Journal of
Pediatric Dentistry
DOI: 10.14744/JPD.2023.11_159
J Pediatr Dent 2024;10(1):9-16

Review Article

Macroglossia Impact on Child's Dentition with Beckwith-Wiedemann Syndrome: A Narrative Review

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Abstract

Beckwith-Wiedemann Syndrome (BWS) is a pediatric overgrowth disorder characterized by developmental aberrations, tissue and organ hyperplasia, and an elevated susceptibility to embryonic tumors. Its incidence stands at approximately 1 in 10,340 live births. This syndrome manifests various distinctive features within the oral cavity, notably macroglossia. The primary objective of this review is to systematically present the scientific evidence about the influence of macroglossia on the dentition of affected children. PubMed and Google Scholar articles published between 2011 and 2023 were systematically searched. The selected reports synthesize the ramifications of macroglossia on the oral and dental aspects of children afflicted with Beckwith-Wiedemann Syndrome. The final analysis encompassed 12 articles, comprising seven case studies, three retrospective observations, one cohort study, and one cross-sectional investigation. It was evident that children with BWS experiencing macroglossia necessitate comprehensive care from both medical and dental professionals due to its substantial impact on various aspects, including tooth development, facial aesthetics, and functional implications such as open bites, occlusion disorders, diastema, drooling, enamel hypoplasia, tooth shape anomalies, dental caries, delayed eruption, skeletal class III malocclusion, and mandibular prognathism. The clinical hallmark of Beckwith-Wiedemann Syndrome is characterized by systemic overgrowth, encompassing macroglossia, which significantly influences oral function and maxillofacial morphology. Several limitations are inherent in this review. Firstly, it is predominantly based on single-center retrospective studies with a limited subject pool. Secondly, the absence of case-control analyses hinders further validation of macroglossia's long-term impact on the dentition of affected individuals beyond adolescence. Consequently, future reviews would benefit from extended follow-up studies over a more prolonged duration to address these limitations comprehensively.

Keywords: Beckwith-Wiedemann syndrome, dentition, macroglossia

Introduction

Beckwith-Wiedemann syndrome (BWS) is a childhood overgrowth disorder characterized by developmental abnormalities, tissue and organ hyperplasia, and an elevated risk of embryonic tumors, occurring at an incidence of approximately 1 in 10,340 live births.[1,2] The clinical spectrum of BWS encompasses a wide range of

How to cite this article: Monica GH, Andriana N, Setiawan AS. Macroglossia Impact on Child's Dentition with Beckwith-Wiedemann Syndrome: A Narrative Review. J Pediatr Dent 2024;10(1):9-16

manifestations, including macroglossia, macrosomia, abdominal wall defects, gigantism, hypoglycemia, ear anomalies, and various tumors such as Wilms tumor and hepatoblastoma.[3] Genetic and epigenetic alterations within the chromosome 11p15 locus are implicated in BWS, which typically presents sporadically in 85% of cases, with the remaining 15% demonstrating familial inheritance.[4,5] Macroglossia, a prominent feature of BWS affecting 80–99% of patients, arises from muscle hypertrophy caused by genetic abnormalities in chromosome 11p15. Clinically, macroglossia is characterized by tongue enlargement, often extending beyond the dental arch, with implications for airway and feeding interventions.[6–8]

This work aims to comprehensively investigate the impact of macroglossia on the dentition of children with Beckwith-Wiedemann Syndrome (BWS) by conducting a systematic review of the existing scientific literature published between 2011 and 2023, with the ultimate goal of contributing to the understanding and management of dental and oral health issues in this patient population.

Methods

A systematic article search was conducted in a narrative literature review research design to identify children's oral and dental aspects with BWS. The systematic search and selection of articles link studies on different topics for reinterpretation or interconnection to develop or review. The population in this study is all data in an electronic database with a combination of specified keywords. The sample in this study was selected based on the inclusion and exclusion criteria applied during the search and selection of articles.

Searching strategy

The search was conducted by identifying articles according to the research topic. In this study, the electronic databases used were Google Scholar and PubMed, with applied keywords, inclusion, and exclusion categories. The keywords are words or phrases related to BWS, macroglossia, and oral and dental aspects.

Inclusion and exclusion criteria

The inclusion criteria used in the electronic database are (1) articles published in the last ten years, (2) articles in English and Indonesian, (3) articles with research conducted on humans, and (4) research including observational and review studies. Exclusion criteria include all articles not meeting the inclusion criteria specified at the time of search.

Review

An electronic database search yielded 80 articles (Appendix 1). After excluding four duplicate articles, the remaining 76 were screened based on abstract titles. Among them, 26 articles met the inclusion criteria. Consequently, 14 articles were excluded during full-text screening, resulting in a final selection of 12 articles.[9–20] Appendix 1 provides an overview of the key characteristics of these articles, including research title, country of origin, researcher names, research design, sample size, methods employed, and research findings for each study covered.

The impact of macroglossia on the dental and oral development

Macroglossia may cause open bites in children with BWS. In addition, occlusion disorders in children with[10–14,19,20] may cause diastema[11–13] in several cases. Furthermore, drooling[10–15] and eating and swallowing difficulties due to the influence of macroglossia in children are also associated with BWS.[10,13,14] In addition, tooth shape anomalies[11] and dental caries[14] can occur due to the influence of macroglossia in children with BWS, as well as delayed eruption[11,15] and class III skeletal disorder due to the influence of macroglossia in children with BWS[11,13,16,17,19] and also mandibular prognathism.[12,13,16,17] All the results are also shown in Table 1.

Overall, the findings from this literature study show that the clinical feature in children with BWS is excess growth that can occur in all organs of the human body as one of the three main characteristics that appear during infancy, one of which is an overgrowth of the tongue or macroglossia. Macroglossia impacts tooth growth and facial appearance, including open bites, occlusion disorders, diastema, drooling, enamel hypoplasia, tooth shape anomalies, dental caries, delayed eruption, skeletal class III, and mandibular prognathism.[10–20]

Some cases due to macroglossia can cause children with BWS to have difficulty eating and swallowing, speaking, and experiencing respiratory problems.[7,20] If there is difficulty eating because of macroglossia, it will cause a lack of nutrition and inaccurate calorie intake. In addition, research has shown that children with BWS have other features of varying severity, such as omphalocele, ear abnormalities, hemihyperplasia, neonatal hypoglycemia, and an increased predisposition to embryonal tumors during childhood.

Complications due to macroglossia in neonates include airway obstruction and dysphagia. If difficulty breath-

Table 1. The results of the analysis of the effect of macroglossia on the development of children's teeth and mouth

Clinical manifesttion	Effect of macroglossia on the development of children's teeth and mouth											
	1	2	3	4	5	6	7	8	9	10	11	12
Open bite	√	√	√	√	√	√	√			√	√	
Occlusion disturbance	√	√	√	√	√					√	√	
Diastema		√		√	√							
Drooling	√	√		√				√	√			
Enamel hypolacia		√										
Dental anomaly		√										
Dental caries					√							
Delayed eruption		√				√						
Class III malocclusion		√		√			√	√		√		
Mandibular prognathism			√	√		√	√					√
Difficulty eating and swallowing	√			√	√			√	√	√	√	
Difficulty speaking									√			
Respiratory disorders					√					√	√	√

1) Lamfoon et al (2021), 2) Callea & Yavuz (2016), 3) Meazzini et al (2020), 4) Abeleira et al (2011), 5) Heo et al (2016), 6) Kawafuji et al (2011), 7) Hikita et al (2014), 8) Shipster, Morgan & Dunaway (2012), 9) Maas et al (2016), 10) Cohen et al (2020), 11) Naujokat et.al (2019), 12) Pawlukowska et al (2023)

ing is due to macroglossia, initial airway maintenance is required through endotracheal intubation or feeding using a gastric tube.[14,19] In addition, because macroglossia limits tongue movement, pronunciation problems can occur and cause protrusion of the supporting structures of the teeth along with inclination of the labial mandibular incisors in the maxillofacial region. The effect on the mandible is substantial, causing a class III malocclusion accompanied by an open bite.

In addition to the functional difficulties caused by macroglossia, BWS affects both cancerous and noncancerous children[10] such as hepatoblastoma, peritoneum or retroperitoneum, Wilms tumor, and adrenal carcinoma.[11] The risk of tumor severity depends on clinical and molecular findings. However, most tumors occur at the age of 8–10 years. Therefore, periodic cancer screening is needed to improve tumor prognosis.

According to Matsuda, children with BWS with macroglossia should undergo tongue surgery during a period of minimal perioperative risk before the tongue can affect jaw growth. Wolford suggested that an overly large tongue can cause negative mandibular growth and that reducing the tongue size can control dental problems.[16] The minimum age for tongue surgery in children is at least six months. However, in cases of less severe BWS, Müssig and Zschiesche recommend prior orthopedic, orthodontic, and physiotherapy interventions.[13] It is also recommended that a multidisciplinary medical and dental team develop clinical guidelines for patients with BWS. Orthodontists, in particular, play an essential role as they can evaluate and manage maxillary and mandibular growth to help determine dental occlusion and oral function. Glossectomy is often indicated to prevent mandibular overgrowth.

In a study of children with BWS, dental caries were found on the proximal surfaces of the maxillary genetic teeth, and early caries was found on the occlusal surfaces of the premolars. Because of the relatively large tongue, children with BWS have extensive interdental space in the maxilla and mandible and contra-occlusion with an anterior open bite. Hypoglycemia occurs in 30–50% of children with BWS, which is known to be caused by hyperinsulinemia due to pancreatic enlargement and cell hyperplasia.[10,11] If hypoglycemia is not identified and treated early, neurological complications such as cerebral lesions may occur, and appropriate treatment should be applied immediately at an early stage. Since hypoglycemia most commonly occurs within 24 hours of birth, a blood glucose test is performed on newborns with megaloblasts and umbilical cord malformations. Hypoglycemia usually resolves spontaneously before age four, but partial pancreatectomy may be considered if hypoglycemia is not controlled. In addition, blood sugar can be evaluated through pre-operative blood tests, and blood sugar can be carefully monitored for early detection of hypoglycemia during the surgical procedure.

Implication for practice

Macroglossia associated with Beckwith–Wiedemann syndrome is seen in 80–99% of patients. Not all patients presenting with macroglossia require tongue

reduction, as mild macroglossia may improve due to average mandibular and skeletal growth. Indications for surgical reduction include airway obstruction, swallowing problems and failure to thrive, dental deformities, speech problems, persistent drooling, trauma to the tongue, and cosmetic concerns.[21] Surgery is one way to improve this manifestation, but parents do not necessarily agree. Further exploration in the future may be considered for an ongoing description of this macroglossia in the pediatric dentition. Dentists and pediatricians, with this understanding, can explain to parents the implications of macroglossia and what if surgery is not performed.

Conclusion

The clinical feature of BWS is an overgrowth in all human body organs, one of which is an overgrowth of the tongue or macroglossia. Macroglossia is the most common manifestation affecting oral function and maxillofacial morphology. In addition, macroglossia can cause complications of endoskeletal problems such as open bite, occlusion disorders, a diastema, drooling, enamel hypoplasia, tooth shape anomalies, dental caries, delayed eruption, skeletal class III, and mandibular prognathism.

Financial Disclosure: Nil.
Conflict of Interest: None declared.
Use of AI for Writing Assistance: Not declared.

References

1. Weksberg R, Shuman C, Beckwith JB. Beckwith-Wiedemann syndrome. Eur J Hum Genet 2010;18(1):8–14.
2. Mussa A, Russo S, de Crescenzo A, Chiesa N, Molinatto C, Selicorni A, et al. Prevalence of beckwith-wiedemann syndrome in North West of Italy. Am J Med Genet A 2013;161(10):2481–2486.
3. Zammit M, Caruana E, Cassar D, Calleja-Agius J. Beckwith-Wiedemann syndrome review: A guide for the neonatal nurse. Neonatal Netw 2017;36(3):129–133.
4. MacFarland SP, Duffy KA, Bhatti TR, Bagatell R, Balamuth NJ, Brodeur GM, et al. Diagnosis of Beckwith–Wiedemann syndrome in children presenting with Wilms tumor. Pediatr Blood Cancer 2018;65(10):e27296.
5. Simmonds JC, Patel AK, Mildenhall NR, Mader NS, Scott AR. Neonatal macroglossia: Demographics, cost of care, and associated comorbidities. Cleft Palate Craniofac J 2018;55(8):1122–1129.
6. Farronato G, Giannini L, Galbiati G, Maspero C. Sagittal and vertical effects of rapid maxillary expansion in Class I, II, and III occlusions. Angle Orthod 2011;81(2):298–303.
7. Brioude F, Kalish JM, Mussa A, Foster AC, Bliek J, Ferrero GB, et al. Clinical and molecular diagnosis, screening and management of Beckwith-Wiedemann syndrome: An international consensus statement. Nat Rev Endocrinol 2018;14(4):229–249.
8. Wang KH, Kupa J, Duffy KA, Kalish JM. Diagnosis and Management of Beckwith-Wiedemann Syndrome. Front Pediatr 2020;7:567.
9. Pawlukowska W, Patalan M, Bagińska E, Giżewska M, Masztalewicz M. Application of original therapy for stimulation of oral areas innervated by the trigeminal nerve in a child with Beckwith-Wiedemann syndrome. Brain Sci 2023;13(5):829.
10. Lamfoon S, Abuzinada S, Yamani A, Binmadi N. Beckwith-Wiedemann syndrome with macroglossia as the most significant manifestation: A case report. Clin Case Rep 2021;9(7):1–4.
11. Callea M, Yavuz I, Unal M, Sahnaz C, Dogan MS, Cammarata-Scalisi F. A case of Beckwith-Wiedemann syndrome with peculiar dental findings. Eur J Paediatr Dent 2016;17(4):315–317.
12. Meazzini MC, Besana M, Tortora C, Cohen N, Rezzonico A, Ferrari M, et al. Long-term longitudinal evaluation of mandibular growth in patients with Beckwith-Wiedemann syndrome treated and not treated with glossectomy. J Craniomaxillofac Surg 2020;48(12):1126–1131.
13. Abeleira MT, Seoane-Romero JM, Outumuro M, Caamaño F, Suárez D, Carmona IT. A multidisciplinary approach to the treatment of oral manifestations associated with beckwith-wiedemann syndrome: A long-term case report. J Am Dent Assoc 2011;142(12):1357–1364.
14. Heo SJ, Shin TJ, Hyun HK, Kim JW, Jang KT, Lee SH, et al. Dental caries treatment of a patient with Beckwith-Wiedemann syndrome: A case report. J Korean Dis Oral Health 2016;12(2):92–95.
15. Kawafuji A, Suda N, Ichikawa N, Kakara S, Suzuki T, Baba Y, et al. Systemic and maxillofacial characteristics of patients with Beckwith-Wiedemann syndrome not treated with glossectomy. Am J Orthod Dentofacial Orthop 2011;139(4):517–525.
16. Hikita R, Kobayashi Y, Tsuji M, Kawamoto T, Moriyama K. Long-term orthodontic and surgical treatment and stability of a patient with Beckwith-Wiedemann syndrome. Am J Orthod Dentofacial Orthop 2014;145(5):672–684.
17. Shipster C, Morgan A, Dunaway D. Psychosocial, feeding, and drooling outcomes in children with beckwith Wiedemann syndrome following tongue reduction surgery. Cleft Palate Craniofac J 2012;49(4):e25-e34.
18. Maas SM, Kadouch DJ, Masselink ACCM, Van Der Horst CMAM. Taste and speech following surgical tongue reduction in children with Beckwith-Wiedemann syndrome. J Craniomaxillofac Surg 2016;44(6):659–663.
19. Cohen JL, Cielo CM, Kupa J, Duffy KA, Hathaway ER, Kalish JM, et al. The utility of early tongue reduction surgery for macroglossia in Beckwith-Wiedemann syndrome. Plast Reconstr Surg 2020;145(4):803E-813E.
20. Naujokat H, Möller B, Terheyden H, Birkenfeld F, Caliebe D, Krause MF, et al. Tongue reduction in Beckwith–Wiedemann syndrome: Outcome and treatment algorithm. Int J Oral Maxillofac Surg 2019;48(1):9–16.
21. Kittur MA, Padgett J, Drake D. Management of macroglossia in Beckwith-Wiedemann syndrome. Br J Oral Maxillofac Surg 2013;51(1):e6-e8.

Appendix 1. General characteristics of the articles

No	Title	Author (country, year)	Research design and sample size	Purpose	Measurement method	Result	Conclusion
1	Beckwith- Wiedemann syndrome with macroglossia as the most significant manifestation: A case report	Lamfoon et al (Saudi Arabia, 2021)[10]	Clinical Case Reports 1 year old baby boy	To review dental problems and update the clinical and molecular diagnosis of BWS and its management with an emphasis on macroglossia.	The patient has macroglossia which causes inability to close the mouth, impaired occlusion, difficulty eating and swallowing, drooling and hemihypertrophy on the left side of the body.	The patient has macroglossia which causes inability to close the mouth, impaired occlusion, difficulty eating and swallowing, drooling and hemihypertrophy on the left side of the body.	Follow-up and monitoring by the dentist is important to maintain function and restore the patient's aesthetic appearance.
2	A case of Beckwith-Wiedemann syndrome with peculiar dental findings	Callea et al (Venezuela, 2016)[11]	Case Study 5-year-old boy	To find out some cases of BWS and describe all the features broadening knowledge of orodentofacial phenotype along with literature review	Intraoral examination	There are typical oral characteristics in BWS patients including: • Delayed eruption • Congenital diastema of the mandibular permanent incisors • Tooth shape anomaly • Tooth enamel defects, namely enamel hypoplasia • Mixed teeth • enamel defects on teeth 21 • Open bite • Skeletal class III • Macroglossia Poor oral hygiene.	BWS cases have orofacial characteristics such as macroglossia, Skeletal class III, Open bite and additional features such as diastema, tooth shape anomalies, and tooth enamel defects. With the medical record of oral manifestations in BWS patients, it can aim to expand knowledge about BWS.
3	Long-term longitudinal evaluation of mandibular growth in patients with Beckwith-Wiedemann Syndrome treated and not treated with glossectomy	Meazzini et al (Italy, 2020) [12]	Observational Retrospective 78 BWS patients (Age 5-15 years)	To compare long-term mandibular growth between a group of BWS patients who underwent glossectomy at an early age and a group of patients who were not operated on.	Lateral cephalometric examination	1. All patients had an open bite on the primary teeth. 2. There was no significant difference in the sagittal position of the maxilla or mandible in patients who were operated on (glossectomy) and those who were not operated on. 3. The maxillary incisor inclination in patients aged 5, 10 and 15 years was statistically greater in the non-operated group (glossectomy). Mandibular growth rates were similar between glossectomy and non-operated patients, with higher mandibular measurement values in both groups of patients compared to the healthy population.	Many BWS patients exhibit progressive mandibular overgrowth from childhood to adolescence and glossectomy does not appear to alter their rate of growth. Consequently, in the absence of airway obstruction, swallowing problems with failure to thrive, impaired feeding and speech problems, based on our data, glossectomy is not recommended in BWS patients to prevent Class III malocclusion.
4	A multidisciplinary approach to the treatment of oral	Abeleira et al (Spain, 2011) [13]	Case Study	1. To describe a 15-year follow-up of patients with BWS	Intraoral examination	1. Have hypoglycemia, which goes away in 23 hours. 2. Intraoral examination showed the	This study recommends that a multidisciplinary medical and dental team develop clinical guidelines

Appendix 1. Cont.

No	Title	Author (country, year)	Research design and sample size	Purpose	Measurement method	Result	Conclusion
	manifestations associated with Beckwith-Wiedemann syndrome			To find out the appropriate treatment plan in patients with BWS and dentoskeletal changes, including macroglossia.		presence of: Perioral muscle hypotonia True macroglossia Severe drooling 3. Having difficulty in swallowing and sucking. 4. There is a progressive anterior open bite secondary to tongue prolapse. 5. When the patient was 7.5 years old had severe vertical mandibular growth with anterior open bite, diastema, class III malocclusion and class I malocclusion. 6. Vertical skeletal growth and dentoalveolar compensation, especially in the maxillary and mandibular anteriors.	for patients with BWS. In particular orthodontists play an important role, as they can evaluate and manage maxillary and mandibular growth to help determine final dentition and oral function.
5	Dental caries treatment of a patient with Beckwith-Wiedemann Syndrome	Heo et al (Korea, 2016) [14]	Case Study Three year old boy	To describe the dental care of children with BWS.	Intraoral examination	1. The patient was diagnosed with BWS with manifestations of omphalocele, complex heart disease, macroglossia and wrinkled left ear. 2. At about 4 months of age, the patient has difficulty swallowing food because the large tongue blocks the throat. 3. Macroglossia causes the patient to have difficulty breathing, diastema, anterior open bite, class III malocclusion. There is caries on the proximal surfaces of the incisors and the occlusal surfaces of the maxillary premolars.	BWS is a disease seen from various clinical features. Macroglossia is the most common feature observed in children with BWS, and can cause feeding problems and breathing difficulties, so caution is required during dental work. In addition, long-term evaluation of bone problems caused by macroglossia is required.
6	Systemic and maxillofacial characteristics of patients with Beckwith-Wiedemann syndrome not treated with glossectomy	Kawafuji et al (Japan, 2011) [15]	Case Study Seven Japanese people who had been diagnosed with BWS (2 boys and 5 girls Age 4 years 2 months – 9 years 2 months)	To analyze individuals who have and who have not undergone glossectomy, so that it has a high impact on jaw growth and occlusion.	Results of cephalogram and dental impressions taken at the first visit	1. Of the seven individuals recorded, all of them had macroglossia. 2. Four patients showed exomphalos, tumor, earlobe abnormalities and hemihypertrophy. 3. All seven individuals exhibited wide dental arches and anterior open bite due to unerupted anterior teeth and proclination. 4. Four individuals had mandibular prognathism	As a characteristic of BWS, individuals exhibit macroglossia resulting in an anterior open bite and wide dental arch. Long facial height and enlarged anterior cranial base and large mandibular body.

Appendix 1. Cont.

No	Title	Author (country, year)	Research design and sample size	Purpose	Measurement method	Result	Conclusion
						All seven individuals showed wide variation in the gonial angle, but the overall facial height appeared to be large.	
7	Long-term orthodontic and surgical treatment and stability of a patient with Beckwith-Wiedemann syndrome	Hikita et al (Japan, 2014) [16]	Case Study 5 years 10 months old girl	This study aims to determine the results of long-term observations of BWS patients who underwent tongue reduction, early orthodontic treatment, and orthodontic-surgical treatment.	Cephalometric test results	1. Anterior open bite with 9.0 mm overjet and -3.0 mm overbite, and narrow maxillary dental arch width with high arched palate resulted in total crossbite. 2. His facial profile is concave with a protruding chin and a long lower face. 3. The tongue is quite long, and the folds of the earlobe are abnormal. Skeletal class III with severe mandibular protrusion	This study suggests that balancing the structure and function of the dentoalveolar and musculoskeletal tissues of the orofacial complex is the key to good treatment outcomes and long-term stability of patients with BWS.
8	Psychosocial, Feeding, and Drooling Outcomes in Children with Beckwith Wiedemann Syndrome Following Tongue Reduction Surgery C.	Shipster, et al (UK, 2012)[17]	Cohort 10 Kids with BWS 9 months to 4 years old	To describe the preoperative and postoperative psychosocial, feeding, and drooling outcomes of children with macroglossia associated with BWS and to investigate the effect of TRS (Tongue reduction surgery) in these areas.	Parental report questionnaire Saliva scale Feeding rating scale	1. All parents of patients reported that macroglossia had a negative impact on the child's facial appearance. 2. Macroglossia causes various feeding difficulties before surgery to prevent lip seal and bolus manipulation during the oral preparatory phase. 3. All case samples experienced excessive salivation and difficulty eating before surgery. After TRS (Tongue reduction surgery) is performed, there is a change in the child's facial appearance because the tongue is no longer protruding and the psychosocial changes are very positive.	In particular, in relation to psychosocial outcomes, a visibly enlarged tongue had a negative effect on a child's facial appearance. There are characteristic feeding difficulties, including poor anterior open bite, food ropulsion and increased salivation before surgery.
9	Taste and speech following surgical tongue reduction in children with Beckwith-Wiedemann syndrome	Maas et al (Netherland, 2016)[18]	Observational Retrospective 10 patients with BWS who had TRS (Tongue reduction surgery) More than 5 years old	To determine the long-term outcome of Tongue reduction surgery (TRS) on taste and speech function in patients with BWS who are more than 5 years old and who have undergone anterior tongue wedge resection surgery.	Questionnaire	1. None of the children had taste problems. 2. Eight out of ten children experience drooling. Six pediatric patients had speech errors, especially the pronunciation of the letters "s" and "t".	That anterior wedge resection is an effective technique for treating macroglossia in children with BWS without long-term complications for speech or taste perception.

Appendix 1. Cont.

No	Title	Author (country, year)	Research design and sample size	Purpose	Measurement method	Result	Conclusion
10	The Utility of Early Tongue Reduction Surgery for Macroglossia in Beckwith-Wiedemann Syndrome	Cohen et al (USA, 2020) [19]	Observational Retrospective 36 patients with BWS who had tongue reduction. (Mean age at tongue reduction was 9 months).	To determine whether BWS patients could benefit from early surgical intervention before 12 months of age.	Intraoral Examination	1. After tongue reduction the patient had a significant reduction in obstructive apnea hypopnea from 30.9±21.8 per hour to 10.0±18.3 per hour (p=0.019) and an increase in oxyhemoglobin nadir saturation from 72±10 percent to 83±6 percent (p=0.008). 2. Although there were no significant changes in feeding and breathing, surgical intervention was clinically significant. Intraoral examination of 36 patients before and after surgery showed an increase in class I occlusion and decreased changes in class III occlusion, anterior open bite, and macroglossia.	Patients with prenatal macroglossia, a postnatal obstructive sleep apnea requiring continuous positive airway pressure, will benefit from tongue reduction surgery before 12 months of age. Therefore, this study recommends that every patient with BWS and severe macroglossia undergo a multidisciplinary evaluation for tongue reduction in the initial management of respiratory distress based on objective data.
11	Tongue reduction in Beckwith-Wiedemann syndrome: outcome and treatment algorithm	Naujokat et al (Germany, 2019)[20]	Cross Sectional 68 Children with BWS (Mean age of patients 2.5 years)	To evaluate perioperative complications, as well as long-term aesthetic and functional outcomes in patients undergoing surgery or conservative treatment.	• Questionnaire • Surgical parameters • Post-surgery results Preoperative documentation	1. Of the 26 patients who underwent tongue reduction surgery, 85% described a disproportionate tongue shape, and 19% showed scars that were quite disturbing appearance. 2. Dentoalveolar and musculoskeletal malformations occurred in both groups at almost the same rate: malpositioned teeth in 62% (surgical) and 80% (conservative), anterior open bite in 58% (operative) and 70% (non-operative).	In the long term, none of the patients had taste disturbances or paresthesias, although tongue shape was disproportionate in 85%. With current treatment algorithms, operative tongue reduction has a positive effect on skeletal, dentoalveolar and functional development with adequate long-term outcomes and high patient satisfaction rates. Supportive therapy is essential for surgical and conservative treatment.
12	Application of Original Therapy for Stimulation of Oral Areas Innervated by the Trigeminal Nerve in a Child with Beckwith-Wiedemann Syndrome	Pawlukowska et al (Poland, 2023)[9]	Case study, 5 months old baby	To present original therapy for stimulation of oral areas innervated by the trigeminal nerve is a good alternative to existing methods of surgical tongue reduction in children with BWS and macroglossia.	Intraoral examintation	After 3 months, a significant improvement in oral alignment and function was achieved. Preliminary observations of therapy application for stimulation regions innervated by the trigeminal nerve in children with Beckwith–Wiedemann syndrome seem promising	The original therapy for stimulation of oral areas innervated by the trigeminal nerve is a good alternative to existing methods of surgical tongue reduction in children with BWS and macroglossia.