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Improved Sleep and Behavior after Adenotonsillectomy in Children with Sleep Disordered Breathing

Karim, Md. Rezaul

University of Rajshahi

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Md. Rezaul Karim

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University of Rajshahi

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DECLARATION

I hereby declare that this thesis titled **"Improved Sleep and Behavior after Adenotonsillectomy in Children with Sleep Disordered Breathing"** was carried out in the Department of Ear, Nose & Throat (ENT), Rajshahi Medical College Hospital, Rajshahi and no part of it has been presented anywhere for any higher degree. The thesis is submitted in partial fulfillment of the requirements for the PhD degree (ENT) to the Institute of Biological Sciences, University of Rajshahi, Rajshahi, Bangladesh.

June, 2020 **Md. Rezaul Karim**
Dhaka, Bangladesh

CERTIFICATE

This is to confirm that **Md. Rezaul Karim** is the sole author of the thesis entitled "**Improved Sleep and Behaviour after Adenotonsillectomy in Children with Sleep Disordered Breathing**". No part of this work has been submitted for another degree or qualification in any other institute at home or abroad.

I am forwarding this thesis to be examined for the degree of Doctor of Philosophy (PhD) in the Institute of Biological Sciences (IBSc), University of Rajshahi, Bangladesh. Md. Rezaul Karim has fulfilled all the requirements for submission of thesis for the PhD degree according to the rules of the University of Rajshahi.

(Dr. M. Firoz Alam)
Professor & Director
Institute of Biological Sciences
University of Rajshahi
Rajshahi 6205
Bangladesh.

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Md. Rezaul Karim

PhD Candidate
Institute of Biological Sciences
Rajshahi University, Rajshahi

ABSTRACT

Background and objective:

Sleep disordered breathing (SDB) is a common problem in preschool and school going children and is generally perceived as a neurodevelopmental condition leading to maltreatment resulting in abnormal behavioural complications and reduced cognition. The present study was undertaken to evaluate whether adenotonsillectomy done in children with SDB improves their behavior, cognition and quality of life.

Methods:

This prospective interventional study of pre-test post-test design was conducted in Rajshahi Medical College Hospital, Rajshahi over a period of 3-years from July 2012 to June 2015 on 50 children (selected based on predefined eligibility criteria) aged 3-8 years who underwent adenotonsillectomy for sleep disordered breathing (SDB) with or without behavioural problem. The outcome variables were sleep disordered breathing, attention-deficit hyperactivity disorder (ADHD), cognitive function and quality of life.

Result:

About three-quarters (74%) of the study children were 6 or > 6 years old with mean age being 6.6 years. Female-to-male ratio was 3:2. Half of the children was rural residents (50%) and 40% belonged to lower middle class. Snoring (86%), upper airway resistance syndrome (90%), obstructive hypoventilation (86%) and obstructive sleep-apnoea syndrome (OSAS) (80%) all demonstrated their dominance before adenotonsillectomy. After intervention major proportions of these symptoms reduced indicating that adenotonsilitis was the

main reason of these symptoms. The major behavioral problems in children before intervention were ADHD (82%), problemetic behaviours on awakening (86%), night-to-night sleep duration variability (78%) and headache (80%). All the major problems responded well following adenotosillectomy ($p < 0.001$). Of the minor problems incidence of enuresis reduced to less than half ($p = 0.027$). Cognitive function like learning disabilities and poor academic performance showed commendable improvement following adenotonsillectomy ($p < 0.001$).

Conclusion:

The study concluded that children diagnosed with SDB experience significant improvement in both sleep and behavior after adenotonsillectomy.

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LIST OF ABBREVIATIONS

Abbreviations	Decode
AT	Adenotonsillectomy
ADHD	Attention-deficit/hyperactivity disorder
AHI	Apnea-hypopnea index
BASC	Behavioural Assessment System for Children
CBCL	Child Behaviour checklist
CPRS	Conners' Parent Rating Scale
CPRS-RS	Conners' Parent Rating Scale–Revised Short Form
DAS	Differential Abilities Scale
DSM	Diagnostic and Statistical Manual of Mental Disorders
HS	Habitual snoring
NEPSY	Neuropsychological Assessment
OSA	Obstructive sleep apnea
OSAS	Obstructive sleep apnea syndrome
PS	Primary snoring
PSG	Polysomnography
SDB	Sleep disordered breathing
SRBD	Sleep-related breathing disorders
TOVA	Test of Variables of Attention
UARS	Upper airway resistance syndrome
WHO	World Health Organization

Chapter 1
INTRODUCTION

1.1 Introduction:

Sleep disordered breathing (SDB) is defined as a continuum of sleep-associated respiratory disorders mainly encompassing snoring, upper respiratory tract resistance syndrome, obstructive sleep apnea syndrome (OSAS), hypoventilation (the most extreme component of the spectrum). The term SDB is primarily used in children than OSAS, for the former term covers a wide variety of breathing problems related to sleep. While prevalence of OSAS is reported to vary from 0.7-3%, the occurrence of SDB snoring and clinical suspicion of the condition in children can reach up to 11% (De Serres *et al*., 2002; Tran *et al*., 2005).

The effect of SDB on the development and actions of children — especially hyperactivity and inattention — is well known. (Chervin *et al*., 2002; Gottlieb *et al*., 2003; O'Brien *et al*., 2003; Golan *et al*., 2004; Huang *et al*., 2004). O'Brien and colleagues (2003), with the help of both polysomnography (PSG) and parental surveys, demonstrated that although children are not usually the victims of SDB with pronounced symptoms of ADHD, it is rampantly prevailing among them with moderate overactive behaviour. However, two studies (Golan *et al*., 2004; Huang *et al*., 2004) have shown that SDB was more likely to occur in children with ADHD and that management of SDB may reduce the behavior in a group of population if their normal snoring and SDB

are ameliorated (Chervin *et al*., 1997). Unlike OSAS, which is partially characterized by a standardized PSG-based apnea-hypopnea index (AHI), SDB could be clinically detected and may not require PSG report to establish the diagnosis of obstructive respiratory disorder (Weatherly *et al*., 2004).

In addition to hyperactivity, snoring and SDB children with poor school performance are found to exhibit neurocognitive disability (Blunden *et al*., 2001; Gozal, 1998; Gozal, 2001; Urschitz *et al*., 2003). Gozal (2001) demonstrated that children with no clinically important hypoxia (as assessed by pulse oximetry) but with frequent snoring showed worse academic performance than those without snore. There is also a tendency to equate sleep-disordered breathing with enuresis, learning difficulties, daytime sleepiness, and somatic complaints (De Serres *et al*., 2002). Behavioral and emotional problems are also not unusual in children with SDB prior to treatment and changes following adenotonsillectomy are the usual findings (Goldstein *et al*., 2000).

The relationship of ADHD with sleep is multifaceted and complex. Sleep abnormality is an inherent characteristic of ADHD based on the criteria of the Mental Disorders Diagnostic and Statistical Manual, Fourth Edition (DSM-IV). It may worsen and intensify the symptoms of the condition. Nevertheless, sleep problems can also lead to ADHD and ADHD-like symptoms, leading to misdiagnosis. (Polanczyk *et al*., 2007; Spencer *et al*., 1998). ADHD is a widespread neurodevelopmental problem estimated to harm about 5.3% of the world's children and adolescents (Wender, 1998) and the survival of about two-thirds of patients in adulthood (Corkum *et al*.,1998; Hodgkins *et al*., 2013). The frequency of sleep abnormalities in people with ADHD ranges from 25-55%

(Owens, 2005; Sung *et al*., 2005; Efron, *et al*., 2014; *et al*., 2006). In a study in Australia, over 60% of ADHD children were reported to have mild to extreme sleep disorders and 22% were under sleep-medications during the study period of one week (Spruyt & Gozal, 2011). Nevertheless, in earlier versions of the DSM, high nocturnal activity and altered sleep-behaviour were identified features in children with ADHD' (Xu *et al*., 2009; Williams, Owen & O'Donovan, 2009).

Attention-deficit hyperactivity disorder is generally considered as a neurodevelopmental disease that may arise from the combination of several genetic and socio-environmental factors with symptoms identified and regulated by different phenotypes (Faraone *et al*., 2005; Floet *et al*., 2010; Rowland *et al*., 2002; Owens *et al*., 2005). Therefore, comorbidity is not uncommon and 59 – 87% of children diagnosed with ADHD possess at least one comorbidity and 20% suffer three or more comorbidities or symptoms of comorbidity (Gaina *et al*., 2007). Interestingly, potential links between sleep and ADHD were first reported in 1957 (Harriet *et al*., 2007) and 1971 (Teng, 2010). In fact, there are some potential consequences of disordered breathing if children with sleep disorder remain untreated. Loud snoring may create a major social problem when a child shares a room with any other family members. SDB can lead to enuresis causing bed-wetting. Children with SDB may not generate sufficient growth hormone, leading to growth retardation and developmental delay. With decreases in physical activity resulting in obesity, SBD can induce the development of enhanced insulin resistance or daytime fatigue.

When repeated heavy snoring, gasping, snoring, or unexplained bedwetting is observed, SDB, of course, should be considered, which among others, may include alteration in mood, misconduct, and poor performance in school. Not every child with academic or behavioral problems will have SDB, but sleep disordered breathing should be considered if a child's snoring persists on a regular basis or exhibits behavioural problem with poor academic performance. The analysis of sleep or PSG is an objective test for breathing with sleep disorder. However, sleep tests may occasionally give inaccurate results, particularly in children and as such PSG is not mandatory to establish the diagnosis of a case of SDB.

Hypertrophied tonsils and adenoids are a common causes for SDB and surgical removal of these organs is generally considered the first line of treatment for children with SDB if the symptoms are problematic. A substantial proportion of children with sleep apnea demonstrates both short and long- term improvement in their sleep and behavior after adenotonsillectomy.

Studies are, therefore, required to investigate the relationship between sleep disordered breathing and its relationship with adenoid and tonsillar enlargement as well as to determine whether adenotonsillectomy done for SDB results in improvement in behavior, cognitive function and quality of life.

1.2 Rationale of the study:

From the background study it appears that children diagnosed with attention-deficit/hyperactivity disorder (ADHD), may also have obstructive sleep apnea (OSA). However, the relationships between sleep and ADHD are complex and

are routinely overlooked by practitioners. The present study intends find the ways for better understanding and treatment of children exhibiting inattentive, hyperactive, impulsive behaviors, by in-depth questioning on sleepiness, SDB or problematic behaviors while sleeping, during the night and upon awakening, as well as night-to-night sleep duration variability.

The present study was therefore undertaken to evaluate the efficacy of adenotonsillectomy (AT) in the treatment of children with sleep disordered breathing (SDB) and whether adenotonsillectomy done for SDB results in better outcome in terms of improvements of behavior, cognition, and overall quality of life. As the proposed study is, by far, the first study to address this issue in the context of our country, the data generated from the study might be of immense significance in the management of children with SDB.

1.3 Research gap:

The relationships between sleep and ADHD are complex and are routinely overlooked by practitioners. In children, often ADHD is considered as a separate disease and is treated accordingly particularly in Bangladesh, although in most cases it is the sequalae of sleep disordered breathing resulting from hypertrophy of tonsils and adenoids. So the present study intended to find the relationship of SDB and ADHD will better inform physicians, particularly pediatric ENT specialists about complex relationship between the conditions, which, in turn, will help them in better understanding of the problem of children presenting with ADHD and deciding the treatment option accordingly.

1.4 Research hypothesis:

A substantial proportion of children with SDB, behavior and cognitive problems improves following adenotonsillectomy.

1.5 Objectives:

1.5.1 General Objectives:

To determine whether behavior and sleep improves following adenotonsillectomy in children with SDB having behavior problem.

1.5.2 Specific objectives:

1. To see the improvement in SDB.
2. To see the improvement in ADHD.
3. To compare the cognitive function before and after adenotonsillectomy

To compare the quality of life before and after adenotonsillectomy.

Chapter 2

REVIEW OF LITERATURE

2.0 An overview:

This chapter primarily described the gross anatomy of tonsils and adenoids, their blood and nerve supply. The adjacent structures (other organs, blood vessels and nerves) surrounding the organs were also be discussed. Then the studies describing the relationship between sleep disorder breathing and ADHD in children were discussed. Lastly and more importantly, the impact of adeno-tonsillectomy on behavior of the children and cognitive function were highlighted.

2. 1 Anatomy of the tonsils and adenoids:

Tonsils and adenoids are tissue lumps like glandular tissues in the neck and other parts of the body. While tonsils are located on either side of the back of the throat (pharynx), adenoids are located where the throat meets the back of the nose. Without the use of special instruments, they cannot be visible through the eyes.

Tonsils and adenoids are usually larger in children, but begin to decrease in size from 8-12 years of age to adult proportions. While tonsils and adenoids are

part of the immune system (defense of the body against potentially harmful germs), they are not essential meaning if they are removed, there is no harm to the immune system or negligible harm to the body defense.

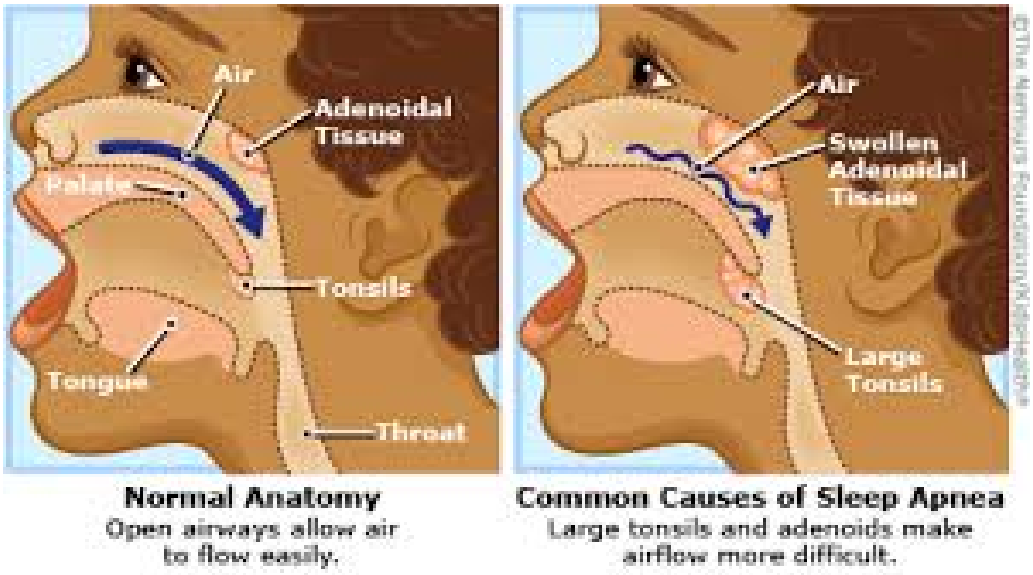


Fig. 1: Anatomy showing locations of tonsils and adenoids

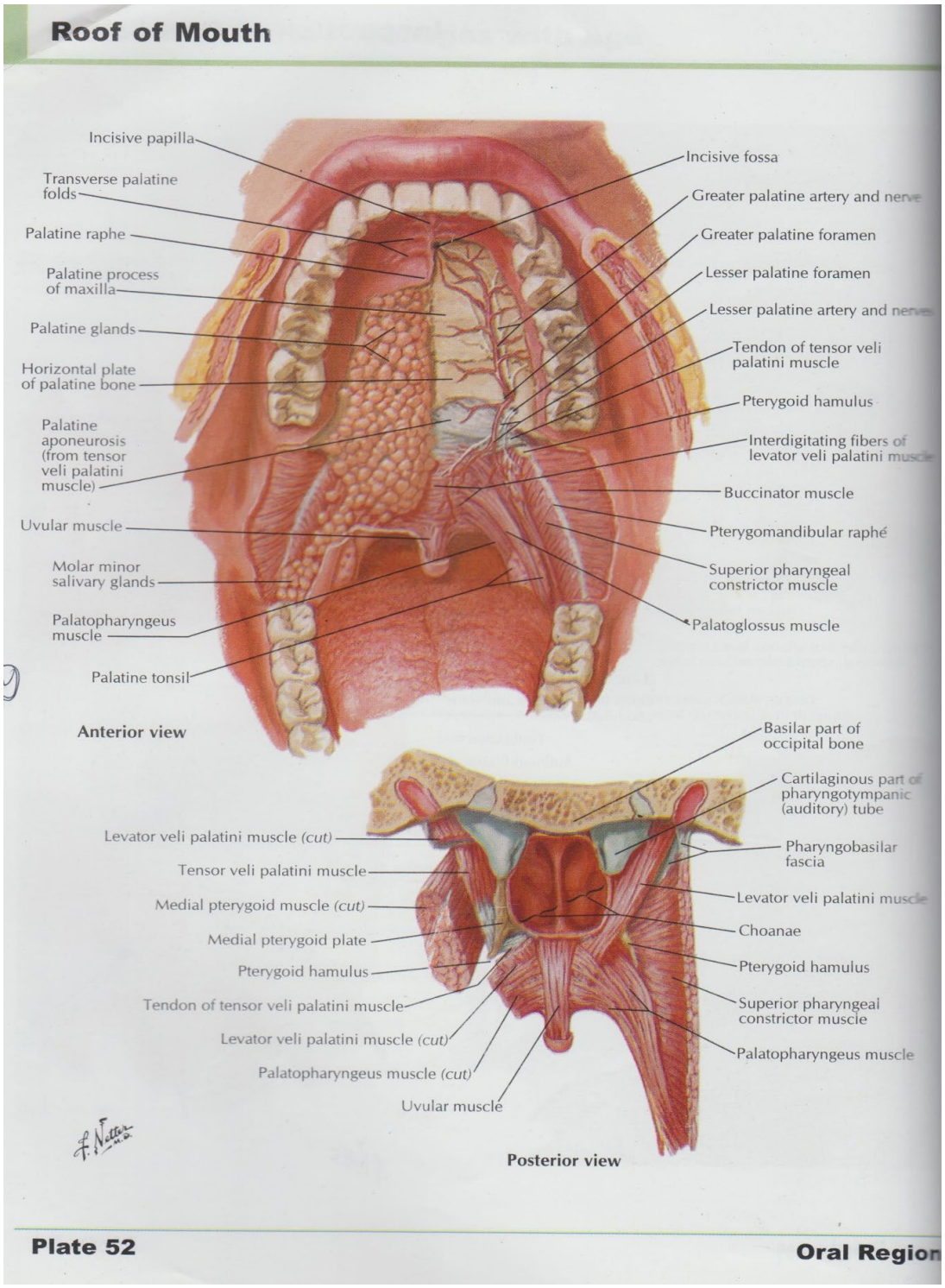


Fig. 2: Showing oral region particularly roof of the mouth

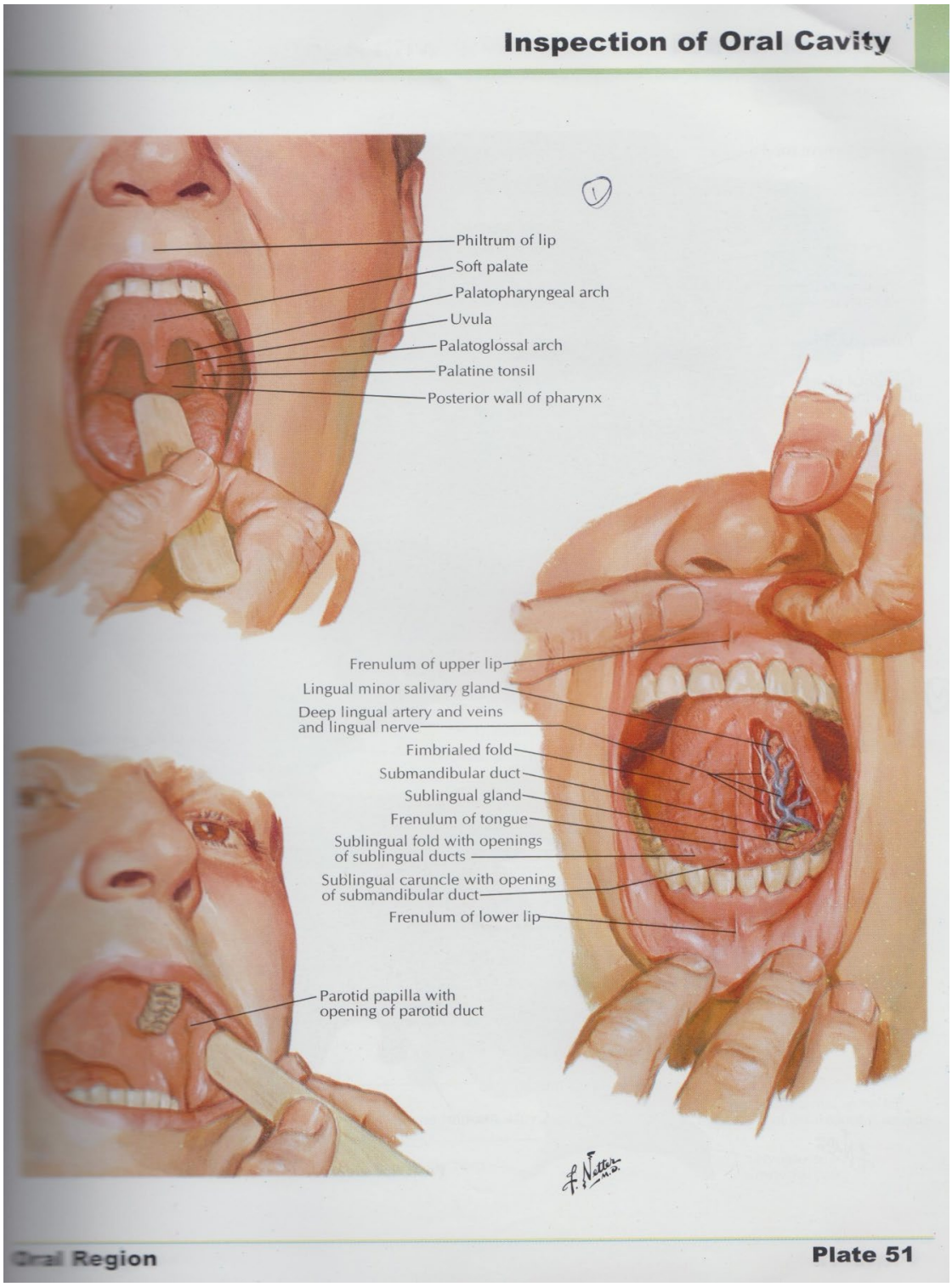


Fig. 3: Inspection of oral cavity shoing palatine tonsil

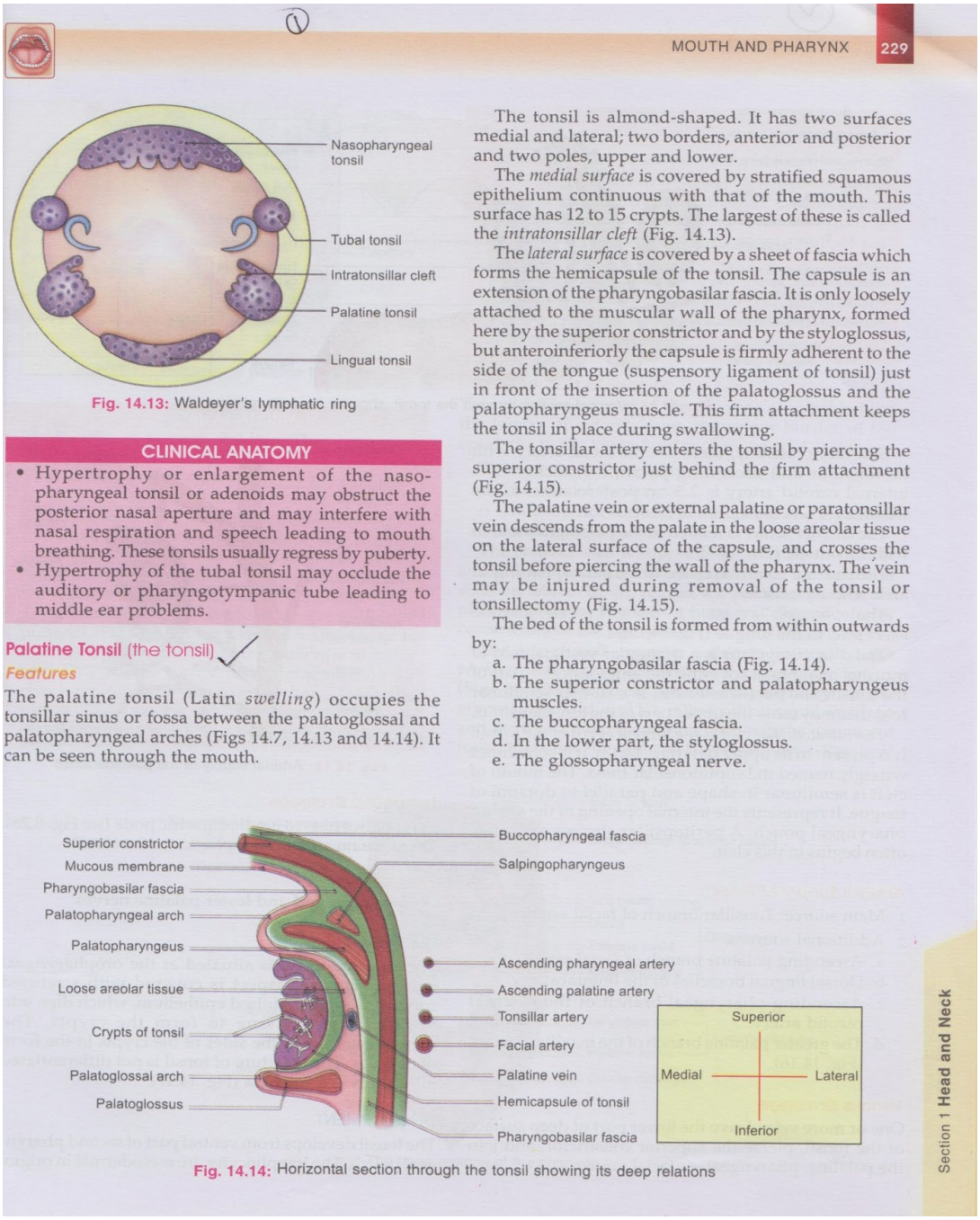


Fig. 4: Clinical anatomy of the tonsil with its associated structures

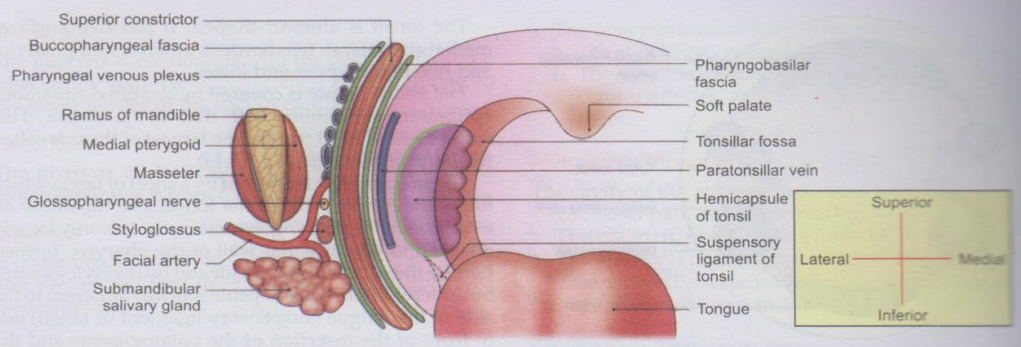


Fig. 14.15: Vertical section through the tonsil, showing its deep relations

Still more laterally, there are the facial artery with its tonsillar and ascending palatine branches. The internal carotid artery is 2.5 cm posterolateral to the tonsil.

The *anterior border* is related to the palatoglossal arch with its muscle (Fig. 14.7).

The *posterior border* is related to the palatopharyngeal arch with its muscle.

The *upper pole* is related to the soft palate, and the *lower pole*, to the tongue (Fig. 14.15).

The *plica triangularis* is a triangular vestigial fold of mucous membrane covering the anteroinferior part of the tonsil. The *plica semilunaris*, is a similar semilunar fold that may cross the upper part of the tonsillar sinus.

The *intratonsillar cleft* is the largest crypt of the tonsil. It is present in its upper part (Fig. 14.13). It is sometimes wrongly named the supratonsillar fossa. The mouth of cleft is semilunar in shape and parallel to dorsum of tongue. It represents the internal opening of the second pharyngeal pouch. A peritonsillar abscess or quinsy often begins in this cleft.

Arterial Supply of Tonsil

1 Main source: Tonsillar branch of facial artery.
2 Additional sources:
   a. Ascending palatine branch of facial artery.
   b. Dorsal lingual branches of the lingual artery.
   c. Ascending pharyngeal branch of the external carotid artery.
   d. The greater palatine branch of the maxillary artery (Fig. 14.16).

Venous Drainage

One or more veins leave the lower part of deep surface of the tonsil, pierce the superior constrictor, and join the palatine, pharyngeal, or facial veins.

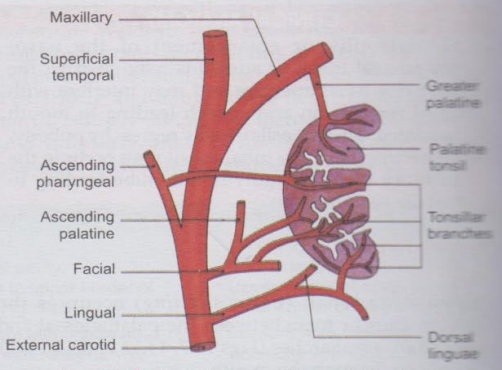


Fig. 14.16: Arterial supply of the palatine tonsil

Lymphatic Drainage

Lymphatics pass to jugulodigastric node (*see* Fig. 8.28). There are no afferent lymphatics to the tonsil.

Nerve Supply

Glossopharyngeal and lesser palatine nerves.

HISTOLOGY

The palatine tonsil is situated at the oropharyngeal isthmus. Its oral aspect is covered with stratified squamous nonkeratinised epithelium, which dips into the underlying tissue to form the crypts. The lymphocytes lie on the sides of the crypts in the form of nodules. The structure of tonsil is not differentiated into cortex and medulla (Fig. 14.17).

DEVELOPMENT

The tonsil develops from ventral part of second pharyngeal pouch. The lymphocytes are mesodermal in origin.

Fig. 5: Ventricular section through the tonsil showing its deep relations

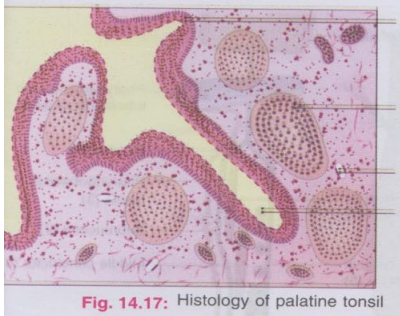


Fig. 14.17: Histology of palatine tonsil

CLINICAL ANATOMY

- The tonsils are large in children. They retrogress after puberty.
- The tonsils are frequently sites of infection, specially in children. Infection may spread to surrounding tissue forming a peritonsillar abscess.
- Enlarged and infected tonsils often require surgical removal. The operation is called *tonsillectomy*. A knowledge of the relationship of the tonsil is of importance to the surgeon.
- Tonsillectomy is usually done by the guillotine method. Haemorrhage after tonsillectomy is checked by removal of clot from the raw tonsillar bed. This is to be compared with the method for checking postpartum haemorrhage from the uterus. These are the only two organs in the body where bleeding is checked by removal of clots. In other parts of the body, clot formation is encouraged.
- Tonsillitis may cause referred pain in the ear as glossopharyngeal nerve supplies both these areas.
- Suppuration in the peritonsillar area is called *quinsy*. A peritonsillar abscess is drained by making an incision in the most prominent point of the abscess.
- Tonsils are often sites of a septic focus. Such a focus can lead to serious disease like pulmonary tuberculosis, meningitis, etc. and is often the cause of general ill health.

Laryngeal Part of Pharynx (laryngopharynx)

This is the lower part of the pharynx situated behind the larynx. It extends from the upper border of the epiglottis to the lower border of the cricoid cartilage.

The *anterior wall* presents:

a. The inlet of the larynx.
b. The posterior surfaces of the cricoid and arytenoid cartilages.

The *posterior wall* is supported mainly by the fourth and fifth cervical vertebrae, and partly by the third and sixth vertebrae. In this region, the posterior wall of the pharynx is formed by the superior, middle and inferior constrictors of the pharynx.

The *lateral wall* presents a depression called the *piriform fossa*, one on each side of the inlet of the larynx (Fig. 14.18). The fossa is bounded medially by the aryepiglottic fold, and laterally by the thyroid cartilage and the thyrohyoid membrane. Beneath the mucosa of fossa, there lies the internal laryngeal nerve. Removal

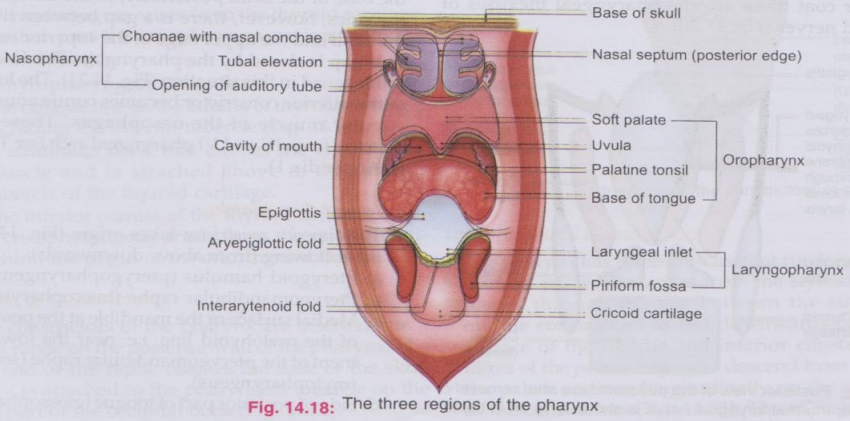


Fig. 14.18: The three regions of the pharynx

Fig. 6: Histology of the palatine tonsil & three regions of the pharynx

2.2 Sleep disordered breathing – An overview:

For adolescents, the term SDB is more often used than OSAS for the former term acknowledges that SDB is a continuum of sleep-associated breathing disorders (SABDs) which primarily involves snoring, upper respiratory tract resistance syndrome (URTS), obstructive hypoventilation, and OSAS. The prevalence of snoring and suspected SDB in children is always much higher (11%) than that of OSAS (0.7-3%) (De Serres *et al*., 2002; Tran *et al*., 2005). The effect of SDB on the development and behaviour of children, that is, hyperactivity and inattention is well-described in the literatures (Chervin *et al*., 2002; O'Brien *et al*., 2003; Golan *et al*., 2004; Huang *et al*., 2004). Several studies (O'Brien *et al*., 2003; Golan *et al*., 2004; Huang *et al*., 2004) using either polysomnography (PSG) or parental surveys or both have reported that SDB is observed more commonly in children with ADHD than among children without ADHD. One research also found that SDB may be associated with children with a moderate hyperactivity disorder (O'Brien *et al*., 2003). Children with habitual snoring and SDB mostly did have ADHD and that treatment of children could reduce ADHD provided their snoring and SDB disappeared (Chervin *et al*., 1997). Unlike OSAS, which is partially characterized by a common PSG-based index of apnea-hypopnea (AHI), SDB could be clinically detected and may not require to be supported by PSG confirmation of an obstructive respiratory condition (Weatherly *et al*., 2004).

Fig. 7: Enlarged tonsils in child with obstructive sleep apnoea

According to the guidelines of the American Academy of Pediatrics (Weatherly *et al*., 2003) and the American Thoracic Society (Schechter, 2002), the diagnosis of OSAS includes a clear result from PSG or some other purposive tests (e.g., a nocturnal cardiopulmonary study). For OSAS assessment, although PSG conducted overnight in a laboratory is accepted as the "gold standard", there are logical explanations why only PSG cannot be sufficient to classify entire children with SDB. Firstly, in a typical sleep study, patients with primary snoring and UARS may display a normal breathing disturbance index. Secondly, analysis of practice trends of otolaryngologists revealed that < 10% of patients ever underwent any objective screening test and < 5% of school-going children were subjected to PSG before adenotonsillectomy (Schechter, 2002). This research type varies from the American Academy of Pediatrics Guidelines. But actually the otolaryngologists follows the fact that for each

child undergoing adenotonsillectomy, there are not sufficient centers to have pre-operative PSG testing. Thirdly, children with SDB may not consistently follow OSAS PSG guidelines (Weatherly *et al*., 2004). For these reasons many otolaryngologists agree that PSG screening should be reserved for very young patients or those with clinical comorbidity (Sterni & Tunkel, 1998).

Lastly, there are insufficient data on normative sleep pattern of the child population. As such variation in quality and perception of sleep study findings in a suspicious diagnosis of SDB or OSAS depends on the definition framed on the basis of AHI. While in healthy children an AHI as small as 1 may be uncommon, it is uncertain whether this value is important clinically.

Specific methods, such as, measures of quality of life (QOL), can be used for children who do not require PSG screening. Several studies (Ali, *et al*., 1996; Friedman *et al*., 2003; Mitchell & Kelly, 2005(a,b); Mitchell *et al*., 2004(a); Stewart *et al*., 2005; Chervin *et al*., 2000) using different evaluation tools have shown that AT results in immense betterment in QOL of children who have PSG-supported OSAS as well as those who have been clinically diagnosed with SDB without verification. While these instruments are useful in assessing result, a questionnaire particularly for SDB prediction and post-operative progress would minimize the gap between reliable PSG information for each child with nocturnal respiratory tract obstruction at one end of the continuum and medical perception of SDB in children on the other end. Chervin and associates (2000) designed the Pediatric Sleep Questionnaire (PSQ) and showed strong accuracy and consistency in its SDB measures, snoring, sleepiness, and behavioral problems. The Conners' Parent Rating Scale –

Revised Short Form (CPRS-RS) survey was selected to measure actions before and after adenotonsillectomy in the present study (Conners, 1997; Pedigo & Erford, 1999). The study was based on earlier studies of QOL improvement following adenotonsillectomy (Friedman *et al*., 2003; Mitchell & Kelly, 2005; Mitchell *et al*., 2004(b). The research was planned at 6 months after adenotonsillectomy to investigate changes in both sleep and behavior without using PSG. However, the study subjects with recurrent infections were excluded if they were the primary cause of adenotonsillectomy. Due to behavioral problems reported by family, patients were not invited to participate in this study. Pediatric otolaryngologists diagnosed children with SDB by history and clinical examination by fiber-optic nasopharyngoscopy. However, all patients were stable and did not have any known or clinical comorbidity, for example, congenital heart disease, neurological impairments like cerebral palsy, Down's syndrome, or craniofacial defects.

Children with severe obstructive sleep apnea are at increased risk of heart failure, hypertension and failure to thrive, and few physicians have concerns about the need to treat sleep disorder (Marcus, 2001). Nevertheless, most children with sleep-disordered breathing (SDB) have milder manifestations for which behavioral disturbances and cognitive impairment are considered to be the main morbidities. (Guilleminault *et al*., 1982; Blunden *et al*., 2000; Chervin *et al*., 2002; Gottlieb *et al*., 2004). Unfortunately, it has not been well examined the best way to identify children with an SDB rate that raises the risk for these outcomes. However, the value of mild SDB treatment is not well known (Rosen *et al*., 2004).

In fact, if SDB is suspected for medical purposes and adenotonsillectomy (AT) therapy is expected, less than 10% of North American children undergo polysomnography to confirm their diagnosis or need for surgery (Weatherly R*et al*., 2003), whereas the American Academy of Pediatrics seeks routine sleep checks for SDB until AT is suggested (American Academy of Pediatrics, 2002). This is because many studies showed a weak correlation between office experiences and the findings of the sleep laboratory (Messner, 1999). Usual polysomnography, however, can neglect mild forms of SDB that are still associated with neurobehavioral morbidity in cross-sectional studies (Gottlieb *et al*., 2004; Rosen *et al*., 2004; O'Brien *et al*., 2004). Few prospective studies explored the degree to which morbidity can respond to treatment in these situations (Guilleminault *et al*., 2004), and none analyzed long-term results, and none integrated a full range of gold standard mental health, attitude, cognitive, and daytime sleep tests.

A double-blind, placebo-controlled, randomized clinical trial is required to make a conclusive remark of the results AT in mild SDB. However, for several reasons, this study design is not feasible at this time. It is unlikely for families and practitioners to be oblivious to AT and fake surgery is not a choice. Some published data set the timing of neurobehavioral change after AT, and long-term randomization to a placebo arm would pose ethical concerns for diagnosed children with SDB.

Disorder of ADHD is commonly associated with sleep disorder or disruption. ADHD's relationships are dynamic and multidirectional with sleep problems, medical comorbidities, and medications. Evidence gleaned from reported

researches which compared sleep in children with ADHD with well-matched controls is well-consistent with ADHD associations with: hypopnea / apnea and peripheral limb movements in sleep or night flexibility in PSG studies; delay in sleep onset, shorter sleep duration in actigraphic studies, bedtime resistance, morning waking problems and daytime sleepiness in subjective studies. The above sleep disorders are also frequently associated with ADHD. Psychostimulant drugs might be associated with sleep disruption and disturbance. Long-acting formularies could have inadequate action, resulting in a rebound of symptoms at bedtime. Present guidelines emphasize diagnosis of sleep difficulties in children with ADHD prior to pharmacotherapy initiation and monitoring of the same during ADHD treatment and, with safe sleeping habits being the first-line choice to address sleep problems. ADHD may induce sleep difficulties as an inherent characteristic of the disorder; sleep problems may trigger or imitate ADHD or vice-versa. They either alone or together may interfere with neurological functioning as both problems share common underlying etiology (Hvolby, 2015).

The relationship between sleep and ADHD is complex and multifaceted. Sleep problems may be an underlying characteristic of ADHD, or the effects of the condition may both intensify or exacerbate it. Nevertheless, sleep problems can also lead to ADHD and ADHD-like symptoms, misleading to correct diagnosis (Cortese *et al*. 2006b; Owens 2008). The findings of limited, disordered sleep that appear to be almost similar to those of ADHD (Gruber, 2009; Beebe 2006; O'Brien 2009). The interrelationships become even cumbersome when psychostimulant drugs are used to treat ADHD, which may in some cases

affect sleep (Spruyt and Gozal, 2011) but paradoxically do better in others via a calming effect (Kooij *et al*. 2001; Jerome, 2001; Kratochvil *et al*., 2005). That is why before starting treatment for ADHD, it is suggested that primary sleep disturbances be omitted (Cortese *et al*. 2013a; Lecendreux and Cortese 2007). Many patients who are benefited from behavioral interventions aimed at improving sleep (Cortese *et al*., 2013a) could be considered as part of the multimodal ADHD management plan prescribed for pharmacotherapy patients (Graham *et al*. 2011; Lecendreux and Cortese 2007; Wolraich *et al*. 2011).

Children with ADHD frequently present psychiatric comorbidities. Majority (87%) of the children with ADHD has at least one comorbidity and 20% possesses ≥ 3 comorbidities (Rowland *et al*. 2002; Spruyt and Gozal, 2011; Hodgkins *et al*., 2013). Sleep problems are more likely to adversely affect the QoL of children with ADHD and their families (Hvolby *et al*. 2008) and may also induce the causation of anxiety disorder, depression or deviant behaviour in opposition (Hvolby *et al*. 2008; Mick *et al*. 2000). So, when treating patients, it is important to take into account the associations of comorbid conditions and associated medications with ADHD and sleep disorders.

Despite extensive research, the complex, multidirectional sleep interactions with ADHD, medication, and psychiatric comorbidities remain obscured. The reciprocal relationship between ADHD and sleep indicates the functional and neuroanatomic overlap between the brain regions implicated in the regulation of attention, excitement and sleep (Owens *et al*. 2013; Owens 2008).

In the middle of the 20th century, over one million tonsillectomies were conducted per year on children in the USA primarily due to chronic infection. Alhough the number of tonsillectomies has decreased in recent decades (Owings & Kozak, 1996), it is still the most commonly performed pediatric surgeries in the USA. Adenotonsillectomy is usually conducted on obstructive rather than infectious signs with increasing frequency (Rosenfeld & Green, 1990). Recent studies of practice patterns showed that more than 20,000 pediatric ATs are conducted by otolaryngologists each year because obstructed respiration of any kind (59%), frequent infections (42%), and OSA (39%). This suggests that obstructive airway problem now supersedes recurrent infection as the most frequent surgical indication for AT (Weatherly *et al*., 2003).

Specific forms of breathing with sleep disorder (SDB) cover primary snoring, termed as habitual snoring not related to oxygen desaturation or sleep excitement. International Sleep Disorder Classification, 1997, characterized UARS, as high intrathoric negative pressure and sleep excitement usually not related with oxygen desaturation or airflow limitations (Guilleminault *et al*., 1996). SDB including OSA, marked by frequent episodes of nocturnal hypopnea or apnea in combination with sleep restlessness, oxygen desaturation and probable hypercapnia (American Thoracic Society, 1996). Although the features of OSA in children remain more or less ambiguous, an index of apnea (AI) above 1/hour or an index of apnea / hypopnea (AHI) above 5/hour for overnight PSG is usually taken as abnormal (Marcus *et al*., 1992; Guilleminault *et al.,* 2005). The incidence of pediatric UARS, including the seldom used oesophageal pressure monitoring (Pes) for diagnosis is not yet known, but has

been shown to be equal to or greater than OSA incidence (Guilleminault *et al*., 1996). Several studies have shown a raised incidence of SDBs in some ethnic groups, including African Americans (Redline *et al*., 1999) as well as in children who are overweight or obese, (Mallory *et al.,* 1989) which also seems to induce an increased prevalence in ethnic groups with higher obesity rates (Villaneuva *et al*., 2005). Data also indicate that SDB is less likely to be resolved in obese children after surgery (Tauman *et al*., 2006; Shine *et al*., 2006; O'Brien *et al*., 2006). OSA was associated with systemic and cardiovascular sequelae such as failure to thrive (Hodges & Wailoo, 1987), systemic hypertension (Enrightet, 2003; Guilleminault *et al*., 2004), corpulmonary or left ventricular hypertrophy (Ross *et al*., 1987; Cloward *et al*., 2003; Massumi *et al*., 1969). The less serious types of SDB are also found to be associated with reduced cognitive abilities (O'Brien *et al*., 2004; Blunden *et al*., 2000; Kaemingk *et al*., 2003), quality of life (QOL) (Franco *et al.,* 2000; De Serres *et al*., 2000; Crabtree *et al.,* 2004) and behavioral abnormalities (Ali *et al.,* 1996; Gottlieb *et al*., 2003) in kids. Even the less extreme types of SDB are observed to bear association with decreased cognitive abilities (O'Brien *et al*., 2004; Blunden *et al*., 2000; Kaemingk *et al*., 2003), QOL (Franco *et al.,* 2000; De Serres *et al*., 2000; Crabtree *et al.,* 2004) and behavioral disorders (Ali *et al.,* 1996; Gottlieb *et al*., 2003) in boys.

A total of 232 articles were found in the search. Analysis of these abstracts reported 25 relevant articles ranging from 19 to 297 subjects with sample sizes that met the eligibility for enrollment. Seventeen of these studies considered a single outcome variable to evaluate the improvement after surgical

intervention; ten studies measured changes in QoL, four studies investigated changes in behaviour, and three studies focused exclusively on neurocognitive behavior improvements. Six studies assessed changes in behavioral activities and memory, and 2 studies evaluated behavior and success in the development of life. Only one study examined changes in all the variables: intelligence, behavior, and QoL.

Previous descriptive studies support a link of SDB with behavior and cognition. The findings show improvement after AT. Guilleminault *et al.,* (1982) studied on 25 children with suffering s from snoring, extreme drowsiness during the day, and abnormal behavior. No obstructive sleep apnea was shown by PSG with Pes, but raised negative esophageal pressure was seen. In a small subset of older patients (Wilkinson Addition Test) objective intelligence tests were conducted and progress was reported. Potsic *et al.,* (1986) looked forward to 100 children with obstruction due to adenotonsillary hypertrophy. Less oral ventilation and fewer behavioral problems were recorded on parent questionnaires among the AT patients after surgery. Stradling *et al.,* (1990) in a study of 61 children with chronic tonsillitis having snoring compared with 31 controls. A parental survey reported major basic issues about their boys, including high rates of violence, learning compromise, and hyperactivity. Postoperative survey responses are identical to the responses from the control group. Gozal (1998) examined 297 children in the lowest 10^{th} percentile of their first grade class. Measurements of nocturnal pulse oximetry and carbon dioxide were used to identify 54 children with abnormalities in sleep-associated gas exchange and evaluation was recommended for AT. Of the 24 children

who underwent surgery, the following year, only 2 remained in the lowest 10% of their class. Some differences in academic performance have been seen in children with gas-exchange disorders who have not undergone surgery or children without known anomalies in gas exchange. While indicative of progress in key outcome measures, these studies lacked established analytical methods recording either beneficial outcome from surgery or the presence of OSA. De Serres *et al.,* (2002) carried out a study in 101 children with SDB using a validated disease-specific QoL system, Obstructive Sleep Disorders 6 questionnaire. Marked improvements in QoL after AT were seen in three-quarters (74%) of the children during their postoperative visit and slight improvement in majority (88%) of children. Similar improvements after AT were shown in studies using other validated QOL instruments. Mitchell and Peers (2004) in a short-term (6 months after OSA surgery) study demonstrated substantial improvements in QoL in 60 children having SDB before AT. The QoL was measured with Parental Obstructive Sleep Apnea 18 (OSA-18) questionnaire, a validated disease-specific quality of life device. After a longer follow-up (9 to 24 months) in 37 children, the study showed continued but less dramatic improvement in QoL with OSA-18. Flanary (2003) studies 55 children with adenoid and tonsillar hypertrophy with symptoms of OSA. The improvements were measured after AT using both a validated general QoL tool, the General Children's Health Questionnaire Parent Form and disease-specific OSA-18 and found advantages in both short-term and long-term QoL.

In another study Diez-Montiel *et al.,* (2006) with the help of OSD-6 questionnaire examined 101 children at least 3 years after AT. They observed

that the QoL related to disease improved over pre-operative levels. Improvements in behavior and cognition (evaluated with the help of validated objective outcome measures) have also been shown following AT done for SDB. Ali *et al.,* (1993) made a comparative evaluation of cognition after AT in 11 children with snoring but no apparent obstruction and 10 non-snoring children. The resulting measure was the Conner Rating Scale, Continuous Performance Test, Wechsler Intelligence Scale, and Matching Family Figures Test. The SDB group exhibited reduced inattention and hyperactivity on the Conner and improved scores on the CPT after AT. Montgomery-Downs *et al* (2000) measured behavioral improvements in a sample of 19 at-risk children with OSA before and after AT with the Differential Ability Scale (DAS) and the Developmental Neuropsychological Assessment (NEPSY) relative to 19 controls. In the OSA subjects, DAS scores were lower than those seen in preoperative controls and significantly improved to match the level of control after surgical intervention. Only the verbal scores of NEPSY were found to be lower in subjects than in controls, and after surgery those scores also improved.

In an uncontrolled study of 36 children undergoing AT, Goldstein *et al* (2002) found abnormal behavior preoperatively in 28% of patients when Child Behavior Checklist (CBCL) was used as a standardized assessment tool for childhood behavior. These behavioral disturbances in all but two patients were resolved after surgery. The mean overall problem score was also significantly reduced. Goldstein *et al.,* (2004) observed significant favourable outcome in disease-specific QoL following OSA-18 surgery as well as improvement in CBCL activity on 64 children before and after AT in terms of SDB.

Improvement of QoL scores and behavioral scores are strongly correlated. Avior *et al.,* (2006) assessed impact of AT treatment on attitude and QOL of 19 children with OSA being clinical diagnosis. The tools used were Test of Attention Variables (TOVA), OSA-18, and CBCL. Improvements were observed two months after surgery in all three measures. Galland *et al.,* (2006) demonstrated statistically significant changes in neurocognitive activity with CPT and actions with the Children's Behavioral Assessment System (BASC) test following AT for moderate SDB in children despite being considered to be behaviorally healthy preoperatively.

Behavioral changes tend to be long-lasting, such as those seen in QOL. Mitchell and Kelly (2005) documented behavioral changes in children with confirmed OSA after completing short-term assessment after AT with BASC (6 months after surgery) which were found to continue after long-term follow-up (9 to 18 months) in another study, Mitchell & Kelly 2006(a,b). A lot of recent studies has also looked at changes in behavior, memory, or QoL in accordance with PSG findings. Friedman (2003) in an attempt to test the neurocognitive activity in 39 children with reported OSA and 20 controls without SDB symptoms with the Kaufman Assessment Battery for Children (K-ABC). Children having OSA had lower scores and a lower composite scale score for general mental development. There was no connection between the ratings of OSA and K-ABC. Following AT, the neurocognitive scores of OSA cohort reached the level comparable to that of control group.

Stewart *et al.,* (2005) used the CHQPF-28 to examine disease-specific QoL with the Tonsil and Adenoid Health Status Instrument and international QoL in

47 children suspected to have OSA. Nearly two-thirds (65.9%) of the children were identified to have OSA by PSG and were subjected to AT. A favourable outcome was observed in terms of both QoL assessment scores and PSG findings among the children who have had surgery a year earlier. In contrast Mitchell and Kelly, 2004(a,b) assessed QoL in children with severe OSA and fobserved significant differences with OSA-18 in general and QoL domain scores. Research conducted by the same researchers (Mitchell & Kelly, 2005) to examine the discrepancies in QoL development among 43 children reported to have worse OSA and 18 children with mild OSA. They demonstrated significantly better outcome in both general and domain scores of OSA-18.

Another earlier study at the same institution (Mitchell *et al.,* 2004) observed more QoL development in children with slight and severe OSA compared to children with moderately severe OSA. A study conducted by Tran *et al.,* (2005) examining changes in 42 children with established PSG sleep apnea. The study observed favourable changes in CBCL and OSA-18 and overall changes in QoL and behavior of the children 3 months after AT compared to a control child who experienced similar surgery but did not have snoring history. Pre-operative cognitive and QoL ratings are associated. No correlation was found between the rate of anomaly on the OSA-18 test at baseline and the severity of OSAS.

In 30 age and sex-specific overweight (in terms of body mass index children) and OSA, Chervin *et al.,* (2006) demonstrated favourable outcome in children's behavior 1 year after AT according to the Conner's studies. Attention improvement was also observed using objective measurements. Nearly half of

children diagnosed with ADHD in the study no longer had the disease one year after intervention. PSG tests at entry or change in PSG following surgery is highly predictive, suggesting either baseline or postoperative behavioral or neurocognitive changes.

Li *et al.,* (2006) conducted a study on 40 children with SDB to see the changes in them 6 months after AT. The study showed marked improvements in both CBCL behavior and care with TOVA. ADHD ratings were average in 78 percent of kids. The changes seen in TOVA research had no association with improved PSG AHI. Such findings showing a lack of visible association between outcome and PSG parameters raise question whether standardization of PSG indicators is a dependable measure to detect clinically significant improvements in SDB or highlights the necessity for more responsive sleep disturbance interventions in children.

The above published studies evaluating whether adenotonsillectomy in children with sleep disorders is associated with attitude, cognitive function and QoL improvements as well as evaluating whether these improvements could be correlated with polysomnographic parameters is of utmost importance to consider whether future studies can provide additional clinically significant details. Summarization of these studies is, therefore of utmost importance. All studies discussed above have shown improvements in one or more of the defined outcome measures, including general or disease-specific QoL, behavioral problems such as hyperactivity and increased aggression or neurocognitive abilities such as memory, attention, or school achievement. A minimal association has often existed between changes in outcome measures

and PSG measures. Studies also suggest that AT performed in children with SDB is often associated with improvements in QoL, behavior and cognitive function to some extent, but well-designed large, randomized-controlled trials (RCTs) are required to provide convincing data about the outcomes of this commonly performed surgery in the general population (Julie *et al*., 2007).

Chapter 3

MATERIALS AND METHODS

3.0 Introduction:

This chapter describes the study design contemplated to test the hypothesis, when and where the study was conducted and who were the population (that what eligibility criteria were used to select the study population). The variables used in the study, particularly the outcome variables were operationalized. Detailed operative procedure was also described. In data analysis section, which data analysis soft-ware was used and how data processing and data analysis were performed were also outlined.

3.1 Study design:

The present study was a prospective interventional study of pre-test post-test design.

3.2 Place and period of study

The study was conducted from July 2012 to June 2015 in Rajshahi Medical College Hospital, Rajshahi. The hospital is located at the heart of the city and is a well-equipped tertiary care hospital to deal with the cases of ENT diseases including pediatric adeno-tonsillar diseases.

3.3 Study population

Children with SDB and ADHD if fulfills the following eligibility criteria were included in the study as study population.

3.4 Eligibility criteria:

3.4.1 Inclusion criteria:

Patients with following characteristics will be included in the study as cases.

- Children, ranging from 3-8 years of age, undergoing adenotonsillectomy for SDB with or without attention-deficit hyperactive disorder.
- Parents voluntarily allowing their children to participate in the study.

3.4.2 Exclusion criteria:

Children with following criteria will be excluded from the study:

- Children with SDB having congenital anomalies.
- Children with severe medical conditions (e.g. cerebral paralysis, epilepsy),
- Parents not willing to allow their children to participate in the study.

3.5 Addressing ethical issues for ethical clearance:

Prior permission was taken from Ethical Review Committee of Institute of Biological Sciences, University of Rajshahi, Rajshahi and Rajshahi Medical College Hospital, Rajshahi to undertake this study. Keeping compliance with

Helsinki Declaration for Medical Research Involving Human Subjects 1964, the parents of the study children were informed verbally and in writing about the study design, the purpose of the study and potential benefits derived from the study. Parents who gave written informed consent to allow their children to participate in the study were included as study sample.

3.6 Sample size determination:

A total of 50 children with SDB and/or ADHD were consecutively included in the study.

3.7 Outcome variables:

The main outcome variables were sleep disordered breathing, ADHD, Cognitive function and quality of life.

3.8 Detailed procedure:

Detailed procedure of surgery and quality of life assessment are given below.

3.8.1 Procedure of Surgery:

A tonsillectomy is a tonsil removal operation. An adenotonsillectomy is an operation in which the adenoids and tonsils are removed. While adenotonsillectomy is an extremely safe procedure, surgery, in some cases, can be a scary experience — especially for kids. Blood tests and urine tests are performed prior to tonsillectomy and/or adenoidectomy. During the operation, general anesthesia was used. Adenotonsillectomy is usually performed as an out-patient procedure, meaning that the child will leave the hospital on the day

of surgery. However, children with obstructive sleep apnea (OSA) and children under the age of 3 had to be admitted overnight to the hospital.

Traditional surgery involves removing the whole tonsil or adenoid and partial (intracapsular) surgery involves removing only the tonsillar tissue that is inflamed. Children who have undergone partial tonsillectomy or adenoidectomy may have less post-operative pain and may come round faster than children undergoing conventional surgery. In ocassional cases, the remaining tonsillary tissue may become enlarged or infected after partial removal, requiring further surgery. A number of different devices were used to perform adeno-tonsillectomy through the mouth. The method used depended on a number of factors, including the preference of the surgeon, the extent of the operation, and the child's age and overall health. The following methods were used.

- **Coblation:** It involved using cool electrical current to remove tonsillar tissue; it may cause less postoperative pain and a faster recovery.
- **Dissection:** It was the most common method which involved removing the tonsils using a scalpel
- **Electrocauterization:** It involved using hot electrical current to remove the tonsils. However, may cause damage to surrounding tissue that increases postoperative pain.
- **Harmonic scalpel:** It was performed using a scalpel that vibrates; it minimized bleeding and damage to surrounding tissue.

- L**aser ablation** It was done using a hand-held laser to vaporize tonsillar tissue. Following tonsillectomy and/or adenoidectomy, some children experienced mild sore throat, ear pain, and a stuffy or runny nose for a week or two who were managed with soft foods (e.g., ice cream, pudding etc.) and cold liquids to relieve discomfort. For relieving pain, acetaminophen was also given.

The details of the steps of operation of adenotonsillectomy are given in appendix-III:

3.8.2 Quality of life assessment:

As medicine moved from "life preservation" to "health promotion" science (World Health Organization, 1947), the Quality of Life (QoL) concept has become increasingly important in the study of medical conditions, their impact and their outcome (Danckaerts *et al.,* 2008). The concept of QoL was defined as an ideal state as one of general well-being in which the daily functioning of an individual, across a wide range of domains, is unaffected by the potentially adverse effects of disease or disorder. Leidy *et al.,* (1999) defined QoL as "the subjective perception of an individual's health status impact on physical, psychological, and social functioning, including disease and treatment." This is consistent with the definition of QoL by the WHO QoL team (WHOQOL, 1995). Nearly all definitions and measures of QoL encompass physical, social and psychological domains. It is also popular to include a mental domain (Eiser & Morse, 2001). While QoL is affected by many proximal forces (i.e., family, friendship) and distal forces (socio-economic and cultural), disease is one of

the most powerful influences (Eiser & Morse, 2001). There is also a growing mental domain (Eiser & Morse, 2001). Although these procedures are increasingly used in the construction of tools for assessing QoL in children and youth, the process has not yet been tested in various patient groups to find its consistency in application.

QoL is seen primarily as a patient-reported outcome (Matza *et al.,* 2004 Spitzer *et al.,* 1995) with a key distinction between an independent assessment (e.g., he / she can't concentrate and that stops him / her from working at school and I think he / she should feel bad about it) and a "subjective" assessment (I can't concentrate, that stops me from working at school and I feel bad about that and it impacts generally on how I feel about myself). In this regard, it seems important to capture their QoL accurately in a child's own study. However, there are several issues that complicate this. Young children (e.g. before age 7 or 8) may lack the comprehension, insight or communication skills to provide valid self-assessment (Bibace & Walsh, 1980). This can be exaggerated in children with learning disabilities; those for whom mental health status or factors that affect their capability to accurately learn or internalize something (e.g., depression) as is usually the case with ADHD, where the child cannot able to reflect and respond to a questionnaire. In these cases, a parent or care-taker may need to rely on a proxy rating. As a result, QoL measures designed for children's populations usually have completed versions of both a child and a parent (Danckaerts *et al.,* 2008).

The present study measured the quality of life through the subjective evaluation of parents on the four dimensions, namely physical, emotional, cognitive and

social. The parents' level of satisfaction on the four domains were assessed before and after adenotosillectomy using a '0-4' Likert Scale, where 0 means 'grossly dissatisfactory' and 4 'highly satisfactory' with 'poor' 1, 'more or less satisfactory' 2, and 'satisfactory' 3 in between them. First the level of satisfaction was assessed separately for responses against each question representing the status of each domain. Then all these satisfaction scores were added together to find an overall level of satisfaction.

3.9 Data collection:

Data were collected using a semi-structured questionnaire (research instrument) containing all the variables of interest by interview of the parents and clinical and psychological examination of the children.

3.10 Statistical analysis:

Data were processed and analyzed using computer software SPSS (Statistical Package for Social Sciences). The test statistics used to analyse the data were **descriptive statistics**, **Chi-square (χ^2) Test, Paired t-Test**. Data presented on categorical scale were compared between children before and after intervention using **McNemar Chi-square (χ^2) Test**, while the changes in continuous variables were compared between children before and after intervention using **Paired-sample t-Test**. The level of significance was set at 0.05 and $p < 0.05$ was considered significant.

Chapter 4

RESULTS

The present study intended to determine the outcome of adenotonsillectomy in children with SDB with or without behavioural problem (ADHD) included a total of 50 children ranging from 3–8 years of age. The main outcome variables were sleep disordered breathing, ADHD, cognitive function and quality of life which were determined before and after tonsillectomy and improvement was measured by comparing the data pertaining to theses variables before and after the procedure. The findings obtained from data analysis are presented below:

The present study demonstrated that nearly three-quarters (74%) of the children were 6 or > 6 years old with mean age being 6.6 years (Table 1). Females were a bit higher (58%) than their male counterparts (42%) (Fig. 8). Half of the patients were rural residents (50%), one-third (34%) urban and the rest 16% were urban slum dwellers (Table 2 & Fig. 9). In terms of socioeconomic status lower middle class comprised the main bulk (40%), followed by poor and middle class (each comprised 24%). Very few were rich and upper class (Table 3).

Results

Pattern of sleep-breathing before and after adenotonsillectomy is shown in Table 4. Snoring, upper airway resistance syndrome, obstructive hypoventilation and obstructive sleep-apnoea syndrome (OSAS) all demonstrated their significant presence before adenotonsillectomy, which after intervention reduced to minimum ($p<0.001$ in each case). The major behavioral problems in children before intervention were attention-deficit hyperactivity disorder (82%), problemetic behaviours on awakening (86%), night-to-night sleep duration variability (78%) and headache (80%). The minor behavioural problems were enuresis (36%) and day time sleepiness (14%). All the major problems responded well following adenotosillectomy ($p<0.001$). Of the minor problems incidence of enuresis reduced to less than half ($p = 0.027$) (Table 5). Cognitive function like learning disabilities and poor academic performance showed commendable improvement following adenotonsillectomy ($p<0.001$) (Table 6 & Fig. 10).

Most children recovered fully from tonsillectomy and adenoidectomy in about 2 weeks. The most common complications observed were pain, bleeding, fever, infection, dehydration and vomiting.

Table 1. Distribution of respondents by their age (n = 50)

Age (years)*	Frequency	Percentage
3-6	13	26
≥ 6	37	74

***Mean age =** (6.6 ± 1.6) years; **range =** (3 – 10) years

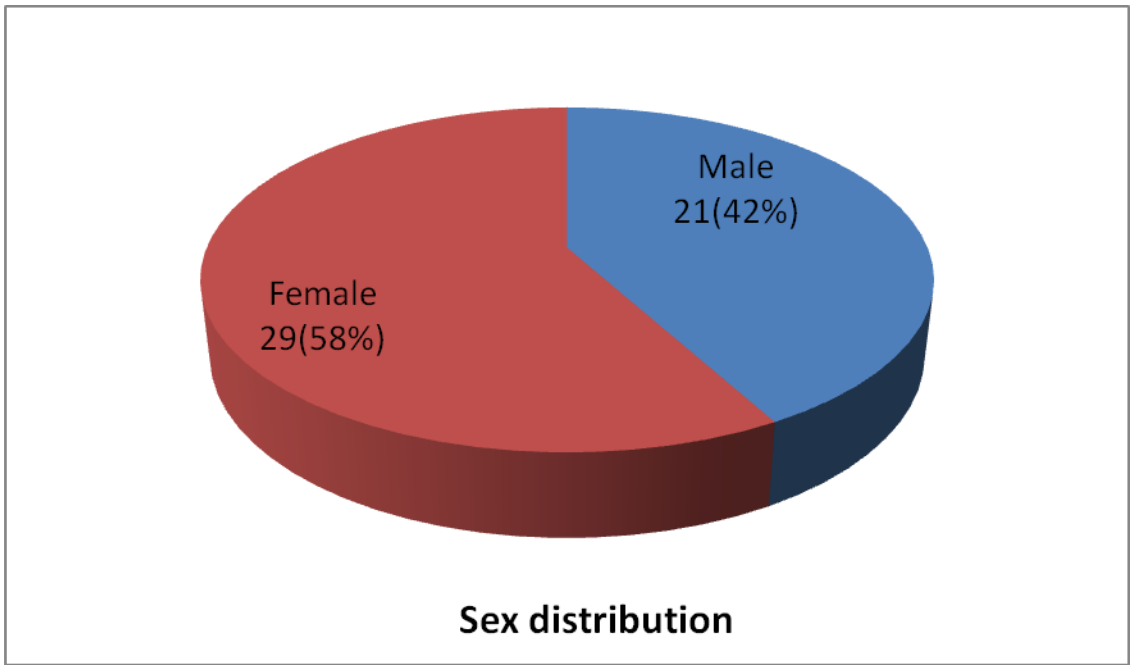


Fig. 8: Distribution of children by gender (n = 50)

Table 2. Distribution of respondents by their Residence (n = 50)

Residence	Frequency	Percentage
Rural	25	50
Urban	17	34
Urban slum	8	16

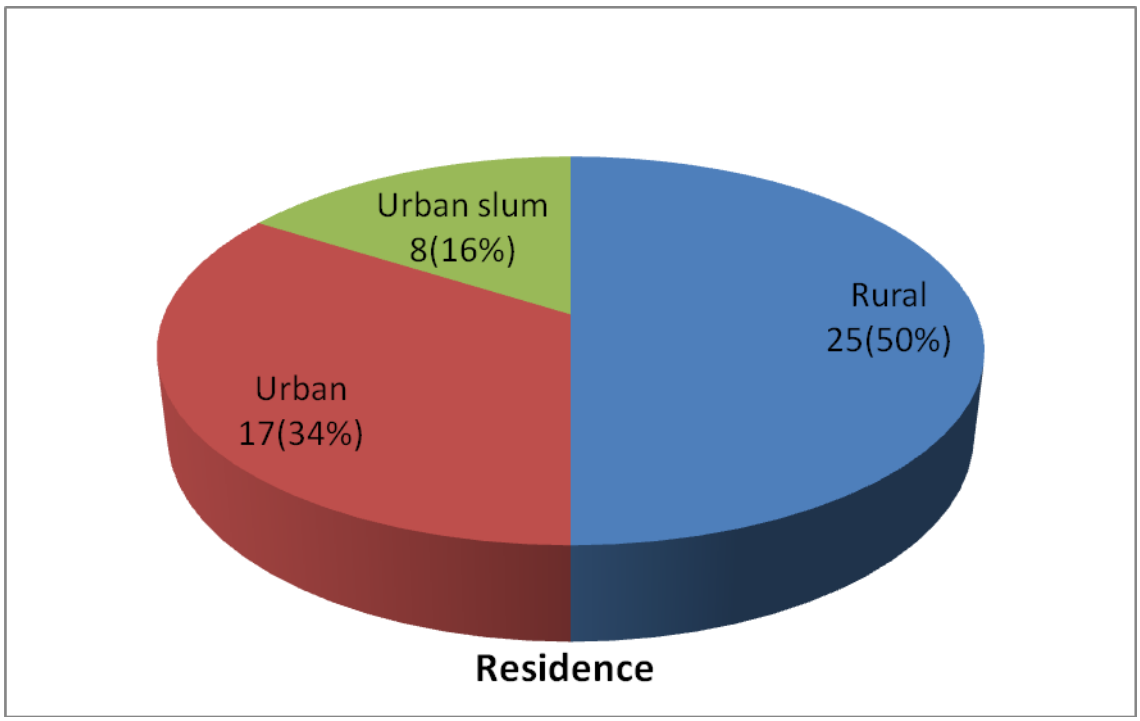


Fig. 9: Distribution of chgildren by their residence (n = 50)

Table 3. Distribution of respondents by their socioeconomic status (n = 50)

Socioeconomic status	Frequency	Percentage
Poor	12	24
Lower middle class	20	40
Middle class	12	24
Upper middle class	4	8
Rich	2	4

Table 4. Pattern of sleep breathing in children before and after intervention

Pattern of sleep breathing	Group		p-value
	Before intervention (n = 50)	After intervention (n = 50)	
Snoring	43(86.0)	11(22.0)	<0.001
Upper airway resistance syndrome	45(90.0)	10(20.0)	<0.001
Obstructive hypoventilation	43(86.0)	7(14.0)	<0.001
Obstructive sleep apnea syndrome	40(80.0)	8(16.0)	<0.001

Figures in the parentheses indicate corresponding **%;**
***MacNemar Chi-squared Test (χ^2)** was done to analyze the data**.**

Table 5. Behavioral problem in children before and after intervention

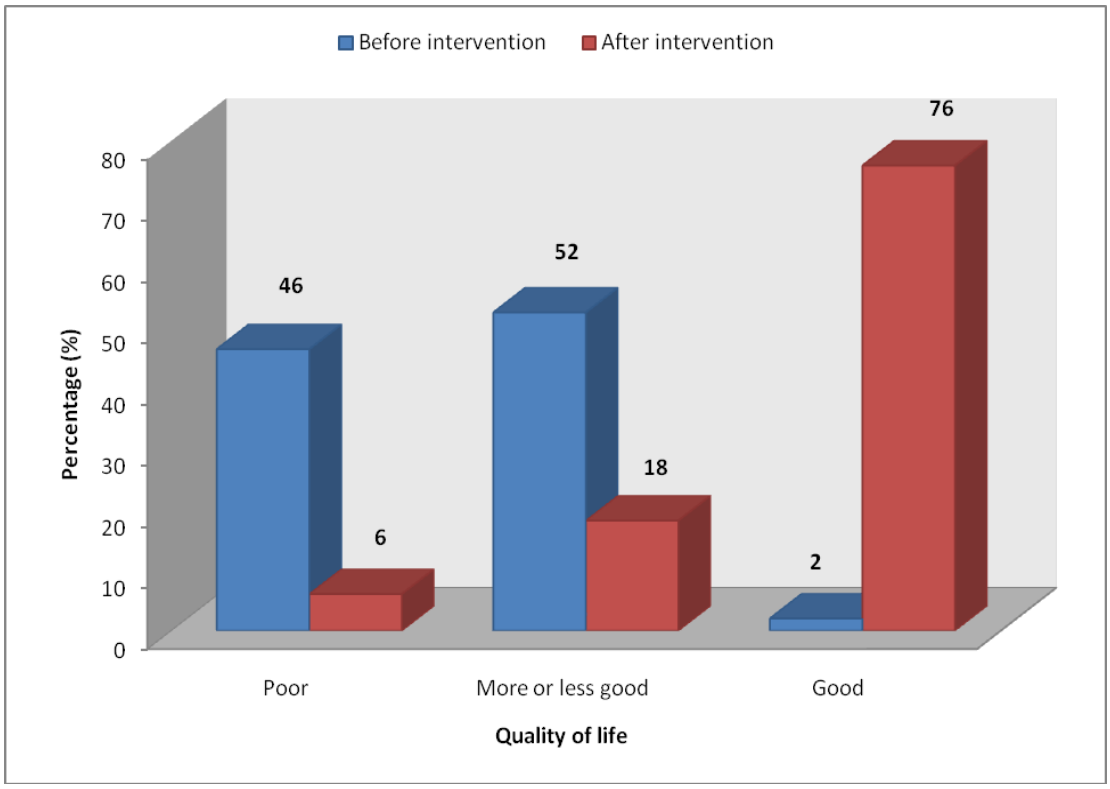
Behavioral problem	Group		p-value
	Before intervention (n = 50)	After intervention (n = 50)	
Attention-deficit hyperactivity disorder	41(82.0)	9(18.0)	<0.001
Enuresis	18(36.0)	7(14.0)	0.027
Day time sleepiness	7(14.0)	10(20.0)	0.607
Problematic behaviors on awakening	43(86.0)	7(14.0)	<0.001
Night-to-night sleep duration variability	39(78.0)	6(12.0)	<0.001
Headache	40(80.0)	10(20.0)	<0.001

Figures in the parentheses indicate corresponding **%;**
***MacNemar Chi-squared Test (χ^2)** was done to analyze the data**.**

Table 6. Cognitive function in children before and after intervention (n = 50)

Cognitive function	Group		p-value
	Before intervention (n = 50)	After intervention (n = 50)	
Learning disabilities	43(86.0)	6(12.0)	< 0.001
Poor academic performance	42(84.0)	7(14.0)	< 0.001

Figures in the parentheses indicate corresponding **%;**
***MacNemar Chi-squared Test (χ^2)** was done to analyze the data**.**



P < 0.001

Fig. 10: Quality of Life before and after intervention

Chapter 5

DISCUSSION

Sleep disorder breathing, as we have seen in the introduction and literature review chapters, is more or less a common pediatric problem and is generally associated with behavioural problems, *viz.* aggression, hyperactivity, ADHD and poor adjustment with surrounding social settings (Goldstein *et al.,* 2002). As such, it is quite usual that the overall health status and QoL of children with SDB would be decreased significantly (Goldstein *et al.,* 2002; Mitchell *et al.,* 2004). Therefore, the result presented in the earlier chapter needs to be compared and contrasted with findings of similar studies conducted at home and abroad to come to conclusion.

The children with SDB mainly presented (74%) to us at early school age (at 6 or >6 years) with mean age being 6.6 years. Studies have demonstrated that primary snoring can affect 10–25% of pediatric population aged 3–12 years, and a subset of these population (around 10%) may have OSAS (Stein *et al.,* 2001; Castronovo *et al.,* 2003).

Gozal (1998) observed that SDB occurs 6–9-times more likely in 1st grade children (aged 6 yrs) who were below 10th percentile for academic achievement. Moreover, neurocognitive activities, such as, memory, learning activities and problem solving functions, are substantially impaired in children with SDB (Owens *et al.,* 2000). A female predominance was observed in the series. Snoring (86%), upper airway resistance syndrome (90%), obstructive hypoventilation (86%) and obstructive sleep-apnoea syndrome (OSAS) (80%) all demonstrated their significant presence before adenotonsillectomy. After intervention a substantial proportion of these symptoms is reduced ($p < 0.001$ in each case) indicating that adenotonsilitis might be the main reason of these symptoms. Poor sleep in children may have negative effects on their daily functioning, mood, behavior and school performance (Owens *et al.,* 2005; Gaina *et al.,* 2007; Harriet *et al.,* 2007). Moreover, sleep problems have adverse effects on QoL. In some cases, sleep problems may be a symptom of ADHD (Teng, 2010; Reine *et al.,* 2010).

The major behavioral problems in our children before intervention was ADHD (82%), problemetic behaviours on awakening (86%), night-to-night sleep duration variability (78%) and headache (80%), The minor

behavioural problems were enuresis (36%) and day time sleepiness (14%). All the major problems responded well following adenotosillectomy and reduced to bare minimum ($p<0.001$). Of the minor problems incidence of enuresis reduced to less than half ($p = 0.027$). Cognitive function like learning disabilities and poor academic performance showed commendable improvement following adenotonsillectomy. Nearly half (46%) of the children had poor and 52% had average QoL as reported by their parents. After intervention over three-quarters (76%) of the children had good QoL which is considered significant and is believed to be the result of adenotonsillectomy ($p<0.001$). Consistent with these findings Julie and associates (2007) found significant improvement in sleep and behavior before and after adenotonsillectomy.

Although polysomnography is believed to be the 'gold standard' for judging OSAS, for selected patients PSG test may not always be mandatory before AT. There are no guidelines as yet for medical practice about the use of PSG and AT eligibility, and majority of the otolaryngologists take decisions or recommendations based on SDB, clinical history and adenoid and/or tonsillary hypertrophy seen in

physical examination. Nonetheless, predictive performance of clinically suspicious OSAS can be as poor as 30% when evaluating PSG as well. (Wang *et al.,* 2007; Montgomery-Downs *et al.,* 2004).

Adenotonsillectomy has been shown to be potentially curative in children with adenotonsillary hypertrophy for the entire range of obstructive sleep disorders – from primary snoring to upper airway resistance syndrome, which may not display irregularities with regular PSG (Chervin *et al.,* 2005). In addition to clinical suspicion of SDB, the use of a tool such as the Pediatric Sleep Questionnaire (PSQ) may aid in identifying patients who would be suitable candidates for AT or who may have residual SDB or related symptoms that did not respond to surgery.

It has been shown that predictive performance for SDB is fortified when parental reporting of multiple behavioral interventions is integrated with snoring history (Chervin *et al.,* 2005). PSQ could therefore be used as a detailed parental questionnaire to evaluate quality of sleep and the Conners' Parent Rating Scale – Revised Short-form (CPRS-RS) to evaluate child behaviour. The CPRS-RS are the most extensively used tools for assessing child behavior. The CPRS-RS could be used over time to investigate, screen or monitor treatment

effects and may also be used as an adjunct to other information, such as, the short form of the Conners' Teacher Rating Scale – Revised. The use of feedback from teachers and parents will definitely provide more data about the child's global behaviour.

As this was a prospective observational study and has clearly shown the associations between AT and improvement in sleep and behavior, the findings support a cause-and-effect relationship between SDB and the onset of behavioral problems. However, as it was not a RCT, this association cannot be fortified. Without comparing with a control group that did not undergo adenotonsillectomy, it cannot be conclusively established that the surgical intervention was the cause of the change in behavior after adenotonsillectomy. Nonetheless, in a 4-year prospective cohort study (Chervin *et al.,* 2005), the PSQ and CPRS were used together to show that SDB symptoms potentially precede the onset of hyperactivity. Such findings give validity to the present study data, which demonstrates that treatment of SDB can lead to alleviation of abnormal behavior and sleep problems.

However, recent studies have indicated that some children have persistent sleep disordered breathing after adenotonsillectomy. Post-operative PSG

may therefore be needed following surgery, especially in children who persist symptoms or who exhibit increased risk factors for persistent apnea following adenotonsillectomy, such as obesity, or neuromuscular problems or craniofacial anomalies. Specific treatments such as weight loss, continuous positive airway pressure (CPAP) or specific surgery in such patients may sometimes be required.

Chapter 6

CONCLUSION

Sleep disordered breathing (SDB) is a familiar problem in preschool and school going children and is generally perceived as a neurodevelopmental condition leading to maltreatment resulting in abnormal behavioural complications and reduced cognition. A substantial proportion of children with SDB undergo adenotonsillectomy followed by resolution of the disorder. Staggering improvements in behavioural problems like hyperactivity, ADHD and quality of life are reported by the parents or caregivers after adenotonsillectomy for SDB. The present study was undertaken to evaluate whether adenotonsillectomy done in children with SDB improves their behavior, cognition and quality of life.

This prospective interventional study of pre-test post-test design was conducted in Rajshahi Medical College Hospital, Rajshahi over a period of 3-years from July 2012 to June 2015. The study population was children aged 3-8 years who underwent adenotonsillectomy for sleep disordered breathing (SDB) with or without attention-deficit hyperactivity disorder (ADHD). A total of 50 children fulfilling the predefined enrollment criteria (aged 3 – 8 years having SDB) were included in the study. The outcome variables were sleep disordered breathing, ADHD, cognitive function and quality of life.

The present study demonstrated that nearly three-quarters (74%) of the children were 6 or > 6 years old with mean age being 6.6 years. A female predominance

was observed in the series with female-to-male ratio being 3:2. Half of the patients were rural residents (50%), one-third (34%) urban and the rest 16% were urban slum dwellers. Lower middle class comprised the main bulk (40%), followed by poor and middle class (each 24%). Very few were rich and upper class. Snoring (86%), upper airway resistance syndrome (90%), obstructive hypoventilation (86%) and obstructive sleep-apnoea syndrome (OSAS) (80%) all demonstrated their significant presence before adenotonsillectomy. After intervention a substantial proportion of these symptoms reduced ($p < 0.001$ in each case) indicating that adenotonsilitis was the predisposing factor for these conditions. The major behavioral problems in children before intervention were attention-deficit hyperactivity disorder (82%), problemetic behaviours on awakening (86%), night-to-night sleep duration variability (78%) and headache (80%). The minor behavioural problems were enuresis (36%) and day time sleepiness (14%). All the major problems responded well following adenotosillectomy ($p<0.001$). Of the minor problems incidence of enuresis reduced to less than half ($p = 0.027$). Cognitive function like learning disabilities and poor academic performance showed commendable improvement following adenotonsillectomy ($p < 0.001$).

The findings of the present study suggest that the children with SDB presented as snoring, upper airway resistance syndrome, obstructive hypoventilation and obstructive sleep-apnoea syndrome (OSAS) show significant improvement after adenotonsillectomy in terms of quality of life, behavior, and cognitive function. However, not every child with snoring need to undergo adenotonsillectomy as the procedure is not without risk. Potential problems that

may occur include anesthesia or airway complications, infection, bleeding, and problems with speech and swallowing. If the SDB symptoms are problematic or intermittent, academic achievement and behavior are not major concerns and the tonsils are not enlarged enough, it may be recommended that a child with SDB should be watched conservatively and surgical treatment should be considered only if symptoms aggravate.

Based on the findings, the following recommendations are put forward:

1. Large-scale, randomized-controlled trials can be undertaken to provide authentic proof of the benefits of commonly performed surgical procedure in children for adeno-tonsillar hypertrophy with or without SDB.

The study findings also suggest some message to be conveyed to general people in order to make them aware of the signs of SDB in children and the steps to be taken by them, because if the diagnosis is delayed some complications, such as cognitive impairment and behavioral problems may continue to persist with poor academic performance and socialization.

Chapter 7

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RESEARCH CELL
RAJSHAHI MEDICAL COLLEGE
RAJSHAHI-6000, BANGLADESH

Ref. RMC/ERC/2013-2014/10 Date: 20/02/2013

ETHICAL REVIEW COMMITTEE

To
Md. Rezaul Karim
PhD Candidate
Institute of Biological Science
Rajshahi University
Rajshahi

Subject: Ethical Clearance

With reference to your application on the above subject, this is to inform you that your Research Proposal entitled "*Improved Sleep and Behavior after Adenotonsillectomy in Children with Sleep Disordered Breathing*" under the supervision of Professor Khalequzzaman, Department of Zoology, University of Rajshahi, Rajshahi has been reviewed and approved by the Ethical Review Committee of Rajshahi Medical College.

You are requested to please note the following ethical guideline as mentioned at page 2 (overleaf) of this memo.

Prof. (Dr.) Md. Abu Rayhan Khandakar
Principal, Rajshahi Medical College &
Chairman, Ethical Review Committee (ERC)
Rajshahi Medical College
Bangladesh

Annexure-II

Consent Form (Bangla)

কোড: ..... তারিখঃ .....

উত্তরদাতার নামঃ .....

আসসালামুআলাইকুম।আমি পিএইচডি প্রোগ্রামের ছাত্র/ছাত্রী। আমি একটি গবেষণা করছি যার শিরোনাম হল "IMPROVED SLEEP AND BEHAVIOR AFTER ADENOTONSILLECTOMY IN CHILDREN WITH SLEEP DISORDERED BREATHING". আমি আপনাকে এই গবেষণায় অংশগ্রহণের আমন্ত্রণ জানাচ্ছি। আপনার কাছ থেকে কিছু তথ্য জানতে চাই। আপনাকে উক্ত গবেষণা কর্মে কিছু প্রশ্নের উত্তর দিতে হবে যা এই ফর্মে উল্লেখ আছে।

আমি আপনাকে জানাতে চাই যে এটি একটি সম্পূর্ণরূপে একাডেমিক গবেষণা কর্ম এবং আপনার প্রদত্ত তথ্য সমূহ অন্য কোন উদ্দেশ্যে ব্যবহৃত হবেনা। আপনার নাম প্রকাশনায় গোপন থাকবে।

এই গবেষণা কর্মে আপনার অংশ গ্রহণ ঐচ্ছিক এবং গবেষণা কর্মের যে কোন সময় এতে অংশ নেয়া থেকে বিরত থাকতে পারবেন। ইন্টারভিউ চলাকালীন কোন নির্দিষ্ট প্রশ্নের উত্তর না দিতে চাইলে, প্রশ্নের উত্তর না দেওয়ার অধিকার আপনি সংরক্ষণ করেন।

আমি আপনার সহযোগিতায় কৃতজ্ঞ হব। আপনি যদি গবেষণায় যোগ দিতে সম্মত হন তবে নির্দিষ্ট স্থানে স্বাক্ষর করুন।

তথ্য গ্রহণকারীর স্বাক্ষর ও তারিখঃ

.....

গবেষণায় অংশগ্রহণকারীর স্বাক্ষর ও তারিখঃ

.....

গবেষকের স্বাক্ষর ও তারিখঃ

.....

Annexure-III

Consent Form (English)

After being fully informed about the objectives, consequence of the study and my right to withdraw myself from the study at any time for any purpose, what so ever, I am ……hereby giving consent to participate in the study conducted by **Md. Rezaul Karim,** Principal/Co-investigator, Department of ENT, Rajshahi Medical College Hospital, Rajshahi.

I fully recognize that my participation in this study will generate valuable medical information that might be used for the interest of patients undergoing adenotonsillectomy for sleep disordered breathing with or without ADHD.

Hospital authority, doctors or any other staff will not be responsible for any adverse consequences during the study.

I shall try my best to comply with the instructions given by the Principal Investigator / Co-investigator throughout the whole period of study.

Signature……. / Thumb impression

Date…….

Appendix – IV

Data Collection Form

(Dept. of ENT, Rajshahi Medical College Hospital, Rajshahi)

Study Title: Improved Behavior and Sleep After Adenotonsillectomy in Children with Sleep Disordered Breathing.

Sl. No…… Date…… Name……

Address……..

Demographic characteristics:

1. **Age:** .....yrs /_____/
2. **Sex:** 1 = Acute 2 = Recurrent /_____/
3. **Residence:** 1 = Rural 2 = Urban 3 = Urban slum /_____/
4. **Socioeconomic status:** 1 = Poor 2 = Lower middle class /_____/
   3 = Middle class 4 = Upper middle class 5 = Rich

Pattern of sleep breathing before intervention:

5. **Snoring:** 1 = Yes 0 = No /_____/
6. **Upper airway resistance syndrome:** 1 = Yes 0 = No /_____/
7. **Obstructive hypoventilation:** 1 = Yes 0 = No /_____/
8. **OSAS (obstructive sleep apnea syndrome):** 1 = Yes 0 = No /_____/

Behavioural problem before intervention:

9. **Attention-deficit hyperactivity disorder (ADHD):** 1 = Yes 0 = No /_____/
10. **Enuresis:** 1 = Yes 0 = No /_____/
11. **Day time sleepiness:** 1 = Yes 0 = No /_____/
12. **Problematic behaviors on awakening:** 1 = Yes 0 = No /_____/
13. **Night-to-night sleep duration variability:** 1 = Yes 0 = No /_____/
14. **Headache:** 1 = Yes 0 = No /_____/

Cognitive functions before intervention:

15. **Learning disabilities:** 1 = Yes 0 = No /_____/
16. **Poor academic performance:** 1 = Yes 0 = No /_____/

17. **Quality of life (rated by parents):** 1 = Poor 2 = Fair /_____/
    3 = More or Less Good 4 = Good 5 = Excellent

Pattern of sleep breathing after intervention:

18. **Snoring:** 1 = Yes 0 = No /_____/
19. **Upper airway resistance syndrome:** 1 = Yes 0 = No /_____/
20. **Obstructive hypoventilation:** 1 = Yes 0 = No /_____/
21. **OSAS (obstructive sleep apnea syndrome):** 1 = Yes 0 = No /_____/

Behavioural problem after intervention:

22. **Attention-deficit hyperactivity disorder (ADHD):** 1 = Yes 0 = No /_____/
23. **Enuresis:** 1 = Yes 0 = No /_____/
24. **Day time sleepiness:** 1 = Yes 0 = No /_____/
25. **Problematic behaviors on awakening:** 1 = Yes 0 = No /_____/
26. **Night-to-night sleep duration variability:** 1 = Yes 0 = No /_____/
27. **Headache:** 1 = Yes 0 = No /_____/

Cognitive functions after intervention:

28. **Learning disabilities:** 1 = Yes 0 = No /_____/
29. **Poor academic performance:** 1 = Yes 0 = No /_____/
30. **Quality of life (rated by parents):** 1 = Poor 2 = Fair /_____/
    3 = More or Less Good 4 = Good 5 = Excellent

(Signature of the Investigator)


Plate 1 & 2: Showing enlarged tonsils and adenoids in children

Plate 3: Showing one tonsil larger than the other

Plate 4: Demonstration is going on about adenotonsillectomy operation (Step I)

Plate 5: The investigator is observing the demonstration (Step II)

Plate 6: The investigator himself doing adenotonsillectomy (Step III)

Plate 7: The investigator himself doing adenotonsillectomy (Step IV)

Plate 8: Showing tonsils & adenoids removed