationship between growth hormone therapy (GHT)- a cornerstone intervention for improving linear growth and metabolic parameters in PWS- and scoliosis progression remains contentious [10]. Docquier *et al.* postulated potential GHT-associated acceleration of scoliotic progression during adolescence, whereas Nagai *et al.* demonstrated comparable scoliosis incidence between GHT-treated (48.8%, 21/43) and untreated groups (41.9%, 13/31), with no statistical significance ($p > 0.05$) [11]. Given the nonspecific early clinical presentation of PWS, genetic confirmation through identification of paternal 15q11-13 deletions or maternal uniparental disomy remains the diagnostic gold standard, with spinal deformities now recognized as key supportive diagnostic criteria [12]. Early detection and intervention for spinal deformities are therefore critical for optimizing patient outcomes [13-15].

Current surgical literature on PWS-associated scoliosis predominantly is scant, with significant knowledge gaps persisting regarding surgical indication criteria, deformity correction strategies, long-term outcome assessments, and perioperative complication mitigation. This retrospective cohort study aims to: i) investigate the clinical characteristics of PWS patients with severe kyphoscoliosis; ii) evaluate the surgical outcomes of spine deformity for PWS patients; iii) comprehensively analyze perioperative complication profiles and associated risk factors, thereby providing evidence-based insights for refining therapeutic protocols.

2. Methods

This retrospective cohort study consecutively enrolled PWS patients with kyphoscoliosis who underwent spinal correction surgery at our institution between 2013 and 2022. The inclusion/exclusion criteria were established as follows:

2.1. Inclusion Criteria

i) Genetic diagnosis of PWS through molecular analysis (patronymic 15q11-13 mutation).
ii) Receiving spinal correction surgery in our hospital.
iii) Follow-up time greater than 2 years.

2.2. Exclusion Criteria

i) Confirmed diagnosis of Angelman syndrome [16].
ii) Presence of concurrent congenital spinal anomalies.
iii) No need for correction surgery.

The recorded clinical data included: definitive diagnosis of Prader-Willi syndrome (PWS), sex, age, BMI, follow-up duration, endocrine disorders, other clinical manifestations, spinal fusion approach, surgery-related complications, and intraoperative blood loss. Standing full-spine radiographs served as the basis for evaluating and measuring spinal parameters in this patient cohort. Preoperative measurements included: major curve patterns; major curve angle using the Cobb method; regional kyphosis angle (defined as the maximum angle between any two vertebrae on sagittal radiographs) > 60° were included for discussion, while those ≤ 60° were excluded; coronal balance distance (C7 plumb line [C7PL] deviation from the central sacral vertical line [CSVL],

with rightward deviation as positive and leftward as negative); and sagittal balance distance (C7PL deviation from the vertical line through the S1 posterior superior corner, with anterior deviation as positive and posterior as negative). On postoperative and final follow-up standing full-spine radiographs, the major curve angle and local kyphotic angle were remeasured using preoperative Cobb angle segments to calculate correction rates and correction loss rates. Formulas: Correction rate = (preoperative major curve angle - postoperative major curve angle) / preoperative major curve angle; Correction loss rate = (final follow-up major curve angle - postoperative major curve angle) / postoperative major curve angle.

3. Results

Between 2013 and 2022, 12 patients with Prader-Willi syndrome and severe kyphoscoliosis underwent spinal correction surgery at our institution, including 7 males (58%) and 5 females (42%). The mean surgical age was 11 ± 2.3 years (range: 5-14 years). The average BMI measured 27.9kg/m^2 ± 3.07 kg/m^2 (range: 21 kg/m^2-32.1 kg/m^2), with 50% of patients classified as obese (BMI ≥ 28 kg/m^2). Mean follow-up duration was 3.2 ± 1.9 years (range: 2.0 years-7.9 years).

The clinical manifestations of this patient cohort varied: 10 cases (83%) presented with endocrine issues, including elevated blood glucose in 9 (75%), decreased growth hormone in 4 (33.3%), decreased IGF-1 in 3 (25%), and decreased sex hormone levels in 1 (8.3%). Other clinical features included: mild intellectual disability in 5 patients (41.7%); snoring during sleep in 6 cases (50%); feeding difficulties during infancy in 2 cases (16.7%); low birth weight in 1 case (8.3%); and mild pulmonary hypertension in 1 case (8.3%) (Table 1).

TABLE 1: Demographic characteristics and clinical manifestations.

ID	Gender	Age	BMI(kg/m^2)	Follow-up duration(years)	Endocrine Problem	Other characteristics
#10828	M	10	29.2	5.2	Decreased growth hormone and testosterone, elevated blood glucose	Mild intellectual disability, snoring, mild pulmonary hypertension
#14887	M	12	24.5	2.0	Decreased growth hormone	Low birth weight infant, feeding difficulties
#15763	M	5	30.3	7.9	Elevated blood glucose	Snoring, feeding difficulties in infancy
#21405	M	12	29.8	2.2	Elevated blood glucose	snoring
#24146	F	13	31.1	3.0	Decreased IGF-1	Mild intellectual disability, snoring
#19127	F	12	32.1	5.3	Elevated blood glucose, decreased growth hormone	Mild intellectual disability, snoring

#40704	M	10	27.6	2.1	-	-
#28037	M	10	28.5	2.3	Elevated blood glucose	-
#25000	M	12	26.9	2.1	Elevated blood glucose, decreased growth hormone	Mild intellectual disability
#46671	F	11	25.9	2.3	Elevated blood glucose	Mild intellectual disability, snoring
#29692	F	11	27.9	2.2	-	-
#29309	F	14	21	2.3	Elevated blood glucose	-

Among the kyphoscoliosis cases, thoracolumbar double curves were observed in 6 patients (50%), atypical long thoracic curves in 3 cases (25%), right thoracic curves in 2 cases (16.7%), and long thoracic curves in 1 case (8.3%). The preoperative mean thoracic Cobb angle measured 78.5 ± 15.6°, while the mean lumbar Cobb angle was 62.6° ± 31.6°. The mean coronal balance distance measured 19.2 mm ± 19.8 mm, while the mean sagittal balance distance was 31.0 mm ± 28.6 mm. The average flexibility of thoracic curves was 37.9% ± 15.5%, and lumbar curves demonstrated 52.3% ± 23.8% flexibility. Five cases (41.7%) exhibited concomitant kyphosis with scoliosis, showing a mean regional kyphotic angle of 80.4° ± 11.4° (Table 2).

TABLE 2: Preoperative kyphoscoliosis information.

ID	Curve type	Thoracic curve Cobb	Lumbar curve Cobb	Thoracic curve flexibility	Lumbar curve flexibility	Coronal balance (mm)	Sagittal balance (mm)	Regional kyphosis angle Cobb
#10828	Thoracolumbar double curve	93	74	35.5%	59.5%	26.9	24.1	-
#14887	Right thoracic curve	55	27	36.3%	62.9%	-6.7	18.6	-
#15763	Atypical long thoracic curve	90	30	55.6%	96.7%	19.3	4.2	-
#21405	Atypical long thoracic curve	91	44	44.0%	65.9%	65	108	-
#24146	Mild long right thoracic curve	-	-	-	-	-8.2	-65	90

#19127	Thoracolumbar double curve	99	134	14.1%	38.1%	48	16.6	82
#40704	Atypical long thoracic curve	58	-	56.9%	-	-9.6	-10.6	92
#28037	Thoracolumbar double curve	84	63	36.9%	49.2%	6.41	26.8	-
#25000	Right thoracic curve	66	-	62.1%	-	-1.97	26.91	-
#46671	Thoracolumbar double curve	62	63	25.8%	50.8%	27.97	17.91	-
#29692	Thoracolumbar double curve	88	70	28.4%	9.8%	-5.76	19.22	73
#29309	Thoracolumbar double curve	77	58	20.8%	37.9%	4.3	34.03	65
Mean ± SD	-	78.5±15.6	62.6° ± 31.6	37.9% ± 15.5%	52.3% ± 23.8%	19.2±19.8	31.0±28.6	80.4 ± 11.4

Regarding surgical approaches, posterior spinal fusion surgery was performed in 9 cases (75%), while 3 cases (25%) received growing rod surgery. The mean number of fused segments measured 13.5 ± 1.3 (range: 11-16), and distal fusion predominantly stopped at stable vertebra (SV) (75%). The mean intraoperative blood loss was 1204 ± 495 mL (range: 700-2200), with an average operative duration of 328.3 ± 71.3 minutes (range: 210-450). Postoperative complications occurred in 5 patients (41.7%): surgical site infection in 3 cases (25%), lower extremity paralysis in 1 case (8.3%), and growing rod decompensation with massive intraoperative hemorrhage (3200 mL) during final-stage surgery in 1 case (8.3%) (Table 3).

TABLE 3: Surgical strategy and outcomes about surgery.

ID	Surgical approach	UIV	LIV	Number of fusion segments	SV	Intraoperative bleeding /ml	Operative time /min	Complications
#10828	Fusion	T2	L4	15	L4	2200	450	SSI
#14887	Fusion	T3	L1	11	L2	800	210	-
#15763	Growth rod	T3	L3	13	L3	750	370	-
#21405	Fusion	T3	L4	14	L4	1800	380	-
#24146	Fusion	T2	L3	14	L3	1300	350	SSI
#19127	Growth rod	T1	L4	16	L4	800	350	Excessive bleeding
#40704	Fusion	T2	L2	13	L2	1100	345	-
#28037	Fusion	T3	L4	14	L4	1000	230	-

#25000	Fusion	T2	L1	12	L1	800	255	-
#46671	Fusion	T3	L4	14	L4	1500	320	SSI
#29692	Growth rod	T3	L3	13	L4	700	395	Neurological deficits
#29309	Fusion	T3	L3	13	L4	1700	285	-
Mean ± SD	-	-	-	13.5 ± 1.3	-	1204 ± 495	328.3 ± 71.3	-

At immediate post-operation, the mean thoracic curve correction rate was 60.2% ± 20.4%; the mean lumbar curve correction rate measured 71.8% ± 17.9%; the mean kyphosis correction rate was 43.7% ±10.1%. At final follow-up, the mean correction loss rate was 9.9% ± 11.1%, 18.7% ± 24.9%, 15.2% ± 25.3% respectively (Table 4).

TABLE 4: Final follow-up information.

ID	Thoracic curve correction rate	Lumbar curve correction rate	Regional kyphosis correction rate	Thoracic curve correction loss rate	Lumbar curve correction loss rate	Regional kyphosis angle correction loss rate
#10828	57.0%	78.4%	-	-6.4%	0.0%	-
#14887	76.3%	70.4%	-	10.0%	0.0%	-
#15763	47.8%	83.3%	-	27.5%	0.0%	-
#21405	65.9%	77.3%	-	0.0%	47.4%	-
#24146	-	-	36.7%	-	-	36.8%
#19127	27.3%	56.7%	53.3%	-1.4%	24.1%	35.7%
#40704	86.2%	-	37.0%	12.1%	-	5.2%
#28037	76.2%	95.2%	-	7.8%	11.7%	-
#25000	68.0%	-	-	10.0%	13.0%	-
#46671	74.2%	90.5%	-	4.3%	5.3%	-
#29692	22.5%	51.4%	56.2%	28.6%	76.5%	21.9%
#29309	61.0%	43.1%	35.4%	16.7%	9.0%	-23.8%
Mean ± SD	60.2%±20.4%	71.8%±17.9%	43.7%±10.1%	9.9%±11.1%	18.7%±11.1%	15.2%±25.3%

4. Discussion

4.1. Clinical Characteristics of Scoliosis in PWS Patients

Patients with Prader-Willi syndrome (PWS) exhibit growth retardation, paraspinal muscle hypotonia, and elevated BMI that increases spinal loading, thereby predisposing to scoliosis. Nakamura *et al.* reported that scoliosis in PWS primarily manifests as lumbar or thoracolumbar curves, whereas idiopathic scoliosis (IS) predominantly involves thoracic curves [9, 17]. IS patients typically demonstrate rapid pubertal growth with a lean, tall stature, while PWS patients display markedly delayed development, paraspinal muscle

hypotonia, and obesity. This study revealed that thoracolumbar double curves with concomitant kyphosis are predominant in PWS patients, characterized by better lumbar curve flexibility and preserved global trunk balance. Therefore, the thoracolumbar double curve or atypical long thoracic curve with kyphosis represents a significant clinical characteristic of scoliosis in PWS patients.

4.2. Conservative Management of Scoliosis in PWS

Due to the typically elevated body weight, poor brace compliance, and rapid curve progression in PWS patients, bracing often fails to control deformity progression. Therefore, brace therapy primarily aims to decelerate curve advancement and delay surgical intervention, thereby preserving growth potential for pediatric patients. The majority of patients ultimately require surgical treatment (Figure 1) [18, 19].

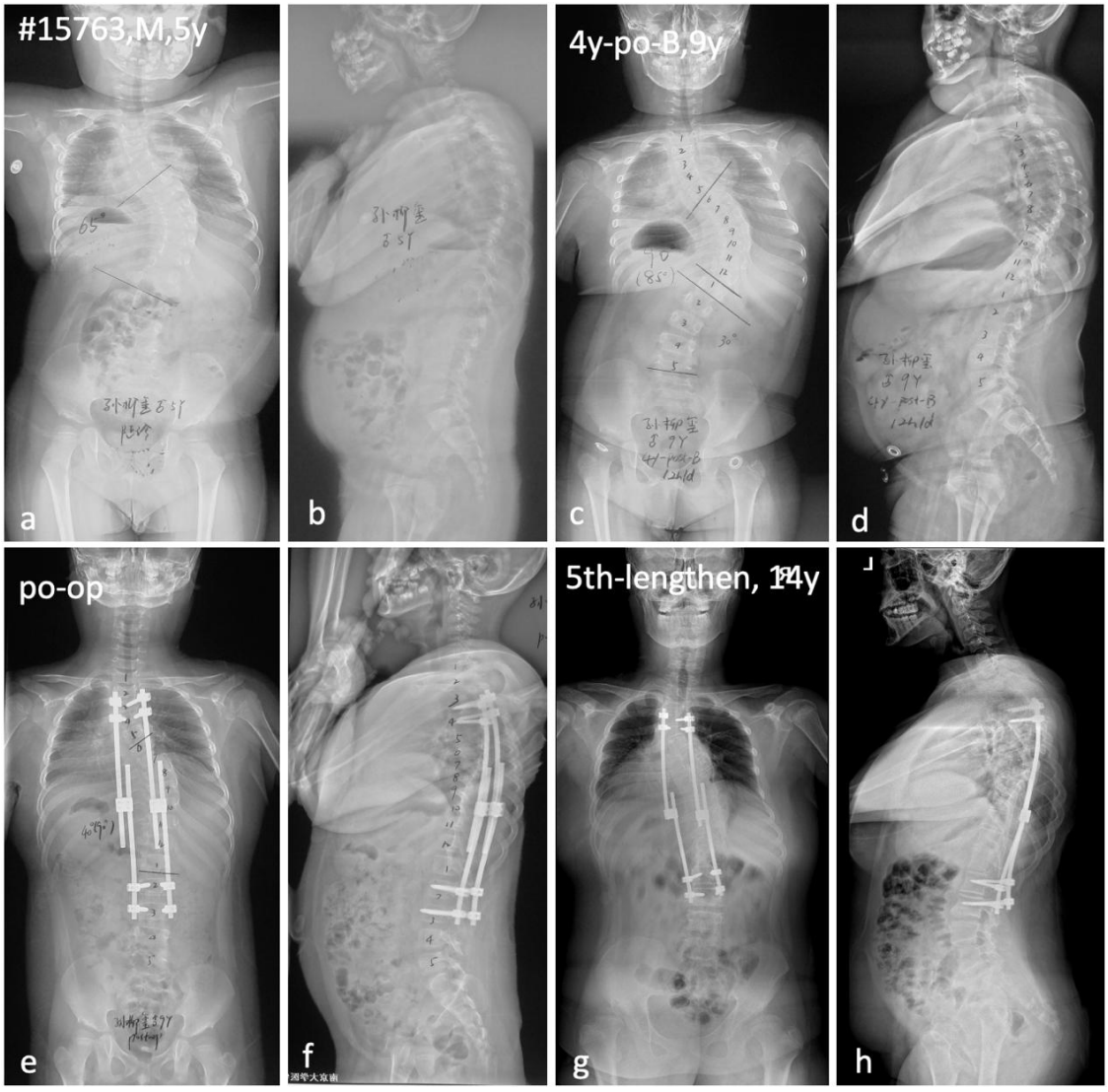

FIGURE 1: a & b) Initial diagnosis at age 5 years revealed a Cobb angle of 65° with a long thoracolumbar curve pattern. **c & d)** After 4 year of bracing, the scoliosis progressed to 90°. **e & f)** The patient underwent posterior spinal growing rod implantation (T3-L3), achieving immediate postoperative correction to 40°. **g & h)** Five years post-implantation and after the fifth lengthening procedure, coronal and sagittal balance was maintained without trunk tilt, demonstrating sustained correction.

4.3. Surgical Strategies and Outcomes

For young children with PWS-associated scoliosis, growing rod techniques are recommended, while adolescents may be considered for fusion surgery. Kroonen *et al.* proposed that surgical indications and strategies for PWS patients with scoliosis may align with those for idiopathic cases, such as surgical intervention for rapid curve progression or trunk imbalance [7]. This study demonstrated suboptimal outcomes with growing rod therapy: one patient developed decompensation and continued curve progression after 3 years of treatment, with excessive intraoperative bleeding during final fusion surgery.

Odent *et al.* observed that patients with severe kyphosis require more extensive surgical correction [20]. Accadbled *et al.* emphasized that paraspinal muscle hypotonia, a key pathogenic factor in PWS-associated scoliosis, renders its biomechanical behavior closer to neuromuscular scoliosis, necessitating extended fusion levels [21]. For thoracolumbar double curves, both curves should be instrumented, with the distal fusion vertebra selected as the stable vertebra (SV). In this study, 9 (75%) surgical cases achieved distal fusion at the SV yielding satisfactory postoperative correction rates. These findings corroborate the aforementioned perspectives.

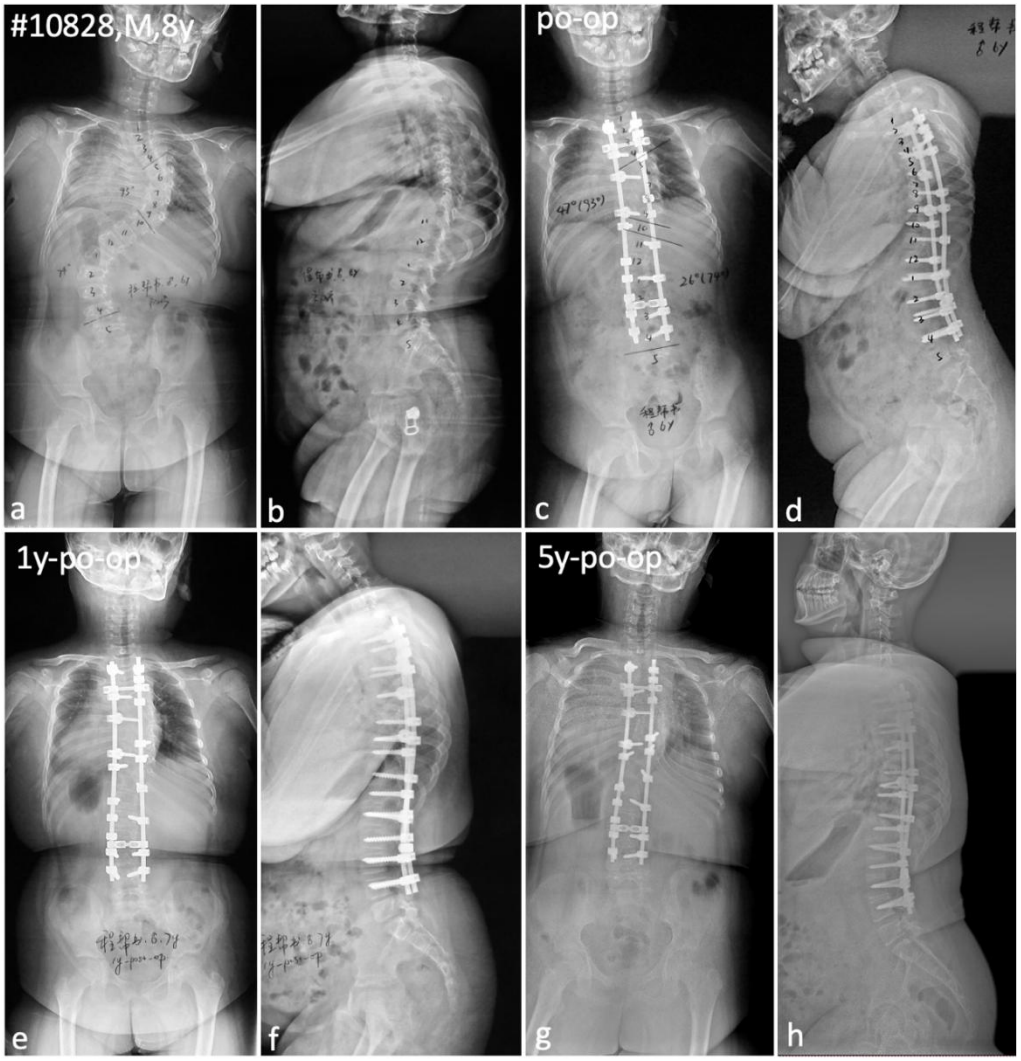

FIGURE 2: a & b) An 8-year-old male with Prader-Willi syndrome (chromosomal analysis revealed a 15q11-13 deletion) presented with thoracolumbar double curves on initial radiographs: thoracic curve 93° and lumbar curve 74°.

c & d) The patient underwent posterior spinal instrumentation and fusion. Due to the extensive curve pattern, distal fixation extended to L4(SV), achieving postoperative correction to 47° (thoracic) and 26° (lumbar). **e-h)** Postoperative 1-year and 5-year follow-up demonstrated maintained correction with improved coronal and sagittal balance.

4.4. Surgical Complications

Neurological complications occur with higher frequency, particularly during revision surgeries. In Accadbled's study, 4 patients (25%) developed neurological injuries: 1 case of transient neurological impairment occurred after primary posterior spinal correction, while 3 cases of permanent neurological deficits followed revision surgeries [21]. Greggi *et al.* reported lower extremity paralysis in 1 of 6 PWS patients undergoing spinal correction, with muscle strength recovering after removal of instrumentation [22]. Among the 12 cases in this study, 1 patient developed bilateral lower extremity paralysis following revision surgery.

Wound infection or poor healing is associated with obesity, excessive subcutaneous adipose tissue, and comorbid diabetes mellitus. In this study, 3 patients developed postoperative SSI. Additionally, frequent comorbidities such as skin rashes and psychological disorders (e.g., self-injurious behaviors) may exacerbate wound infection risks. Accadbled *et al.* reported a postoperative wound infection rate of 5/16 (31%), with 3 cases requiring debridement and drainage, ultimately achieving satisfactory wound healing and spinal fusion outcomes [21].

Previous literature has documented complications including implant dislodgement, instrumentation loosening, and respiratory dysfunction, which were not observed in this cohort. Prader-Willi syndrome (PWS) exhibits extreme rarity, and surgical refusal by some patients contributed to the limited cohort size in this study. Furthermore, the definitive therapeutic efficacy and potential complications of corrective surgery require longer-term follow-up and multicenter analytical studies.

5. Conclusion

Scoliosis in PWS patients predominantly manifests as thoracolumbar double curves or atypical long thoracic curves, frequently accompanied by kyphosis, while demonstrating relative good flexibility. Posterior spinal fusion extending to the SV improved good correction outcomes. Surgical challenges included excessive bleeding, SSI and neurological deficits. These findings emphasize the necessity of individualized surgical strategies to optimize outcomes in this high-risk population.

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