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ORIGINAL RESEARCH

Effect of Adenotonsillectomy on the Symptomatology and Growth of Children with Obstructive Adenotonsillar Enlargement

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Abstract

Background: Obstructive adenotonsillar enlargement, a common childhood disorder in Ear, Nose and Throat (ENT) practice, is associated with obstructive sleep apnea syndrome (OSAS) and growth failure.

Objective: To assess the effect of adenotonsillectomy on symptomatology and somatic and biochemical markers of growth in children with obstructive adenotonsillar enlargement.

Setting and design: A prospective interventional and controlled study was conducted among children 2-8 years old with the diagnosis of adenotonsillar enlargement who attended the ENT Clinic of a Teaching Hospital in Nigeria.

Methods: The study group consisted of 43 children who underwent adenotonsillectomy, while the control group consisted of 43 age and sex-matched children without features of obstructive adenotonsillar enlargement. The symptomatology score, weight, height, serum growth hormone (GH), and insulin-like growth factor-1 (IGF-1) were measured pre-surgery and six months post-surgery among the study and the control groups.

Results: There was a statistically significant difference in symptomatology scores among the study group six months post-surgery ($p < 0.001$). The weight, height, and serum levels of GH and IGF-1 significantly increased in the study group six months after the surgery.

Conclusion: Adenotonsillectomy positively affects the symptomatology, somatic growth and biochemical markers of growth in children with obstructive adenotonsillar enlargement.

Keywords: Adenotonsillar Enlargement, Insulin-like Growth Factor (IGF-1), Growth Hormone, Obstructive Sleep Apnea.

Introduction

Obstructive adenotonsillar enlargement is a common childhood ENT disorder which can be associated with obstructive sleep apnea

syndrome (OSAS).^[1,2] It is common among children 3 to 5 years of age and responsible for most of the OSAS, which affects them.^[2] Studies have shown that chronic OSAS can cause complications like growth retardation, pulmonary hypertension, right-sided heart failure and *Cor pulmonale*.^[2] Apart from these, adenotonsillar enlargement causes great physical and psychological stress to the patients and their parents, leading to absence from school and work, poor school performance, sleep deprivation, frequent hospital visits, and economic burden.^[3]

The procedure is performed by Otorhinolaryngologists worldwide.^[4] In Nigeria, the commonest indication for adenotonsillectomy is obstructive sleep apnea syndrome resulting from adenotonsillar enlargement and many children across different centres in Nigeria undergo Adenotonsillectomy annually.^[4] OSAS resulting from adenotonsillar enlargement is also an identified cause of growth failure in children, and the obstruction is usually treated with adenotonsillectomy.^[5] The pathophysiology of growth failure among affected children has been ascribed to decreased calorie intake due to tonsillar obstruction, increased energy expenditure associated with laboured breathing, hypoxemia and interruption of growth hormone and insulin-like growth factor-1 (GH-IGF-1) secretion.^[5,6] Obstructive adenotonsillar enlargement interrupts the secretion of growth hormone, which is secreted in a pulsatile manner during REM sleep. Adenotonsillectomy eliminates airway obstruction, thereby restoring physiological sleep homeostasis in children, and this may explain the improvement in growth after the adenotonsillectomy.^[6,7]

Studies have been conducted across the globe on the effect of adenotonsillectomy on somatic growth indices and biochemical markers of growth (GH and IGF-1). In Nigeria, there are some studies on adenoid and tonsil

enlargement and its surgery; some were on the presentation of adenotonsillar enlargement, indications for adenotonsillectomy, the outcome of adenotonsillectomy on sleep-disordered breathing and evaluation of adenoidal enlargement.^[2, 8, 9, 10] However, there needs to be more documented work on the effect of adenotonsillectomy on growth and biochemical markers of growth among children in Nigeria. This study aimed to assess the impact of adenotonsillectomy on symptomatology, somatic growth indices and biochemical markers of growth (serum levels of GH and IGF-1) in children with obstructive adenotonsillar enlargement pre-surgery and six months post-surgery and to compare the parameters with those of controls.

Methods

This prospective, interventional and controlled study was conducted at the ENT Clinic of Lagos University Teaching Hospital (LUTH), Lagos, Nigeria, between October 2018 and July 2020. The study population comprised all consecutive children aged 2-8 years who attended the clinic during the study period. Eighty-six children participated in the study. The study group comprised 43 children diagnosed with obstructive adenotonsillar enlargement and booked for elective adenotonsillectomy.

The protocol for this study was approved by the Lagos University Teaching Hospital (LUTH) Health Research Ethics Committee, Idi Araba, Lagos, with the assigned number ADM/DCST/HREC/APP/2288.

A structured questionnaire was administered to the parents or guardians of each child to obtain patients' data, symptomatology of adenotonsillar enlargement and medical history. Obstructive adenotonsillar enlargement was assessed by taking an adequate history of upper airway obstructive symptoms airway, a physical examination of

the oropharynx with related ENT areas and a plain radiograph of the postnasal space. On physical examination of the oropharynx, the size of the tonsils was graded according to the Brodsky Tonsillar Enlargement Grading Scale.^[13]

Adenoid enlargement was assessed on the lateral radiograph of the postnasal space using landmark parameters described by Fujioka.^[14] Adenoidal nasopharyngeal ratio (ANR) greater than 0.5 defined obstructive adenoidal enlargement.^[15] All consecutive children aged 2-8 years with a diagnosis of adenotonsillar enlargement and those with parental consent for surgery were recruited into the study. The severity of symptoms was graded before and after the surgery using previously validated symptomatology score (SS) parameters.^[9] The extent of improvement of the symptoms after surgery was estimated by a standardised response means (SRM) score. SRM was calculated by dividing the change score by the standard deviation of the change score. The symptomatology scores were generated using a set of questions designed to grade the severity of the most common symptoms of adenotonsillar enlargement that indicate breathing and sleep disturbances. The following numeric values were assigned to snoring and mouth breathing: 0—absent, 1—occasionally during sleep, 2—regularly during sleep, and 3—regularly during sleep and daytime. Obstructive breathing during sleep was assigned the following values: 0—absent, 1—occasionally, 2—<5 episodes, 3—>/5 episodes. The domains of nasal discharge and daytime hypersomnolence were assigned the following values: 0—never, 1—occasionally, and 2—regularly.

The SS represented the sum of the individual domain scores. These were recorded before and six months after adenotonsillectomy for each child. The maximum score any child could have was 13. An SS of less than six was regarded as 'mild' airway obstruction, scores between 6 and 9 were considered moderate obstruction, and

scores more than nine were regarded as severe obstruction. The 'SS change score' was calculated by subtracting the post-operative mean total and mean domain SS scores from the corresponding pre-operative values.

The height and weight were measured before surgery and six months after adenotonsillectomy in both the intervention and the control groups. Height was measured using a Harpenden stadiometer and was read to the nearest 0.1cm, while a stable weighing scale was used to measure the body weight and was read to the nearest 0.1kg.^[16]

Three millilitres of venous blood samples were drawn from the study group on the day preceding the surgery. Blood samples were also drawn from the control group as they initially presented to the ENT clinic and six months later. The blood samples were centrifuged for 15-20 minutes at 2000rev. Serum was extracted from the blood samples and stored at -80°C pending analysis. Samples were analysed for GH and IGF-1 using an ELISA Kit (manufactured by Bioassay Technology Laboratory, China). This was repeated six months (post-adenotonsillectomy) in the study and control groups.

At six months after surgery, post-operative symptomatology was reassessed. Children with congenital airway abnormalities, previous adenotonsillectomy, sickle cell disease and children whose parents refused to give consent were excluded from the study. The control group was recruited from consecutive children who presented to the ENT clinic with ear wax impaction, foreign bodies in the ear and nose, and without features of obstructive adenotonsillar enlargement. The control group was matched for age and sex during the study period. Written informed consent was obtained from consecutive parents/caregivers of eligible participants in the best language understood.

Data analysis and management

All collected data were collated and analysed using Statistical Product and Service Solution (SPSS) version 25. Continuous variables were presented as mean, median and standard deviation, while categorical variables were presented as frequency and percentage. Measurement differences were calculated by subtracting the pre-operative data from the post-operative data. Analysis of variance (ANOVA) was used to evaluate the relationship between tonsillar grades and symptomatology scores. The paired t-test was used to assess the changes in the serum levels of IGF-1, GH, and growth indices between baseline values and the values at the end of the study in each group. The differences between pre-operative and post-operative data were calculated and compared between the intervention and control groups using independent samples t-test. P values ≤ 0.05 were accepted as significant.

Results

Forty-five children (45) were recruited into the study, two of which were lost to follow-up. They were compared with forty-three sex- and age-matched children in the control group, making 86 participants in all. Both groups had 31 (72.1%) males and 12 (27.9%) females. The mean age was 4.02 ± 1.70 years in the study group and 4.19 ± 1.67 years in the control group. Over fifty-five per cent of the children in the study group were less than five years of age. All the children in the study group presented with snoring, while 95% presented with nasal obstruction, 93% with mouth breathing, 93% with recurrent nasal discharge and 93% observed apnea during sleep. The least common symptom was excessive daytime sleepiness found in 20 (46.5%) participants.

Tonsillar Grade

Twenty-three (53.5%) children in the study group had grade 3+, 18 (41.9%) had grade 4+ tonsils and two (4.7%) had grade 2+. The total mean for the ANR was 0.76 ± 0.07 . The total mean ANR for children under five was 0.79 ± 0.04 , while children older than five years had a total mean ANR of 0.72 ± 0.0 . The difference was statistically significant. ($p < 0.001$)

Symptomatology score (Tables I and II)

Table I shows the relationship between mean symptomatology score (SS), age, sex and tonsillar grade. SS was significantly higher in children less than five years ($p = 0.023$). However, there was no significant difference in SS between males and females, and there was no correlation between SS and tonsillar grades. Table II shows a change in mean symptomatology score six months post adenotonsillectomy. The total mean change in symptomatology score of 9.21 (95%CI) and total standard response mean of 3.27 were indicative of marked improvement in obstructive symptoms after adenotonsillectomy. The highest mean change score was 2.51, with a Standardized Response Mean of 3.59, recorded in the snoring symptom domain, while excessive daytime sleepiness showed the smallest score of 0.77 with SRM = 1.03.

Weight and Height (Table III)

The mean weight in the study group before surgery was 14.7 ± 3.92 kg, which increased to 18.60 ± 3.96 kg six months after surgery with an increment of 3.9kg ($p < 0.001$). The mean weight of the control group also increased with statistical significance ($p = 0.036$). The mean height in the study group increased from 1.01 ± 0.13 m to 1.05 ± 0.13 m ($p < 0.001$) while in the control group, it increased from 1.03 ± 0.12 m to 1.04 ± 0.14 m ($p = 0.723$).

Table I: Mean symptomatology score in relation to age, sex and tonsillar grade

Variable	Frequency	Pre-study group symptomatology	F or t-Statistics	p-value
Age			2.096	0.042*
<5	25	10.00±2.57		
≥5	18	8.28±2.778		
Sex			-0.940	0.353
Male	31	9.03±2.95		
Female	12	9.92±2.19		
Tonsillar grade			0.527	0.595
2+	2	11.00±2.82		
3+	23	9.30±2.52		
4+	18	8.94±3.11		

Table II: Mean symptomatology score changes after adenotonsillectomy

Symptom domains	Pre-surgery mean score	Post-surgery mean score	Mean change in score (95% CI)	Standard deviation of change in score	Standardised response mean (SRM)
Snoring	2.51	0.00	2.51(2.30- 2.73)	0.70	3.59
	2.47	0.00	2.47(2.18- 2.75)	0.93	2.66
Mouth breathing					
Observed apnea during sleep.	1.81	0.00	1.81(1.49- 2.14)	1.05	1.72
Nasal discharge	1.72	0.07	1.65(1.45- 1.85)	0.65	2.54
Day time somnolence	0.77	0.00	0.77(0.54- 1.00)	0.75	1.03
Total symptomatology score	9.28	0.07	9.21(8.34- 10.08)	2.82	3.27

Table III: Changes in anthropometric indices six months post-tonsillectomy

	Baseline mean weight±SD (Kg)	mean	Mean weight±SD (kg) after six months	Paired t-test	p-value
Study group	14.70±3.92		18.60±3.96	-14.075	<0.001
Control	16.80±3.25		18.22±2.91	-2.135	0.036
P value	0.008		0.498		
	Baseline mean height ± SD (m)	mean	Mean height ± SD (m)after six months	Paired t-test	p-value
Study group	1.01±0.13		1.05±0.13	-6.142	<0.001
Control	1.03±0.12		1.04±0.14	-0.356	0.723
P value	0.517		0.732		

GH and IGF-1 (Table IV)

The mean baseline serum level of GH in the study group was 2.85±2.79ng/ml, which increased to 6.14±2.54ng/ml six months after surgery with a significant difference of 3.29ng/ml (p = 0.009) while that of the control

group increased from 5.95±2.32ng/ml to 6.88±2.54ng/ml with a difference of 0.93ng/ml (p = 0.080).

The IGF-1 in the study group increased from 31.42±14.41ng/ml to 44.98±8.92ng/ml, giving a difference of 13.56ng/ml (p<0.001) while that

of control group increased from 39.91±15.98 to 43.22±14.23 with a difference of 3.31ng/ml (p = 0.313).

Table IV: Comparison levels of Growth Hormone (GH) and Insulin-like Growth Factor-1 (IGF-1) after six months

	Baseline mean GH± SD (ng/ml)	Mean GH± SD (ng/ml) after six months	Paired t-test	p-value
Study group	2.85±2.79	6.14±7.99	-2.722	0.009*
Control	5.95±2.32	6.88±2.54	-1.773	0.080
P value	<0.001	0.564		
	Base line IGF-1(ng/ml)	Mean IGF-1(ng/ml) After six months	Paired t-test	p-value
Study group	31.42±14.41	44.98±8.92	-11.635	<0.001*
Control	39.91±15.98	43.22±14.23	-1.014	0.313
P value	0.011*	0.494		

Discussion

This study found a significant improvement in symptoms and increased somatic growth and biochemical growth markers after adenotonsillectomy. Snoring was the most improved symptom, evidenced by the highest standardised response mean (SRM), while excessive daytime sleepiness was the least. These findings are comparable to the report of Orji *et al.* [9]

The mean total symptomatology score (SS) of the study group reduced from a pre-operative value of 9.28 to a post-operative value of 0.07, giving a mean change in symptomatology score of 9.21, an indicator of a marked improvement in symptoms. This is similar to what has been reported in the literature. According to Greg *et al.*, 26 of 27 children studied had complete resolution of symptoms three months after adenotonsillectomy. [21] Borovich *et al.* studied the effect of adenotonsillectomy on quality of life using the Pediatric Sleep Questionnaire Sleep-related Breathing Disorder (PSQ-SRDB). They reported that children who underwent adenotonsillectomy had a better quality of life compared with control. [19]

Adenotonsillar enlargement has been reported to be common in preschool-age children. [9,16] The mean ANR and mean symptomatology scores reported in this study were higher in children under five, constituting about fifty-five per cent of the study group. These values indicate severe airway obstruction in this age group due to the size of the adenoid and tonsils compromising the airway patency in this age group. Amuta *et al.* observed that with increasing age, airway obstruction in children with obstructive adenotonsillar enlargement declines significantly. [22] This may explain why these children had greater pre-operative symptomatology scores than older ones.

Various studies reported positive changes in somatic growth indices following surgery. [23,26] A significant increase in the mean weight was observed in the study group six months post-surgery, but when compared to the control group, it could be described as a catch-up weight gain, as described previously. There was also a significant increase in height six months post-surgery in the study group. This may be attributed to increased food intake and elimination of laboured breathing following relief of oropharyngeal and nasopharyngeal obstruction after the surgery. However, it must

be noted that the study group had a baseline mean weight, which was lower relative to the control group matched for age and sex. This showed one of the effects of obstructive symptoms and its consequences, such as growth failure. However, we did not find a significant difference in height between the study group and the controls before and after surgery. Our findings are comparable to what has been reported in various studies. [23 - 25, 27] Eliot *et al.* studied growth after adenotonsillectomy for obstructive sleep apnea. [23] Four hundred and sixty-four children who had OSAS were randomised to early adenotonsillectomy and watchful waiting. They found a significant increase in weight in the adenotonsillectomy group. Ersoy *et al.*, Vontetsianos *et al.* and Fernandes *et al.* also demonstrated a significant increase in weight and height following adenotonsillectomy. [24 - 26] In contrast to our finding, there was no significant difference in weight between the control and study group before surgery in the Fernandes *et al.* study. [25] Their control group comprised children with obstructive adenotonsillar enlargement who did not undergo surgery, in contrast to children without adenotonsillar obstruction, which was used as a control in this study. Farmarzi *et al.* also reported a significant increase in weight and height in the study group six months after adenotonsillectomy. [5] This is, however, different in this study, and the disparity may be due to a larger sample size of 100 children compared to 43.

The serum levels of GH and IGF-1 were also significantly lower among the study group than those of control group before surgery. Though the pathophysiology of growth failure due to obstructive adenotonsillar enlargement is not fully understood, the interruption of growth hormone-insulin-like growth factor-1 axis secretion is a suggested mechanism. [5,6] Growth hormone is secreted in the anterior pituitary gland in a pulsatile manner during REM sleep. [6] Sleep disturbances have been shown to decrease the amount of short-wave

sleep (SWS) occurring in children with adenotonsillar enlargement. This effect is expected to decrease sleep-associated GH secretion. The effects of GH on skeletal growth are mediated mainly by stimulation of insulin-like growth factor-1 (IGF-1). Adenotonsillectomy thus may influence the GH-IGF-1 axis by increasing the secretion of GH and IGF-1, as shown in the study group with a significant increase in serum levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) in the study group at six months after surgery. This may also explain the 'catch-up' weight gain observed in the study group after surgery.

A significant increase in serum level of IGF-1 after surgery was found in this study in agreement with Mohammad *et al.* who, in evaluating the effects of adenotonsillectomy on serum levels of IGF-1 and Insulin-like Growth Factor Binding Protein-3 (IGFBP-3) and growth indices in children with adenotonsillar enlargement or recurrent tonsillitis, also reported a significant increase in IGF-1 in the study group six months after surgery. [5] Aydogan *et al.*, however, reported no statistically significant difference in pre-operative and post-operative values of height and IGF-1. [27] Most of the published reports evaluated the effect of adenotonsillectomy on serum level of IGFBP-3 and that of IGF-1. IGFBP3 is the carrier of IGF-1, and its function is primarily to prolong the half-life of IGF-1. [26] Serum growth hormone was measured in this study to determine the direct effect of adenotonsillectomy on growth hormone. The present study is one of the few studies that measured the impact of adenotonsillectomy directly on GH before and six months after adenotonsillectomy. A significant increase in the serum levels was found six months after surgery. Chiba *et al.* assayed urinary GH excretion and reported an increase in growth hormone in seven out of ten children following adenotonsillectomy. [27] However, in contrast to our finding, Vontetsianos *et al.* found no statistically significant increase in GH and IGF-

1 after surgery in the study of possible pathogenetic mechanisms of improved somatic growth following adenoidectomy and tonsillectomy in 57 young children. [25]

This study had some limitations. Growth hormone is secreted in a fluctuating manner. It peaks during sleep and by the time of waking up. As a result, a 24-hour pooled sample is more reliable than a random sample, limiting the accuracy of the growth hormone measurements in this study. Polysomnography is the gold standard for evaluating OSAS but it is rather expensive and not readily available in a poor-resource setting like Nigeria. Thus, the assessment of Sleep Disordered Breathing (SDB) based on clinical and physical examinations with radiological demonstrations of enlarged adenoids and tonsils limited the accuracy of the diagnosis of OSAS.

Conclusion

Obstructive adenotonsillar enlargement has significant deleterious effects on children's growth. Adenotonsillectomy significantly reduces obstructive symptoms and positively affects both the somatic growth and biochemical markers of growth in children with obstructive adenotonsillar enlargement.

Authors' Contributions: BBA conceived and designed the study. IJA did the literature review and analysed and interpreted the data with DAO. IJA drafted the manuscript. BBA and SAO revised the draft for sound intellectual content. All authors approved the final version of the manuscript.

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