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Research Article

Oral soft tissue conditions in Down syndrome patients

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Abstract

Introduction: Down syndrome is an abnormality caused by an extra chromosome 21. Oral soft tissue conditions are one of the most frequently reported clinical features in Down syndrome because their prevalence is relatively high. The purpose of this study was to determine the various oral soft tissue conditions in children with Down syndrome from various literatures. **Methods and Material**: The literature review was conducted using the Scoping Review method following the frameworks published by Arksey and O'Malley (2005) and developed by Levac, et al. (2010) and Peters, et al. (2015). Screening and selection of studies was carried out using PRISMA-ScR. Articles were searched using keywords, boolean operators, limit functions, and inclusion criteria on the Pubmed, EBSCOHost, ScienceDirect, and Google Scholar search engines. **Results**: There were 12 articles that met the criteria and were analyzed. The most commonly reported oral soft tissue conditions in Down syndrome are fissured tongue, macroglossia, and cheilitis. Fissured tongue varies from 28% - 78%, macroglossia varies from 36.8% - 94%, total & angular cheilitis varies from 6.3% - 51%. Incompetent lip, geographic tongue, everted lower lip, chapped lower lip, protruded tongue, gingivitis, and several other soft tissue conditions have also been reported in only a few articles. **Conclusion**: The most common frequently oral soft tissue conditions reported in the Down syndrome population are fissured tongue varies from 28% - 78%, macroglossia varies from 36.8% - 94%, and total & angular cheilitis varies from 6.3% - 51%.

Keywords: Cheilitis, Down syndrome, Fissured tongue, Macroglossia, Oral soft tissue conditions

INTRODUCTION

Down syndrome is an abnormality caused by the existence of an extra chromosome 21. This triggers the disturbance in neurology, physical, mental, and intellectual development of Down syndrome individuals.[1,2] Based on the location of chromosome abnormality, Down syndrome is divided into 3 categories. Said categories are: trisomy 21 (94%), translocation (5%), and mosaicism (1%).[3,4] Trisomy 21 is caused by the existence of an extra chromosome 21, which normally is diploid, but because of this condition it becomes triploid; that causes the individual to have 47 total chromosomes.[5] Translocation type Down syndrome is caused by the existence of a segment of chromosome 21 sticking to another chromosome pair.[3,4] Mosaicism type Down syndrome or partial trisomy is caused by the existence of a nondisjunction event on late cell division stages.[3,4]

Down syndrome is one of the most common chromosomal abnormalities that happens all over the world. According to WHO, out of a 1.000 people, 1 to 10 of them suffer from this condition.[6] It is estimated that the number of people suffering from Down syndrome reaches 8 million people globally.[7] According to data from Indonesia Center for Biodiversity and Biotechnology (ICBB), there are more than 300.000 Indonesian children with Down syndrome. According to Riskesdas (2013), out of 1.000 people, 1.3 of them suffer from Down syndrome.[6,7]

The existence of extra chromosome 21 in Down syndrome individuals causes mental retardation and developmental delays in children.[8] This further causes the existence of comorbidity characteristics that influence the growth and development of Down syndrome children.[4,9] Individuals with Down syndrome usually have a higher risk for getting infection, orofacial or maxillofacial dysmorphology/anomaly, and also systemic abnormalities.[1,3,10] They are more susceptible to infections due to defects in their immune system. These defects mainly occur on the natural killer cells, neutrophils, lymphocyte T cells, and lymphocyte B cells.[11,12] They also have higher risks for oral health problems including oral soft tissue and periodontal anomalies, dental anomalies, periodontal diseases, and malocclusion.[3,13]

Oral soft tissue condition is one of the most common clinical features that is reported between various oral manifestations on Down syndrome individuals.[1] Oral soft tissue / mucosa condition is the clinical state of the oral mucosa (a moist wet layer that contacts with the external environment of the mouth cavity). The oral mucosal condition is generally identified as an oral disease and a normal variation of the oral mucosal condition.[14] It may manifest due to the comorbidity of Down syndrome children. It may also manifest because of poor oral hygiene.[8] This condition is caused by the low IQ score of the Down syndrome children, that they do not have the ability or consciousness to maintain their oral hygiene.[8,15] The existence of hypotonia and the lack of muscular coordination also causes Down syndrome children to have difficulties on toothbrushing.[16,17] The existence of malocclusion on Down syndrome children also facilitates plaque retention that hinders mouth hygiene maintenance.[18,19] Therefore, Down syndrome children need family members, caregivers, or surrounding people to help maintain their oral hygiene and health. However, the majority of family members of Down syndrome children focus more on comorbidity or existing common medical conditions, so that oral health are oftentimes neglected.

Based on initial searches conducted through PubMed and Google Scholar database, it is shown that there are quite a lot of research conducted on oral condition abnormality of Down syndrome children, especially the oral hard tissue, however study literatures that focus on oral soft tissue condition on Down syndrome children with scoping review research design have not been conducted in Indonesia. The aim of this research is to know various oral soft tissue conditions on down syndrome children, because it is important in helping to identify oral health conditions and can be beneficial in care priority management which has implications for the multidisciplinary oral mucosa health care needed by these groups of individuals in Indonesia.

MATERIALS AND METHODS

The strategy for article research in this qualitative study is to use the scoping review method, which follows the work steps and methodological framework published by Arksey and O'Malley (2005) and further developed by Levac et al. (2010) and Peters et al. (2015).[20–22] Research instruments used were a laptop, Microsoft Software, search engines (PubMed, EBSCOhost, ScienceDirect, and Google Scholar), Mendeley application, scientific journal articles, and internet access. Screening and the selection of studies were done with Preferred Reporting Items for Systematic Review and Meta-analysis Scoping Review (PRISMA-Scr).[23]

Articles were obtained through electronic database searches conducted in PubMed, EBSCOhost, ScienceDirect, and Google Scholar using "AND" and "OR" Boolean operators and the limit functionality of each database. Article searches were conducted by combining multiple keywords across search engines (Table I). The samples that were used in this study are articles that meet certain inclusion criteria listed below:

1. Articles that discuss oral soft tissue lesions or conditions in individuals with Down syndrome.
2. Articles that were published in the past 15 years (2007-2022).
3. Full-text articles that can be accessed in English and Indonesian as languages that are able to be understood by the writer.
4. Articles that are included in national and international journals.

While the exclusion criteria in this study are:

1. Articles that do not discuss oral soft tissue conditions/lesions in individuals with Down syndrome.
2. Articles that were not published in the past 15 years.
3. Non-full-text articles and non-accessible articles.
4. Articles not in English or Indonesian
5. Duplicate articles on different search engines.

The systematic screening and selection of studies that are looked into in this paper are done using PRISMA-ScR, with reasons on why those full-text articles were excluded (Diagram 1). Data analysis was conducted using thematic analysis. Thematic analysis is a method of qualitative research done to identify, describe, and report patterns or themes in certain data.[24]

Table I: Research protocol

Electronic database search engine	Search topic strategy	Amount of articles
PubMed	*((Down syndrome OR Down's syndrome OR trisomy 21 OR sindrom Down OR trisomi 21)) AND ((child OR infant OR baby OR adolescent OR anak)) AND ((oral lesion OR soft tissue oral lesion OR oral mucosa OR oral mucosa lesion OR oral manifestation OR lesi oral OR lesi jaringan lunak oral OR mukosa oral OR lesi mukosa oral OR manifestasi oral))* *Filters: full text from 2007 - 2022*	198
EBSCOhost	*(Down syndrome OR trisomy OR Down's syndrome OR Down's OR trisomy) AND (baby OR children OR infant OR adolescent) AND (oral lesion OR soft tissue oral lesion OR oral mucosa lesion OR oral manifestation)* *Limiters - full text, references available, published date: 20070101-20221231*	671
ScienceDirect	*(Down syndrome OR Down's syndrome OR trisomy 21) AND (oral lesion OR soft tissue oral lesion OR oral mucosa OR oral mucosa lesion OR oral manifestation)* *Filters: 2007 - 2022*	71
Google Scholar	*(oral soft tissue lesion OR oral mucosa lesion) "Down syndrome"* *Filters: 2007 - 2022*	1.680

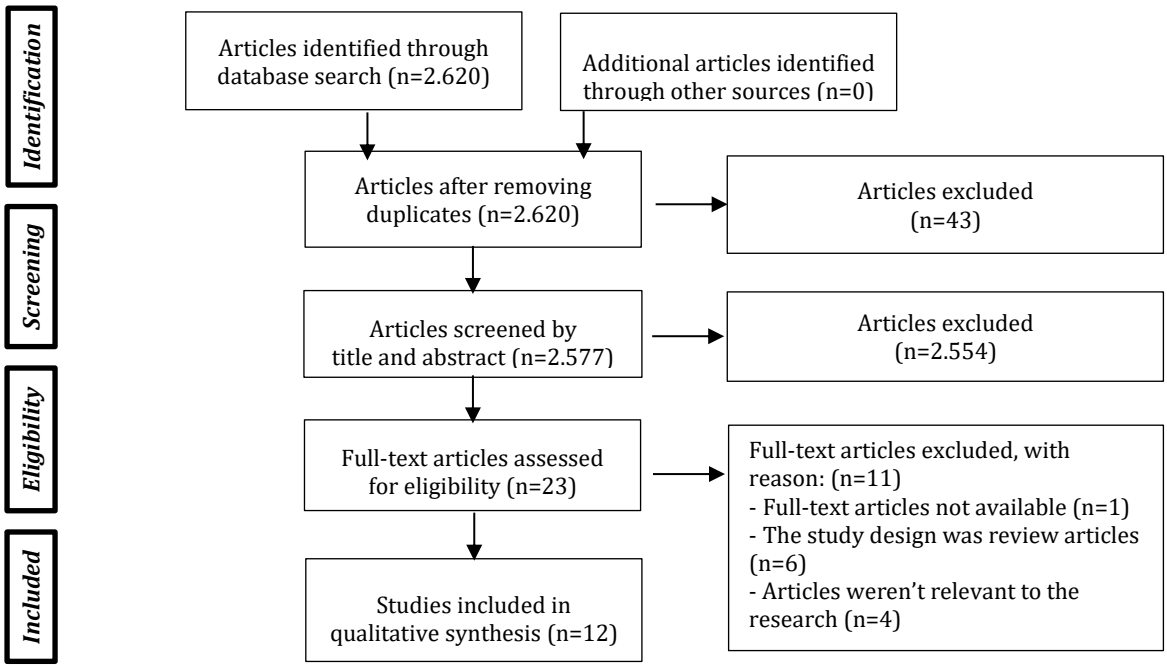

Diagram 1: PRISMA-ScR Flowchart summarizing the selection process

RESULTS

A total of 12 studies that met the inclusion criteria were obtained from the search results and study selection, with general characteristics that varied from the selected studies (Table 2). The results of this scoping review study showed that there are various conditions of the oral soft tissues in people with Down Syndrome (Table 3).

Fissured tongue is the most common oral mucosa condition presented in Down syndrome patients. It was reported in 10 different research articles with a variation value between 28% to 78%.[1,3,17,25–31] Meanwhile, angular cheilitis with a variation value between 6.3% to 51%[1,3,17,27–30] , and macroglossia with variation value between 36.8% to 94%[3,17,26–28,30,31] , were also common oral mucosa conditions each reported in 7 different research articles; lip fissure / cheilitis with a variation value between 13% to 14% were reported in 3 different research articles[1,25,27]; incompetence lip with a variation value between 7.8% to 100% were reported in 3 different research articles[3,17,26]; gingivitis reported in 3 different research articles [1,32,33]; geographic tongue reported in 2 different research articles[25,30]; everted lower lip, chapped lower lip, and protruded tongue were reported in 2 different research articles[3,17]. In addition, several other oral soft tissue conditions were also reported in 5 different research articles (Table 3)[1,17,28,30,32].

Table II: Characteristics of the studies

Author	Publication Year	Country Origin	Article Title	Journal	Research Purposes	Type of Study
M. Daneshpazhooh et al.[25]	2007	Iran	Mucocutaneous Findings in 100 Children with Down Syndrome	Pediatric Dermatology	To assess the mucocutaneous findings in Down syndrome patients in Iran.	cohort study
S. Asokan et al.[17]	2008	India	Oral findings of Down syndrome children in Chennai city, India	Indian Journal of Dental Research	To assess the common oral findings and anomalies of Down syndrome (DS) children in Chennai city, India.	Descriptive cross-sectional study
R. Al-Shawaf & W. Al-Faleh[26]	2011	Saudi Arabia	Craniofacial characteristics in Saudi Down's syndrome	King Saud University Journal of Dental Sciences	To study the craniofacial manifestations in the Saudi Down's syndrome patients in comparison with those in normal subjects.	Comparative cross-sectional study
R. Sureshbabu et al.[27]	2011	India	Phenotypic and dermatological manifestations in Down Syndrome	Dermatology Online Journal	To evaluate the frequency of phenotypic and dermatological manifestations in patients with Down syndrome in south India.	cohort study
D. Shukla et al.[28]	2014	India	Dentofacial and Cranial Changes in Down Syndrome	Osong Public Health and Research Perspectives	To determine the prevalence of certain oral characteristics usually associated with Down syndrome and to determine the oral health status of these patients.	cross-sectional study
F. Camacho et al.[29]	2014	Spain	Phenotypical and Dermatological Findings of Down Syndrome in Southern Spain	European Journal of Pediatric Dermatology	To describe the prevalence of dermatological and systemic entities among DS patients in the Trichology Unit Health Care Area, with special reference to AA.	Prospective study (cohort)
G. Al-Sufyani et al.[33]	2014	Yemen	Oral Hygiene and Gingival Health Status of Children with Down Syndrome in Yemen: A Cross-Sectional Study	Journal of International Society of Preventive & Community Dentistry	To assess the oral hygiene and gingival health status among Yemeni children with Down syndrome.	cross-sectional study
S. Al-Maweri et al.[1]	2015	Yemen	Lip and Oral Lesions in Children with Down Syndrome: A Controlled Study	Journal of Clinical and Experimental Dentistry	To assess the prevalence of orolabial lesions and conditions, with particular emphasis on the incidence of fissured tongue, angular cheilitis and lip fissures, among a group of Yemeni patients with DS, as compared to healthy controls.	control cross-sectional study
B. Ghaith et al.[30]	2019	United Arab Emirates	Oral Health Status among Children with Down Syndrome in Dubai, United Arab Emirates	Journal of International Society of Preventive & Community Dentistry	To assess the oral health status in Down syndrome (DS) children in Dubai, United Arab Emirates.	Quantitative case-control study
C. Tipe et al.[32]	2019	Peru	Oral Epidemiological Profile and Risk Factors in Adolescents with Different Degrees of Down Syndrome in a Vulnerable Peruvian Rural Population	Journal of Contemporary Dental Practice	To assess the epidemiological profile of 12- to 16-year-old adolescents with Down syndrome in the Special Basic Education Center in Lima-Peru.	descriptive cross-sectional study
H. Fansa et al.[31]	2019	Saudi Arabia	The Prevalence of Oral and Dental Anomalies in Down Syndrome Children in Western Region, Saudi Arabia	International Journal of Health Sciences and Research	To determine the prevalence of some selected oral and dental anomalies in Down syndrome children in Makkah and Jeddah, Saudi Arabia.	cross-sectional study
S. Ashwinirani et al.[3]	2020	India	Oral and Perioral Manifestations in Down's Syndrome Patients	BLDE University Journal of Health Sciences	To assess the oral and perioral features of DS patients and to compare age and gender wise distribution of these findings.	Descriptive study

Table III: Sample characteristics and soft tissue oral condition findings in Down syndrome patients

Author		M. Danesh-pazhooh et al.[25]	S. Asokan et al.[17]	R. Al-Shawaf dan W. Al-Faleh[26]	R. Sureshbabu et al.[27]	D. Shukla et al.[28]	F. Camacho et al.[29]	G. Al-Sufyani et al.[33]	S. Al-Maweri et al.[1]	B. Ghaith et al.[30]	C. Tipe[32]	H. Fansa et al.[31]	S. Ashwinira-ni et al.[3]
Study population		Iran	India	Saudi Arabia	India	India	Spain	Yemen	Yemen	United Arab Emirates	Peru	Saudi Arabia	India
Sample amount		100	102	30	95	77	57	101	50	106	107	50	100
Control		N/A	N/A	available	N/A	N/A	N/A	N/A	available	available	N/A	available	N/A
Sex distribu-tion	Male	47	57	14	59	70	34	64	31	63	59	30	63
	Female	53	45	16	36	7	23	37	19	43	48	20	37
Mean Age (Range) year		11.20 (3-20)	N/A (0-15)	15.93 (12-24)	11.97 ± 8.8 (0-40)	N/A (1-30)	16.7 (2-29)	10.52 (6-16)	12.66 (6-18)	9.3 ± 2.8 (4-18)	N/A (12-16)	8.0 (4-14)	N/A (8-16)
Fissured tongue		28%	41.2%	70%	52.6%	67.5%	70.2%		78%	67.9%		74%	73%
Macroglossia			62.7%	60%	36.8%	58.4%				46.2%		94%	53%
Angular Cheilitis			22.5%		6.3%	22.1%	28.1%		38%	21.7%			51%
Cheilitis/ Lip Fissure		13%			13.7%				14%				
Incompetence lip			7.8%	100%									48%
Geographic tongue		4%								8.5%			
Everted lower lip			65.7%										61%
Chapped lower lip			10.6%										21%
Protruded tongue			41.2%										45%
Gingivitis								28.7% (severe) 47.5%(moderate) 23.8% (mild)	98%		58.8% (mild) 29.8% (moderate)		
Other oral conditions			*Angle of mouth pull down* (63.7%), *defects in palate* (23.5%), *enlarged tonsils* (22.5%)			*Ankyloglossia* (13%), *lack of lip seal* (51.9%)			gingival hyperplasia (18%), fibroma (8%), *cheek biting* (2%), herpes labialis (2%), *traumatic ulcer* (4%),	*Atrophy of tongue* (7.5%), *Irritation fibroma* (1%), *Ulcer* (2.8%), *Trauma to soft tissue/lip* (2.8%),	Periodontitis (85.9% mild, 2.8% moderate)		

***N/A**, not available

Characteristics of the Studies

There were 7 research articles that used a cross-sectional study design[1,17,26,28,31–33], 3 articles used a cohort study design[25,27,29], one article used a quantitative case-control study design[30], and one other article used a descriptive study design[3]. The sample sizes of all the research articles varied from 30 to 107 individuals, while the ages of the study sample ranged from 0 to 40 years old.[1,3,32,33,17,25–31] Research locations on 4 articles were conducted in India[3,17,27,28], 2 articles were conducted in Saudi Arabia[26,31], 2 articles were conducted in Yemen[1,33], and the other 4 articles were conducted in Iran[25], Spain[29], United Arab Emirates[30], and Peru.[32]

DISCUSSION

Based on the data, it is known that there are several oral soft tissue manifestations in Down syndrome individuals from toddlers to young adults. The average age category of the sample that reported in 8 studies according to the Ministry of Health was from late childhood to adolescence, while the average age of the sample in the 4 other studies was not reported (Table III).[1,25–27,29–31,33,34]

The most common oral soft tissue condition in Down syndrome patients are fissured tongue and macroglossia. Fissure tongue is an asymptomatic benign lesion, with deep arches on the anterior 2/3 of dorsal surface and the edges of the tongue as its characteristic.[5,28,35] Fissured tongue is more commonly found in Down syndrome patients than the normal population.[1,25] Fissured tongue in Down syndrome patients are caused by mouth breathing and the presence of tongue protrusion, which causes the tongue to be cracked and dry.[36–39] The prevalence of fissured tongue in the studies reviewed has a variation value between 28% to 78% in 10 different studies . Most of the studies reviewed reported that the fissured tongue in Down syndrome has an average value above 60%, excluding a study conducted by Daneshpazhooh et al. at 28%, Asokan et al. at 41,2%, and Sureshbabu et al. at 52.6%.[17,25,27] This is caused by differences in sample collection method, sample grouping system, and study location. However, in this study, it can be observed that the average prevalence value of fissured tongue increases with age. It is also found that fissured tongue is more common in males. The data found in this study matches with other previous studies used as reference.[1,3,17] The increasing age is a factor that affects the development of crack and fissure on the tongue of Down syndrome patients.[26,40] Local factors such as food diet and oral hygiene also contributes to the development of tongue fissure.[26] It is commonly found that fissured tongue is associated with geographic tongue. The relevant clinical reason for the development of geographic tongue in Down syndrome patients is because of the prior existing fissured tongue that acts as bacterial reservoir and causes glossitis, therefore the geographic tongue develops.[30] Two studies by Daneshpazhooh et al. dan Ghaith et al. states that geographic tongue condition is not commonly found in Down syndrome individuals; the prevalence value of geographic tongue is 4% and 8,5% in said studies respectively.[25,30]

Macroglossia in Down syndrome individuals also varies from 36.8% to 94% in 7 different studies. Macroglossia that is found in Down syndrome are relative macroglossia caused by inadequate lymphatic drainage, muscle weakness (hypotonia), and low mouth position.[26,30,41] Other than said factors, the smaller size of the oral cavity in Down syndrome population also causes the tongue to seem bigger than the normal population.[3,41] Macroglossia can also be followed by the development of fissured tongue in Down syndrome individuals (Shukla et al.).[28] Most of the studies that are reviewed in this paper, reports the average presence of macroglossia in Down syndrome individuals to be above 50%, except the study conducted by Sureshbabu et al. (36.8%) and Ghaith et al. (46.2%).[27,30] According to Sureshbabu et al. macroglossia is more significantly present in children than adults.[27]

Cheilitis also becomes one common condition of oral soft tissue in Down syndrome individuals, the condition is reported in 8 different studies that reviewed in the current study.[1,3,17,25,27–30] However, the percentage of cheilitis that are reported is smaller than the percentage of fissured tongue and macroglossia, with a total average percentage value of 24.5%. Cheilitis is usually found in patients over 4 or 5 years of age.[25,27] The reported types of cheilitis consist of angular and total type, however the prevalence of cheilitis reported in the study by Daneshpazhooh et al. included both types, which was 13%.[25] In 8 studies that are reviewed in the current study, angular cheilitis are more frequently reported with an average value of 27.1% than total type cheilitis with an average value of 21.9%. According to Asokan et al. and Al-Maweri et al., angular cheilitis incidence is higher in Down syndrome individuals than the normal population.[1,17] The increased incidence can be caused by the presence of *Candida albicans* as the result of drooling and immune defects in Down syndrome individuals.[1,3]

Incompetent lips are also reported in 3 different studies that are reviewed in the current study, with a variance value of 7.8% to 100% in researched samples.[3,17,26] The open mouth condition that are found in Down syndrome group are caused by narrow nasopharynx, tonsil and adenoid abnormal enlargement, or a protruded tongue.[26] The reported findings of incompetent lips has significant variance value. This condition may be due to the differences in population.[17] According to a study conducted by Ashwinirani et al., incompetent lips in Down syndrome individuals increased with age.[3] Incompetent lips may increase because of mouth breathing and tongue protrusion. This condition is further caused by the narrow respiration tract in down syndrome individuals, therefore mouth breathing becomes the continuous parafunctional habit and increases over time.[36–39] Most individuals with incompetent lips are found to have severe periodontal and gingival disease.[17] Periodontal and gingival disease such as gingivitis and periodontitis usually appear due to poor oral hygiene followed by local and systemic factors in the Down syndrome individuals.[1,33] Periodontal and gingival diseases usually start developing in the early stages of life and its severity increases with age.[32] According to studies conducted by Al-Sufyani et al., Al-Maweri et al. and C. Tipe, mild, moderate, and severe gingivitis in Down syndrome patients were reported

with a total average value of 58.53%.[1,32,33] Other than that, mild and moderate periodontitis in Down syndrome individuals were also reported in a research conducted by C. Tipe.[32]

In 2 researches conducted by Asokan et al. and Ashwinirani et al., everted lower lip and chapped lower lip were reported in Down syndrome individuals[3,17]. Everted lower lip in Down syndrome individuals is caused by the hypotonic condition on the lower lip, followed by tongue protrusion which is located on the lower lip.[42,43] Chapped lower lip in Down syndrome individuals is also caused by the hypotonic condition of the lower lip. This condition causes the mouth to be open, which further causes mouth breathing, drooling, and chapped lower lip.[43] Everted lower lip is more common in Down syndrome with an average value of 63.35% than chapped lower lip with an average value of 20.8%.[3,17] The existence of these oral manifestations are not related to the individuals' age. Protruded tongue in Down syndrome individuals is also reported in 2 researches conducted by Asokan et al. and Ashwinirani et al. that has the value of 41.2% and 45% respectively.[3,17] Protruded tongue in Down syndrome individuals are caused by the hypotonic condition on orofacial muscles, this further causes the mouth to be open permanently and the tongue to be protruded past the normal position of the tongue.[42] The prevalence of protruded tongue in Down syndrome individuals decreased with age.[17] Tongue protrusion can cause speech disorders in patients.[26] The constant condition of tongue protrusion also can cause ulceration, and if not treated can become secondary infection or even experience necrosis.[26]

Other oral soft tissue conditions in Down syndrome individuals were also reported sporadically in some studies that are reviewed in the current study. The other oral soft tissue conditions in Down syndrome patients are: angle of mouth pull down (63.7%), palatal defect (23.5%), and tonsil enlargement (22.5%) in a research conducted by Asokan et al.[17] Ankyloglossia (13%) and lack of lip seal (51.9%) were reported by a research conducted by Shukla et al.[28] Gingival hyperplasia (18%), fibroma (8%), cheek biting (2%), herpes labialis (2%), and traumatic ulcer (4%) were reported in a research conducted by Al-Maweri et al.[1] Atrophy of tongue (7.5%), fibroma (1%), ulcers (2.8%), and trauma to soft tissue/lip (2.8%) were reported in a research conducted by Ghaith et al.[30]

The prevalence of said oral soft tissue conditions are more commonly found in Down syndrome subject group than normal subject group. This circumstance is reported on research conducted by Al-shawaf & Al-Faleh, Al-Maweri et al., Ghaith et al., and Fansa et al. that compare Down syndrome subject group with normal subject group.[1,26,30,31] Factors that may contribute in said circumstance are the existence of congenital conditions and clinical conditions that are caused by the developmental disorders in people with Down syndrome, causing this group to be more susceptible to oral soft tissue conditions.[44]

As recommendation and suggestion for further studies, it is important to conduct further studies on clinical oral soft tissue abnormality based on Down syndrome types, so that more diverse and specific data can be obtained. Research limited only on oral soft tissue conditions on Down syndrome children is still minimal. Therefore, it is recommended to conduct further studies based on age category on children for the future. Other than that, further studies conducted are recommended to have a control group that can be used to directly compare the prevalence value of each oral soft tissue condition present in Down syndrome population with the normal population.

CONCLUSION

The result of this research study shows the most common frequently oral soft tissue conditions reported in the Down syndrome population are:

1. Fissured tongue varies from 28% to 78%.
2. Macroglossia varies from 36.8% to 94%.
3. Total and angular cheilitis varies from 6.3% to 51%.

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