

# MUCOCILIARY CLEARANCE TIME IN PATIENTS WITH AND WITHOUT RHINITIS ;

A case control study //

Dissertation submitted in part fulfillment of the requirements for the Degree of Masters of Medicine in Ear, Nose and Throat-Head and Neck Surgery, University of Nairobi.

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## DECLARATION

This thesis is my original work and to the best of my knowledge, has not been presented for a degree in any other university.

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This thesis has been submitted with my approval as the university supervisor.

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## DEDICATION

To you my *God*,  
For your ways and wonders!!

To you the mortal who waits upon  
The immortal.

To you, who in the grip of pain,  
Dare entrust it to the mortals.

To my grandmother,  
You cared, you didn't wait!

To Teta and Gift,  
The reason for reasons!

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## **ABBREVIATIONS**

ENT/HN	Ear, Nose, Throat Head and Neck
KNH	KENYATTA NATIONAL HOSPITAL
SCT	Saccharin Clearance Time
NMCC	Nasal Mucociliary Clearance
FESS	Functional Endoscopic Sinus Surgery
MCT	Mucociliary Clearance Time

# ABSTRACT

## MUCOCILIARY CLEARANCE TIME IN PATIENTS

### WITH AND WITHOUT RHINITIS

Rhinitis may be allergic or non allergic. Allergic rhinitis, perennial or seasonal is the most common type of rhinitis, affecting approximately 20% of the population while nonallergic rhinitis affects 5-10%. While rhinitis is not a life-threatening condition, complications can occur and the condition can significantly impair quality of life.

**Aim:** To measure the mucociliary clearance time in patients with and without rhinitis

**Setting:** ENT, H&N, and orthopedic departments at KNH

**Results:** 130 cases between the age of 18 and 40 years and matched controls were inducted. Females accounted for 65% of patients treated with rhinitis while sneezing was the commonest presenting symptom (96.2%), The average mucociliary clearance time was significantly different, 12.64 and 7.80minutes in cases and controls respectively ( $p = <0.01$ ). Nasal crusting as well as the rheology of mucus were significant factors in determining mucociliary clearance time ( $p=0.05$ )

**Conclusion:** In our study group, neither age nor sex affected MCT, Rheology of mucus and nasal crusting significantly affect MCT. Nonetheless, there is an overlap between normal values in cases with rhinitis and controls.

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# 1. INTRODUCTION

Rhinitis may be allergic or non allergic. Allergic rhinitis, perennial or seasonal is the most common cause of rhinitis, affecting approximately 20% of the population. Nonallergic rhinitis affects 5-10% of the population, and nearly half of these individuals seek treatment for relief of their symptoms. While rhinitis is not a life-threatening condition, complications can occur and the condition can significantly impair quality of life, which leads to a number of indirect costs.

## 1.1 Definitions

### 1.1.1 Rhinitis

Rhinitis is defined as inflammation of the mucous membranes lining the nasal passages. It is characterized by a symptom complex that consists of any combination of the following: sneezing, nasal obstruction, nasal itching, postnasal dripping, rhinorrhea and occasionally nasal pains. [1, 3, 4]

#### 1.1.1.1 Allergic rhinitis

Allergic rhinitis is defined as the clinical expression of tissue changes in the upper airway and adjacent structures following interactions of IgE and specific allergens, characterized by the symptoms of nasal congestion, rhinorrhea, postnasal drainage, sneezing, nasal itching, and occasionally impaired sense of smell (and taste). Allergic rhinitis can be seasonal, usually indicative of pollen-allergen sensitivity, or it can be year-round, frequently related to sensitivity to perennial, indoor aeroallergens. It can also be classified as intermittent or persistent or mild, moderate or severe. [3,4]

The distinction between allergic and nonallergic rhinitis can be difficult clinically. The presence of concurrent symptoms in the eyes or upper respiratory tract such as ocular itching, scratchiness, tearing or redness, palatal itching, or asthma symptoms such as coughing, chest tightness, wheezing and shortness of breath



are more likely to suggest allergic rhinitis. The presence of co morbid conditions, such as allergic eczema or asthma, also point toward a diagnosis of allergic rhinitis. [4]

### **1.1.1.2 Non-allergic rhinitis**

Nonallergic rhinitis is characterized by chronic nasal symptoms, often identical to those of allergic rhinitis but without allergic causation. The diagnosis of non-allergic rhinitis is frequently a diagnosis of exclusion when diagnostic testing cannot substantiate an allergic etiology. There is no universally accepted classification of non-allergic rhinitis. The symptoms can be similar to allergic rhinitis, but with a decrease in the amount of nasal itch and in the number of sneezing episodes and conjunctival complaints. [1, 3, 4]

Nonallergic rhinitis is subclassified into Infectious rhinitis, Recumbency rhinitis, Occupational rhinitis, Hormonal rhinitis, Drug-induced rhinitis, Gustatory rhinitis, Nonallergic rhinitis with eosinophilia syndrome (NARES), Non airflow rhinitis and Idiopathic rhinitis. The exact prevalence of nonallergic rhinitis is not known but estimates indicate that up to 50 percent of patients with rhinitis actually have nonallergic causes [3]

## 2. Background of the study

### 2.1 Historical background

Measurement of cilia beat frequency started in 1844 with Martius who used a stroboscope to estimate frequency beat. This is unreliable at frequencies about 6-20Hertz [40] because of the phase difference between groups of cells and metachronous movement. Nearly a century later, in the 1930s, investigation of ciliary movement began with Proetz. Later in 1974, the saccharine test was described. [27]

### 2.2 Cilia

Columnar epithelial cells are often but not always covered by cilia. These ciliated cells contain several mitochondria, most of which cluster in the apical part of the cell. Ciliogenesis takes place after replication and transformation of the cell centrioles to basal bodies. Cilia originate from basal bodies, which also serve to anchor them to the cell. [2]

Cilia are long, thin, mobile projections from the luminal surface of the cell. Cross-sectional view shows a ring of nine doublet microtubules surrounding two single central microtubules. The cilia in the human nose are 0.3 $\mu$ m in diameter, 4-6 $\mu$ m long and there are about 100 per cell. [2,7,8,15]

Cilia are present on the surface of mucosal cells in the airways, oviducts, ependymal lining of the brain, central canal of the spinal cord, middle ear mucosa, and ductuli efferentes (between testis and epididymis). Rudimentary cilia that have incomplete ultrastructure compared with the 9+2 pattern are found in the brain, pineal gland, pancreas, adrenal glands and other structures. [15]

Biopsies from the anterior part of the nose (lower edge of the inferior turbinate, one centimeter posterior to the front edge) disclosed only single islands of cilia

covering about 10% of total surface. Each island corresponds to one cell. Further back in the airways most cells carry cilia, which may form a dense 'long-haired carpet'. Thus ciliated epithelium covers the posterior 1/3 of the nasal cavity as well as the Eustachian tube, part of the middle ear, rhinopharynx and larynx. Ciliated cells are also found in the trachea and the cartilaginous sections of the bronchial tree, but are absent in peripheral airways. [2]

The basement membrane is seen as a thin continuous double-membrane under the epithelial cells. Underneath this membrane is a thicker layer of collagen and reticulin fibrils, the connective tissue membrane. In the light microscope, these two membranes are called the basement membrane. In the anterior part of the nose the basement membrane is thickened both in rhinitis patients and in symptom free individuals. [2]

The lamina propria is the layer between the epithelium and periosteum or perichondrium. It can be subclassified into a cell rich surface layer, a middle glandular layer and a basal layer rich in sinusoid blood vessels. The lamina propria consists of connective tissue cells and fibrils, ground substance, wandering cells, glands, blood vessels and nerves. [2]

## 2.2.1 Glands

The glands of the lamina propria of the nasal mucosa consist of anterior serous glands and the small, scattered seromucous glands. Patients with nasal hypersecretion (common cold, perennial rhinitis) or subjects exposed to frost have watery secretions seen in the upper part of the internal ostium. Each droplet covers the duct opening of one of the anterior serous glands described by Bojsen-Møller in 1965 and the watery secretions are formed by a confluence of numerous droplets. All the glandular acini are serous. [6]

The seromucous glands start their development in life two weeks before the goblet cell. Initially found in the anterior part, they spread in the antero-posterior

direction similar to the goblet cells. The ducts in these glands have several parts; the first part of the main duct is the ciliated duct, collecting duct, mucous tubules and terminally the serous tubules. Proteinous secretion is released from glandular cells of the serous secretory tubules. The primary secretion is collected in the collecting duct, which possesses marked ability to modify and control the ion and water concentration of final glandular secretion. In the ciliated duct goblet and ciliated cells form a mucociliary apparatus assisting in the expulsion of secretion from the gland opening. [2]

### 2.2.1.1 Secretion

Nasal fluid is a mixture of mucous and serous material from goblet cells and seromucous glands, directly from the blood as a transudate, condensed water from the expired air, tears, cells and micro-organisms. The gel structure of mucoid secretion is due to mucus from goblet cells and seromucous glands. Disintegrating epithelial and inflammatory cells may add to the viscosity. [2] The major components of nasal fluid are:

- Water (95-97%)
- Mucin (2.5-3%)
- Electrolytes (1-2%)
- Proteins (derived from plasma or synthesized locally in the mucosa)

Mucin represents the major group of macromolecules in airway secretion. It forms long threads or fibrils, which account for the visco-elastic properties of the secretion. The glycoproteins of airway mucin may be neutral or acidic. The neutral portion (due to fucomucin) is small in amount in man. Acidity is due to sialic acid (neuraminic acid) and/or sulphated groups (sialomucin and sulphomucin). [2,8]

Sodium, chloride and calcium concentrations in airway secretion are comparable to those of serum, while potassium concentration is about three times higher.

Other proteins with enzymatic properties have been detected in the respiratory secretions, including lactic dehydrogenase, several proteolytic enzymes (proteases) and protease inhibitors

The arterioles of the nasal respiratory mucosa are conspicuous by the total absence of internal elastic membrane, so the endothelial basement membrane is continuous with the basement membrane system of the smooth muscle cells.

The nasal blood vessels have a characteristic porosity of the endothelial basement membrane. This renders these vessels readily influenced by agents such as histamine and drugs carried in blood, than blood vessels elsewhere. [2]

## **2.2.2 Filtration and mucociliary mechanism**

The lower respiratory passages have a protective mechanism through which particulate matter and bacteria are trapped by the mucus film, ciliary action in the tracheobronchial tree and the cough reflex. The nose serves as the preliminary barrier where these are filtered. The defensive function of the nose rests upon the efficiency of the mucociliary mechanism to move mucus to the pharynx to be swallowed. The vibrissae also assist in filtration by arresting large particles. [2,8,10,15, 27]

### **2.2.2.1 Mucociliary mechanism**

The mucociliary system of the airway forms a highly efficient defense mechanism that protects the lungs against inhaled particles including living organisms like bacteria, viruses, fungi, mycoplasma as well as chemical irritants. The vital part of this system is an adequate quantity of mucus with appropriate rheological quality and adequately functioning cilia, which allow the continuous exchange of the covering fluid layer and removal of engulfed particles. Any disturbance in this system leads to stagnation of secretions and secondary infection. [11, 12,27]

The mucociliary system is regarded as the means for purification at the tracheobronchial level, but at the nasal level it acquires more value as it is

directly involved in filtration and air conditioning functions. The nose is an easily accessible organ, so in many centres the measurement of nasal mucociliary clearance has been used as a screening procedure for congenital abnormalities that would alter mucociliary clearance in the nose and lungs. [13]

#### **2.2.2.1.1 Mucous blanket**

A film of mucus that covers the surface of the nasal mucosa – mucous blanket, forms the most important aspect of the protective function by filtration. This mucous blanket is extremely thin, elastic, highly viscous and has a fair degree of tensile strength. [2,8,10,27]

The mucous blanket consists of two layers. An outer layer of viscous mucus rests upon a thin layer of serous fluid, which facilitates the movement of the cilia. The ends of the cilia are in contact with the overlying film of mucus, thus ensuring ease of vibration of the cilia and movement of the overlying mucus layer.

[2,8,10,27]

Finely divided particulate matter, dust soot, pollen and microorganisms are filtered out of the inspired air by adhering to the mucus film. The nasal mucous has a bacteriostatic effect derived from the bacteriolytic enzyme lysozyme, which causes swelling and lysis of some micro-organisms [2,8,10]

Efficient functioning of the nasal mucus blanket as a filter is dependent on its continuous removal and renewal. This is effected by the activity of the ciliated epithelium maintaining the overlying mucous blanket in constant motion.

Renewal of the mucus is ensured by activity of the mucosal glands. This association of ciliary motion and mucus secretion forms the self-cleansing mechanism of the nose [2,8,10,27]

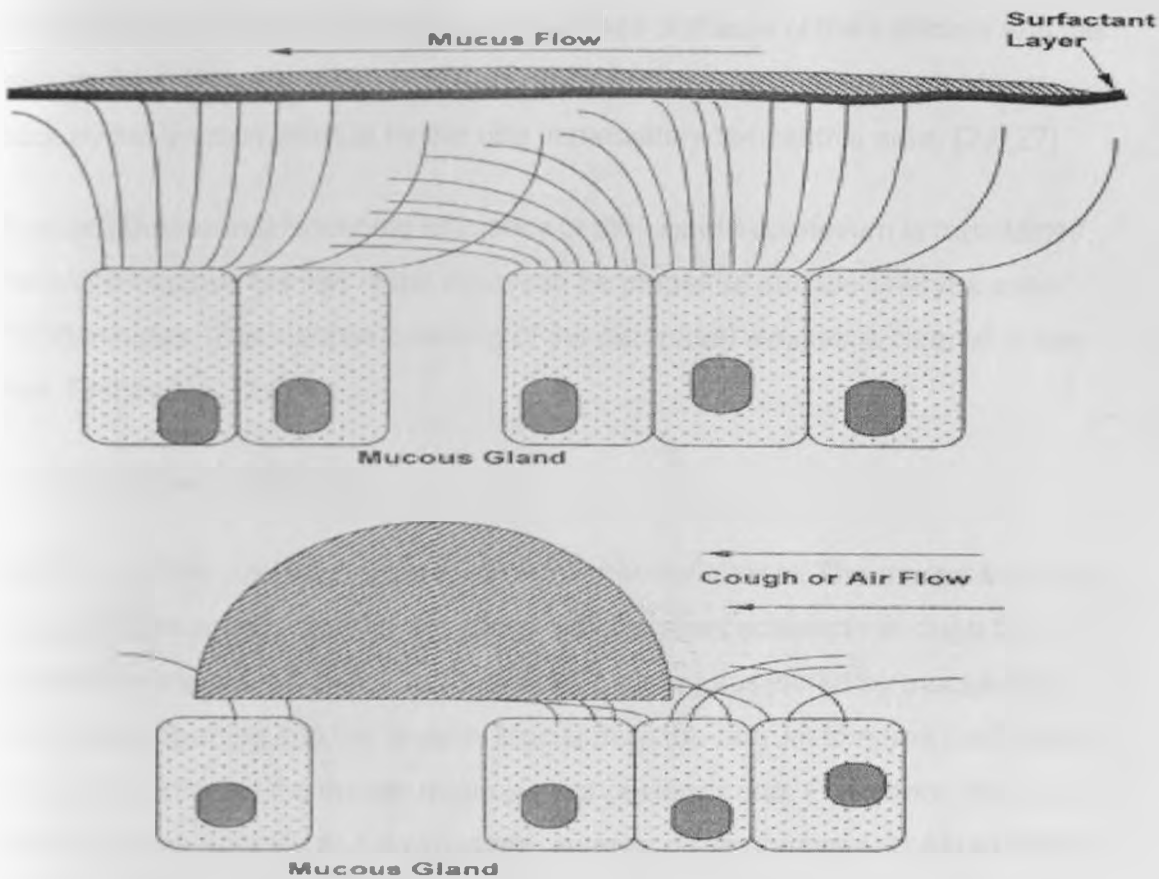


FIG 1 CILIARY CLEARANCE VERSUS COUGH CLEARANCE. TOP: AIRWAY EPITHELIUM, CILIA, AND SURFACTANT AND MUCUS LAYER DURING NORMAL OPERATION OF CILIA. BOTTOM: HYPERSECRETION AND COUGH CLEARANCE IN THE PRESENCE OF CILIARY DYSFUNCTION

[43]

### 2.2.2.1.2 Ciliary action

Ciliary movement is described as consisting of a forward or effective stroke and a backward or recovery stroke. The effective stroke is more rapid and constitutes the propulsive phase. The cilium remains rigid and movement is vigorous. The recovery stroke is less rapid and less vigorous, and the cilium is relatively limp.

[2,8,10]

The cilia of the nasal mucosa beat at a frequency of 12-16Hz (10-15beats/second) at the nasal temperature of 30<sup>0</sup>C. This produces a streaming movement of the overlying mucus, which has been estimated at 0.25-0.75cm/min. The movement, as a general rule, is more rapid in the posterior two thirds of the nasal chambers than in the anterior third, and more active in the

protected meatal recesses than on the exposed surfaces of the turbinate and the septum. The mucous covering of the non-ciliated pre-turbinal region is drawn back by the traction exerted by the cilia immediately behind this area. [2,8,27]

Provided the normal functional efficiency of the ciliated epithelium is maintained, the entire mucous blanket of the nose can be propelled into the pharynx every 20-30 minutes. The mucous covering of the paranasal sinuses is cleared in less than 10 minutes. [2,8]

### **2.2.2.1.3 Ciliary pathways**

*From the middle and inferior meatuses, main antral stream:* The mucus from the mucosa of the anterior part of the lateral wall passes backwards through the middle and inferior meatuses. In the middle meatus, it is joined by mucus from the sinuses opening into the recess. Mucus from the antrum streams back along the upper portion of the middle meatus to its posterior end. From here, this main stream passes laterally and downwards, anterior to the pharyngeal ostium of the pharyngotympanic tube. The stream continues down just behind the posterior pillar of the fauces. A portion is directed anterior to the posterior pillar between the tonsil and the posterior pillar. Streams from the superior meatus and the sphenoid sinuses join the main stream. [2,8,27]

*From the superior meatus:* Including mucus from the posterior ethmoidal cells, the stream passes into the nasopharynx and divides into two portions. The larger anterior stream extends down in front of the Eustachian opening and joins the main antral stream. The smaller posterior portion passes behind the Eustachian orifice and downwards through the fossa of Rosenmüller, and then curves forward to join the main stream. [2,8,27]

*From the sphenoid sinus:* From the ostium of the sphenoid sinus mucus passes down to the top of the nasal choana and then backwards on the roof of the nasopharynx, spreading in a fanwise manner into a series of streams, which



pass outwards and join the main antral stream just below the lower margin of the palate. [2,8,27]

Combined these streams pass down posterior to the posterior pillar to the level of the dorsum of the tongue. A small part is conveyed across the tongue to the glosso-epiglottic pouch. The larger part continues down to the piriform sinus from where mucus is swallowed. [2,8]

### **2.2.2.2 Factors affecting mucociliary clearance**

Protection of the respiratory epithelium rests to an important extent on ciliary activity. [15] Several factors have been found to affect it.

#### **2.2.2.2.1 Drying**

Drying of slight degree causes cessation of ciliary activity, while prompt moistening restores it. Drying for a few minutes results in destruction of cilia. Several conditions may result in excessive drying in the nose;

- Prolonged breathing of excessively dry air
- Inadequate secretion by mucosal glands
- Deviation of inspired air stream by septal deflections, spurs or polypi

Deviated inspiratory air current is restricted to an area of mucosa in excess of the local capacity to saturate the air. This results in excessive local evaporation, increased viscosity of the nasal mucus, local stasis of mucus and eventually cessation of ciliary activity. [2,8,10,27]

#### **2.2.2.2.2 Temperature**

The optimal range of temperature for ciliary activity studied in excised human nasal mucosa is 28-33°C. The normal human nasal temperature has been recorded as about 32°C. Fall of temperature depresses the frequency of ciliary motion, and at about 7-10°C all activity ceases. Warming to normal nasal

temperature restores activity. Rise in temperature results in depression of activity at 35<sup>0</sup>C and in coagulation and irreversible arrest at 43-45<sup>0</sup>C. [2,8,10,27]

### **2.2.2.2.3 Saline solutions**

With isotonic saline (0.9% sodium chloride solution) cilia remain active for prolonged periods. Hypertonic solutions inhibit ciliary activity. Activity ceases in 4.5-5% saline solution, but returns when the mucosa is replaced in normal saline solution. With hypotonic saline solution (0.3-0.2% saline solution) all ciliary motion ceases and the mechanism is permanently damaged. [2,8,10]

### **2.2.2.2.4 Changes in Ph**

Ciliary action is readily paralyzed by acidic solutions. If the pH is reduced to 6.4 or less, ciliary action is arrested. A rise in pH is better tolerated. Ciliary activity is increased in dilute alkaline solution. Cilia will function for longer periods in saline solution at a pH of 8.5. The effect of dilute acids and alkalis is reversible. Neutralization restores normal ciliary action. Rise in temperature tends to lower the pH while a fall in temperature increases it. [2,8,10,16]

### **2.2.2.2.5 Drugs**

Adrenaline (1:10,000) causes reversible inhibition of ciliated cells when they are exposed to it for 20 minutes. Immediate and irreversible cessation of ciliary motion is produced by 1:1,000 adrenaline solution.

Ephedrine sulphate (0.5% solution) does not affect ciliary action. Even with 2% ephedrine, ciliary action is not markedly affected. Acetylcholine causes an increase in the rate of ciliary beating. [17,18,19]

Cocaine (2.5% solution) has little immediate effect. Continuous application for one hour stops ciliary activity. 5% solution causes arrest of ciliary motion in 2-3 minutes; the cilia cannot be resuscitated. 10% solution produces immediate and complete ciliary paralysis. [2,8,10.]

Ether and chloroform in high concentrations in inspired air have no effect on the nasal cilia in the living animal. Both liquids, on direct application, however, cause immediate ciliary paralysis. [2, 8, 10]

Commonly used topical preparations containing steroids or antihistamines as the active ingredient have not been shown to have a detrimental effect on nasal mucociliary function in humans despite reports that isolated cilia beat less effectively when perfused with these drugs or the preservatives that are added to these drugs. [27]

#### **2.2.2.2.6 Viruses and bacteria**

*Haemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Pseudomonas* release toxins that disrupt epithelial cells with the loss of a confluent ciliary field. Neutrophils that gather at the site of purulent infection produce an elastase that is directly toxic to respiratory epithelium. [28]

Viruses responsible for common cold disrupt the ciliated cell's microtubules and there is an increase in mucus tethering at sites of mucus glands making it difficult for the remaining cilia to transport mucus. [27]

#### **2.2.2.2.7 Allergic rhinitis**

Changes in ciliary structure occur in patients with allergic rhinitis and changes in secreted mucus occur in times of acute allergen challenge. There is likely to be an improvement in mucociliary transport owing to the alternation in rheological properties of mucus and an increase in the ciliary beat frequency. [29]

Results from studies of mucociliary clearance are inconclusive; some suggesting an increase while others suggest that mucociliary transport decreases in response to an allergen challenge. In patients with positive skin test, saccharin clearance times are prolonged. [31] Ciliary abnormalities have been detected in

patients described as having perennial rhinitis but not all studies have been able to show this. [30]

#### **2.2.2.2.8 Chronic rhinosinusitis**

In these patients, ciliary denudation has been demonstrated but in areas where cilia were preserved, ciliary motility appeared normal. Prolonged saccharin clearance in patients with maxillary sinusitis has been attributed to abnormalities of the mucus. The mucosa of patients with chronic sinusitis shows edema, shedding of epithelial cells and squamous metaplasia. Ciliary abnormalities have been reported including compound cilia and deviation from the 9+2 filament arrangement. [32]

#### **2.2.2.2.9 Nasal polyposis**

The ciliated surface of polyps can undergo squamous metaplasia. Where the cilia are preserved, the mucus blanket is moved in a normal fashion, but because of the pedunculated swelling of mucosa, the direction may be changed. Such patients have disturbed mucociliary time as measured by the saccharine test and gamma scintigraphy. [33]

#### **2.2.2.2.10 Aging**

The results of a study of 90 healthy subjects, whose age ranged from 11 to 90 years showed that aging was associated with a decrease in ciliary beat frequency and increase in NMCC time. There was no significant change with age of the orientation of the central microtubules of cilia, which reflected the direction of ciliary beat. There was also no sex difference in ciliary beat frequency with aging. A significant increase in the occurrence of microtubular defects, including disarrangement of microtubules and the presence of extra microtubules or single microtubules, was noted with aging. Ciliary beat frequency, NMCC time, and percent of ciliary cross-sections displaying single tubules were significantly different in subjects under and over 40 yr of age, respectively. [41]

## 2.2.3 Regulation of ciliary action

Ciliary motion is an inherent property of ciliated cells. Effective stroke may be due to initial shortening of the contractile filaments on one side and recovery stroke by the subsequent contraction of the contractile elements within the cilium on the opposite side. Excised portions of ciliated mucosa show sustained normal ciliary activity in the absence of the nervous system. [2,8]

## 2.2.4 Effect of nasal cycle on mucociliary clearance

The nasal cycle is a well-recognized physiological phenomenon where each nose alternates between phases of congestion and decongestion. [24]

Hypothetically, the nasal cycle exists in order to replenish the water content of nasal mucus, allowing continued humidification of inspired air. [9] Some workers have noted asymmetry in mucociliary clearance at the morning peak of the nasal cycle [24] although others have found no significant difference at different times of the day or in different phases of the cycle. [26]

## 2.2.5 Diseases of cilia

Ciliary assessment should involve structural and functional evaluation of cilia, as these may not occur concurrently. Functional impairment can be classified as:

- Immotility
- Slowing of ciliary beat
- Dyskinesia when neighboring cilia beat in an uncoordinated fashion

Infection of respiratory mucosa has been shown to cause slowing of ciliary beating or dyskinesia in vitro. Damage of the 9+2 ultrastructure has however not been reported in respiratory infection. [20] Sloughing of damaged nasal mucosa occurs in common cold and influenza but no ciliary ultrastructure damage has been reported. [21] There is also no evidence that chronic infective and

inflammatory conditions such as cystic fibrosis and asthma are associated with abnormal ciliary ultrastructure. [22]

5-10% of cilia show disease in children and adults who have no apparent nasal disease. In Kartagener's syndrome there is absence of dynein arms of the nine peripheral microtubules. These individuals have only 40% of their cilia working and they also lack coordination. [34] In primary ciliary dyskinesia impaired mucociliary clearance has been shown to be due to structural defects of the ciliary axoneme [35]

In Young's syndrome (obstructive azoospermia with recurrent sinobronchial disease) there is a disorganisation of ciliary orientation, which is more pronounced at the ciliary tip but the other features are normal [36] Nasal cilia (Rothmund-Thomson) syndrome is an isolated lack of cilia in the nasal mucosa. The condition presents with chronic rhinitis. [37]

Immunodeficiency is associated with deranged mucociliary transport. Patients with immunodeficiency have slower nasal mucociliary transport and more extensive mucosal damage than those with selective IgA deficiency. [38]

In cystic fibrosis the primary abnormality is not with the cilia but with the production of abnormal mucus probably secondary to defective chloride transport. [39]

## **2.2.6 Methods used to test nasomucociliary flow**

Several techniques have been utilized to measure mucociliary clearance. These include: [24,27]

- 1) Andersen's saccharin test
- 2) Visible dyes or particles
- 3) Small metal discs (imaged by fluoroscopy)
- 4) Radiolabelled particles (detected by gamma scintigraphy)

### 3. LITERATURE REVIEW

Of the methods used to test nasomucociliary clearance, the Andersen's test has become the most useful screening test in clinical practice and compares well with the imaging studies. The advantages of this test include the fact that it is easy to learn, it is cheap, readily available, lacks toxicity, and has no radioactivity, has a high level of tolerance, results are reproducible and can be performed in a clinical setting. [14,23]

However, the test can be difficult to perform in children and cannot be repeated in a short time since the sweetness takes some time to disappear. [25,]

An evaluation of the use of SCT as a measure of nasal function done in 1999 by Havas and Thomas in 50 patients found it to be a reliable and reproducible test. However, due to individual variation in diagnosis of normal and abnormal mucosa, normative values could not be set. [44].

In 1998 Lale A M et al made a review on assessment of mucociliary transport. 42 patients who were starved waiting to undergo surgery for non-nasal procedures and who had no nasal complaints were included. The saccharin test was conducted and their mean SCT was 13.3 minutes (range 5.3-32.5). It is likely that patients who had a SCT of more than 20 minutes have a disturbed nasal mucociliary clearance. They concluded that SCT longer than 60 minutes indicated significant cilia or mucus abnormality while those prolonged beyond 20 in presence of a treatable nasal problem, the SCT would improve on treatment. [27]

Prior M.J et al, while assessing mucociliary clearance time in 40 patients with chronic mucoid rhinitis, they found that 39 of them had prolonged SCT beyond 20 minutes. They also report that similar findings were reported in other studies. [42]

In their study on nasal mucous clearance in patients of perennial allergic rhinitis conducted on 60 patients, Yadav et al. using the SCT tested 30 adult patients with a triad of intermittent sneezing, nasal obstruction and rhinorrhoea who have been having the symptoms for 2-5 years. 30 controls were also tested. The mean nasal MCT in allergic rhinitis was  $4.16 \pm 0.11$ , which was significantly lower as compared to the controls,  $8.21 \pm 0.25$  minutes. The decrease in nasal MCT may be attributed to the fact that secretions in allergic rhinitis are alkaline in nature and alkaline pH is better for ciliary function. [45] Schuhl, However, found a prolonged MCT in long standing cases of allergic rhinitis and explained it on basis of changes in rheology of nasal mucus. [46]

Radiotherapy, in a dose-dependent fashion has been found to affect MCT and so does chemotherapy. Gupta et al drew these conclusions when they conducted a study using the SCT on effects of irradiation on nasal mucociliary clearance in head and neck cancer patients. The low irradiation group had a mean saccharin clearance time of  $30.64 \pm 1.12$  after irradiation, the chemoradiation group a mean of  $31.68 \pm 1.32$ , the high irradiation group a mean of  $33.72 \pm 2.50$  minutes while the controls had a mean of  $9.08 \pm 0.28$ . [47]

Nakagawa et al documented a similar range of values for MCT when they studied MCT in acutely ill patients. 18 cases and 18 controls were analysed. Non-smokers from the control group had an average MCT of 11.5 minutes, which correlated with other studies. SCT was found to be prolonged in the acutely ill as well as smokers. [48]

A SCT of  $10.97 \pm 3.22$  in normal individuals was obtained as opposed to  $12.61 \pm 4.30$  minutes in coal mine workers. Cinai et al documented these findings in their study on mucociliary clearance in coal workers in 77 subjects in 2004. The findings show that coal particles affect NMCC, though the difference in the SCT was not significant. [49]



## 4. JUSTIFICATION

Chronic rhinosinusitis is a diverse group of infections. At presentation the patient may have some or all of the following symptoms: nasal obstruction, sneezing, nasal itching, anosmia, rhinorrhoea, post-nasal discharge. [1,3,4] Allergic rhinitis and its sequelae remain the commonest cause of outpatient visits in most clinics. A study carried out on college students in the catchment area of KNH showed that 13% suffered from allergic rhinitis. [5]

Various workers have documented a relationship between nasal disease and mucus clearance, which invariably results in stasis of secretion, and ultimately infection. [2,8,10] Wang et al found a significant improvement in NMCC in patients with sinusitis after undergoing FESS. They recommended the SCT as a simple, safe, reliable and objective technique of assessing the results of surgery. [50]

When deranged, medical or surgical measures can be used to correct the condition and restore the patient to normal or near normal. [27] But what are the values for mucociliary clearance in patients with rhinitis in our population and what is the effect of rhinitis on mucociliary clearance?

As far as documentation is concerned, there are no reports of a study on mucociliary clearance in Kenya or even Africa and the studies conducted elsewhere have a significant overlap in clearance time that would not apply to individual patients.

It is therefore timely to conduct such a study, which will be a basis for determining severity of a nasal or even an airway condition and also quantifying and qualifying the outcome after treatment

# 5. MATERIALS AND METHODS

## 5.1 Objectives of the study

### 5.1.1 Global objective

1. To compare the mucociliary clearance time in patients with rhinitis with normal subjects

### 5.1.2 Specific objectives

1. To document the mucociliary clearance time in patients with rhinitis
2. To find out the mucociliary clearance time in normal subjects
3. To establish the relationship between duration of symptoms and ciliary activity

## 5.2 Type of study

This was a case control study.

## 5.3 Setting

The study was conducted in the ENT department and the orthopedic clinics and wards at KNH.

## 5.4 Duration of study

After approval by the ethical committee, data was collected from the month of January to April 2008.

## 5.5 Sample size determination

The determination of sample size was calculated using the formula below. (55)

$$n = \frac{P1(100-P1) + P2(100-P2)}{e^2}$$

Where

n - the sample size determined.

e- required size of standard error, in this case standard error if precision of 95% CI is required.

P1 – Study with the biggest sample size

P2 – Study with the smallest sample size

$$n = \frac{77 \times 23 + 18 \times 82}{25}$$

$$= 129.88$$

n = 130 per group, therefore total n is 260.

## **5.6 Materials and method**

### **5.6.1 Materials**

Saccharin granules

Crocodile microforceps

Galipot,

Stopwatch

### **5.6.2 Method**

#### **5.6.2.1 Sampling of patients**

All subjects aged 18-40 seen during the study period, giving an informed consent (Refer to Annex I) and meeting the inclusion criteria were recruited consecutively. History was taken then anterior rhinoscopy performed on the subjects to rule out any abnormalities; morphological or pathological. Normal subjects were patients seen in the orthopedic clinics and wards who were under follow up for traumatic conditions. Patients with conditions treated with steroids or oncological conditions were excluded. Eligible patients were entered in the control group while patients under follow up for rhinitis were entered in the cases. These were matched for sex and age.

##### **5.6.2.1.1 Definition**

Rhinitis is defined as inflammation of the mucous membranes lining the nasal passages [1, 3, 4] Subjects included had a symptom complex that consists of any combination of the following: sneezing, nasal obstruction, postnasal dripping, rhinorrhea and facial pains.

## **5.6.2.2 Inclusion criteria**

### **5.6.2.2.1 Cases**

- All patients under follow up for any type of rhinitis
- Such patients not on medication for the past two weeks
- All patients giving consent
- Patients who have never undergone intranasal or transnasal surgery
- Aged between 18-40 years
- Patients without co-morbidities
- Patients who are not expectant
- Non smokers

### **5.6.2.2.2 Controls**

- Subjects who give an informed consent
- Subjects aged between 18-40 years
- Subjects who had no symptoms of allergy or rhinitis for the past 2 weeks.
- Patients who have never undergone intranasal or transnasal surgery
- Subjects without a respiratory tract infection at the time of testing
- Subjects without other known illnesses
- Non smokers

## **5.6.2.3 Exclusion criteria**

### **5.6.2.3.1 Cases**

- Subjects who do not meet the inclusion criteria

### **5.6.2.3.1 Controls**

- Subjects who do not meet the inclusion criteria

#### **5.6.2.4 Saccharin test of nasomucociliary flow**

To perform the test, a saccharin particle (1.5-mm diameter) was carefully placed on the floor of nasal cavity about 1 cm behind the anterior end of the inferior turbinate. The subject was asked not to sniff, sneeze, smoke, eat or drink during the test and avoid deep breathing [27] The subject was also asked to swallow every 30 seconds and to report the first change in their sensation of taste. The time taken by the subjects to perceive sweet taste in the pharynx was taken as MCT in that nose. The test was repeated on each side and the average of two was taken as the NMCT. This was done to exclude the effect of nasal cycle on mucociliary clearance. [10 14]

##### **5.6.2.4.1 Reference values**

- Normal: 7-15 minutes [27,30,31,42,46]
- In acute allergy, saccharin is tasted in 5 minutes or less.
- With infection and late-stage allergy, saccharin is tasted in 9-19 minutes.
- With atrophic rhinitis and chronic sinusitis, saccharin is tasted in 20-29 minutes

#### **5.6.2.5 Collection of data**

Each patient was assisted by the principal researcher to fill a questionnaire. Findings of the saccharine test were reported by the subject and documented in the questionnaire. This made the basis of analysis.

#### **5.6.3 Analysis**

With the help of a statistician, data collected was entered in a computer and analysed by SPSS statistical package. Descriptive statistics such as means, median, frequency and standard deviation were calculated, including comparisons for sex and age. Tests of statistical significance were carried out using the Chi square test and Mann- Whitney test where applicable.

## 5.6.4 Quality control

The patient evaluation sheet was pre-tested before commencement of the study and necessary modifications made before final data entry was initiated in order to minimize errors. No incidents of patients sneezing or sniffing in the course of the test were encountered as this was overcome during the pre-testing.

## 5.6.5 Shortcomings

- ✓ Errors in reading saccharin test results (observer error)
- ✓ Unhealthy controls
- ✓ Inconsistency in duration of use of medications
- ✓ Obstructing hypertrophied inferior turbinate in some cases.

## 5.6.6 Ethical consideration

- Study participants were included only on voluntary consent.
- Patients who declined to participate in the study were treated the same as those included in the study.
- There was no extra cost to the patient during the study.
- The study was conducted after approval by the ethical committee of the KNH
- The results will be published and availed for use by members of the medical fraternity

# 6.Results

Data from 260 subjects, 130 cases and an equal number of controls was collected using a questionnaire. These were matched for sex and age. Majority of the cases were patients seen in the ENT filter clinic as referrals from public and private health facilities in the country while a few were taken from the ENT consultant clinic. Controls were patients visiting the outpatient orthopedic clinics with injuries caused by trauma.

Data collected was coded under the SPSS package and analyzed. Tests of statistical significance were calculated using Chi-square and Mann - Whitney tests.

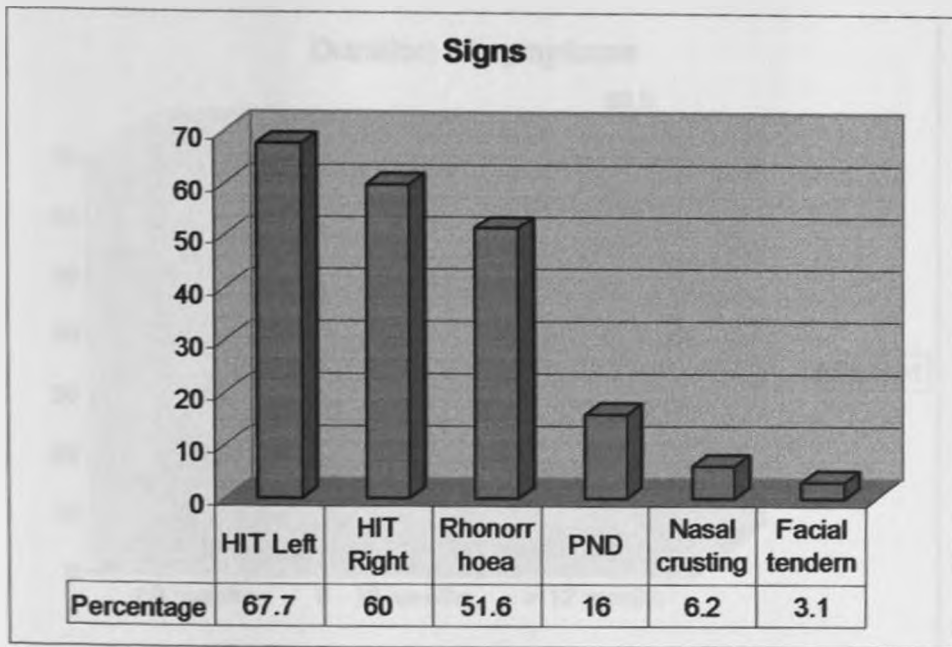
Following are the obtained results.

Table 6.1: Age distribution

Age	Frequency	Percent
<20	11	8.5
20 - 25	36	27.5
26 - 30	41	31.5
31 - 35	26	20
36 - 40	16	12.5
Total	130	100

Table 6.1 shows the age of cases included in the study. The age group of 26 - 30 had the highest frequency, 41(31.5%), the median age being 27 years. The same statistics apply to the controls since they were matched for sex and age.

Figure 6.2: Presenting signs



The bar graph above shows the frequency of signs found on examination. 88(67.7%) had hypertrophy of the left inferior turbinate while 78(60%) and 66(51.6%) had hypertrophy of the right inferior turbinate and rhinorrhoea respectively.



Figure 6.3: Duration of symptoms

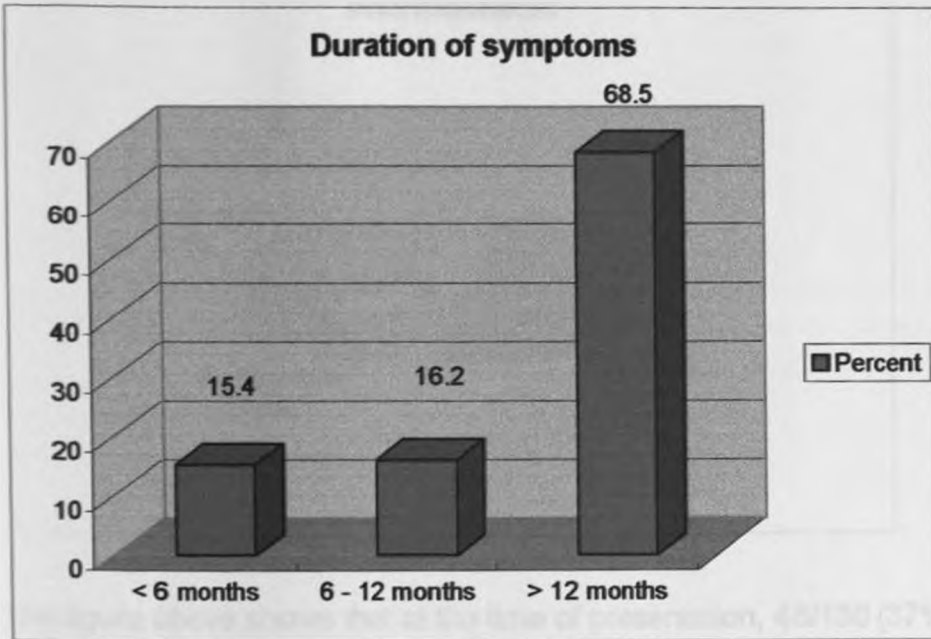
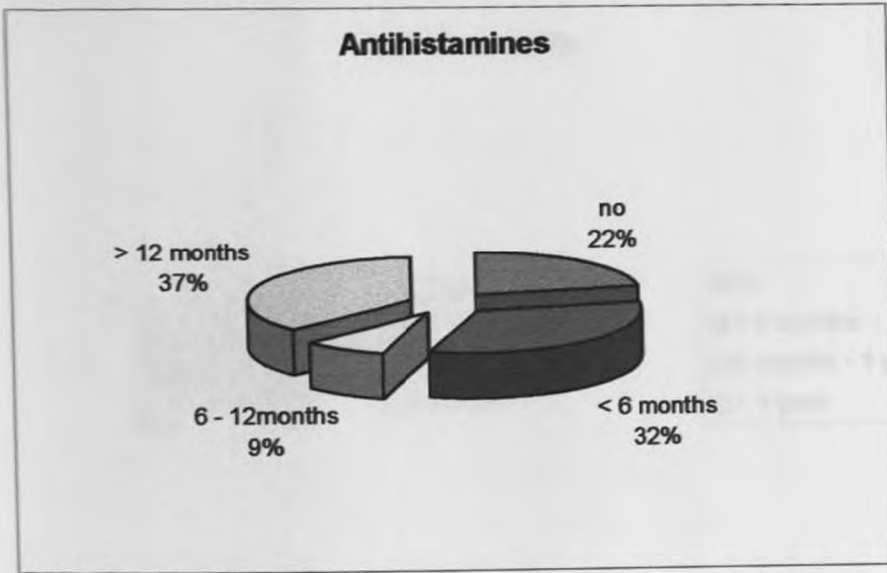


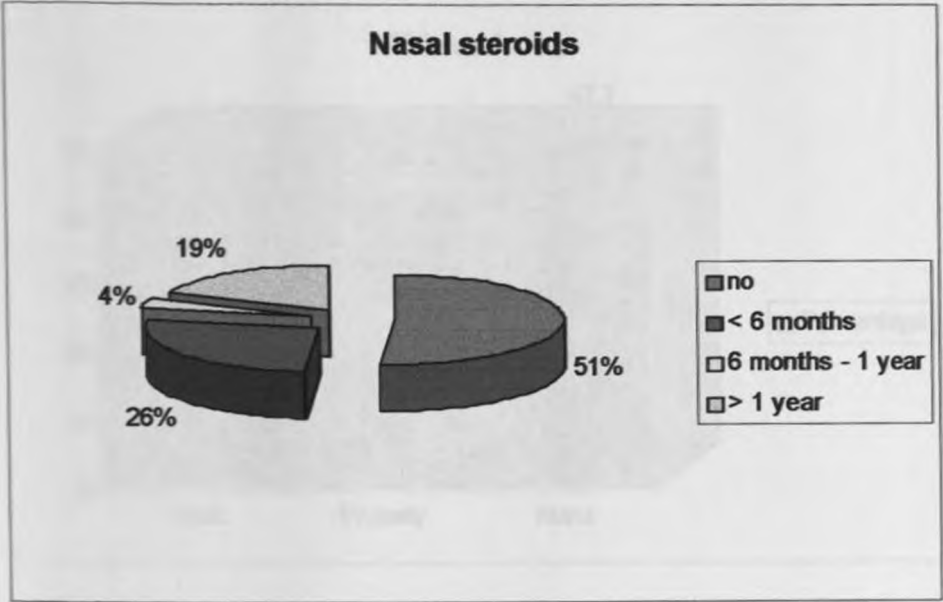
Figure 6.3 shows that 20 (15.4%) had duration of symptoms of less than six months, 21 (16.2%) between six months and one year while 89 (68.5%) of them had the symptoms for more than a year.

Figure 6.4: Use of antihistamines



The figure above shows that at the time of presentation, 48/130 (37%) had used antihistamines interruptedly for over a year, 11/130 (9%) for between six months and one year while 29/130 (22%) had not used antihistamines at all as a form of treatment.

Figure 6.5: Use of nasal steroids



67 (51.5%) of the cases had never used intranasal steroid sprays, 35 (26.2%) had used them for less than 6 months while 24 (18.5%) had used the steroids intermittently for over a year as shown in the figure above.

Figure 6.6: Rheology of mucus

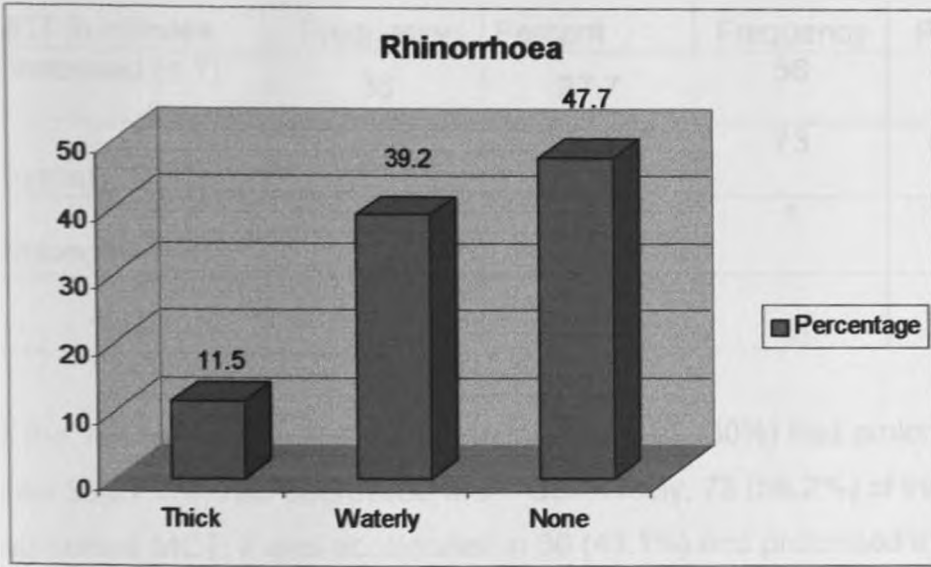


Figure 6.6 shows that 15 (11.5%) reported having thick mucus, 51 (39.2%) had watery mucus while 62 (47.7%) had no mucus at the time of presentation. It is worth noting that this observation is subjective and patient dependent.

Table 6.3: MCT in minutes in cases and controls

	Cases (n=130)			Controls (n=130)		
	Right nose	Left nose	Average	Right nose	Left nose	Average
Minimum	0.57	2.09	1.34	1.09	2.17	2.11
Maximum	42.21	66.01	54.07	18.44	16.13	15.64
Median	8.32	11.22	9.67	7.21	7.21	7.51

The average MCT in cases was 9.67 minutes with a range of 1.34 to 54.07 minutes, while the average MCT in the controls was 7.51 minutes with a range of 2.11 to 15.64 minutes as shown in the table above. Differences in the MCT in both nostrils could be due to the nasal cycle. The range of nasal clearance was widespread between the cases hence the adoption of the maximum, minimum and the median.

Table 6.4: Average MCT in minutes in cases and controls

MCT in minutes	Cases (n=130)		Controls (n=130)	
	Frequency	Percent	Frequency	Percent
Decreased (< 7)	36	27.7	56	43.1
Normal (7 – 15)	55	42.3	73	56.2
Prolonged (> 15)	39	30.0	1	0.8
Total	130	100.0	130	100

Of the 130 cases 55 (42.3%) had normal MCT, 39 (30%) had prolonged MCT while 36(27.7%) had decreased MCT. Conversely, 73 (56.2%) of the controls had normal MCT; it was accelerated in 56 (43.1%) and prolonged in 1 (0.8%) as summarized in the table above.

Table 6.5: Age in years

Average MCT in minutes	n=130	Median	Minimum	Maximum
Decreased (< 7)	36	25.50	18	40
Normal (7 – 15)	55	28.00	18	40
Delayed (> 15)	39	27.00	18	40

P=0.552

The following table shows age distribution in the cases. The median age in accelerated, normal and prolonged MCT was 25.5, 28 and 27 respectively. This was not significant.

Table 6.6: Comparison between MCT and symptoms

Symptom	Yes		No		P value
	n	MCT	n	MCT	
Runny nose	123	9.66	7	9.72	0.562
Nasal blockage	123	9.72	6	7.58	1.018
Sneezing	125	9.67	5	7.76	0.327
Post nasal drip	58	9.68	70	9.67	0.574
Facial pains	18	9.58	109	9.67	0.359
Headache	52	8.62	74	10.41	1.464

There was no significant difference in the symptom presentation in relation to the MCT in the cases. This is summarized in the table above.

Table 6.7: Comparison between MCT and signs

Sign	Yes		No		P value
	n	MCT	n	MCT	
Nasal crusts	9	20.02	121	9.57	0.024
HIT – R	78	9.65	52	9.74	1.029
HIT –L	88	9.65	42	9.96	0.849
PND	31	10.84	99	9.65	0.195
Facial tenderness	5	7.85	125	9.66	1.046

Nasal crusting was a significant sign ( $p=0.024$ ) in abnormal MCT. In 8 cases that had nasal crusts, the MCT was 20.02 minutes while it was 9.57 minutes in 121/130 cases that did not have nasal crusts. The table above shows these findings.

Table 6.8: Comparison between quality of rhinorrhoea and MCT

Rhinorrhoea	Total	MCT in minutes
Thick	15	19.74
Watery	51	8.77
None	64	9.61

$P < 0.01$

The table above shows that rhinorrhoea significantly affected the MCT. Thick rhinorrhoea was associated with delayed MCT. ( $P < 0.01$ )

Table 6.9: Comparison between MCT and rhinorrhoea

Average MCT	Rhinorrhoea			Total
	Thick	Watery	None	
Decreased (< 7)	0	21	14	35
	.0%	60.0%	40.0%	100.0%
Normal (7 – 15)	3	21	31	55
	5.5%	38.2%	56.4%	100.0%
Delayed (> 15)	12	9	17	38
	31.6%	23.7%	44.7%	100.0%
Total	15	51	62	128
	11.7%	39.8%	48.4%	100.0%

$P < 0.01$

Table 6.9 shows that the consistency of mucus was a significant factor that affected the MCT. None of the cases with thick mucus had a decreased MCT. ( $p < 0.01$ )

Table 6.10: Comparison between duration of symptoms and MCT

Duration	Total	MCT
< 6 months	20	9.25
6 – 12 months	21	8.89
> 12 months	89	10.16

P=0.420

The duration of symptoms between onset and presentation did not significantly affect the MCT as shown in table 6.10. (p=0.420)

Table 6.11: Comparison between MCT and duration of symptoms

Average MCT	Duration of symptoms			Total
	< 6 months	6 – 12 months	> 12 months	
Decreased (< 7)	8	7	21	36
	22.2%	19.4%	58.3%	100.0%
Normal (7 – 15)	5	11	39	55
	9.1%	20.0%	70.9%	100.0%
Delayed (> 15)	7	3	29	39
	17.9%	7.7%	74.4%	100.0%
Total	20	21	89	130
	15.4%	16.2%	68.5%	100.0%

P=0.204

MCT was not significantly affected by the duration of symptoms as shown in the table above. (p=0.204)



Table 6.12: Comparison between use of antihistamines and MCT

Antihistamines	Total	MCT
None	59	8.89
<6 months	42	9.61
6 – 12 months	11	6.27
> 12 months	48	12.02

P=2.16

Table 6.12 shows that neither did use of neither antihistamines nor duration of use affect the MCT significantly. (p=2.16)

Table 6.13: Comparison between MCT and duration of use of antihistamines

MCT	Antihistamines				Total
	None	< 6 months	6 – 12 months	> 12 months	
Decreased (< 7)	7	12	7	10	36
	19.4%	33.3%	19.4%	27.8%	100.0%
Normal (7 – 15)	14	21	2	18	55
	25.5%	38.2%	3.6%	32.7%	100.0%
Delayed (> 15)	8	9	2	20	39
	20.5%	23.1%	5.1%	51.3%	100.0%
Total	29	42	11	48	130
	22.3%	32.3%	8.5%	36.9%	100.0%

P=0.052

In the table above, there was no significant difference between cases that had never been exposed to antihistamines as compared to those who had used them for a variable duration. (p=0.052) Classification of antihistamines was not considered.

Table 6.14: Comparison between duration of use of nasal steroids and MCT

Steroid sprays	Total	MCT
None	67	9.67
< 6 months	34	8.79
6 – 12 months	5	10.5
> 12 months	24	16.06

P=0.602

Use of steroids for whichever duration did not affect the MCT as shown in the table above. (p=0.602)

Table 6.15: Comparison between MCT and duration of use of nasal steroids

Average MCT	Nasal steroids				Total
	none	< 6 months	6 – 12 months	> 12 months	
Decreased (< 7)	16	13	2	5	36
	44.4%	36.1%	5.6%	13.9%	100.0%
Normal (7 – 15)	31	13	2	9	55
	56.4%	23.6%	3.6%	16.4%	100.0%
Delayed (> 15)	20	8	1	10	39
	51.3%	20.5%	2.6%	25.6%	100.0%
Total	67	34	5	24	130
	51.5%	26.2%	3.8%	18.5%	100.0%

P=0.590

There were no significant differences in the MCT in patients who used topical nasal steroids for any duration as well as those who had never been exposed to them as shown in the table above.

Table 6.16: Comparison between MCT and Sex

Average MCT	Sex		Total
	Male	Female	
Decreased (< 7)	10	26	36
	27.8%	72.2%	100.0%
Normal (7 – 15)	24	31	55
	43.6%	56.4%	100.0%
Delayed (> 15)	11	28	39
	28.2%	71.8%	100.0%
Total	45	85	130
	34.6%	65.4%	100.0%

P=0.180

Although females dominated in all MCT clusters, MCT was not affected by the sex of the cases as shown in table 12. (p=0.180)

Table 6.17: Comparison between MCT and nasal crusting

Average MCT	Nasal crusts		Total
	Yes	No	
Decreased (< 7)	1	35	36
	2.8%	97.2%	100.0%
Normal (7 – 15)	2	53	55
	1.9%	98.1%	100.0%
Delayed (> 15)	6	33	39
	15.4%	84.6%	100.0%
Total	9	121	130
	6.3%	93.8%	100.0%

P=0.018

Presence of nasal crusts affected MCT as shown in the table above resulting in delayed MCT. 6 of the 9 cases that had nasal crusting had delayed MCT. (p=0.018)

## 7.DISCUSSION

Rhinitis, allergic or non allergic is characterized by a complex of symptoms. These could consist of a combination of any of the following: sneezing, nasal obstruction, nasal itching, postnasal dripping, rhinorrhea and occasionally nasal pains. [1, 3, 4] In our study majority of the cases had a combination of sneezing, nasal obstruction and rhinorrhoea, 65% of whom, were females.

There is no agreement on the limits for normal MCT. Some studies quote <20 minutes as being the normal cut off [42] while others propose 7-15 minutes [27,30,31,42,46]. In our study, the later was considered the normal range. In their study, Prior et al obtained a mean of 12 minutes in their cases while the controls had a mean of 8 minutes [42] The current study agrees with previous workers, obtaining a mean of 12.6 and 7.8 minutes for the cases and controls respectively.

Ultrastructure of cilia has been shown to change beyond the age of 40 years but remains normal below this age. The changes observed were not related to sex. [41] In our study, cases below 40 years were included and neither was age or sex found to affect the MCT.

The phenomenon of the nasal cycle, alternating congestion and decongestion was first described in 1885. It has been shown that 70-80% of adults manifest this cycle. This cycle is however influenced by physical and environmental factors. [24] These findings concur with our study that demonstrated a difference in the MCT readings between the nostrils.

Up to 98% of the subjects tested, both cases and controls manifested a discrepancy in the readings from both nostrils irrespective of presence or absence of turbinate hypertrophy. Anderson demonstrated areas of the turbinate where clearance could be slow hence the inter-individual differences in the MCT. [27] This could justify our findings

There were cases where there was complete obstruction of the nasal cavity by a hypertrophied inferior turbinate which impeded proper placement of the saccharine granule as described by Anderson. This could have possibly affected the MCT.

In unison with other studies such as that by Lale et al and Stanley et al [27,30], our study did not show any detrimental effect after use of topical steroids or antihistamines. Of importance is that of patients included in our study, they had intervals when they were not using the antihistamines or nasal steroids. These intervals were not standardized neither were the types of drugs used considered. Patients who had used topical vasoconstrictors for duration longer than 2 weeks were excluded from the study to avoid the confounding condition of rhinitis medicamentosa over the MCT. Nonetheless, studies have showed that ephedrine sulphate (0.5% solution) does not affect ciliary action. (17,18,19)

Prolonged MCT in patients with rhinosinusitis and atrophic rhinitis is attributed to the changes in the rheology of mucus including oedema. Changes in the ultrastructure of cilia have also been reported. [27, 32] It has been documented that bacteria release toxins that disrupt epithelial cells resulting in loss of a confluent ciliary field. Also of interest is that neutrophils gather at the site of purulent infection to produce an elastase that is directly toxic to respiratory epithelium thus delaying the MCT. (28) In our study, cases with thick mucus had significantly prolonged MCT some extending even beyond 60 minutes.

Immunodeficiency has been shown extensively to be associated with deranged mucociliary transport. Patients with immunodeficiency have slower nasal mucociliary transport and more extensive mucosal damage and rhinitis is a common presentation in this group. [38] Patients with overt immunosuppression were excluded in our study but no attempts were made to establish the serostatus of the cases or the controls. It is therefore possible that some of the included subjects could have had a degree of immunosuppression.

The saccharine test is a simple cheap and effective way to measure mucociliary clearance time and has become widely accepted. [14,23,42] In our study, no difficulties were encountered during the testing and we therefore agree with its application in research and clinical practice.

## 8.CONCLUSION

In our study group, including subjects in the age range of 18 to 40 years, MCT was not affected by age. Sex has also not been showed to affect MCT.

Presence or absence of sneezing, headache, hypertrophy of the turbinates, nasal obstruction or postnasal drip does not affect MCT

The rheology of mucus significantly affects the MCT Patients with thick mucus have delayed MCT as compared to those with waterly mucus.

Patients with nasal crusting have extremely delayed MCT possibly suggestive of atrophic rhinitis

The normative values of MCT remain debatable with overlap between the cases and controls.

## 9. Recommendations

- ✓ The Anderson saccharine test should be adopted for use in screening patients suspected to have mucociliary clearance impairment.
- ✓ The Anderson saccharine test can be used as a measure of treatment outcome
- ✓ A follow up study should be conducted to establish the relationship between crusting, atrophic rhinitis and MCT.
- ✓ A follow up study to measure MCT in different types of rhinitis.
- ✓ A follow up study to establish factors that determine prolonged MCT.



# 10.BUDGET

ITEM	COST (Kshs)
Ethical and research committee fee	1,000/=
Saccharin granules	3,000/=
Internet surfing and downloading	5,000/=
Stationery, photocopies and statistical software (SPSS)	15,000/=
Secretarial services	10,000/=
Data compilation and analysis	20,000/=
Contingency (15%)	8,100/=
<b>TOTAL</b>	<b>62,100/=</b>

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# APPENDIX I:

## GENERAL PATIENT INFORMATION AND CONSENT FORM

### General patient information

We would like to seek your consent to participate in a study aimed at measuring the speed at which mucus is cleared from the nose to throat. This will help us know the normal range as compared to the abnormal time and will in future, be used to show the severity of a nasal problem and the benefit gained after treatment

### How to participate

1. We will ask you questions seeking to know when the disease started and any treatment given
2. We shall record any findings of examinations done before the test is conducted and the outcome of the test in the minutes.
3. The test will take an hour at most depending on the time it takes to taste the saccharin. This test needs not to be repeated.
4. Similar findings from all the participants will be used to compute the timing and the factors associated with the timing.

### What is the procedure?

A granule of saccharine (sweet tasting substance) will be placed in your nose. You will be required to sit calmly, not to sneeze or to sniff. Swallow every 30 seconds and report once you sense the sweet taste

### How does your participation affect you?

It does not adversely affect you in any way because;

1. You will receive the same treatment you would receive without participating in the study
2. No treatment will be given to you in addition to what you require and you would ordinarily get were you not participating in the study. But the results may be used in future for comparison of your current and future state and outcome of treatment
3. All information given will be confidential.

4. Results of the test will be made known to you at the end of the test, and their significance explained to you

**Are there any hidden dangers?**

1. Not at all
2. The saccharin granules are totally safe and have been approved for research purposes
3. Refusing to consent or withdrawing from the study will not affect the management you receive.

**How does your participation help us?**

1. The findings from the study will help us improve management of patients with similar problems like yours in future.
2. Findings of this study may be published in scientific journals or be presented at scientific conferences with the aim of improving knowledge and harnessing research about this illness
3. You are free to discuss this with family members and we shall be ready to answer any questions raised. If you understand everything said and has accepted it then you can sign the consent form provided

**CONSENT FOR STUDY**

I.....of.....IPNO.....  
study no.....Hereby consent to be included in the MTT study. This study shall include clinical examination and the introduction of a saccharin grain into the nostrils. I understand all the above as it has been explained to me. I also confirm that no monetary or material gains have been promised or given to me for participating in the study.

Signature of patient \_\_\_\_\_ Date \_\_\_\_/\_\_\_\_/2008



## **MAELEZO YA UTAFITI KWA MGONJWA NA KIBALI CHA UTAFITI**

Tungependa kukuomba ruhusa (kwa hiaru yako) kukuhusisha kwenye utafiti huu. Utafiti huu ni kuhusu mda unaochukuliwa kwa unyevu mapuani kufagiwa hadi kwa koo. Kutokana na utafiti huu tutafaidaka kwa kuwa tutaweza kujua mda unaofaa kwa mtu asiye mgonjwa katika pua na hivyo kuweza kupima kiasi cha nafuu anayopata mgonjwa akitibiwa shida katika pua.

### **JINSI YA KUSHIRIKI**

1. Tutakuuliza maswali kutaka kujua ni lini ugonjwa ulianza na ni matibabu gani uliyopewa.
2. Tutakupima na kurekodi ugonjwa ulio nao na pia kutumia chembe ya sukari ili kupima mda utakaohitajika ili uuhisi utamu mdomoni kutoka kwa pua lako.
3. Habari hii itakusanywa kutoka kwa watu wengi walio na shida kama yako na itatumiwa kujua zaidi juu ya ufagiaji huu.

### **KUSHIRIKI KUNAKUDHURU VIPI?**

Hakukudhuru kwa njia yoyote ile.

1. Utapata matibabu sambamba na wale wasioshiriki.
2. Hakuna chochote utakachopewa kukushawishi kushiriki kwenye utafiti huu.
3. Habari yoyote utakayotoa itawekwa kwa siri.

### **KUNA MADHARA YOYOTE ULIOFICHWA YANAYOWEZA KUTOKANA NA UTAFITI HUU**

1. La hasha.
2. Hata kukataa kushiriki hakutabadili matibabu utakayopewa.
3. Chembe za sukari zitakazo tumiwa zimehalalishwa kwa utafiti na hazina madhara yoyote yale.

### **KUSHIRIKI KWAKO KUTATUFAIDI VIPI?**

1. Kushiriki kwako ni muhimu kwa tutaweza kuelewa zaidi mambo kuhusu ugonjwa wako.
2. Matokeo haya yatatumika hata na madaktari wenzetu walioko kwengineko.
3. Uko huru kujadiliana na watu wa familia yako kabla ya kukubali kushiriki na maswali yoyote mutakayouliza yatajibiwa. Iwapo umeelewa maelezo haya yote vizuri na umekubali kushiriki basi utatia sahihi kwenye kibali cha utafiti kudhibitisha ya kwamba umekubali.

# KUKUBALI KWA MGONJWA KUHUSISHWA KWA UTAFITI WA

## MARADHI YA MAPUA

Mimi \_\_\_\_\_ Kutoka \_\_\_\_\_

IPNO \_\_\_\_\_ Nambari ya utafiti \_\_\_\_\_ Ninakubali kuwa mojawapo wa

wagonjwa watakao husika na utafiti wa maradhi yamapua. Nimeelezwa ya

kwamba kuhusika kwa utafiti huu ni kwa HIARI YANGU mwenyewe na si kwa

LAZIMA. Na weza kujitoa kwenye utafiti wakati wowote na bado nitapata

matibabu kama wagonjwa wengine. Nimeelezwa na ni meelewa hii yote na

**Daktari Kaitesi BM**

Sahihi ya mgonjwa \_\_\_\_\_

Sahihi ya daktari \_\_\_\_\_ Tarehe. \_\_\_\_\_ / \_\_\_\_\_ /2008

# Appendix II

## MCT STUDY QUESTIONNAIRE

Name:

Study No.:

Date:

Age:

Sex

DIAGNOSIS .....

### SALIENT SYMPTOMS:

Runny nose      yes  no       headache      yes  no

Nasal blockages      yes  no       sneezing      yes  no

Facial pains      yes  no       Postnasal drip      yes  no

Duration of symptoms      < 6months

6 - 1year

>1year

### SALIENT SIGNS:

Rhinorrhoea      Thick       Watery       None

Nasal crust      yes  no       HIT Right      yes  no

Postnasal discharge      yes  no       HIT Left      yes  no

Facial tenderness      yes  no       Facial swelling      yes  no

**PAST TREATMENT**

Antihistamines	Duration	< 6 months	<input type="checkbox"/>
Yes		6mo – 1 year	<input type="checkbox"/>
No		> 1 year	<input type="checkbox"/>
Nasal steroids	Duration	< 6months	<input type="checkbox"/>
Yes		6mo – 1 year	<input type="checkbox"/>
No		> 1 year	<input type="checkbox"/>

**TEST RESULTS**

Cases:	Right .....	mins	left.....mins	Average (MCT).....
Controls:	Right.	mins	Left..... mins	Average (MCT).....

*Thanks*

# Appendix III

## The Anderson saccharin test

To perform the test, a saccharin particle (1.5-mm diameter) is carefully placed on the floor of nasal cavity about 1 cm behind the anterior end of the inferior turbinate. The subject is asked not to sniff, sneeze, smoke, eat or drink during the test and avoid deep breathing. The subject is also asked to swallow every 30 seconds and to report the first change in their sensation of taste. The time taken by the subjects to perceive sweet taste in the pharynx is taken as MCT in that nose. The test is repeated on each side and the average of two is taken as the NMCT. This is done to exclude the effect of nasal cycle on mucociliary clearance.