COMPARATIVE STUDY OF MIDDLE MEATAL ANTROSTOMY PATENCY WITH OR WITHOUT APPLICATION OF MITOMYCIN C

BY

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DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA.
In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY
IN
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Under the Guidance of

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PRIOR PERMISSION TO START OF STUDY

The Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has examined and unanimously approved the Synopsis entitled **"Comparative Study of Middle Meatal Antrostomy Patency with or without Application of Mitomycin C"** being investigated by Dr.KARNIKA R K & Dr. K C Prasad in the Department of ENT at Sri Devaraj Urs Medical College, Tamaka, Kolar. **Permission is granted by the Ethics Committee to start the study.**

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ABSTRACT

Background:

Chronic sinusitis produces long-term inflammation of the mucous lining of the sinuses. Functional endoscopic sinus surgery (FESS), as described by Messerklinger, has been fully accepted for treating chronic sinus disease, with the assumption that restoration of sinus ventilation and correction of mucous apposition will allow restoration of the muco-ciliary clearance system. One problem the surgeon often encounters is that of post-operative adhesion occurring between the middle turbinate and the lateral nasal wall in the region of the ethmoid sinuses**.** If severe, the recurrence of symptoms is often due to these synechiae, and further surgery may be required to restore normal function. Various surgical approaches, as well as the use of systemic drugs3 and site-specific barriers, have been used to minimize inflammation and injury during surgery so as to reduce the risk of adhesion formation. Mitomycin C is an antibiotic-antineoplastic agent isolated from Streptomyces caespitosus. It acts as an alkylating agent by selectively inhibiting deoxyribonucleic acid (DNA) synthesis and cross-linking DNA. At higher concentrations, cellular ribonucleic acid and protein synthesis are also suppressed. The purpose of this study was to determine whether mitomycin C could be used to prevent the closure of maxillary sinus antrostomies9 – 11 and to prevent frontal recess stenosis while promoting drainage of the ethmoidal and sphenoid sinus by preventing post-operative scarring.[1,2]

Objective: To study the role of mitomycin C in reducing adhesion formation following middle meatal antrostomy

Study design: Prospective Interventional Comparative study

Patients: Fifty patients were selected suffering long-term problems with bilateral chronic rhinosinusitis, with no relief obtained from medical therapy for more than 12 weeks. Patients with unilateral chronic rhinosinusitis and undergoing unilateral FESS, Acute exacerbation of symptoms, established asthma, uncontrolled hypertension, uncontrolled diabetes, suspected cystic fibrosis, drug induced and hormonal causes of rhinitis, presence of bleeding diathesis, previous history of nasal surgeries, Patients refusing to undergo CT scan, patients refusing endoscopic surgery, patients with established or impending complications were all excluded from the study.

Material and Methods: Diagnostic nasal endoscopies and non-contrast computerized tomography of nose and paranasal sinuses were undertaken and following confirmation of the diagnosis, functional endoscopic

sinus surgery (FESS) was carried out bilaterally using the Messerklinger technique. On completion of the surgery, a cotton wick soaked in mitomycin C was placed in one or other side of the nose in the middle meatus. Follow up was for three weeks, three months and six months, patients were assessed for subjective and objective improvement in their symptoms.

Results: In the study there was significant difference in Grade of Ostia between cases and controls at 3 months and 6 months. Grade of Ostia at intraoperative period among cases and controls was Grade 1 (1cm*1cm). At 3 weeks among cases and controls, not much difference were found compared to ostia size made intra-operatively. At 3 months among cases and controls was Grade 2. There was significant difference in Median Grade between two groups. At 6 months among cases and controls was Grade 2 and Grade 3 respectively. There was significant difference in Grade of Ostia between two groups

Conclusion: Mitomycin C may be topically applied in post-operative FESS cases to reduce adhesion formation and hence the need for revision surgery.

Key words: Paranasal Sinusitis; Endoscopy; Mitomycin; Postoperative Complications

LIST OF ABBREVIATIONS

1.	ARS	Acute Rhinosinusitis
2.	CRS	Chronic Rhinosinusitis
3.	CRSsNP	Chronic Rhinosinusitis without Nasal polyposis
4.	CRSwNP	Chronic Rhinosinusitis with Nasal polyposis
5.	FESS	Functional Endoscopic Sinus Surgery
6.	ESS	Endoscopic Sinus Surgery
7.	IPPV	Intermittent Positive pressure ventilation
8.	MAP	Mean Arterial Pressure
9.	PNS	Paranasal sinus
10.	DNE	Diagnostic nasal endoscopy

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INTRODUCTION

INTRODUCTION

Chronic Rhinosinusitis (CRS) represents a significant disease burden worldwide, affecting at least 11% of the population. Prevalence of chronic rhinosinusitis has been increasing in India over past few years due to urban lifestyle and pollution, consequently carrying with it a substantial economic burden to healthcare systems, to patients and to the economy from loss of productivity in the workplace. In fact _sinusitis' was cited as one of the top ten most costly physical health conditions, as it has an increasing incidence in middle age with a significant socio-economic impact and impairment of quality of life.[3.]

Functional endoscopic sinus surgery (FESS) has become a fully accepted technique for treating chronic sinus disease which is unresponsive to medical treatment. The goal of the procedure is to improve the drainage and ventilation of osteo meatal complex in middle meatus. As Osteo meatal complex, represents the final common pathway for drainage and ventilation of the ethmoid, maxillary, and frontal sinuses. The goal of naming this area is to emphasize the concept that inflammation in the OMC can lead to anatomic and functional obstruction of the anterior sinuses.[4]

However, it is accepted that the recurrence of symptoms after FESS is due to stenosis formation in the middle meatal antrostomy site. These post-operative changes cause obstruction of the middle meatus, resulting in reduction of ventilation and drainage of mucus from the paranasal sinuses. Topical application of Mytomycin C after completion of middle meatal antrostomy procedure decreases the incidence of post operative stenosis formation.[4]

AIMS & OBJECTIVES

OBJECTIVES OF THE STUDY

1. 1.To document the patency of middle meatal antrostomy with topical Mytomycin C on one side and without Mitomycin C on other side in patients undergoing Middle meatal antrostomy, in 50 chronic rhinosinusitis patients.

2. To Compare the size of the Antrostomy site of both the sides 3weeks, 3 Months and 6 Months post-operatively.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

Throughout the history of medicine, innumerable efforts have been made to illuminate and examine the inside of various hollow cavities and orifices in our body. The interior of nose and paranasal sinuses, with their narrow passages and fissures, bony walls, allocated heavy demands on the design of instrumentation to be used for this purpose. This motive, propagated the development of the nasal endoscopy.[5]

Killian, in 1915, published a review on the "History of endoscopy, from the earliest times to Bozzini", in which he recorded all the attempts to view the upper airways prior to the beginning of 19 century. [5]

Philip Bozzini, in 1806 published an article describing the first "Light conductor, or description of a simple device and its use for the illumination of the internal cavities and spaces of live animal body" Bozzini, in 1806 stated that he was able to see some areas behind sft palate with the aid of his light conductor. In 1838,

Baumes presented to the Medical Society in Lyons, a mirror, that could be used for the examination of choanae and the larynx which was the size of two Frane piece.[5]

Czermak, in Vienna-1859 developed a technique similar to laryngoscopy of Turck, which helped him to visualise the nasopharynx, the choanae and posterior aspect of nose with aid of a small mirror. This procedure was given the name –Rhinoscopy.[5]

The earliest attempts of rhinologists were directed toward infectious conditions of the nose and sinuses. Prior to the era of introduction of penicillin, sinus and otologic disease were responsible for 1 in every 40 mortalities associated with Intracranial infections.7 As such, the earliest rhinologic operations were in-scripted towards the complicated sinusitis and were more destructive in nature. Heightened attention was paid for frontal sinus as complications from these infections caused the greatest risk of mortality. Simple frontal sinus incision and drainage were reported as early as 1870. [5]

Kuhnt, in 1895, described more extensive operations to obliterate the frontal sinus by removing the anterior wall.[5]

Reidel, in 1898 described removal of both the anterior wall and floor, though the disfiguring nature of the procedure remained a major barrier to acceptance.9 External procedures remained common, yet advancements in surgical technique recognized the importance of procedures that would provide for normal drainage of the frontal sinus through its outflow tract.Caldwell‘s landmark description of the canine fossa approach to the maxillary sinus codified an open approach to this location that would be familiar to the modern rhinologist.10
In 1908, Knapp published his method of Surgery of Frontal recess through an external ethmoidectomy.[5,6]

In 1921, Lynch had also developed an external approach for fronto-ethmoidectomy, which was modified by subsequent surgeons who employed mucosal flaps to reduce the rate of stenosis of the frontal sinus drainage pathway.

Lothrop, in 1917, introduced the concept of creating a median frontal sinus drainage pathway which surpassed some of the advances in the modern practice of rhinology. [5,6]

For the longest of time between the development of modern endoscopic sinus surgery and the destructive operations of the frontal sinus, osteoplastic flap procedures represented the pinnacle of frontal sinus.In 1904, Hoffmann initially described, Obliteration of the frontal sinus through an osteoplastic flap preserving a normal contour of the frontal bone while removing the offending sinus mucosa.

Then, Goodale and Montgomery published in 1956, the classical description of frontal sinus osteoplasty, including obliteration with abdominal fat.18, But these operations was found to be associated with complication rates above 50% and early failure in 10–15% of cases.

Endoscopes, or their early analogs, over the past 100 yrs had been introduced into nearly every anatomical space. Hirschmann and Valentin, became the first nasal endoscopist in 1901, when he introduced a modified cystoscope into the nose,22 likewise Reichert, lay claim to the first endoscopic sinus surgery when he utilized a 7-mm endoscope through an oral-antral fistula to operate on a diseased maxillary sinus.23 Although Maltz had, by 1925, recognized the diagnostic value of endoscopy in evaluating the nose and sinuses, a process he referred to as ―sinuscopy" was limited by the technology of his era.[5,6]

British Professor Harold Hopkins in 1959, replaced Rod Optic endoscope system for an Operating Microscope which was applied for ethmoid labyrinth These operating Microscope were initially revolutionized for Otology.[5,6]

Karl Storz, in 1967, first put into production, providing the keystone instrument that would facilitate a great leap forward in surgery of the nose and paranasal sinuses. Draf is credited with the first published report of endoscopic examination of the nose in 1973.25 The Hopkins rod rigid nasal endoscopes made it possible to examine in detail the clefts and recesses of the nose. The ability to enter middle meatus of the nose enabled the inspection of anterior ethmoid sinuses, key area of infectious paranasal sinus disease.[5.6]

During 1951-56, Hopkins made fundamental improvements in the optics of endoscopy. These included a light source that was separate from the instrument, an excellent resolution, with high contrast, a large field of vision in spite of the small diameter of the endoscope, and perfect fedility of colour.[5,6]

Today, nasal endoscopic examination in combination with tomography the identification of small, circumscribed changes in paranasal sinuses. These small changes are frequently of considerable pathophysiologic significance."[5,6]

Messerklinger establish a systemic endoscopic diagnostic approach to the lateral wall of nose. His studies beginning in 1950 demonstrated that, in most cases the frontal and maxillary sinuses are involved indirectly by primary disease that originates in narrow spaces of nose and in the anterior ethmoid. This discovery led to the development of endoscopic diagnostic technique that focussed on changes on the lateral wall of nose and identified and isolated changes, with the aid of rigid endoscope and tomography of sinuses. Messerklinger observed that the eradication of primary anterior ethmoid disease by means of a circumscribed, limited endoscopic surgical procedure resulted in the recovery of massive mucosal pathology, in the adjacent, large paranasal sinuses, within a few weeks.[5,6]

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATION

EMBRYOLOGY OF NOSE

Nasal Cavity is first recognized in the 4 week as the olfactory or nasal placode. The placode sinks to form the olfactory pit. This then deepens to form the nasal sac. The maxillary process of the 1" arch grows anteriorly and medially to fuse with nasal fold and frontonasal process. This closes off the nasal pits to form the primitive nasal cavity.[7]

Initially mouth and primitive nasal cavity are separated by bucco-nasal membrane. This thins as nasal sac extends posteriorly and eventually breaks down to form the primitive choana. The floor anterior to the choana is formed from mesenchymal extensions of medial nasal folds to produce premaxilla which gives rise to the upper lip, medial crus of lower lateral cartilages.[7,8]

The maxillary process also grows ventrally from dorsal end of mandibular process to join the lateral nasal process around the nasomaxillary groove. The ectoderm in this region canalizes to form the nasolacrimal duct.[7,8]

The lateral nasal folds form the nasal bones, upper lateral cartilages, and interal crus of lower lateral cartilage..Palate begins to form anteriorly with fusion, maxilla and frontonasal processes. Nasal septum is formed from the midline ridge developing from frontonasal process in roof of oral cavity and extends posterior to the opening of Rathke's pouch."[9,10]

The palatal process from lateral maxillary mesoderm grows medially towards septum and towards each other. Fusion is complete except a midline dehiscence which forms site of future incisive canal. It separates the nasal cavity and nasopharynx from oral cavity as they also form soft palate and uvula."[9,10]

ANATOMY OF NOSE

EXTERNAL NOSE:

The external nose is shaped like a triangular pyramid with its root above and base directed downwards. The base is perforated by two nostrils or anterior nares, separated by median septum. Each side of external nose ends in a rounded eminence, the alae nasi, which forms the outer boundary of the nostril. The nasal bones form the bridge, and each is united above with frontal bone and laterally to frontal process of maxilla. Two paired cartilages, the upper and lower lateral cartilage and one unpaired cartilage, the septal, complete the external framework.[10,11]

The chief muscles acting of external nose are the compressors and dilators of ala nasi supplied by facial nerve.Blood supply to the external nose is from maxillary and ophthalmic arteries. The anterior facial vein and ophthalmic vein forms the venous supply, lymphatics drain into the submandibular and pre-auricular lymph nodes.

The skin of the external nose receives its sensory supply from the two upper divisions of the trigeminal nerve; ophthalmic and maxillary[10,11]

NASAL CAVITY:

Each nasal cavity is divided into three parts i.e. nasal vestibule, olfactory region and respiratory region. Nasal vestibule is most anterior and it extends from the nostril anteroinferiorly to the nasal valve posterosuperiorly. The nasal valve is situated between caudal end of upper alar cartilage laterally and septum medially. The area of demarcation is limen nasi, with skin containing hair follicles, sebaceous and sweat glands.[10,11]

It is a space of importance since it is here that the nasal cavity is 2 the narrowest, limited to a triangular shape of only 0.3 cm on each side. The olfactory region is confined to the upper part and the superior turbinate representing an area of 10 cm². The rest of the nasal cavity constitutes the respiratory region and its surface may reach 120 cm² [11,12]

The turbinates. lateral wall of each nasal cavity has superior, middle and inferior Each turbinate overhangs a meatus. The space above or medial to superior turbinate is sphenoethmoidal recess, to which sphenoidal sinus open. Posterior ethmoids drain into superior meatus. The anterior ethmoidal, frontal and maxillary sinuses open into middle meatus. [11,12]

Middle meatus contains several structures of importance. An enlargement is found at anterior end of the middle meatus, which is part of ethmoidal bone, called as the uncinate process. A little further back is another eminence which is called bulla ethmoidalis, which represents a protrusion into the meatus of one of the air cells of the ethmoidal labyrinth." Between these two enlargements is a groove which is known as hiatus semilunaris, which leads to a narrowing called infundibulum.[11,12]

Arterial supply is via the lateral branches of sphenopalatine, greater palatine, superior labial. Venous drainage occurs to pterygoid plexus. Lymphatics drain into the submandibular nodes anteriorly and to the lateral pharyngeal, retropharyngeal and upper deep cervical nodes posteriorly.[11,12]

Main sensory supply to the nasal cavity is derived from the maxillary division of the trigeminal nerve through branches arising in pterygopalatine ganglion.

Sympathetic nerve supply arises from the superior cervical ganglion. It produces vasoconstriction and decreased secretion from the

nose. Parasympathetic supply arises from the pterygopalatine ganglion via nerve to pterygoid canal. It produces vasodilation and increased secretion." [11,12]

NASAL SEPTUM :

The nasal septum is formed by the perpendicular plate of ethmoid, vomer, septal cartilage, nasal crests of the maxillary and palatine bones. The main arterial supply of the nasal septum arises from the septal branch of sphenopalatine artery. The antero-inferior part of the septum or Little's area is where the septal branches of sphenopalatine, greater palatine, superior labial and anterior ethmoidal artery anastomose. Venous drainage occurs to pterygoid plexus. The anterior septum drains in to the submandibular nodes while posterior drains in to retropharyngeal and anterior deep cervical nodes. The nerve supply is by nasopalatine nerve posteriorly and anteriorly by the anterior ethmoidal branch of nasociliary nerve and anterosuperior alveolar nerve.[11,12]

NASAL MUCOUS MEMBRANE

Nasal mucous membrane consists of fairly dense connective tissue. The mucous membrane is predominantly olfactory epithelium superiorly adjacent to the cribriform plate. Respiratory epithelium is composed of ciliated and non-ciliated pseudo stratified columnar cells, basal pluripotent stem cells, and goblet cells. Seromucinous glands found in the sub mucosa are more important in mucous production in nasal cavity than goblet cells which are numerous in sinuses.[11,12]

NERVE SUPPLY OF NOSE

Nerve supply to the nose is extremely rich and is via the general sensory, parasympathetic and sympathetic innervations. The main sensory supply comes from maxillary division of Vth CN from its pterygopalatine branches (nasopalatine, greater palatine, short palatine nerve). The floor and the anterior end of the inferior turbinate are supplied by branches of anterior superior alveolar nerve. The secretory nerve fibers are derived from the sympathetic and parasympathetic systems. Sympathetic fibers are derived through superior cervical ganglion via the sympathetic plexus of internal carotid artery and join with the parasympathetic fibers in the pterygoid canal. These supply the nasal vasculature via the greater superficial petrosal nerve to form nerve to pterygoid canal. Parasympathetic fibers are derived from the superior salivary nucleus in the medulla via the nerves intermedius to form the vidian nerve and reach sphenopalatine ganglion, where they relay before reaching the nasal cavity and also supply blood vessels of the nose causing vasodilatation. The special sensory olfactory nerves are distributed in a network in the mucosa in the upper third of nasal septum, roof and corresponding area.[11,12]

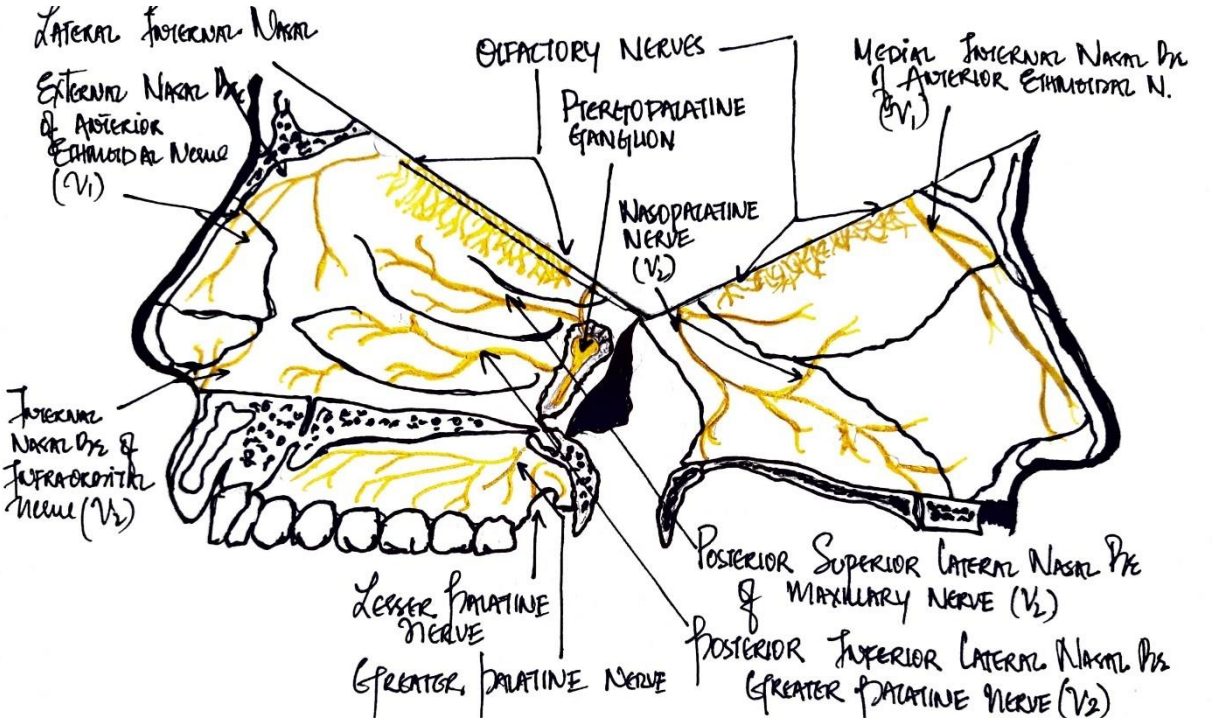


Image-1: Image showing Nerve supply of the lateral wall and the septum of Nose

BLOOD SUPPLY

The nasal cavity derives its blood supply from branches of both internal and external carotid arteries. Anterosuperior quadrant of nose is supplied by anterior and posterior ethmoidal arteries which are branches of sphenopalatine and greater palatine both branches of maxillary artery and by superior labial branch of facial artery. The dividing line between the two carotid system is at the level of the middle turbinate.[11,12]

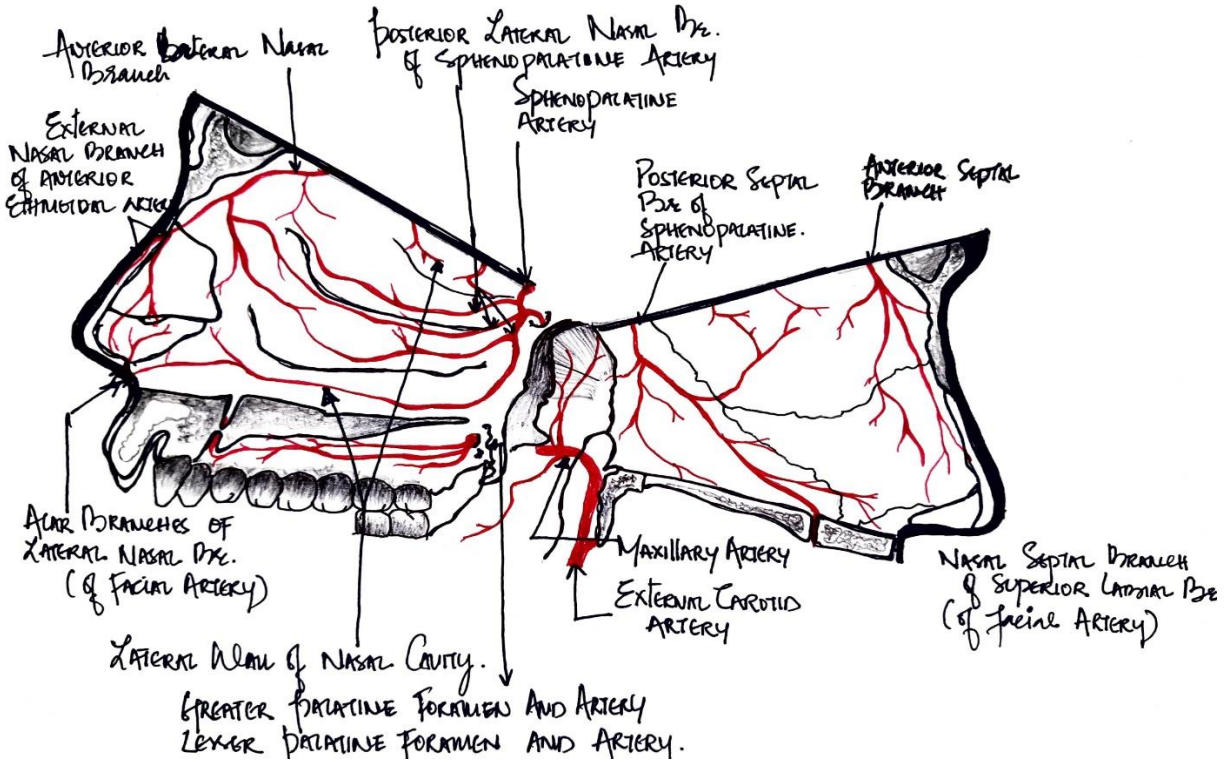


Image-2: Image showing Nerve supply of the lateral wall and the septum of Nose

Venous drainage is by formation of cavernous plexus beneath mucous membrane and drain through the sphenopalatine and facial veins. Lymphatic drainage from the nose is to the submandibular nodes and to the superior nodes of deep cervical chain. Drainage from the posterior part id to the middle and deep cervical chain.[11,12]

OSTEOMEATAL COMPLEX:

Neuman coined this word to describe the region comprising middle meatus with the anterior air cells. This is the most important area for normal sinus functioning and any pathology in this area will disrupt the physiology and leads to sinus dysfunction. In the middle meatus there are several important structures. Anteriorly, the first landmark is a hook shaped bone called uncinate process. Posterior to uncinate process is a groove known as hiatus semilunaris which leads to ethmoidal infundibulum. The ethmoidal bulla is a bulge posterior to the hiatus, which is a part of anterior ethmoidal group of cells. [11.12]

The frontal sinus opens into the superior most aspect of the ethmoidal infundibulum called the frontonasal recess, while the anterior ethmoidal cells open into the infundibulum. The osteum of the maxillary sinus opens posteroinferiorly into the infundibulum.[11.12]

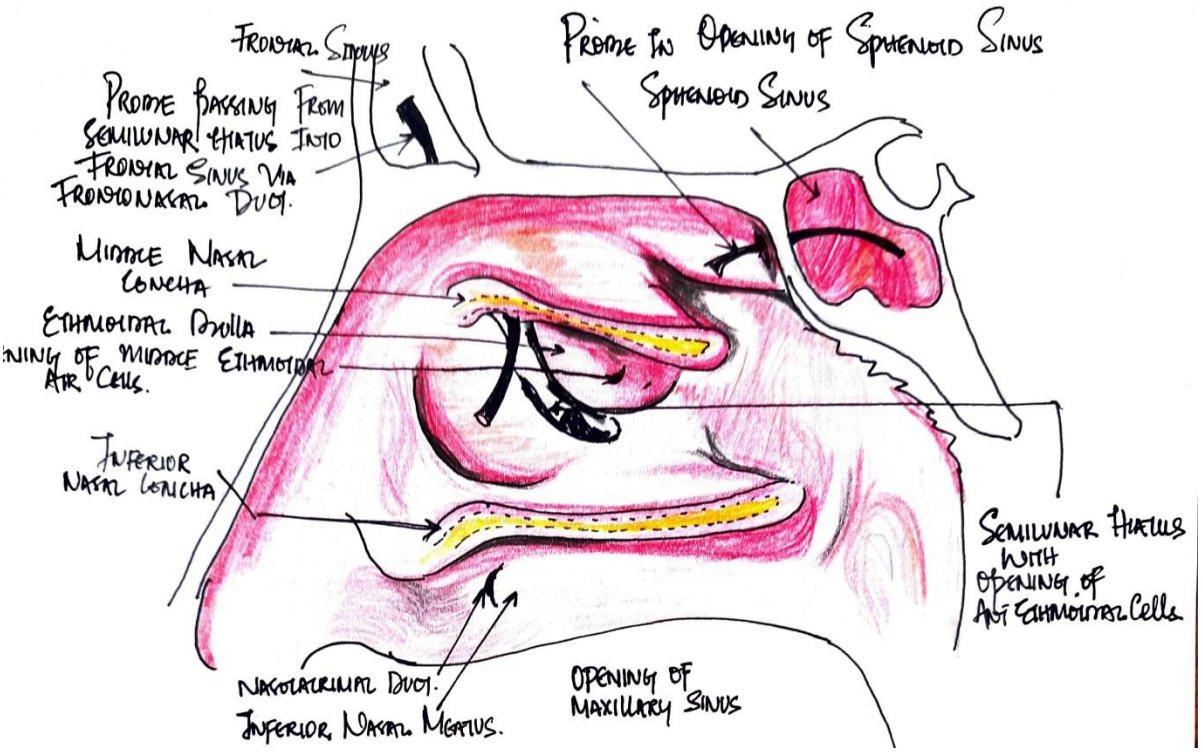


Image-3: Image showing the osteo-meatal complex of the Nose.

PHYSIOLOGY OF NOSE

The chief functions of nose are respiration and olfaction. In addition to being the sensory organ of smell, the nose also plays an important role in the cleansing and conditioning of inspired air. It also contributes to heat exchange, humidification, filtration, nasal resistance, nasal fluids and ciliary function, voice modification and the nasal neurovascular reflexes."[11.12]

Filtration: is accomplished by the nasal mucous blanket which covers the mucosal membrane and is constantly propelled posteriorly by the cilia. Mucous blanket is adhesive and causes the bacteria and dust to adhere to it."[11.12]

EMBRYOLOGY OF PNS

MAXILLARY SINUS:

The maxillary sinus is the first sinus to appear at seven to ten weeks as a shallow groove expanding from the primitive ethmoidal infundibulum into the mass of the maxilla. It continues to grow during childhood at an estimated annual rate of 2 mm vertically and 3 mm anteroposteriorly and in particular with development of the middle third of the face as the dentition erupts. It reaches its final size in the seventeenth to eighteenth year of life. The maxillary sinus in an adult has a volume of around 15 cm^2 and is roughly pyramid shaped. The base of this pyramid is formed by the medial wall of the maxillary sinus with the apex of the pyramid towards the zygomatic recess.[11.12]

ETHMOID SINUS:

At 9th to 10th week of gestation, six major furrows appear on the lateral wall of nose. These furrows are separated by ridges which have an ascending portion called ramus ascendens and a posteroinferior portion called ramus descendens.

The inferior turbinate is also called the maxilla-turbinal and is an individual bone. The first ethmoturbinal regress & the descending portion gives rise to the uncinate process, the ascending process forms the agger nasi. The first furrow gives rise to the infundibulum & the frontal recess. 9.10 Middle turbinate is formed from the second ethmoturbinal, superior from the third. The fourth & fifth ethmoturbinals regress during development.[11.]

THE SPHENOID SINUS :

The sphenoid sinus is recognizable at around the third intrauterine month as an evagination from the sphenoethmoidal recess and again a small cavity is found at birth At the third year of life, pneumatisation of the sphenoid bone progresses and at age seven has frequently reached the floor of the sella.2.[12]

THE FRONTAL SINUS:

The frontal sinus is the most variable in size and shape and may be regarded embryologically as an anterior ethmoidal cell. From the most anterior and superior segment of the anterior ethmoid complex, the frontal bone is gradually pneumatized, resulting in frontal sinuses of variable size. At birth, the frontal sinuses are small and, on x-rays, cannot usually be differentiated from other anterior ethmoidal cells, substances reach olfactory area, to enhance the sense of smell[12]

ANATOMY OF PARANASAL SINUSES

The paranasal sinuses arranged in pairs, include two groups: anterior and posterior. The former include maxillary sinus, the frontal sinus and anterior: ethmoidal sinus. The posterior group comprise of posterior ethmoidal and sphenoidal sinus.

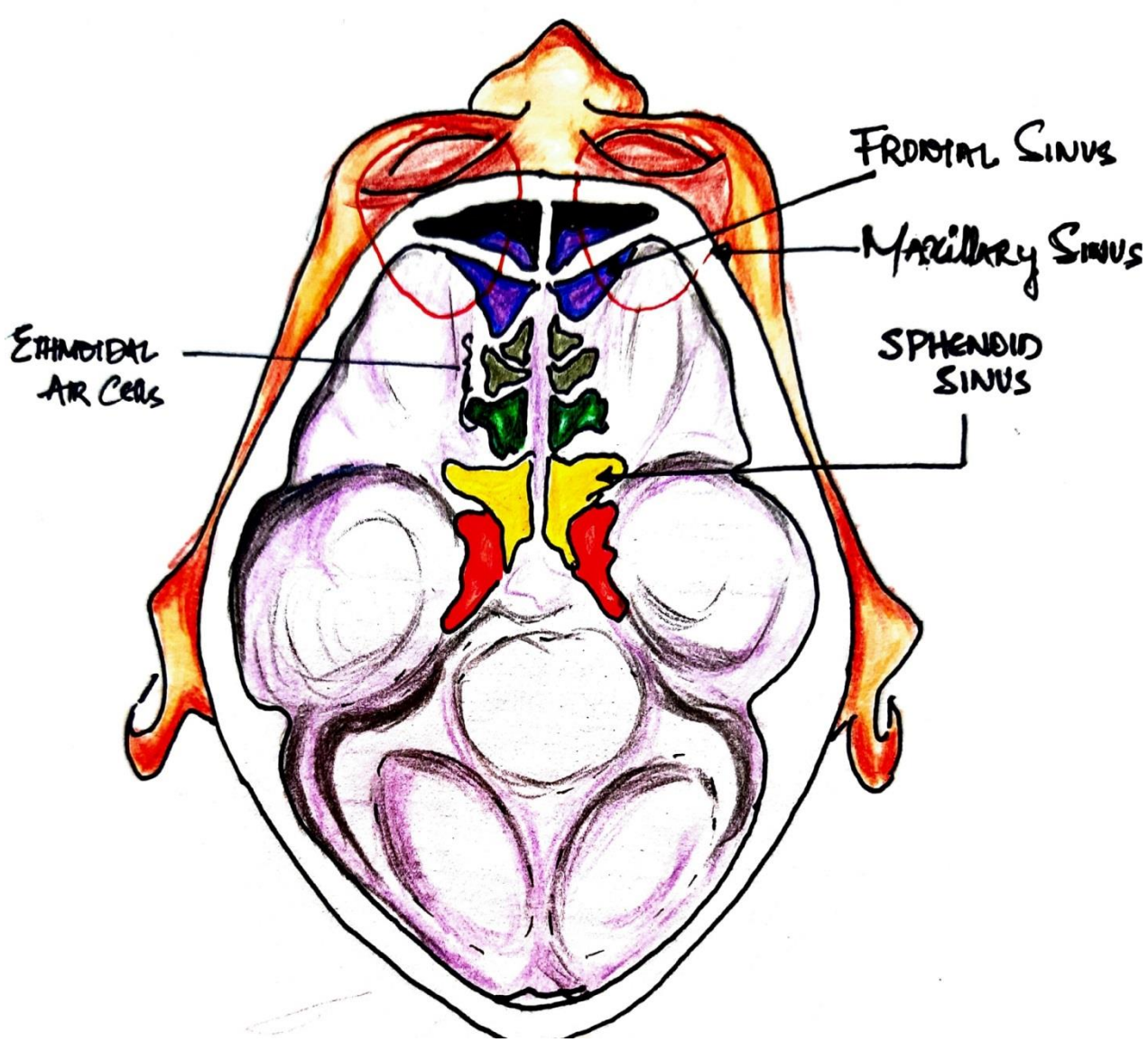


Image-4: An axial section of the cranial cavity depicting all the paranasal sinuses.

MAXILLARY SINUS:

It is present since birth, but attains its maximum size around 15 to 17 years of age. Each sinus is pyramidal in shape, apex pointing towards the zygomatic process. The volume of each sinus in an adult is approximately 15 ml and is composed of a single, nonpartitioned cavity.[12.113]

The medial wall of the maxillary sinus is composed of the lateral nasal wall constituents including the inferior turbinate, uncinate process of the ethmoid bone and projections of the maxilla, palatine and lacrimal bones. The natural ostium of the maxillary sinus is present in superior- posterior aspect of medial wall measures approximately 3 mm in diameter. The mucociliary function of the maxillary sinus physiologically clears secretions to the natural ostia and infundibulum. The accessory Ostia is present in 25% of the population, lies posterior to the natural ostea. [12,13]

The superior wall/ roof of the maxillary sinus is formed by orbital floor. The infraorbital nerve, a sensory branch of the second division V CN.The anterior wall of the maxilla separates the malar soft from the anterior border of the maxillary sinus. The bone over the canine tooth is typically the thinnest portion of the anterior wall.

The floor/ inferior wall of the maxillary sinus is composed of palatine and alveolar segments of the maxilla. In adults the floor is positioned approximately 1 cm inferior the nasal floor. The bony separation between the maxillary sinus and the upper dentition is variably thick and may allow for direct communication.[12.13]

The posterior wall of the maxillary sinus bounds the PPF medially and the infratemporal fossa (ITF) laterally. Potential anatomic variants of the maxillary sinus include hypoplasia and septations.[12.13]

MAXILLARY SINUS

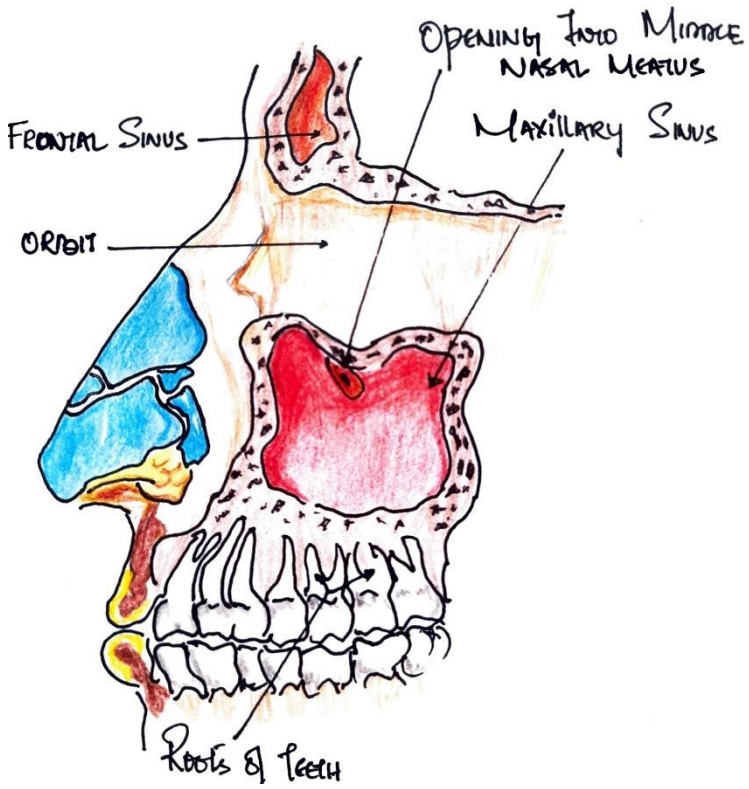


Image-5: Image showing maxillary sinus.

ETHMOIDAL SINUS:

It is present at birth and in the adult life and they vary in number, size and shape. The ethmoid sinus is composed of multiple, individual cells separated by thin walled partitions within the ethmoid bone. The complexity and variability of this area has led many to refer to this area as a ~~l~~labyrinth." Adding to the challenging nature of ethmoid sinus surgery is the proximity of critical neurovascular structures at the borders.

The medial boundary is composed of the middle turbinate, superior turbinate and the olfactory fossa of the cribriform plate. The latter structure may be less than 1 mm thick, is tightly adherent to the underlying dura and has a variable depth in relation to the roof of the ethmoid cavity (fovea ethmoidalis). [12.13]

Kero‘s classification: The distance between the lowest point of the olfactory fossa and the fovea ethmoidalis. Type I 1–3 mm, type II 3–7 mm, type III 8–16 mm. [12.13]

More important to understanding and identifying the potential hazard of a deeply recessed (type III) olfactory fossa when dissecting in the superior–medial aspect of the ethmoid sinus cavity. Asymmetry of the anterior skull base from side to side may also occur (Fig. 4.13). The lateral boundary of the ethmoid cavity is the thin-walled lamina papyracea portion of the ethmoid bone. The collinear position of the lamina papyracea with the maxillary sinus ostium serves as a useful landmark during ethmoidectomy. Additionally, close inspection of the lamina papyracea will often reveal a yellow coloration from the underlying orbital fat. Natural or disease related dehiscence of the lamina papyracea places the medial orbital structures at risk during endoscopic sinus surgery. The posterior boundary of the ethmoid sinus cavity is the anterior face of the sphenoid sinus.[12,13]

An embryologic and anatomic distinction exists between the anterior and posterior ethmoid sinuses, including physiologic clearance points (middle meatus versus superior meatus), number of cells (greater number of anterior cells), and size of cells (larger posterior cells).

The anterior and posterior cavities are separated by the ground lamella (also known as basal lamella) of the middle turbinate. The ethmoid bulla is a reliable landmark given that it is usually the largest of the anterior ethmoid cells and is positioned posterior to the uncinate process.Tracing the anterior surface of the ethmoid bulla superiorly will lead to the frontal recess, as may be done with an ~~–in~~tact bullar" approach to the frontal sinus. The bulla may directly attach to the anterior skull base superiorly, may be attached by a single vertical lamella called the bulla lamella or may have a superior partition above which there is a space termed a suprabullar recess separating the bulla from the skull base. A vertical partition along the posterior surface of the ethmoid bulla may create a space between the bulla and the ground lamella, termed the retrobullar recess.[12,13]

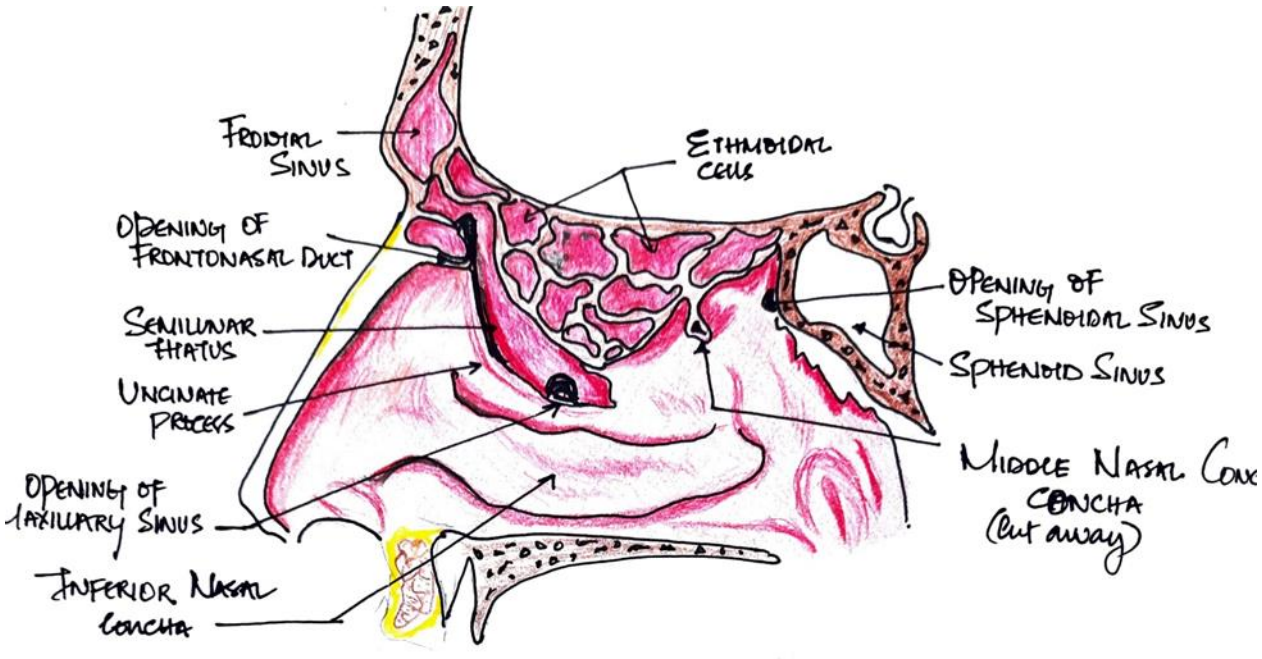


Image-6 Agger Nasi, Uncinate Process, Infundibulum, and Hiatus Semilunaris

These septations often adjoin the posterior wall of the sinus overlying the carotid artery or Optic Nerve.10 As such, caution should be exercised to ensure atraumatic removal of septations and avoidance of catastrophic vascular injury. [12.13]

Pneumatization of the sphenoid sinus is highly variable and can extend as far laterally as the sphenoid wings, and inferiorly to the clivus and foramen magnum. Pneumatization occurs in a progressive fashion during childhood namely incomplete or partial pneumatization.

Pneumatization patterns includes three types, sellar (80%), presellar (17%), and conchal (3%),12 as originally proposed by Hammer and Radberg. Preoperative imaging is crucial to evaluating such variations in sphenoid sinus anatomy in order to ensure safe entry.

The sphenoid sinus ostium is located approximately two thirds up the anterior wall of the sphenoid sinus, positioned 21.21 ± 6.02 mm superolateral to the posterior choana and 4.85 mm ± 2.89 mm lateral to the midline. [14]

The sinus ostium can be visualized by lateralization of the superior turbinate in the sphenoethmoid recess, enclosed by the septum medially, superior turbinate laterally, cribriform plate superiorly, and the nasal floor inferiorly. The sphenoid sinus can also be entered through the posterior ethmoidal cells via the medial–inferior triangle of the sphenoid face.

This approach avoids risk to the optic nerve and carotid artery in the superior–lateral triangle. Transpterygoid approach is another was to access the sphenoid sinus. [15]

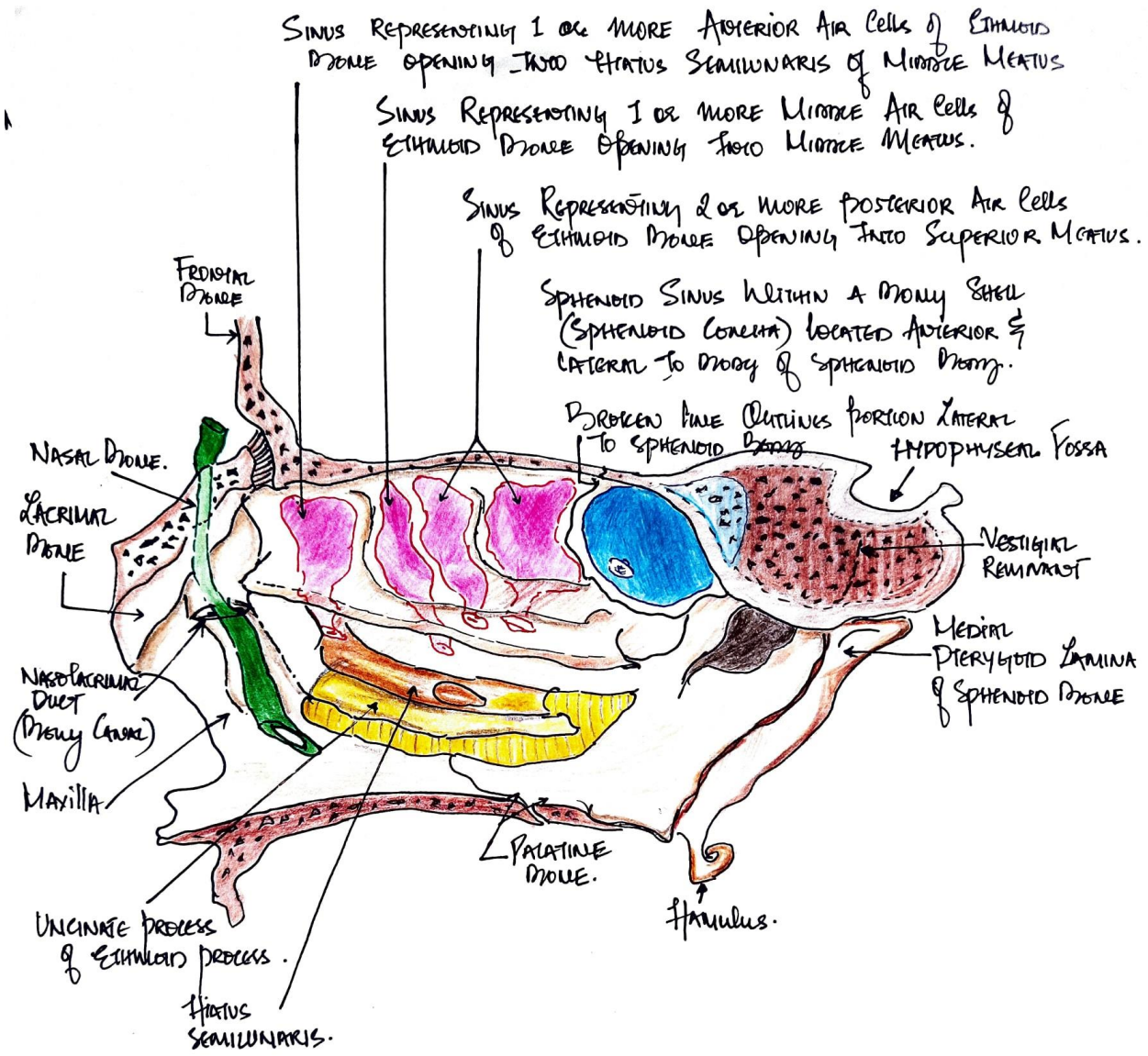


Image-7 Anterior and Posterior ethmoidal air cells and its drainage Pathways, Sphenoid sinus.

FRONTAL SINUS:

The anatomy of the frontal sinus and its outflow tracts are highly complex. The frontal sinus represents pneumatization within the frontal bone of the skull, defined by a thicker anterior and thinner posterior table. The paired frontal sinuses are separated by an inter-sinus septation and are typically asymmetric. The posterior table separates the frontal lobe from the frontal sinus. The floor of the frontal sinus is the orbital roof.

The frontal sinus outflow tract has an hourglass configuration. The three components of the outflow tract from superior to inferior, are the infundibulum, frontal sinus ostium and frontal recess. The frontal sinus infundibulum is a funnel shaped space at the medial, posterior, inferior aspect of the frontal sinus that narrows towards the narrowest point of the hourglass, the frontal sinus ostium.

The widening of the outflow tract inferior to the ostium and into the middle meatus is termed the frontal recess. The frontal recess is defined by the surrounding structures: (1) the lamina papyracea laterally, (2) the anterior portion of the middle turbinate medially, (3) the ethmoid bulla or supra-bullar recess posteriorly, and (4) agger nasi cell, frontal beak and frontal cells anteriorly.

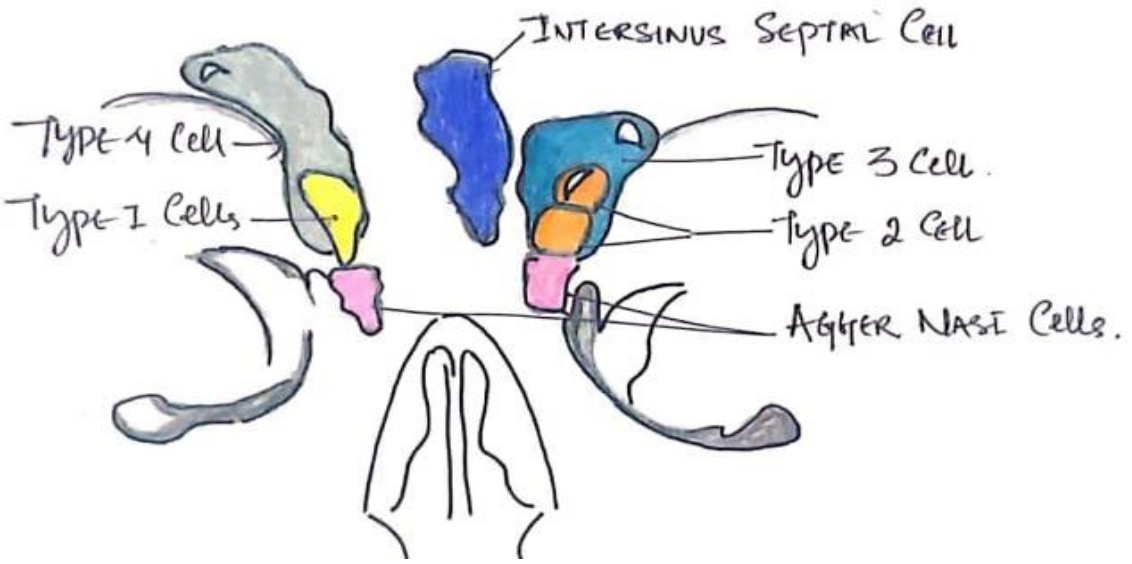
The relationship between the superior attachment of the uncinate and the frontal recess is variable, influencing the drainage pattern of the frontal recess. Attachment of it to the lamina papyracea results in the infundibulum terminating in a blind pouch superiorly termed the recess terminalis. The frontal recess in this situation opens medial to the infundibulum, between the middle turbinate and the uncinate process.

In the second variant, the uncinate process attaches to the fovea ethmoidalis. In this situation, the frontal recess clears directly into the ethmoid infundibulum, lateral to the uncinate process.
This is the same drainage pattern for the third variant in which the uncinate process attaches to the middle turbinate.

Frontal cells refer to anterior ethmoidal cells that originate in the infundibulum and pneumatize within the frontal sinus outflow tract. Originally classified by Bent and Kuhn,9 the clinical significance of frontal cells relates to their potential for outflow tract obstruction. Additionally, understanding the pattern is critical for successful endoscopic surgery of the frontal recess.

Frontal cells are located above the agger nasi cell.
A type 1 frontal cell is a single air cell within the recess.
A type 2 cell is a group of two or more cells within the recess.
A type 3 cell is a single cell that extends from the recess into the frontal sinus.
A type 4 cell is an isolated cell completely within the frontal sinus

FIGURE 8: TYPES OF FRONTAL AIR CELLS.



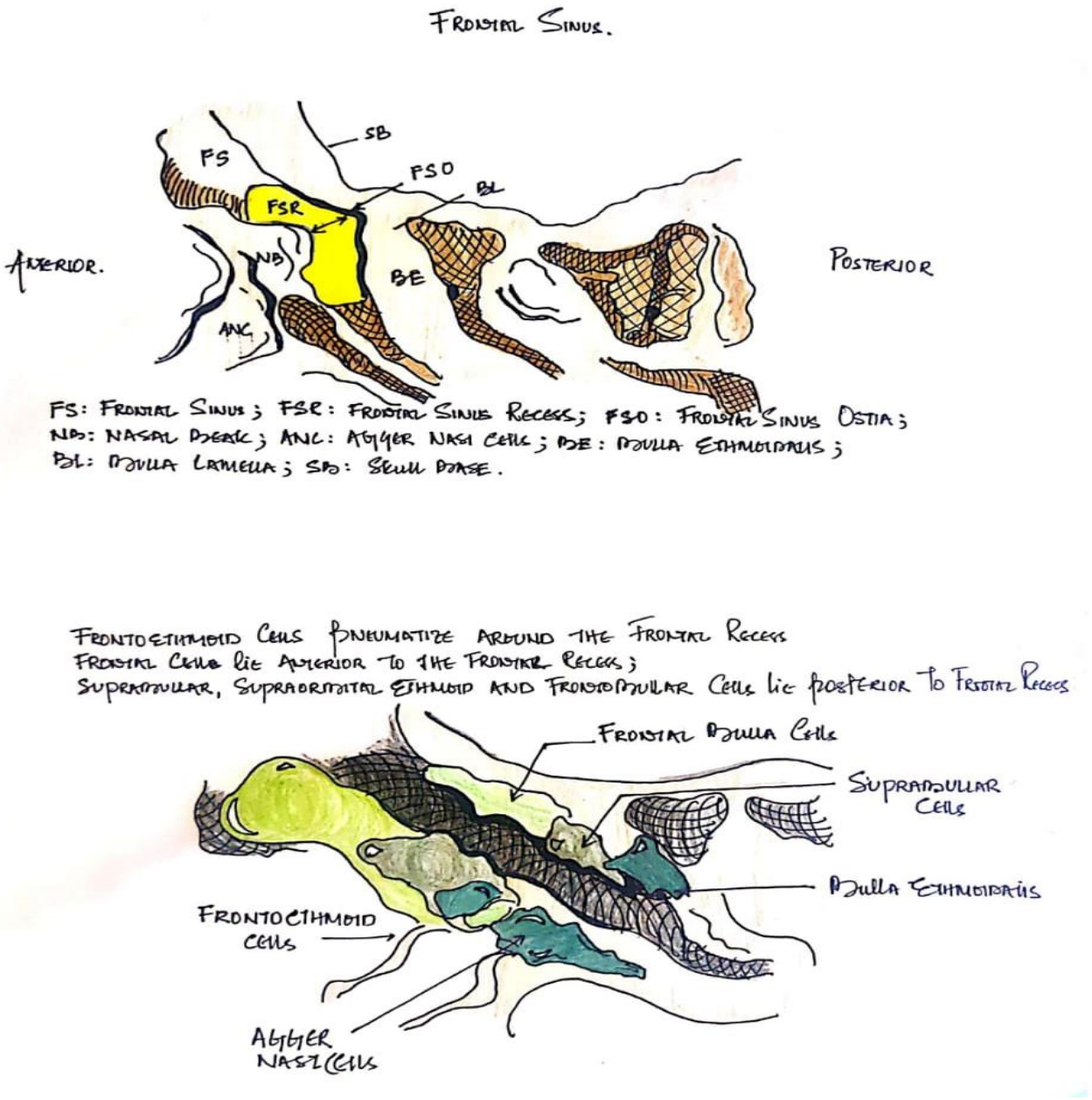


FIGURE 9: Frontoethmoid cells pneumatize around the frontal recess. Frontal cells lie anterior to the frontal recess; suprabullar, supraorbital ethmoid, and frontobullar cells lie posterior to the frontal recess.

Air conditioning: They serve as supplementary chambers for conditioning the inspired air by heating and moistening. Vocal response: They act as resonating chambers and add to quality of voice. Thermal insulators: They protect the structures in orbit and cranial fossac from the intratemporal variations.

Balance of head: It reduces weight of the bones of the face, thereby aiding in the balance of head,

MUCOCILIARY CLEARANCE

Drainage and ventilation are two most important factors in the maintenance of normal physiology of paranasal sinuses. It depends upon the amount of mucus produced, composition of mucus, effectiveness of ciliary beat, mucosal resorption, condition of ostia and ethmoidal clefts,"

The mucus film has two layers: an inner serous layer, called the sol phase, in which cilia beat and an outer more viscous layer, the gel phase, which is transported by the ciliary beat. This functions like a conveyor belt. Normal nasal mucus exists at a pH range of 7.5 to 7.6."[1]

In maxillary sinus, secretion transport starts from the floor of sinus in a stellate pattern. The mucus from anterior, medial, posterior, lateral wall and roof of sinus converge at the natural osteum. This is finally drained into middle meatus. Frontal sinus has active inward transportation of mucus. Due to whorled pattern of cilia, mucus is circulated again and again. Finally mucus from frontal sinus drains into frontal recess. The anterior ethmoidal cells drain into middle meatus and posterior ethmoidal cells into sphenoethmoidal cells. In the sphenoidal cells, mucus undergoes a spiral transport and Drains into sphenoethmoid cells. All these secretions finally drains into lateral nasal wall and from there to Nasopharynx.

CHRONIC RHINOSINUSITIS

The term "sinusitis" refers to a group of disorders characterized by inflammation of the mucosa of the paranasal sinuses. Because the inflammation nearly always also involves the nose, it is now accepted that "rhinosinusitis" is the preferred term to describe this inflammation of the nose and paranasal sinuses[12].

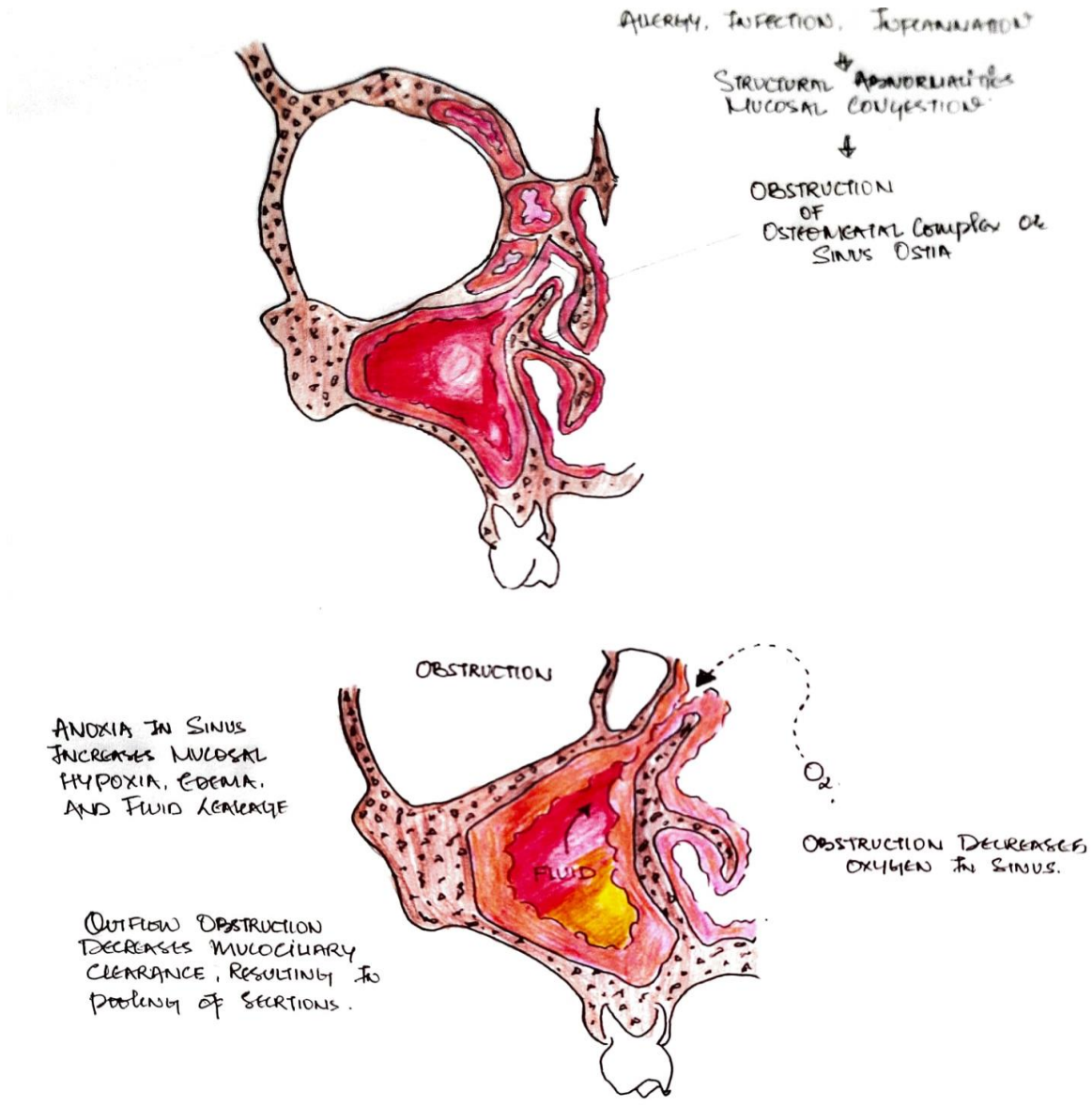


Image-10: Image showing pathophysiology of Chronic rhinosinusitis.

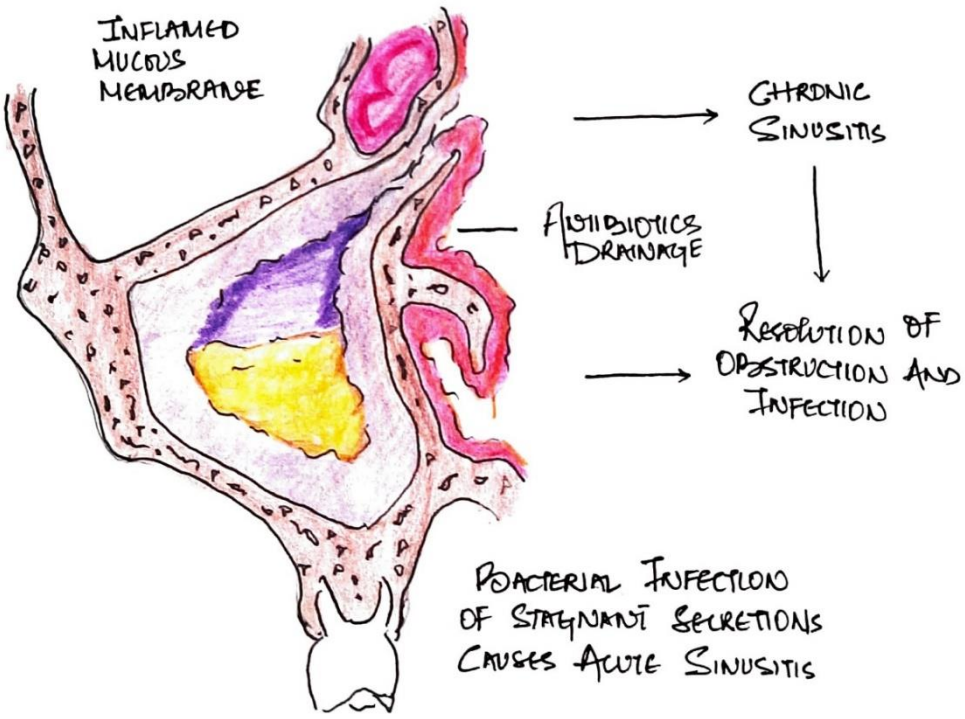


Image-11: Image showing mucosal edema with purulent secretion retained in the maxillary sinus.

To highlight the role of inflammation better, newer definitions have been applied to rhinosinusitis, that is, a group of disorders characterized by inflammation of the mucosa of the nose and paranasal sinuses. Chronic rhinosinusitis (CRS) is rhinosinusitis of at least 12 consecutive weeks duration[12].

Therefore, CRS is a group of disorders characterized by inflammation of the mucosa of the nose and paranasal sinuses of at least 12 consecutive weeks duration [12,13]

A widely accepted set of classifications or definitions was developed by the Rhinosinusitis Task Force of the American Academy of Otolaryngology-Head and Neck Surgery and reported by Lanza and Kenned

CLASSIFICATION	DURATION
ACUTE RHINOSINUSITIS	7 DAYS to <4WEEKS
SUB ACUTE RHINOSINUSITIS	4-12 WEEKS
RECURRENT ACUTE RHINOSINISITIS	>4 EPISODES OF ARS per year
CHRONIC RHINOSINUSITIS	>12WEEKS
ACUTE EXACERBATION OF CHRONIC	Sudden worsening of CRS with return to baseline after

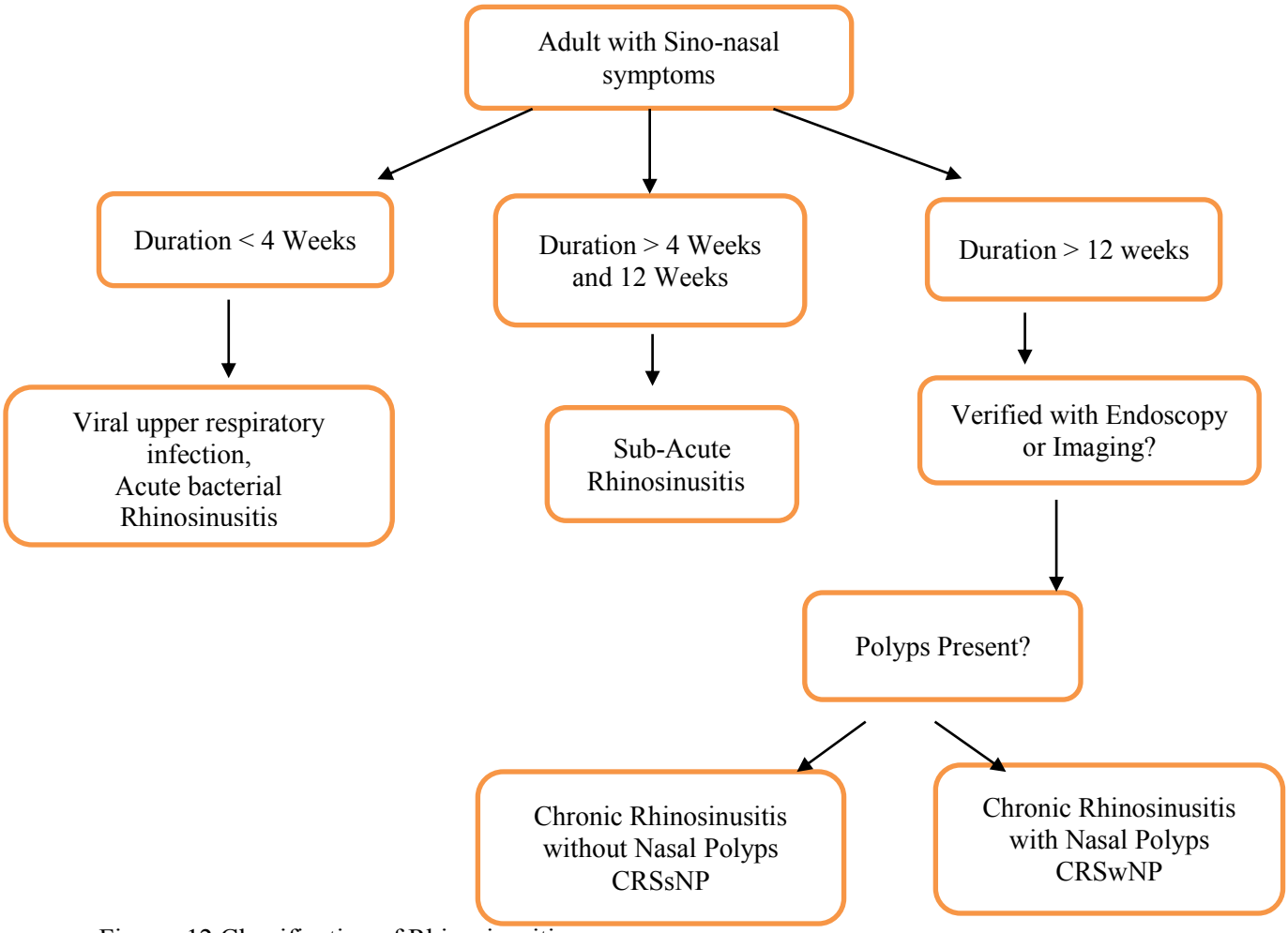


Figure: 12 Classification of Rhinosinusitis

Acute Rhinosinusitis (ARS) Adult

Sinonasal inflammation lasting less than 4 weeks associated with the sudden onset of symptoms. Symptoms must include both:

1. Nasal blockage/obstruction/congestion OR nasal discharge (anterior/posterior)
2. AND Facial pain/pressure OR reduction/loss of smell
3. Radiology and endoscopy are not required for diagnosis[14,15]

Acute Rhinosinusitis (ARS) Pediatric

Sinonasal inflammation lasting less than 12 weeks associated with the sudden onset of symptoms. Symptoms must include two or more of the following:

1. Nasal blockage/obstruction/congestion
2. Discolored nasal discharge (anterior/posterior)
3. Cough (daytime and night-time[14,15]

Recurrent Acute Rhinosinusitis (RARS)

Four or more episodes of ARS per year with distinct symptom-free intervals between each episode. Each episode must meet the above criteria for ARS.[14,15]

Chronic Rhinosinusitis (CRS)

Sinonasal inflammation persisting for more than 12 weeks, with a combination of at least two of the following symptoms and confirmed by endoscopic or radiographic findings:

1. nasal obstruction/congestion/blockage
2. anterior or posterior (mucopurulent) nasal drainage
3. loss or decreased sense of smell
4. facial pressure/pain/fullness AND presence of polyps[14,15]

Diagnostically, CRSsNP and CRSwNP differ only in the objective finding of nasal polyposis. Additional regional and systemic symptoms associated with CRS include oropharyngeal discomfort, otalgia, halitosis, dental pain, cough, malaise, headache and fatigue.

Acute Exacerbation of Chronic Rhinosinusitis (AECRS)

Sudden worsening of CRS symptoms with a return to baseline symptoms, often after treatment

Greater than or equal to 12 weeks of: Two or more of the following symptoms:

Nasal discharge (rhinorrhea or post-nasal drip), Nasal obstruction or congestion, Hyposmia, Facial pressure or pain

Cough (in Pediatric CRS)

AND

One or more of the following objective findings:

Evidence of inflammation on nasal endoscopy or computed tomography

Evidence of purulence coming from paranasal sinuses or ostiomeatal complex

AND

CRS is divided in to CRSsNP or CRSwNP based on the presence or absence of nasal polyps[14,15]

The taskforce in order to accommodate the different needs gave definitions that can be applied in appropriate studies. In this way the taskforce tried to improve the comparability of studies and hence enhanced the evidence based diagnosis and treatment of patients with rhinosinusitis and nasal polyps.

CRS is best considered as a group of heterogeneous disorders due to a multitude of causes that result in mild to severe symptomatic inflammation of the sinonasal mucosa. The management of this complex disease is therefore a challenge. The most simplified classification divides CRS into those patients who have nasal polyps (CRSwNP) and those without (CRSsNP)[15]

CHRONIC RHINOSINUSITIS DIFFERENTIATION BY INFLAMMATORY MEDIATORS:

CRSwNP	➢ Tissue Oedema, low Tumour growth factor -beta and lot T-reg activity ➢ High tissue eosinophilia and IgE, increased IL-5 and IL-13 (Th2 polarisation)
CRSsNP	➢ Fibrosis, less eosinophilic infiltration ➢ Increased interferons- gamma, tumour growth factor – beta and T-regulatory activity (Th 1 polarisation)

Although all cases of rhinosinusitis involve inflammation of the mucosal linings, in practical setting, the main focus is on those patients in whom this inflammation leads to symptoms. Because of this important relationship to symptoms, the Rhinosinusitis Task Force's definitions include a group of symptoms to be applied

to these conditions to allow for clinical diagnosis .[16]

TASK FORCE CRITERIA: Rhinosinusitis symptoms/signs (requires two major factors, or one major and two minor).

MAJOR SYMPTOMS	**MINOR SYMPTOMS**
Facial Pain/Pressure	Headache
Facial Congestion/Fullness	Fever (Non Acute)
Nasal Obstruction/ Blockage	Halitosis
Nasal Discharge/ Purulence/ Discoloured Posterior Drainage	Fatigue
Hyposmia/ Anosmia	Dental Pain
Purulence on nasal examination	Cough
Fever (Acute RS only)	Ear Pain/ Pressure/Fullness

Epidemiology

CRS is the fifth most common diagnosis for an antibiotic prescription worldwide.11,16. Despite its prevalence, there is a paucity of accurate epidemiologic data for CRS, especially for CRSsNP. Patient surveys in the United States have found a 15%–16% prevalence of CRS. A study conducted in Canada, Korea, Scotland, Europe, and Sao Paulo shows prevalence of CRS ranges from 1%–11%. 11,17,18 Men and women are both affected by CRSwNP. In general, nasal polyps occur in all races and become more common with age, with the average age of onset being 42 years.[17,18]

Etiology

Numerous hypotheses have been proposed with a great deal of overlap, supporting a multifactorial basis. One classification method separates potential contributing entities into host and environmental factors. The heterogeneous nature of CRS is important to understand when planning treatment for this diverse group of patients whose disease may have arisen from very different underlying etiologies[19,20]

Factors associated with CRS:

SYSTEMIC HOST FACTORS	LOCAL HOST FACTORS	ENVIROMENTAL FACTORS
ALLERGY	ANATOMIC	MICRO-ORGANISM (Bacteria. Viruses. Fungi)
IMMUNODEFICIENCIES	NEOPLASM	NOXIOUS CHEMICALS
MUCOCILIARY DYSFUNCTION	ACQUIRED MUCOCILIARY DYSFUNCTION	MEDICATIONS
GRANULOMATOUS DISEASE	PREVIOUS TRAUMA OR SURGERY	
GERD		
ASPIRIN INTOLERANCE		

CRSwNP in the Caucasian population is associated more closely with high tissue eosinophilia and increased T helper (Th)-2 cytokine expression (interleukin [IL]-5 and IL-13) as well as nasal obstruction and smell loss, whereas CRSsNP may have more Th-1 polarization and less eosinophilic infiltration.[21]

Defects in the coordinated mechanical barrier and/or the innate immune response of the sinonasal epithelium has also been proposed as a mechanism for CRS. [22,23]

This susceptibility may be based on host genetic factors, predisposing some individuals to mechanical barrier failure in the presence of environmental stress. CRS is a common problem in patients with Kartagener‘s syndrome, primary ciliary dyskinesia, and cystic fibrosis. Inability of the sinonasal cilia to transport viscous mucus causes ciliary malfunction leading to CRS. Epithelial damage or host barrier dysfunction will result in colonization of the sinonasal mucosa with Staphylococcus aureus. Subsequent secretion of super-antigenic toxins may lead to a skewed Th-2 host inflammatory response with generation of local polyclonal immunoglobulin E (IgE), promotion of eosinophil survival and mast cell degranulation with alteration of eicosanoid metabolism. The sum of these local tissue effects may lead to polyp formation.[24,25]

The role of microbes as causative agents in CRS is not clear, but microbial infection and biofilms may contributeto the propagation of CRS. S. aureus is the most common bacterial pathogen identified in CRS patients. Coagulase-negative Staphylococcus and anaerobic and Gram-negative bacteria are also commonly cultured from CRS patients [25,26]

Diagnosis

Symptoms : At the first notification of the problem, the diagnosis of rhinosinusitis is presumed on symptoms alone. The symptoms are mainly the same in acute rhinosinusitis (ARS), CRSsNP and CRSwNP, but the pattern and intensity may vary. Litvack et al in their study reported a significantly increased risk of hyposmia (odds ratio = 2.4 and anosmia (Odds ration =13.2) in nasal polyposis patients compared to CRSsNP. (14) After inquiring the symptoms, anterior rhinoscopy remains the first step in clinical examination, although it is of limited value [27]

Examinations

1**) Nasal endoscopy**

Nasal endoscopy involves passing a frequently rigid, or sometimes flexible, endoscope through the nostril to examine the nasal cavity, middle and superior meati, nasopharynx and mucociliary drainage pathways. Nasal endoscopy has a major contribution in the diagnosis of CRS and affords significantly better illumination and visualization of the nasal cavity compared to anterior rhinoscopy.[28,29]

2**) Imaging**

The plain sinus x-ray has limited usefulness for the diagnosis of rhinosinusitis and for evaluation of the response to therapy. CT scanning is the modality of choice for the paranasal sinuses due to optimal display of differences between air, bone and soft tissue. As mentioned before, CT scanning is not the primary step in the diagnosis of rhinosinusitis, but has the aim to affirm the symptoms and findings of endoscopic examination after failure of medical therapy. Because of many insignificant abnormalities found in the normal population during scans.15, the diagnosis of CRS based on imaging, in absence of symptoms, is inappropriate.[30,31]

3) **Nasal cytology, biopsy and bacteriology**

Generally, cytology has not proven a useful tool in diagnosis of rhinosinusitis. However, lavage with 0.9% saline, micro-suction, nasal brushes, nasal tampons, disposable scrapers, etc. are techniques which are largely used for clinical research.[32,33]

CRS is diagnosed based on clinical symptoms and objective evaluation. Symptoms must be present for at least 12 consecutive weeks. Several studies have shown using symptoms alone to diagnose CRS can be nonspecific. Therefore, nasal endoscopy or imaging must also be used to confirm the presence of sinonasal disease to increase the specificity of diagnosis.[34,35]

Endoscopic findings suggestive of CRS include mucopurulent discharge, nasal polyps or polypoid change, and/or mucosal edema obstructing the middle meatus.[36]

Computed tomography (CT) is considered the gold standard for imaging in CRS. Although CT scans cannot distinguish between inflammation and infection, they do seem to correlate fairly well with the extent of disease. Findings consistent with CRS include isolated or diffuse mucosal thickening, bone changes, or air-fluid levels.[37]

TREATMENT:

Medical treatment.

Medical treatment involved in CRS include:

- Allergen and/or irritant avoidance
- Douching
- Corticosteroids
- Decongestants
- Antibiotics
- Antifungals
- Antileukotrienes
- Aspirin
- Immunotherapy
- Other therapies

Corticosteroids

Systemic corticosteroids (oral, intramuscular) can reduce the size of nasal polyps to an extent that is comparable with surgery. Topical corticosteroids reduce the recurrence of nasal polyps and should be used routinely in the long term, preferably employing a molecule with low systemic absorption in drop form in the head upside down position. In non-polypoid chronic rhinosinusitis, topical corticosteroid shows modest efficacy in reducing symptoms during acute exacerbations when combined with antibiotics.[37,38]

Antibiotics

Antibiotics are needed for acute severe bacterial sinusitis; their place in the chronic form is controversial. Two routes are available: topical and oral. Oral short course is used in the treatment of acute exacerbations of CRS.[37,38]

Antihistamines /Antileukotrienes

There is little evidence of the efficacy of antihistamines in chronic rhinosinusitis, presumably because the majority have little or no effect on nasal blockage, Leukotriene antagonists, such as Montelukast, Zafirlukast, and Zileuton, have been evaluated in numerous studies involving patients with CRSwNP[37.38]

SURGICAL TREATMENT

Functional endoscopic sinus surgery (FESS): FESS has now become well established for the treatment of chronic rhinosinusitis refractory to medical treatment

Steps:

1) Uncinectomy

2) Middle meatal antrostomy

3) Anterior Ethmoidectomy

4) Posterior ethmoidectomy

5) Clearance of frontal recess and frontal sinusotomy

6) Sphenoidectomy

SITE	COMPLICATION
ORBIT	NASOLACRIMAL DUCT DAMAGE EXTRA-OCCULAR MUSCLE INJURY INTRA-ORBITAL HAEMORRHAGE/EMPHYSEMA OPTIC NERVE DAMAGE
INTRACRANIAL	HEAMORRHAE CEREBROSPINAL FLUID LEAK >MENINGITIS
NASAL	HAEMORRHAHE

CONTROL OF BLEEDING

The presence of significant bleeding in the surgical field is a critical factor in the potential success or failure of FESS. When significant bleeding is present, recognition of anatomical landmarks becomes difficult.

Bleeding obscures surgical planes and makes the identification of the drainage pathways of the sinuses difficult. Cell walls become difficult to distinguish from the lamina papyracea or skull base and the risk of causing complications increases. If the patient has significant inflammation of the sinuses, from chronic infection or the presence of pus/fungal debris, increased vascularity will often contribute to more bleeding.23,26 If the surgeon attempts to manipulate an instrument in the surgical field after the discernible anatomy is covered in blood, the risk of a complication increases. In addition, greater surgical trauma may occur, cells may be left behind and there is an increased likelihood of postoperative scarring and failure of the surgical procedure. It is therefore critical to optimize the surgical field and, in so doing, make the surgical dissection as easy as possible.[37,38]

Bleeding is more common close to large vessels. Stamberger has included 3 areas which are responsible for extensive bleeding during sinus surgery.

1. Anterior ethmoidal artery located in an osseous channel close to ethmoid roof

2. Branch of sphenopalatine artery close to the posterior end of middle turbinate.

This is more prone for injury in patients with well pneumatized middle turbinate (concha bullosa)

3. Damage to sphenopalatine artery while attempting to widen the sphenoidal ostium Surgical bleeding during FESS has been classified into: Arterial, Venous and Capillary Out of these three types of bleeding it is the capillary bleed that causes the most trouble during FESS [38.39]

MITOMYCIN C

Mitomycin-C is an antibiotic produced by Streptomyces caespitosus with both antineoplastic and antiproliferative properties. [41]

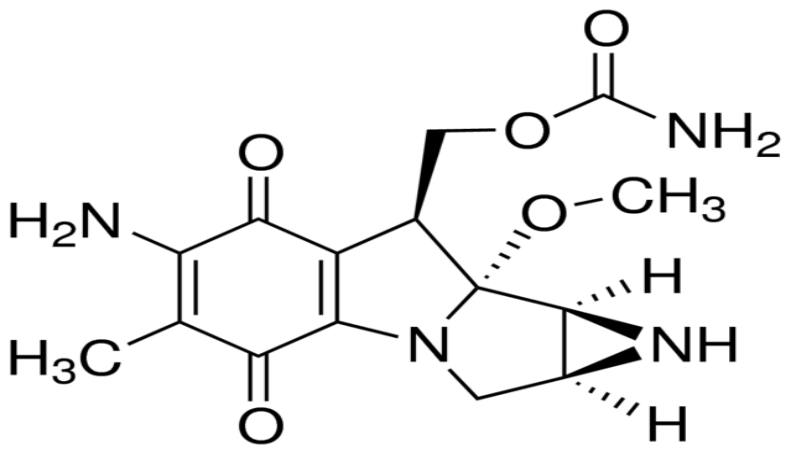


FIGURE 11: MITOMYCIN C

Mechanism of Action:

After intracellular enzymatic or Spontaneous chemical alteration, mitomycin becomes a bifunctional or trifunctional alkylating agent. The drug inhibits DNA synthesis and cross-links DNA at the N6 Position of Adenine and at the O6 and N7 positions of guanine. Attempts to repair DNA lead to strand break.

MMC is a potent radiosensitizer, teratogen and carcinogen in rodents. Resistance has been described to deficient activation, intracellular inactivation of the reduced Q-form and Pgp-mediated drug efflux. [41,42]

As an antineoplastic drug, it functions as an alkylating agent that causes cross-linking of DNA and inhibits RNA and protein synthesis. Topically, it functions as an antiproliferative agent inhibiting fibroblast activity; however, the exact mechanism is not well understood.[41,42]

The use of mitomycin-C to reduce scar formation has been most described in the ophthalmology literature. It has been used successfully as a medical adjuvant to prevent stenosis after glaucoma surgery, dacryocystorhinostomy, optic nerve sheath fenestration, and pterygium surgery.
More recently, the use of mitomycin-C has been reported in the otolaryngology literature as a successful adjuvant treatment in the endoscopic laser management of laryngeal and tracheal stenosis. Myelosuppression and other systemic complications have not been reported with the topical use of mitomycin-C.[43,44]

Wound healing is a sequential cascade of overlapping processes that occur in a careful, regulated, and reproducible manner. Growth factors are glycoproteins or peptides that contribute to wound healing by controlling the proliferation and migration of cells that modulate epithelialization, angiogenesis, and collagen metabolism. [44,45]

Two of the major growth factors that have a direct effect on wound healing are basic fibroblast growth factor (bFGF) and transforming growth factor (TGF)-1. By manipulating growth factors, it may be possible to modify the wound healing process in different clinical states. Modulators are external agents that alter the autocrine growth factor milieu, thereby allowing optimal wound healing. Once a modulator‘s effect is known, it can be placed into a wound to achieve the desired healing response.

The effects of mitomycin-C on wound healing have been investigated. Occleston et al.4 showed initial increase in the production TGF- 1 and bFGF by Tenon‘s capsule fibroblasts exposed to mitomycin-C. [44,45] These levels then decreased toward those of controls by day 48 after treatment. In this study, mitomycin-C caused a significant reduction in collagen type I and fibronectin production compared with those of controls. [44,45]

Scar formation is a natural outcome of wound healing, a process that primarily involves the proliferation, transformation and migration of the fibroblast cells, resulting in tissue remodelling. The resident fibroblast cells, in response to an injury, undergo transient transformation into a more contractile and migratory phenotype called myofibroblast cells.4 This transformation marks the onset of wound healing and is mediated by factors such as transforming growth factor-β family (TGF-β) of cytokines and other factors.5–7 These cells have the ability to synthesise more extracellular matrix proteins, growth factors and receptors required for quick wound closure compared with the fibroblast cells.[46,47]

Earlier studies have only shown that when exposed to higher concentrations of MMC the viability of human nasal mucosal fibroblasts (HNMFs) significantly reduces, which clinically might present as mucosal burns. The need is therefore to understand the influence of MMC on the process of wound healing in order to arrive at an optimum concentration that would prevent scarring of the tissue without adversely affecting cell and tissue health.[48]

Thus, in this study, the functional aspects of wound healing such as cell contraction and migration have been studied in response to the application of MMC to HNMFs. The normal wound healing process has been simulated in vitro using the collagen contraction and wound healing assays, and to our best knowledge, this is the first study that addresses the influence of MMC treatment on wound healing in HNMFs.[49,50]

MATERIALS & METHODS

MATERIALS AND METHODS

SOURCE OF DATA :

This Comparative study was conducted in patients who had chronic Rhinosinusitis with failure of medical management, who presented to the Department of E.N.T in R.L Jalappa Hospital & Research Centre attached to ~~–S~~ri Devaraj Urs Medical College, Tamaka, Kolar from January 2010 to October 2021.

INCLUSION CRITERIA:

1. **P**atients in the age Group of 16-65 years diagnosed having Chronic Rhinosinusitis with Failure of conservative treatment for at least 12 consecutive weeks duration and undergoing ~~–B~~ilateral Middle Meatal Antrostomy".

EXCLUSION CRITERIA:

1. Patients with unilateral chronic rhinosinusitis and undergoing unilateral FESS.
2. Patients with Acute exacerbation of symptoms.
3. Patients with established asthma, uncontrolled hypertension, uncontrolled diabetes, suspected cystic fibrosis.
4. Patients with drug induced and hormonal causes of rhinitis.
5. Patients with presence of bleeding diathesis.
6. Patients with previous history of nasal surgeries.
7. Patients refusing to undergo CT scan, patients refusing endoscopic surgery, patients with established or impending complications

TYPE OF STUDY: Prospective Interventional Comparative study

METHOD OF COLLECTION OF DATA

- Patients with chronic rhinosinusitis after qualifying the inclusion criteria and exclusion criteria were enrolled in the study after written informed consent regarding their enrollment in the study, type of intervention and follow up, after explaining the possible complications.

- A detailed clinical history was elicited. A meticulous ENT examination was performed. Clinical criteria for diagnosis of chronic Rhinosinusitis i.e Task force criteria were adopted. A diagnostic nasal endoscopy was done.

- Patients were enrolled in the study only after obtaining informed consent by explaining the intervention, its benefits and possible complications.

- Complete blood count (CBC), Renal function test (RFT), Serum Electrolytes, Coagulation profile, Electrocardiogram (ECG), Chest X-Ray (CXR), Computed tomography of Nose and paranasal sinuses (PNS) were done as a part of GA work up.

- The common complications: The reported complications following surgery are bleeding, infection, severe post- oprative pain, dry eyes, The common complications : The reported complications following surgery are bleeding, infection, severe post- operative pain, dry eyes, dry mouth, numbness of cheek or palate.

SURGICAL TECHNIQUE:

FESS:

1. Under General anaesthesia, patient positioned in reverse Trendelenberg position, Endoscope- ‗0' degree 4 mm rigid endoscope was used, along with a high definition camera.
2. Infiltration - 0.5 to 1 ml of 1: 2,00,000 adrenaline solution was injected in the lateral wall of the Nose, on the anterior, posterior part of middle meatus in the region of sphenopalatine foramen using a 25 gauge spinal needle.
3. Medialization of middle turbinate with the help of Freer's Elevator is done in order to visualize the Uncinate process and Infiltration given over Uncinate Process.
4. A ball tipped right angled probe is used to palpate the free edge, confirming position of Uncinate Process. If poorly performed it may result in failure of the Endoscopic Sinus surgery procedure, uncinectomy done.
5. Maxillary sinus Ostia identified and Middle Meatal antrostomy done using conventional instruments. In all cases, we have kept the middle turbinate mucosa as intact as possible.
6. At the completion of the procedure, after through saline wash and strict hemostatsic control, a cottonoid saturated with !ml of mitomycin C in a concentration of 0.5mg/ml was placed on the right side for a period of 3 minutes. This methodology was used in order to avoid Bias as each patient would serve as his or her own control.
7. After application of mytomicin C, care was taken not to irrigate the nasal cavity with normal saline to avoid washing out of the Drug.

8. At the end of the procedure, both nasal cavities were tamponade with merocele packing. This packing was removed after 24 hours after surgery. All patients were discharged within 10 days of hospital stay in stable condition.

9. Post operative clots and crusts were removed in a weekly basis for a period of 4 to 8 weeks, if required. Patients were followed up for 3weeks, 3months, 6months. The final follow up was after 6 months postoperatively. During the time of follow up, an observer who was blinded, a professor from the other unit performed the Diagnostic nasal endoscopy for the assessment antrostomy stenosis.

MEASUREMENTS

The Ostia size of the antrostomy were determined using a self-made probe with a circular tip measuring 1cm*1cm in diameter. This dimension was chosen since an antrostomy is considered stenosed if its diameter is smaller than 5mm*5mm. Although an acceptable antrostomy size has yet to be identified, many authors who consider antrostomy size to be adequate propose this diameter. To reduce visuospatial distortion, the probe will be placed in the same plane as the antrostomy and near to the center of the endoscope's field of view. When the endoscopic image of the probe occupie > 40% of the complete endoscopic field of vision for exact measurements, the stenosis will be assessed.

The antrostomy might be quantified reliably and consistently by taking an image under these settings. During this study, the patients‘ medical records were checked for bouts of recurrent sinusitis.

IMAGE 13: SELF MADE PROBE: MEASURING 1CMX1CM

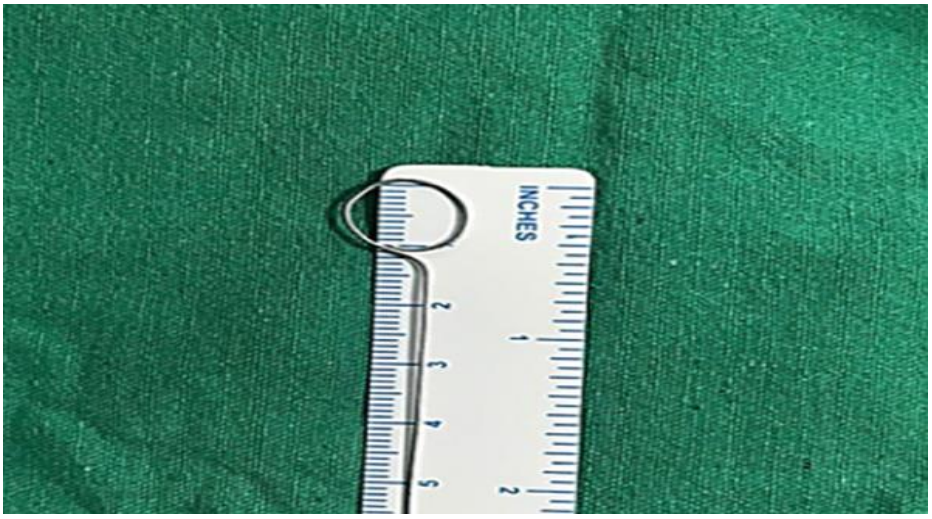
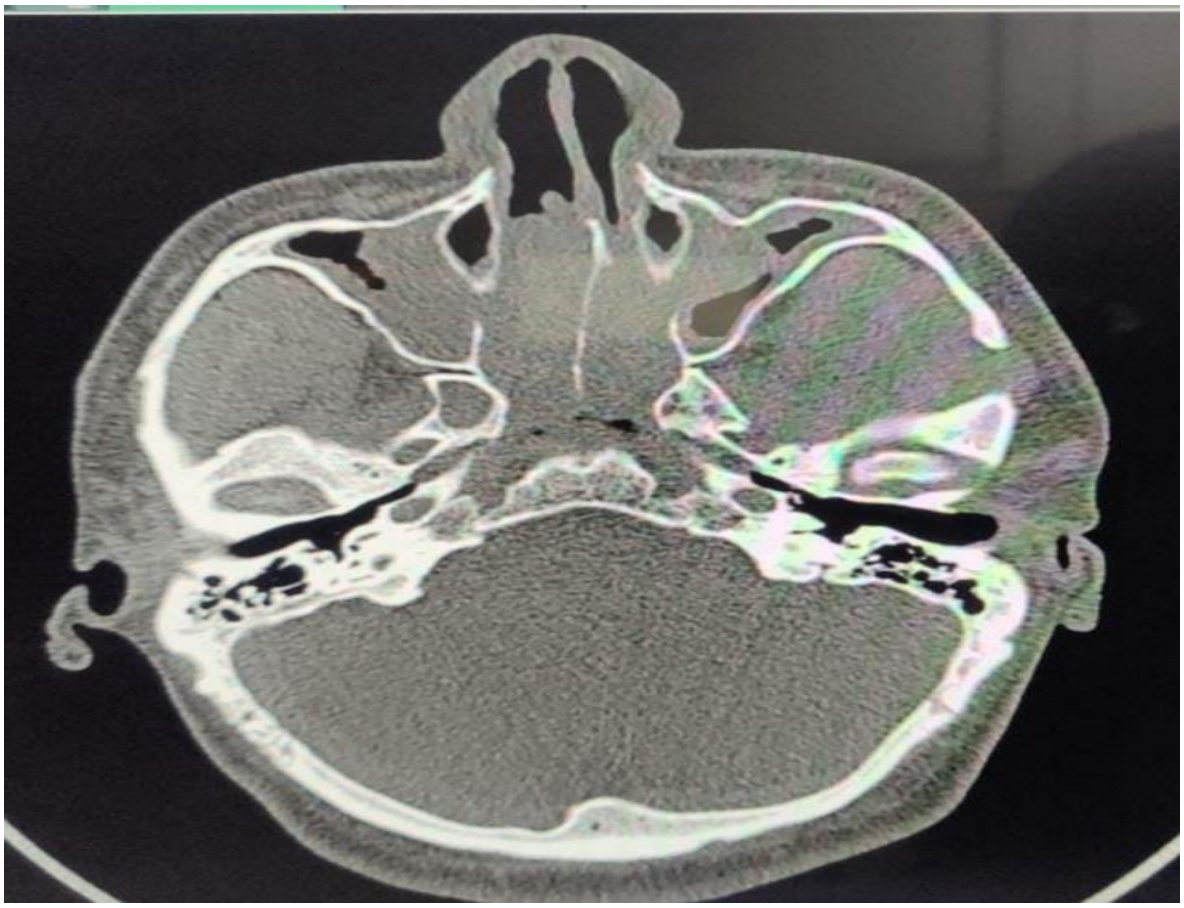


IMAGE 14: CASE 1: CT SCAN



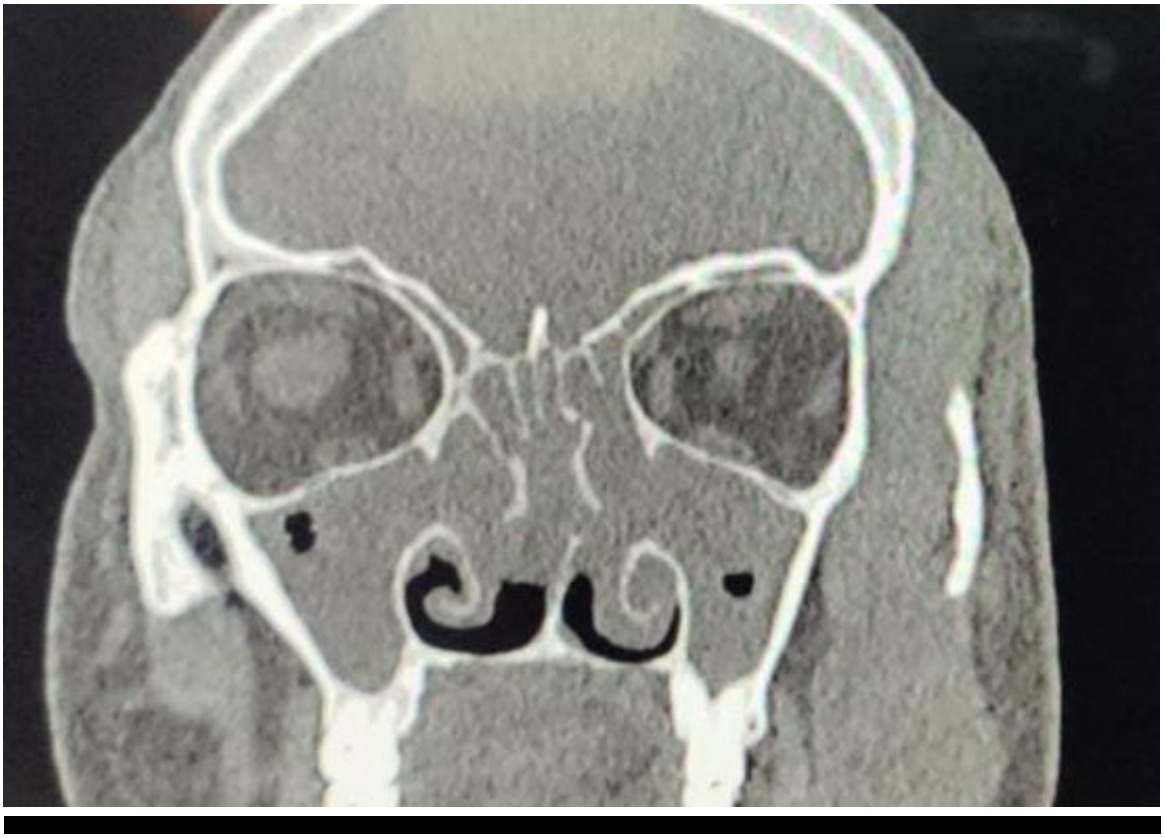
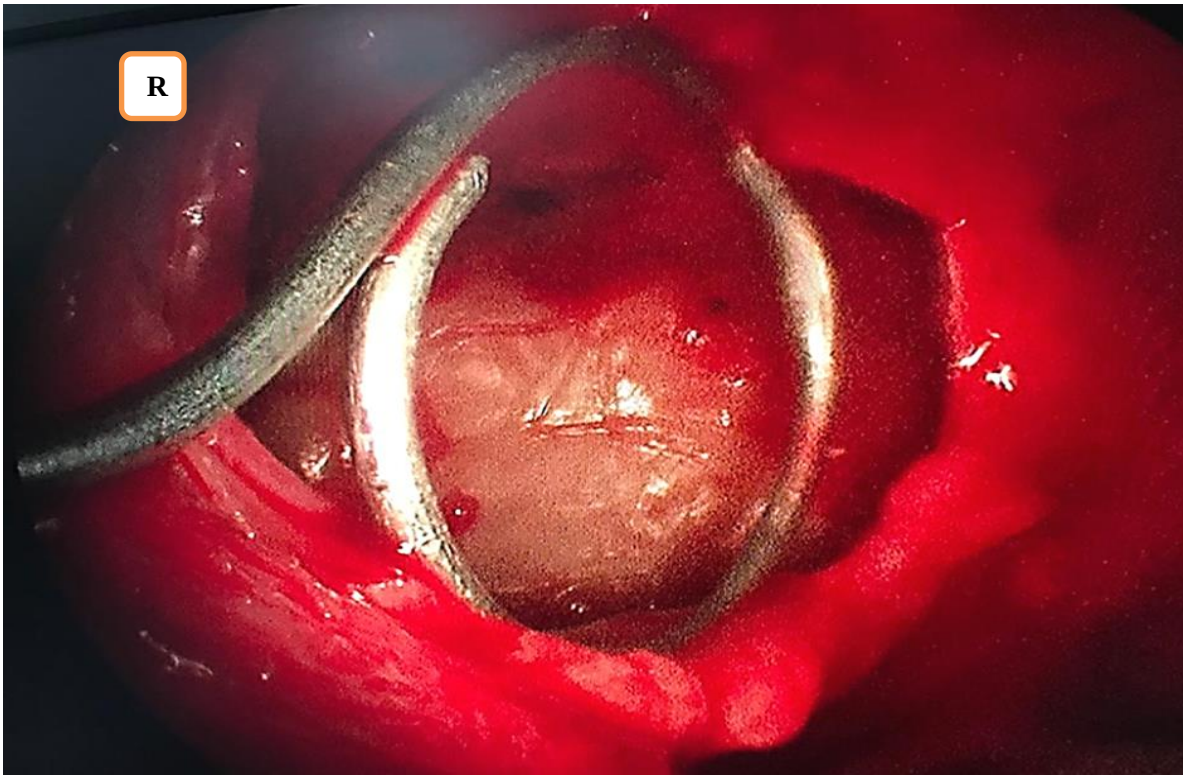


IMAGE 15: INTRA-OPERATIVE IMAGES:
OSTIA MEASURING 1CMx1CM



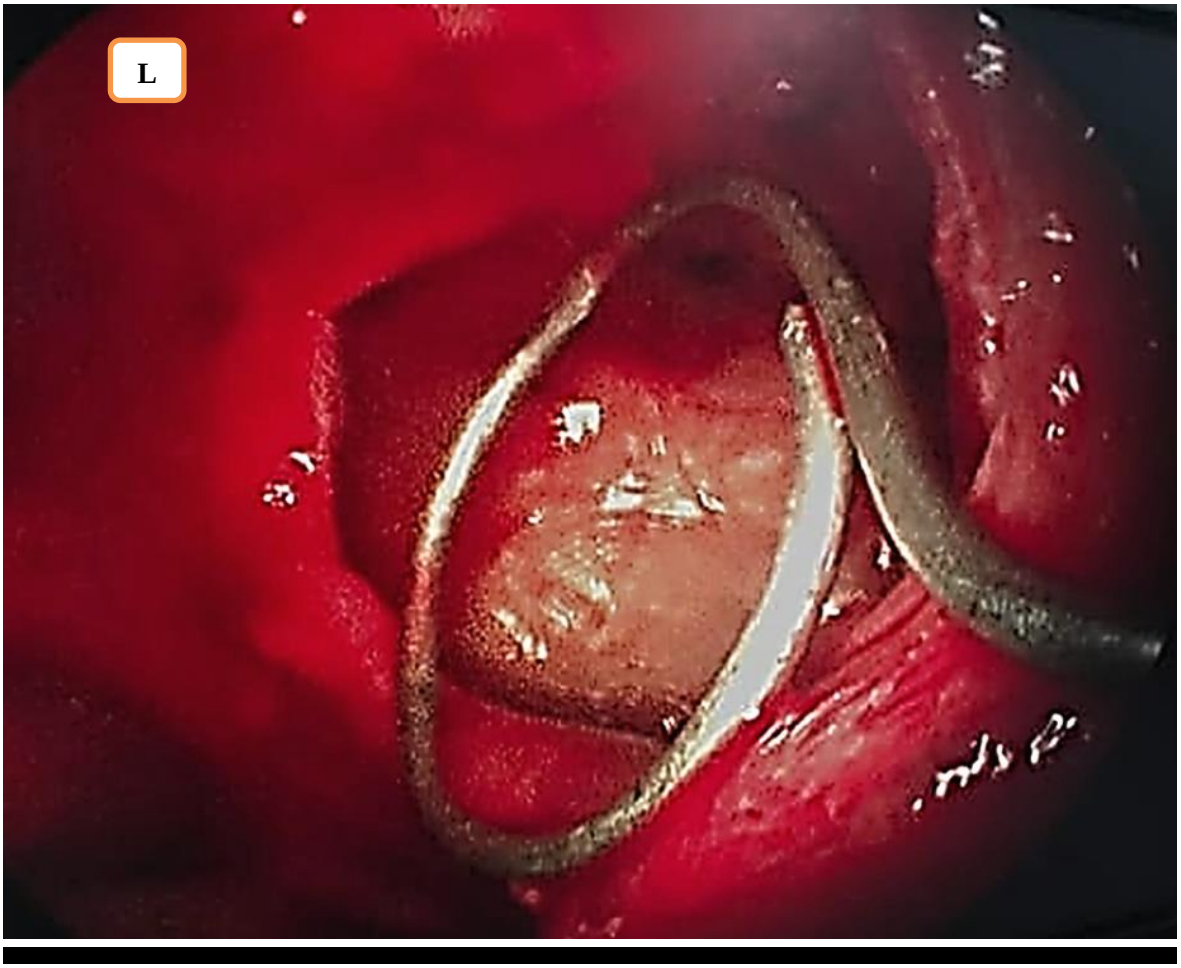
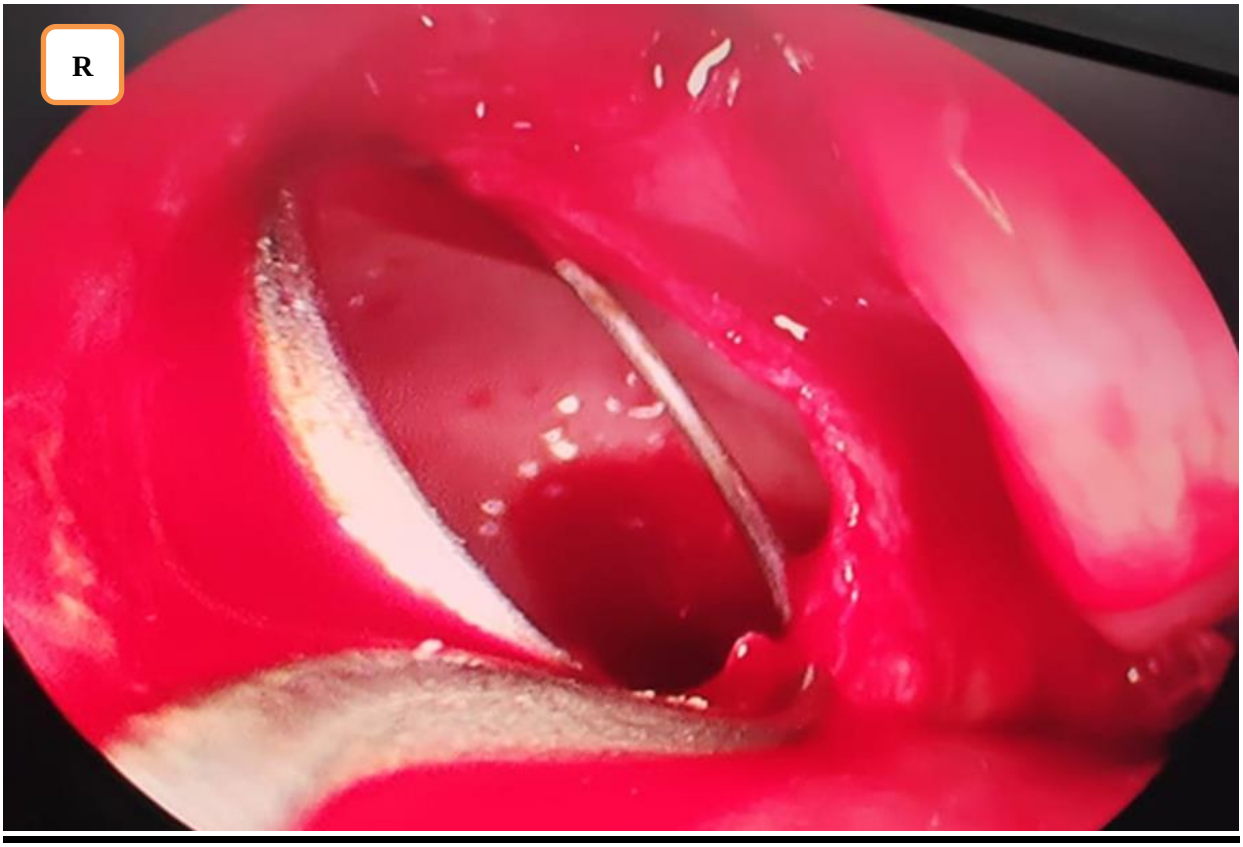


IMAGE 16: FOLLOW UP: 3 WEEKS



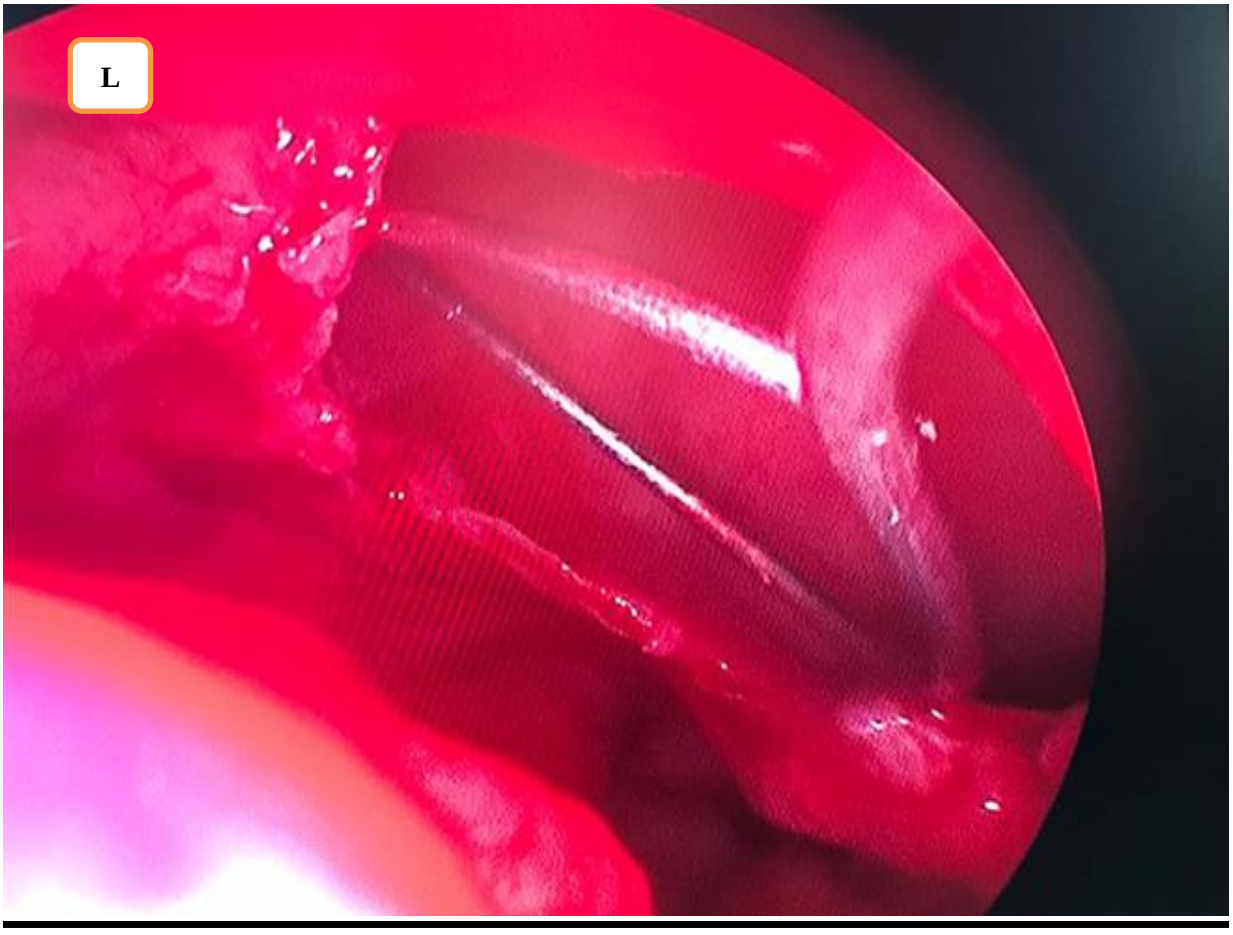
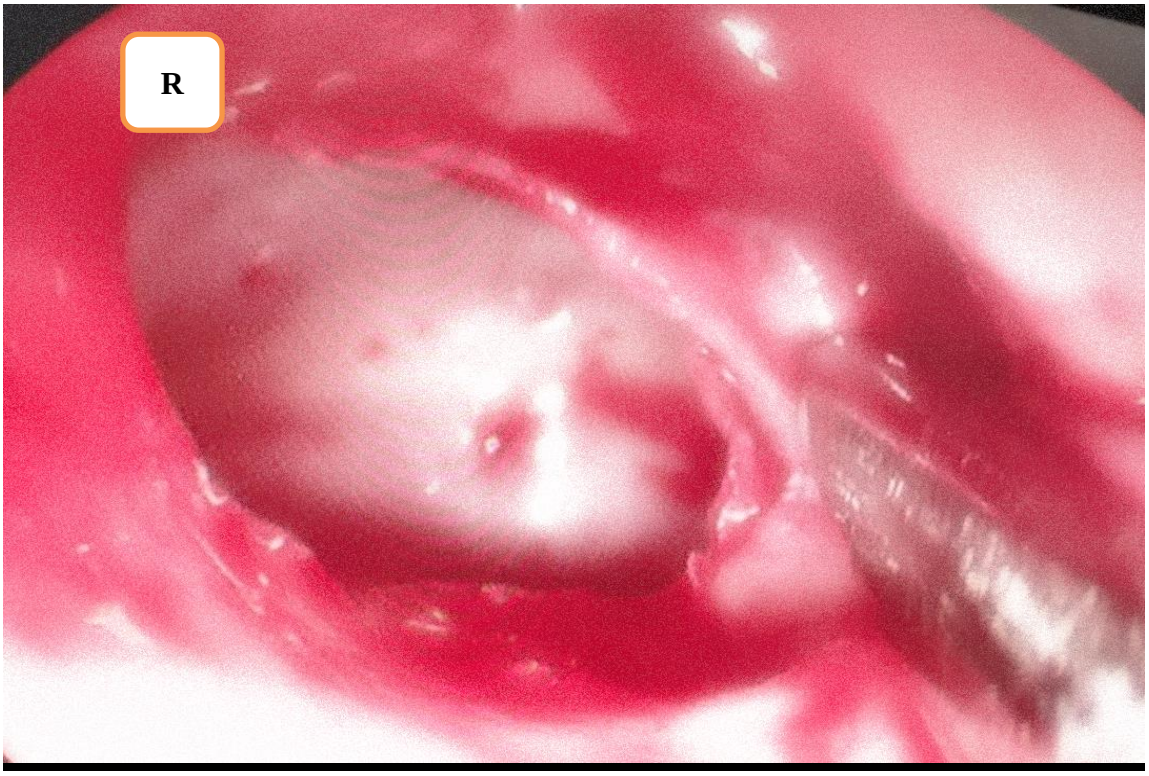


IMAGE 17: FOLLOW UP: 3RD MONTH



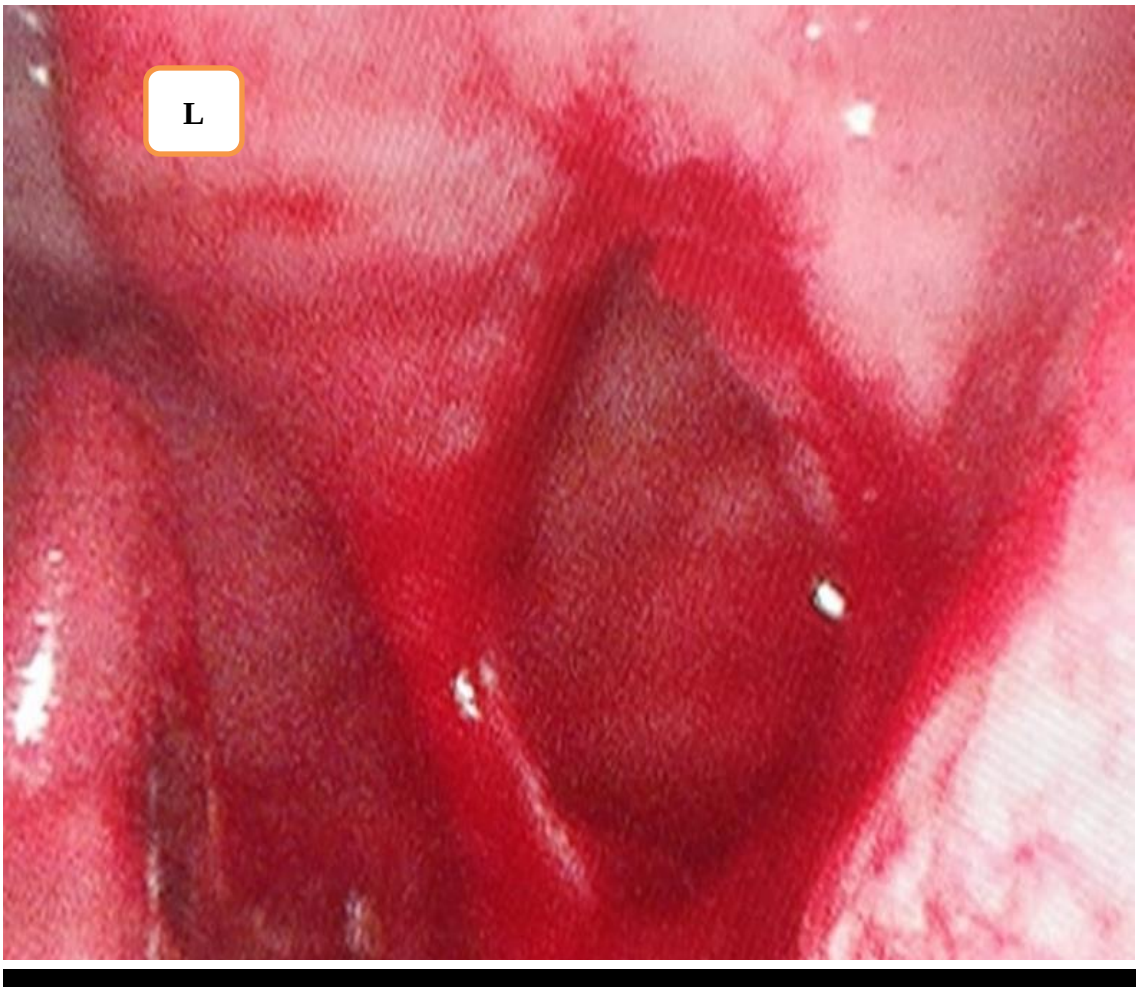
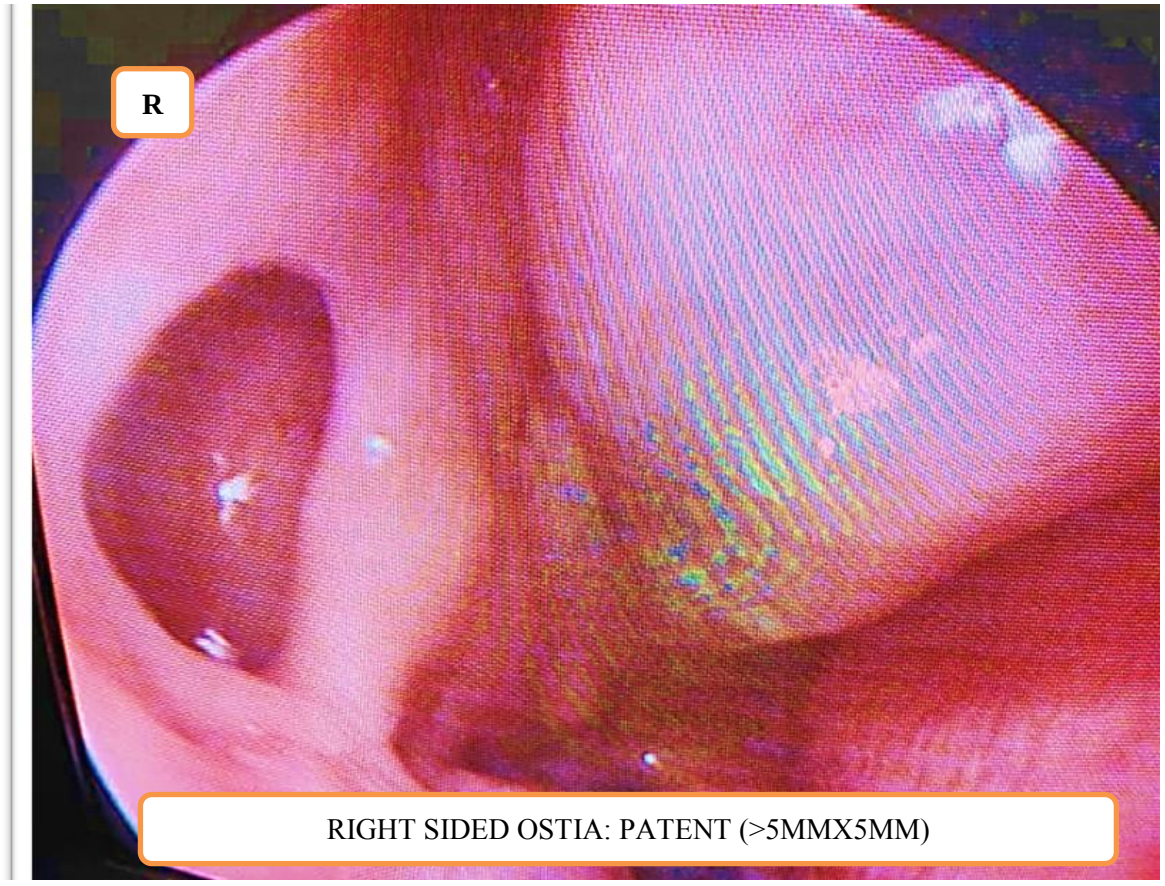
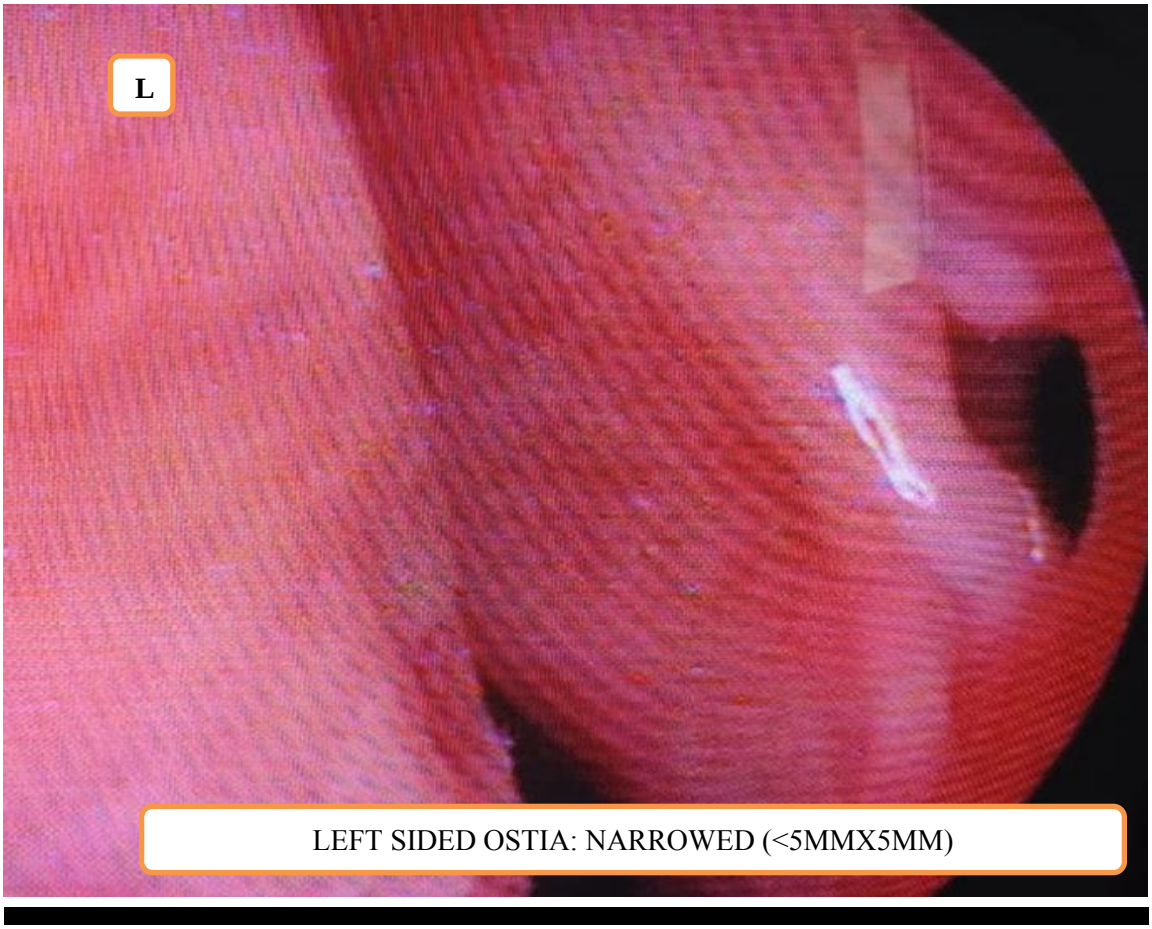
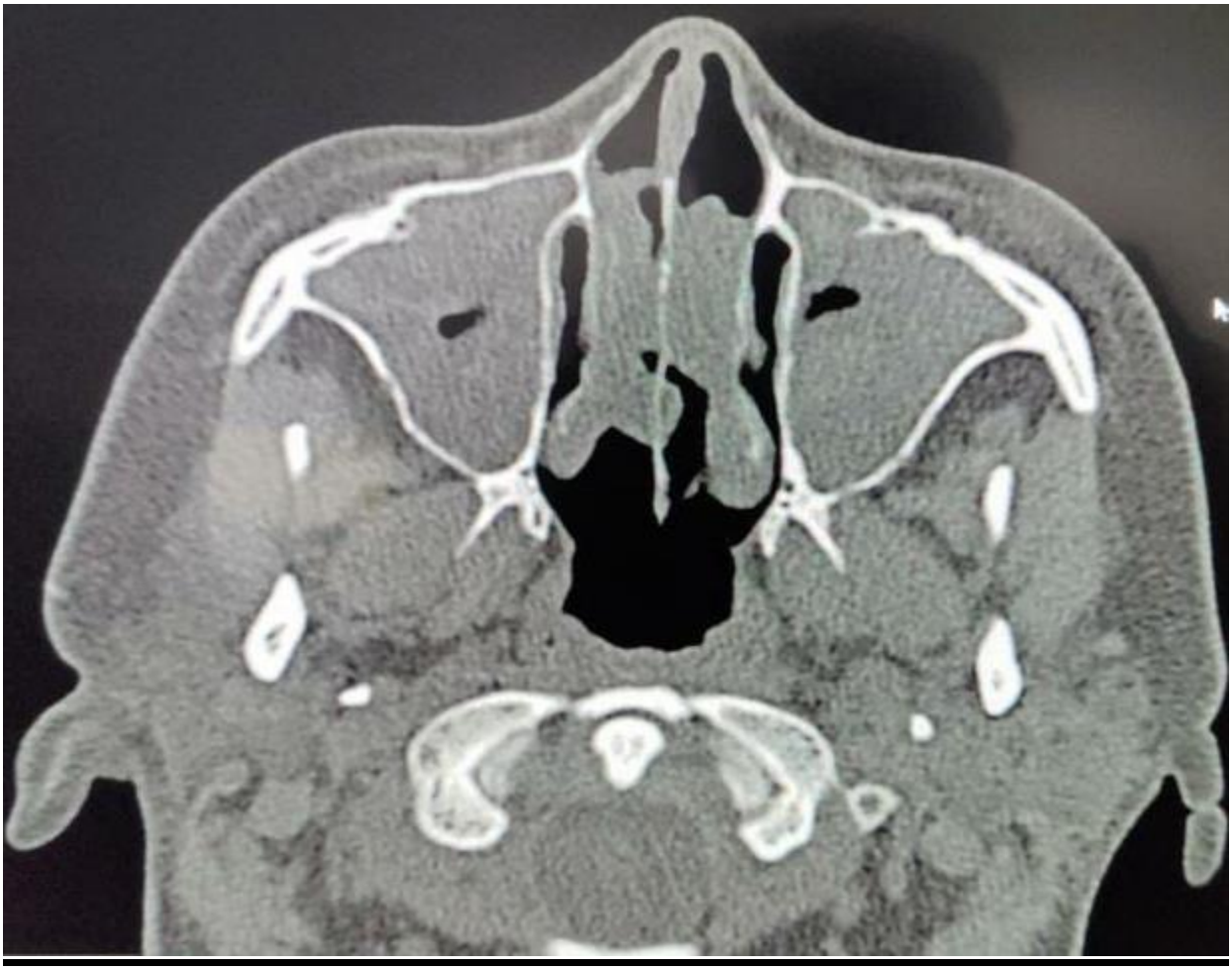


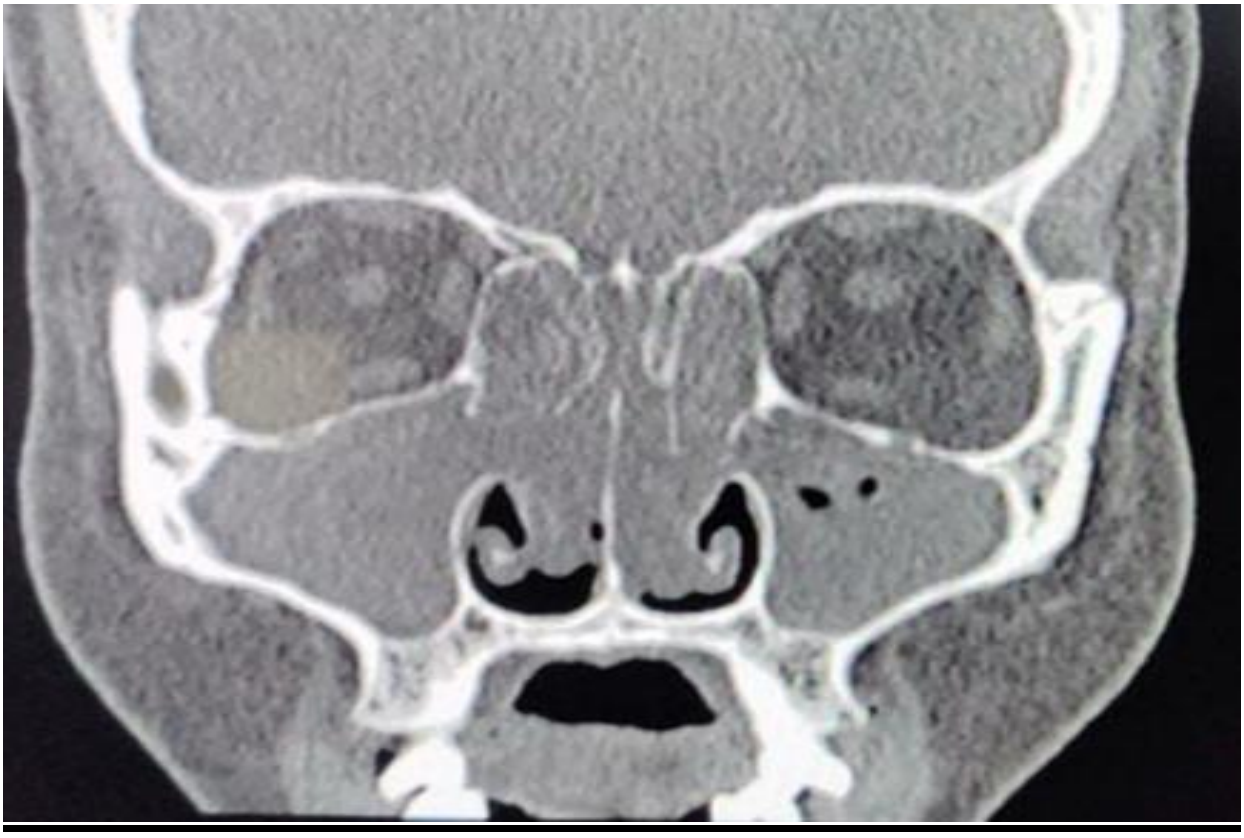
IMAGE 18: FOLLOW UP: 6TH MONTH



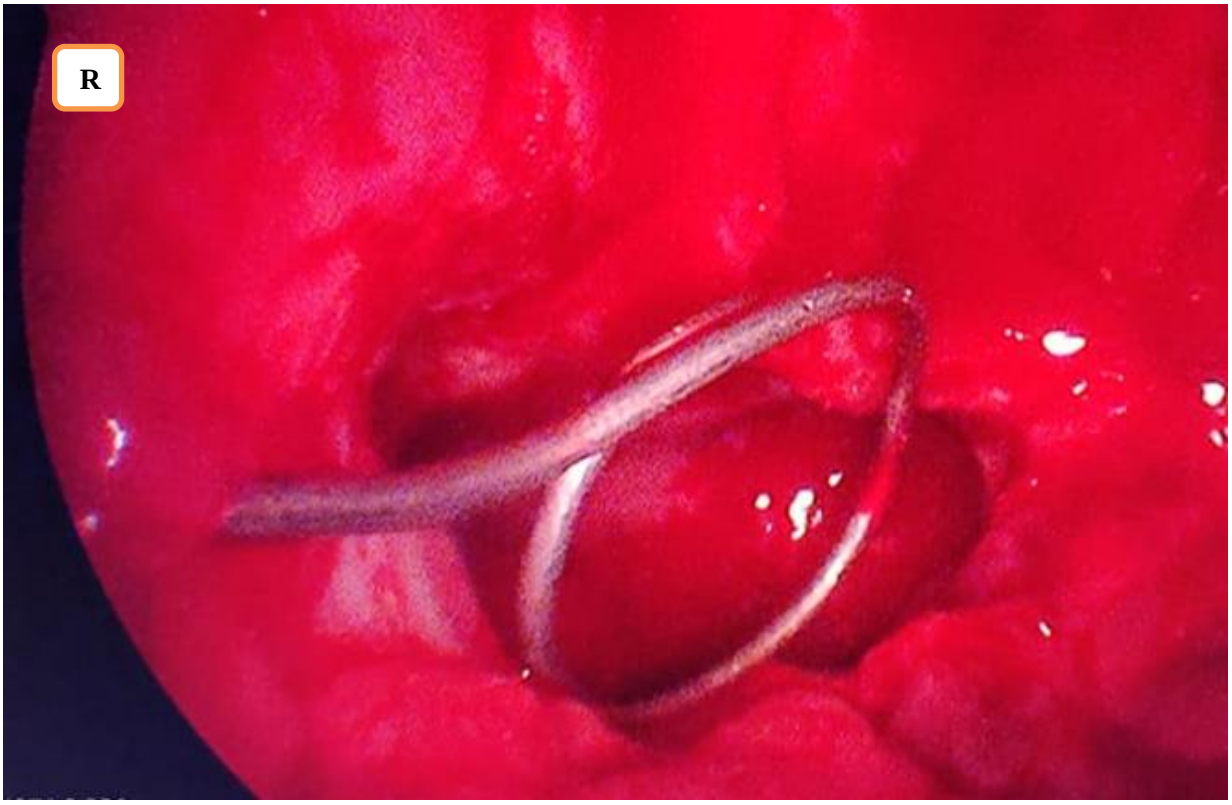


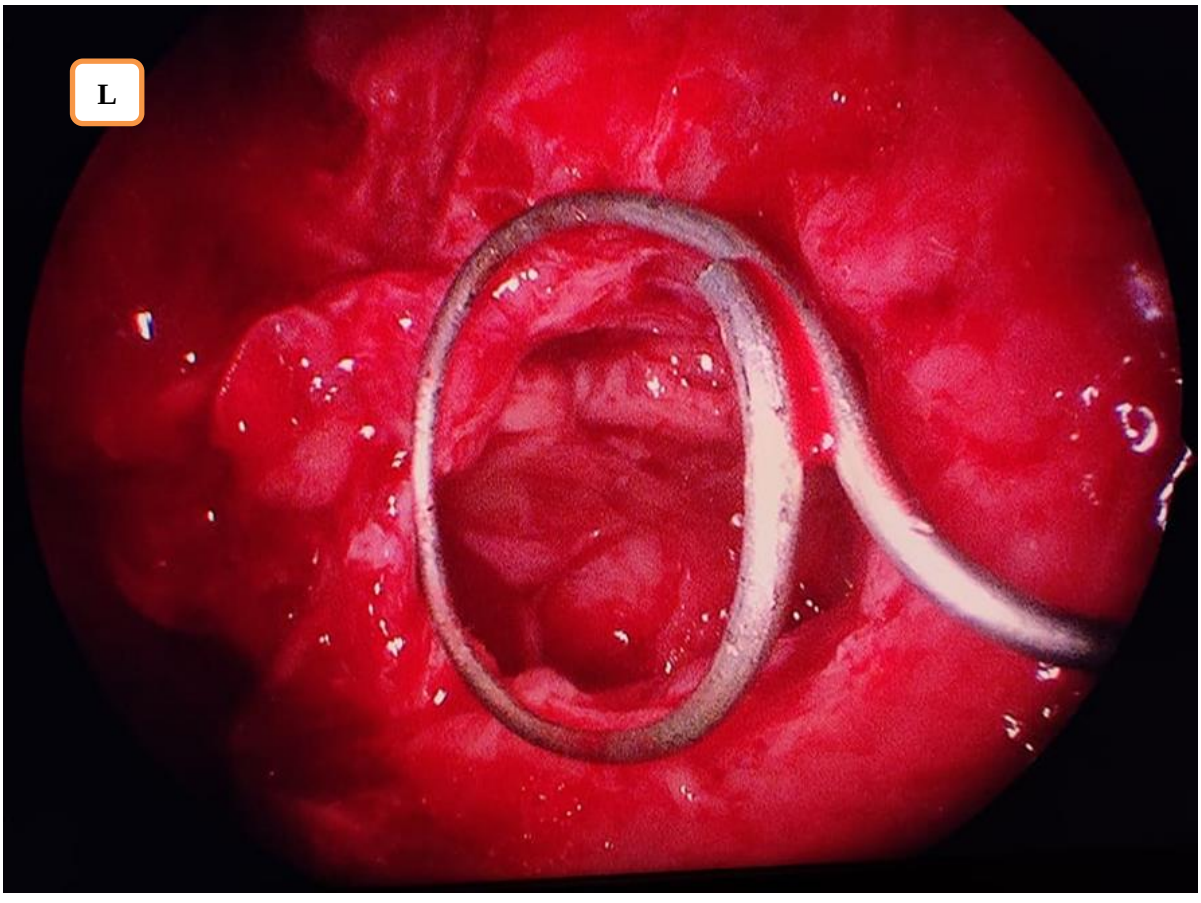
CASE 2: CT SCAN



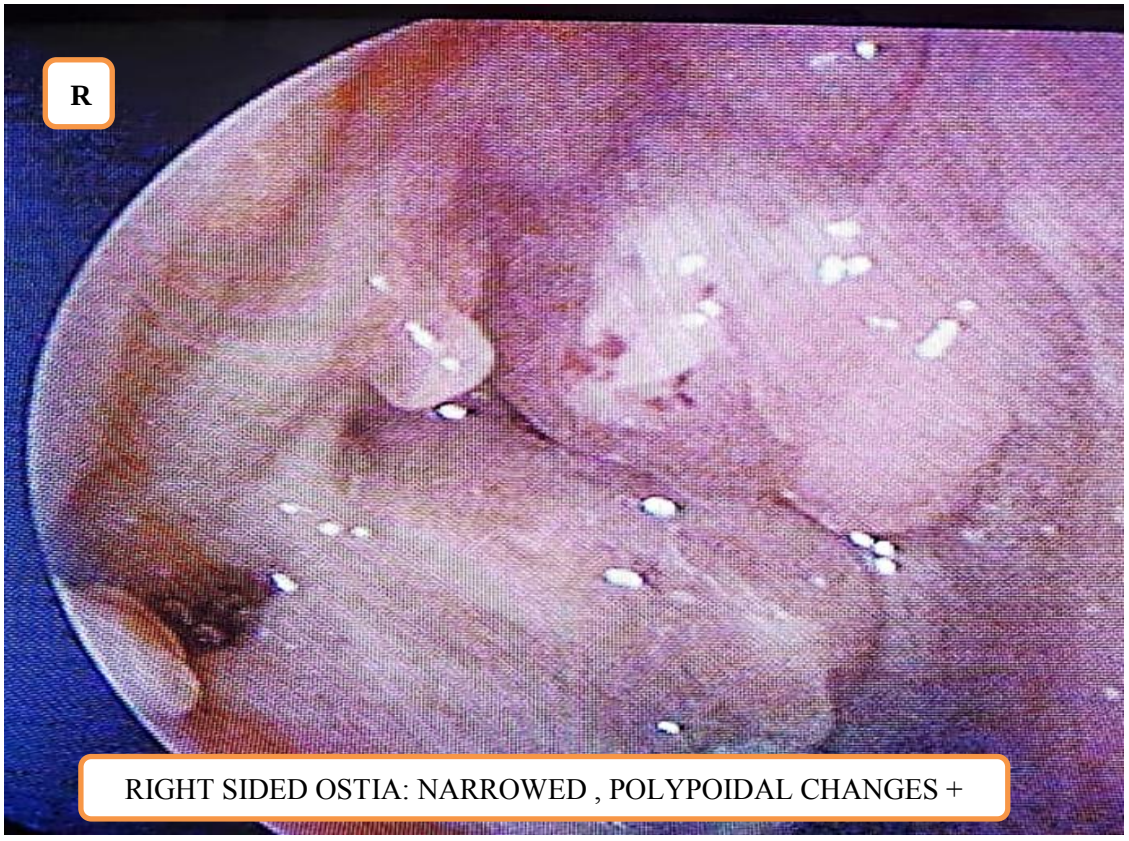


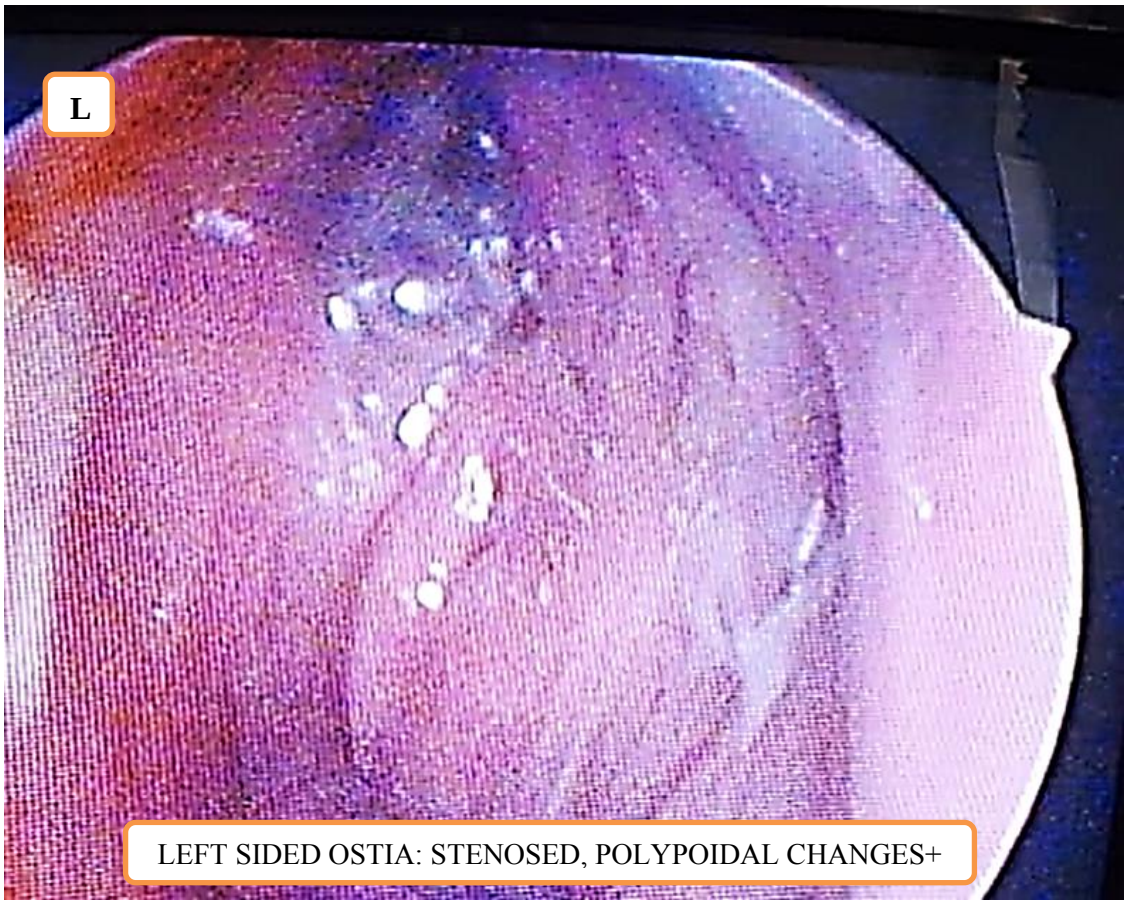
INTRA-OPERATIVE IMAGES:
OSTIA MEASURING 1CMx1CM





FOLLOW UP: 6TH MONTH





Statistical analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test** was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. **Mann Whitney U test** was used as test of significance to identify the mean difference between two quantitative variables.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Formula

$H_0 : P_1 = P_2;$ $\quad\quad$ $H_a : P_1 \neq P_2$

$$n = \frac{\left\{ Z_{1-\frac{\alpha}{2}} \sqrt{2\,\bar{P}\left(1-\bar{P}\right)} + Z_{1-\beta} \sqrt{P_1\left(1-P_1\right) + P_2\left(1-P_2\right)} \right\}^2}{\left(P_1 - P_2\right)^2}$$

Where,

$$\bar{P} = \frac{P_1 + P_2}{2}$$

P_1 : Proportion in the first group

P_2 : Proportion in the second group

α : Significance level

$1-\beta$: Power

RESULTS

RESULTS

Table 1: Age distribution of subjects

		Count	%
Age	<20 years	6	12.0%
	21 to 30 years	15	30.0%
	31 to 40 years	13	26.0%
	41 to 50 years	7	14.0%
	51 to 60 years	6	12.0%
	>60 years	3	6.0%
	Total	50	100.0%

Mean age of subjects was 35.94 ± 13.549 years. Majority of subjects were in the age group 21 to 30 years (30%).

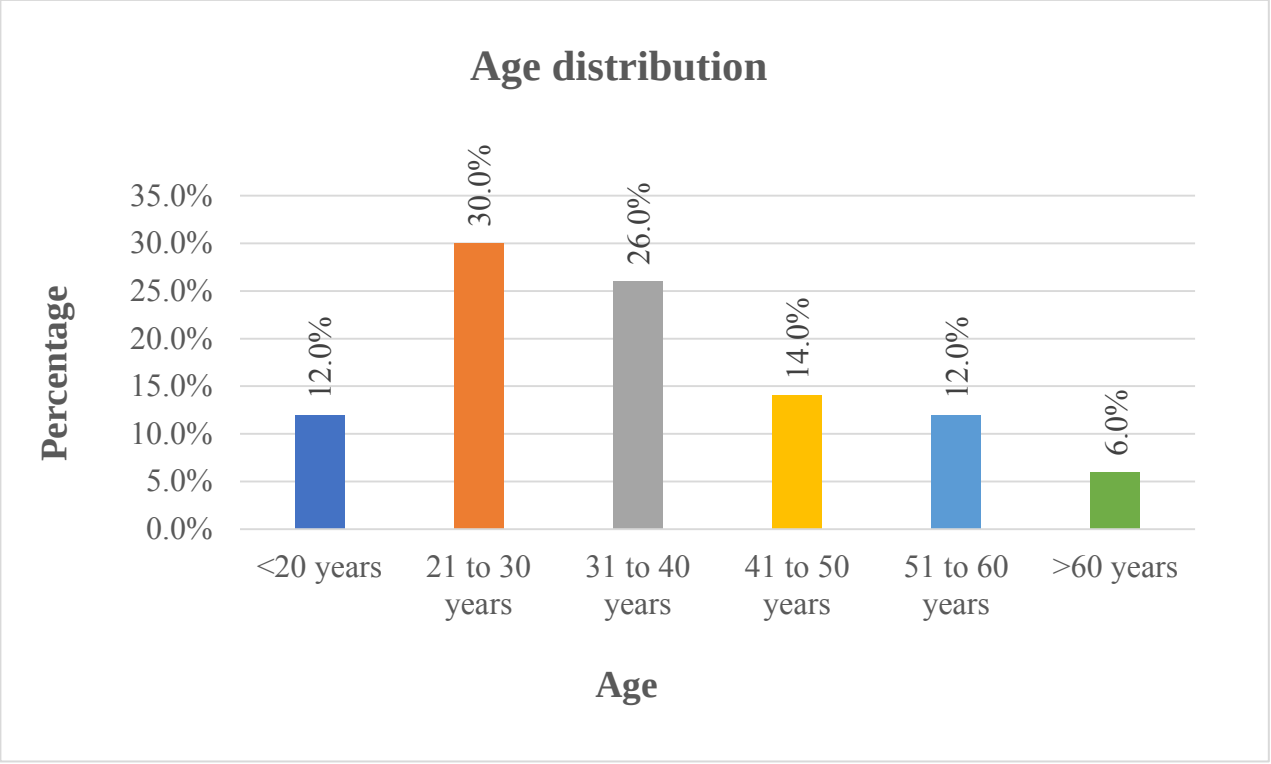


Figure 1: Bar diagram showing Age distribution of subjects

Table 2: Gender distribution

		Count	%
Gender	Male	28	56.0%
	Female	22	44.0%
	Total	50	100.0%

In the study 56% were males and 44% were females.

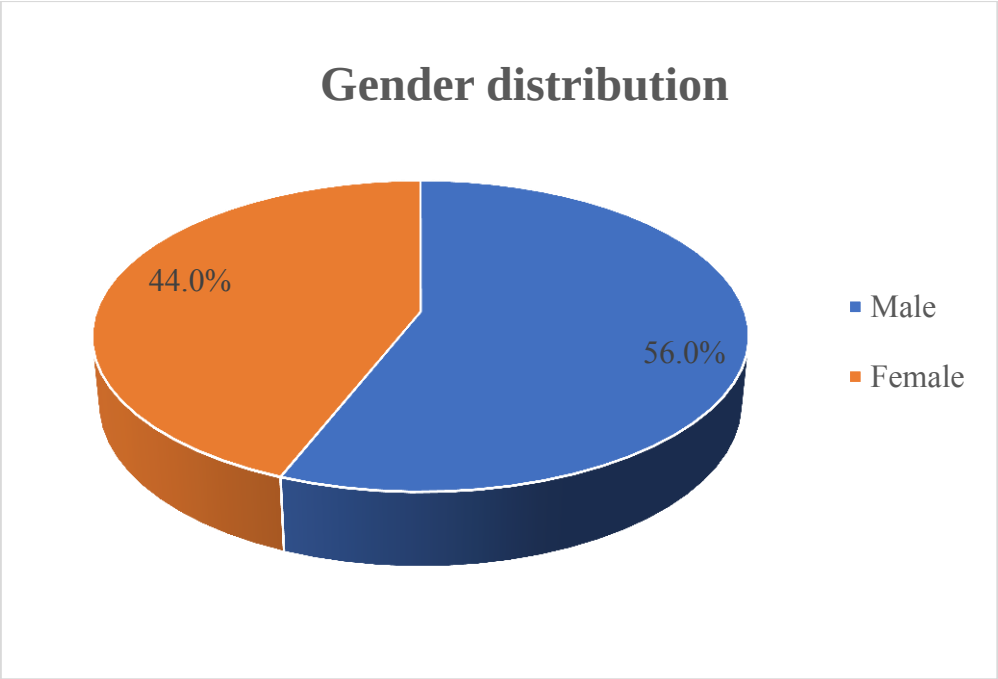


Figure 2: Pie diagram showing Gender distribution

Table 3: Operative Procedures distribution

		Count	%
Operative Procedures	FESS	24	48.0%
	FESS+ Septoplasty	24	48.0%
	FESS+ Septoplasty+ Planectomy	1	2.0%
	Middle Meatal Antrostomy	1	2.0%

In the study 48% underwent FESS, 48% underwent FESS+ Septoplasty, 2% underwent FESS+ Septoplasty+ Planectomy and Middle Meatal Antrostomy respectively.

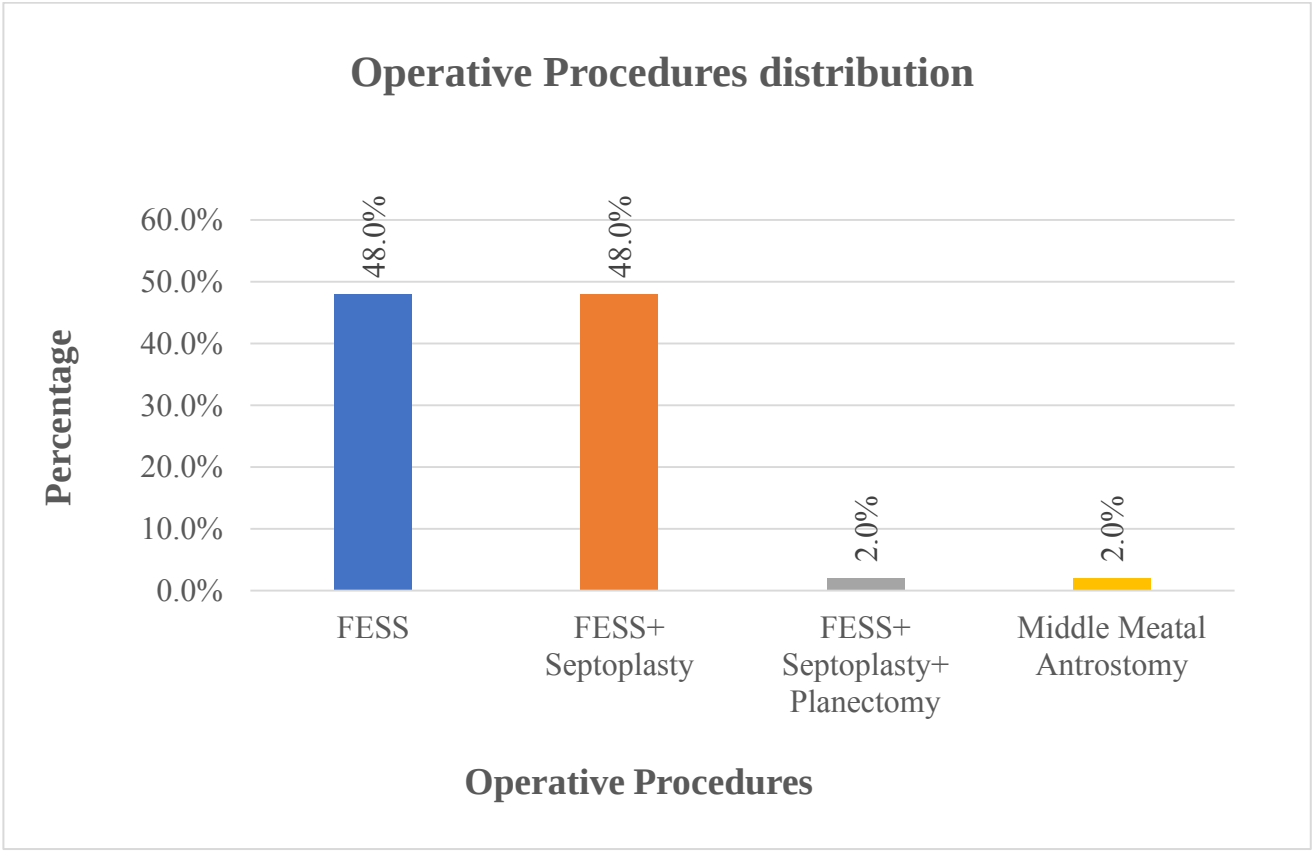


Figure 3:Bar diagram showing Operative Procedures distribution

Table 4: Intra Operative Measurements comparison between Cases and Controls

		Group					
		Cases		Controls		Total	
		Count	%	Count	%	Count	%
Intra Operative Measurements	1*1 cm	50	100.0%	50	100.0%	100	100.0%
	>5*5 mm	0	0.0%	0	0.0%	0	0.0%
	<5*5mm	0	0.0%	0	0.0%	0	0.0%
	Stenosed	0	0.0%	0	0.0%	0	0.0%
	Total	50	100.0%	50	100.0%	100	100.0%

In the study at Intra Operative period, 100% had Grade 1 (1*1cm) size in both cases and controls.

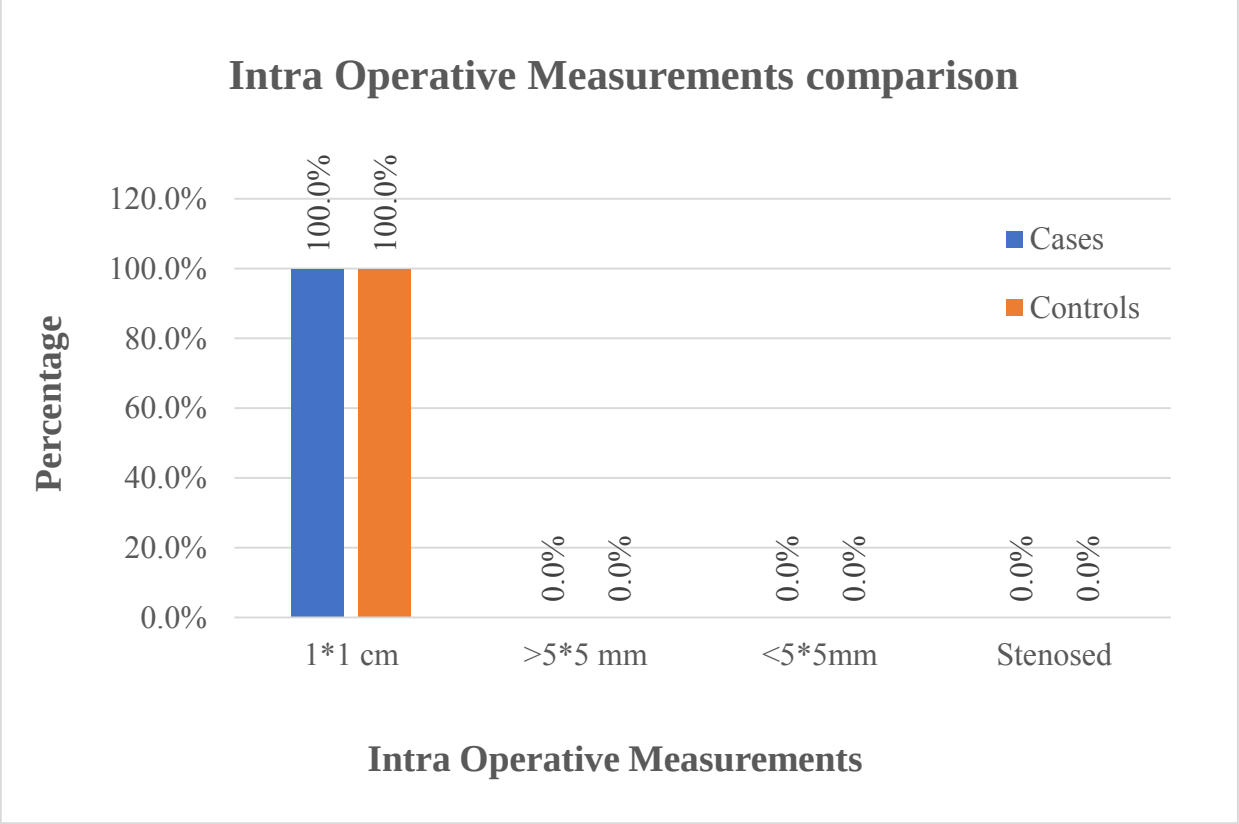


Figure 4: Bar diagram showing Intra Operative Measurements comparison between Cases and Controls

Table 5: 3 Weeks Measurements comparison between Cases and Controls

		Group					
		Cases		Controls		Total	
		Count	%	Count	%	Count	%
3 Weeks	1*1 cm	0	0.0%	0	0.0%	0	0.0%
	>5*5 mm	50	100.0%	50	100.0%	100	100.0%
	<5*5mm	0	0.0%	0	0.0%	0	0.0%
	Stenosed	0	0.0%	0	0.0%	0	0.0%
	Total	50	100.0%	50	100.0%	100	100.0%

In the study at 3 weeks, 100% had Grade 2 (>5*5 mm) size in both cases and controls.

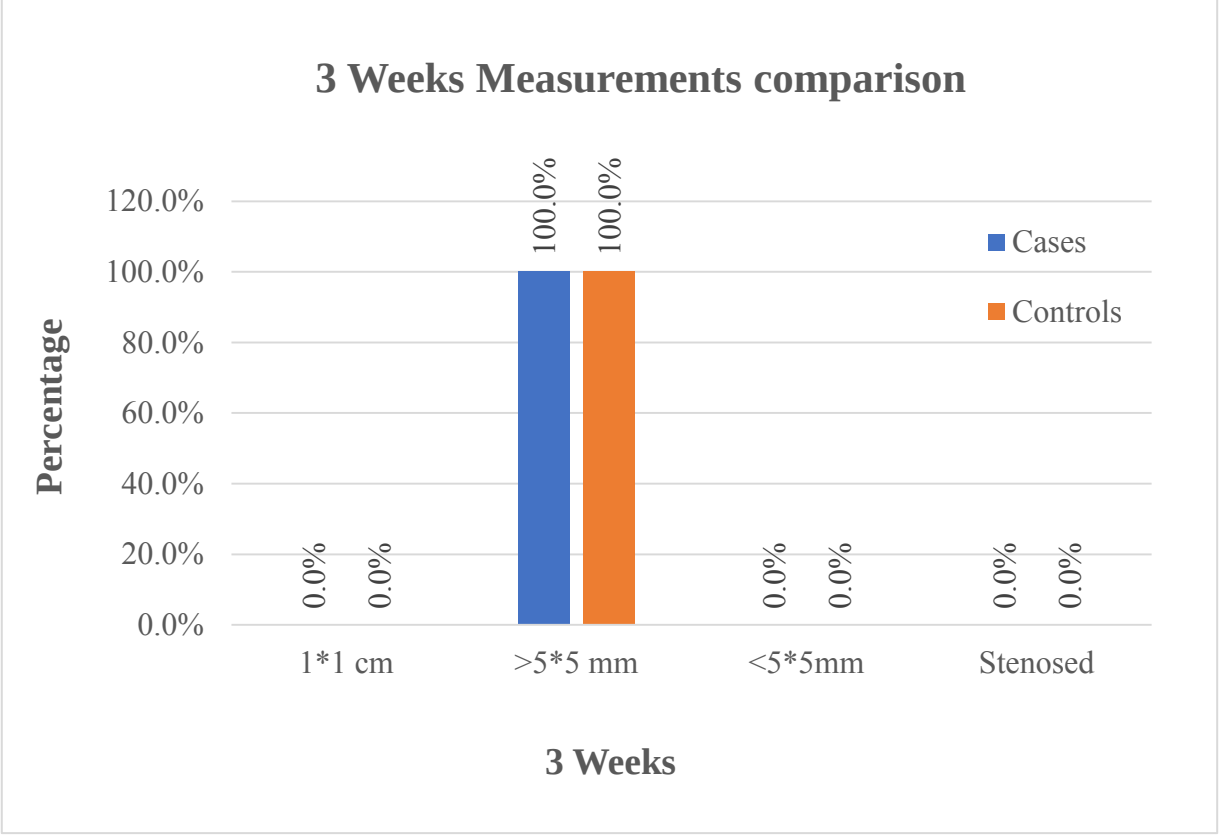


Figure 5: Bar diagram showing 3 Weeks Measurements comparison between Cases and Controls

Table 6: 3 Months Measurements comparison between Cases and Controls

		Group					
		Cases		Controls		Total	
		Count	%	Count	%	Count	%
3 Months	1*1 cm	0	0.0%	0	0.0%	0	0.0%
	>5*5 mm	42	84.0%	29	58.0%	71	71.0%
	<5*5mm	8	16.0%	18	36.0%	26	26.0%
	Stenosed	0	0.0%	3	6.0%	3	3.0%
	Total	50	100.0%	50	100.0%	100	100.0%

$\chi 2 = 9.226$, df =2, p = 0.01*

In the study at 3 months among cases, 84% had Grade 2 (>5*5 mm) and 16% had Grade 3 (<5*5mm) size. Among controls, 58% had Grade 2 (>5*5 mm) and 36% had Grade 3 (<5*5mm) and 6% had Grade 4 (Stenosis). There was significant difference in Grade of Ostea between two groups.

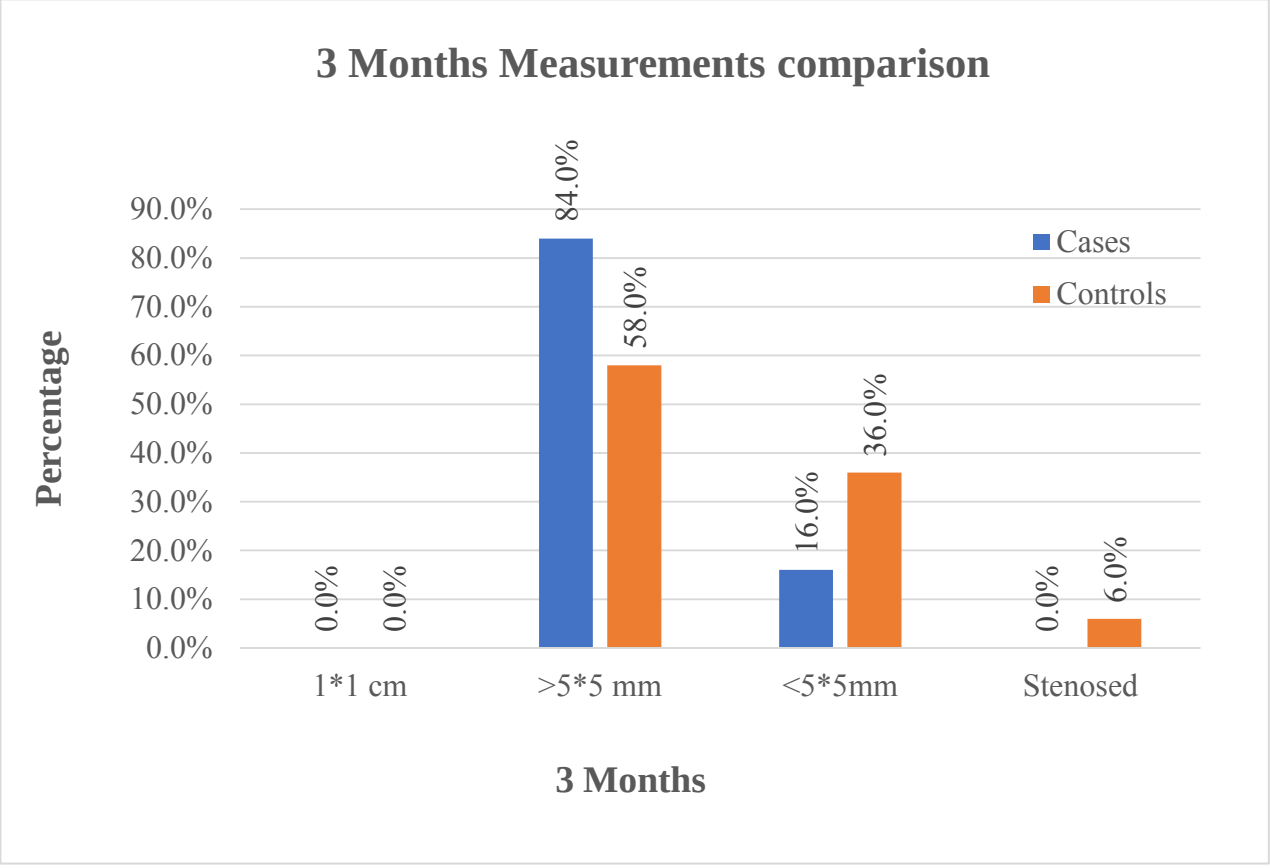


Figure 6: Bar diagram showing 3 Months Measurements comparison between Cases and Controls

Table 7: 6 Months Measurements comparison between Cases and Controls

		Group					
		Cases		Controls		Total	
		Count	%	Count	%	Count	%
6 Months	1*1 cm	0	0.0%	0	0.0%	0	0.0%
	>5*5 mm	34	68.0%	17	34.0%	51	51.0%
	<5*5mm	16	32.0%	22	44.0%	38	38.0%
	Stenosed	0	0.0%	11	22.0%	11	11.0%
	Total	50	100.0%	50	100.0%	100	100.0%

$\chi 2 = 17.61$, df =2, $p < 0.01$*

In the study at 6 months among cases, 68% had Grade 2 (>5*5 mm) and 32% had Grade 3 (<5*5mm) size. Among controls, 34% had Grade 2 (>5*5 mm) and 44% had Grade 3 (<5*5mm) and 22% had Grade 4 (Stenosis). There was significant difference in Grade of Ostea between two groups.

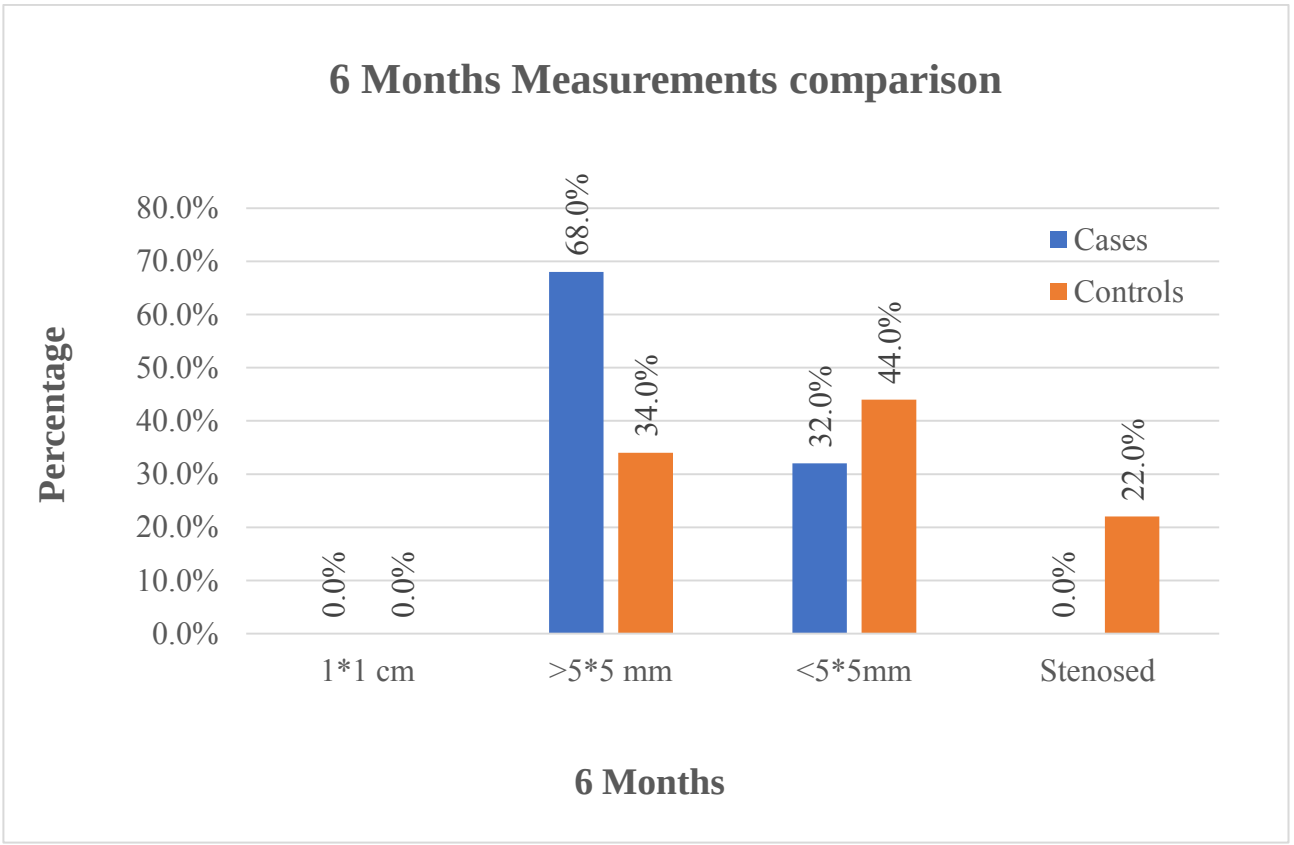


Figure 7: Bar diagram showing 6 Months Measurements comparison between Cases and Controls

Table 8: Grade of Ostea comparison between Cases and Controls

	Group			P value
	Cases	Controls	Total	
	Median	Median	Median	
Intraoperative Measurements	1	1	1	1.000
3 Weeks	2	2	2	1.000
3 Months	2	2	2	0.003*
6 Months	2	3	2	<0.001*

In the study there was significant difference in Grade of Ostea between cases and controls at 3 months and 6 months.

Grade of Ostea at intraoperative period among cases and controls was Grade 1.

At 3 weeks among cases and controls was Grade 2.

At 3 months among cases and controls was Grade 2. There was significant difference in Median Grade between two groups.

At 6 months among cases and controls was Grade 2 and Grade 3 respectively. There was significant difference in Grade of Ostea between two groups.

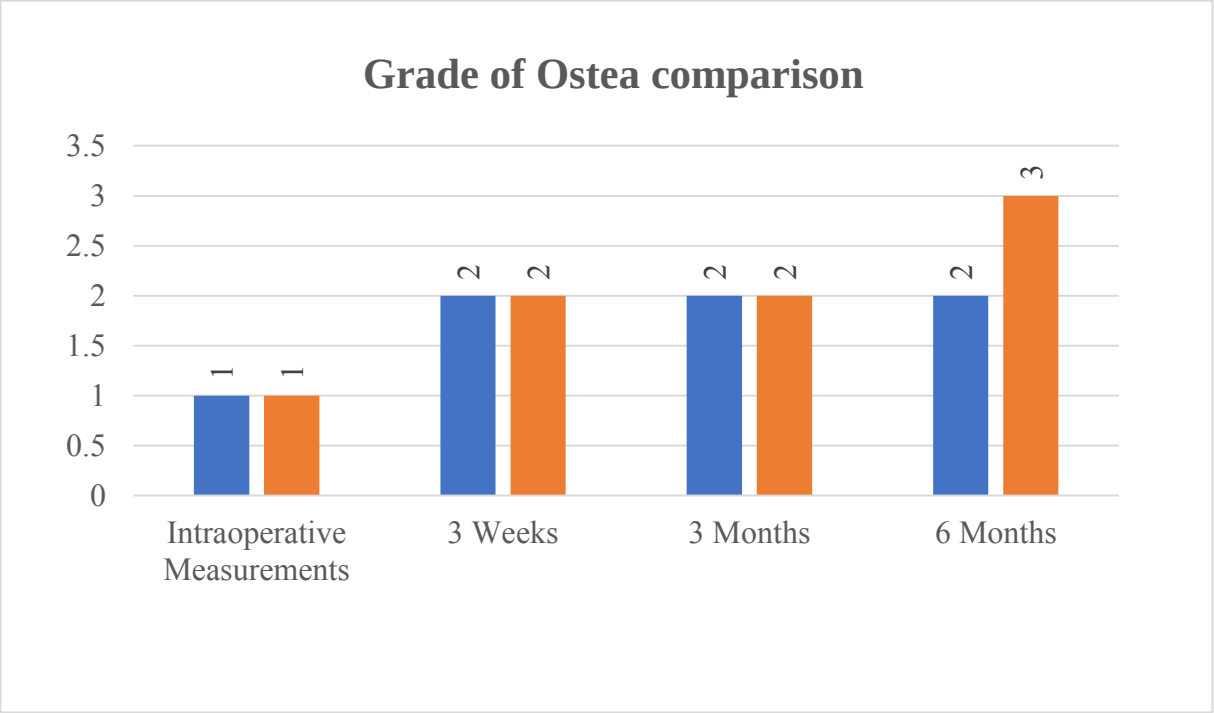


Figure 8: Bar diagram showing Grade of Ostea comparison between Cases and Controls

Table 9: Association between Operative Procedures and Stenosis

		Ostea			
		Stenosed		Not Stenosed	
		Count	%	Count	%
Operative Procedures	FESS	4	17.4%	19	82.6%
	FESS+ Septoplasty	3	12.0%	22	88.0%
	FESS+ Septoplasty+ Planectomy	0	0.0%	1	100.0%
	Middle Meatal Antrostomy	0	0.0%	1	100.0%

$\chi 2 = 0.628$, df =3, p = 0.890

In the study among subjects with FESS, 17.4% had stenosis, among subjects who underwent FESS+ Septoplasty, 12% had Stenosis and among subjects who underwent FESS+ Septoplasty+ Planectomy and Middle Meatal Antrostomy 0% had stenosis. There was no significant difference in Stenosis with respect to Operative Procedures.

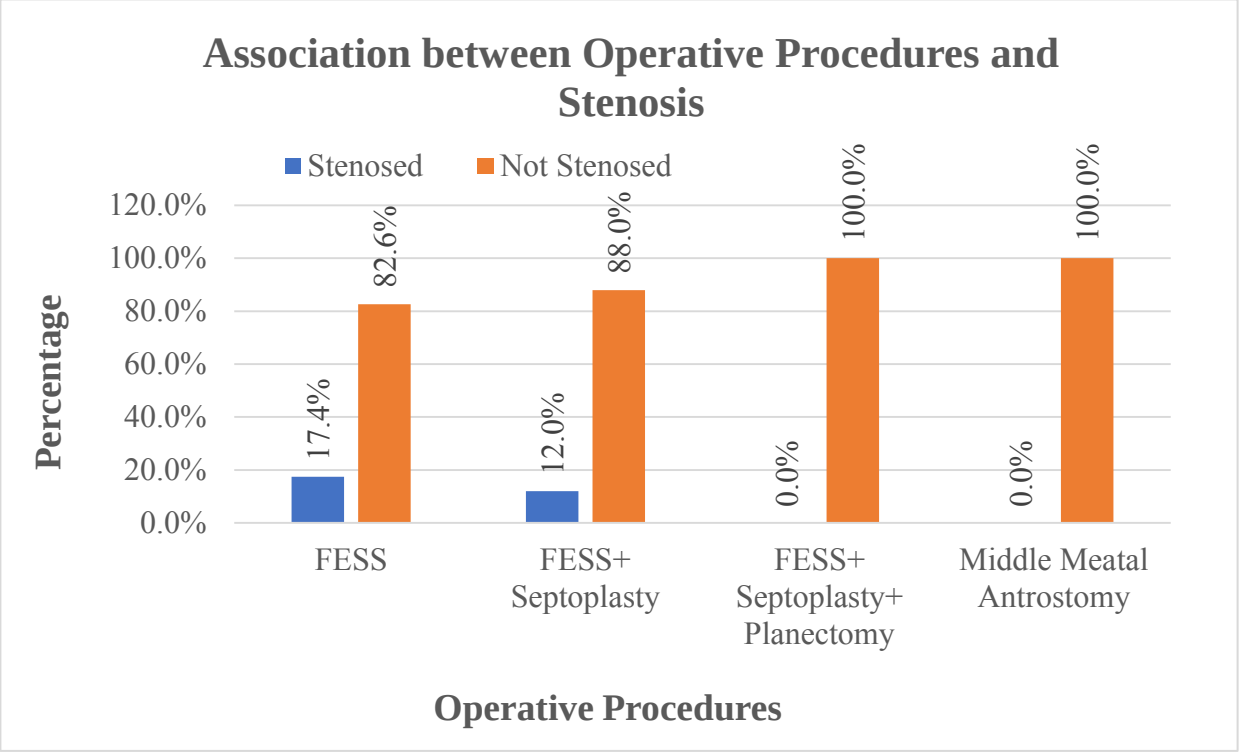


Figure 9: Bar diagram showing Association between Operative Procedures and Stenosis

Table 10: Association between Diagnosis and Stenosis

		Ostea				P value
		Stenosed		Not Stenosed		
		Count	%	Count	%	
Maxillary Sinusitis	Yes	0	0.0%	8	100.0%	0.213
CRSwNP	Yes	4	22.2%	14	77.8%	0.209
CRSsNP	Yes	3	15.0%	17	85.0%	0.868
Allergic Rhinosinusitis	Yes	0	0.0%	6	100.0%	0.292

In the study there was no significant association between Diagnosis and Stenosis. Among subjects with CRSsNP, 25% had stenosis and among subjects with CRSsNP + DNS, 11.8% had stenosis.

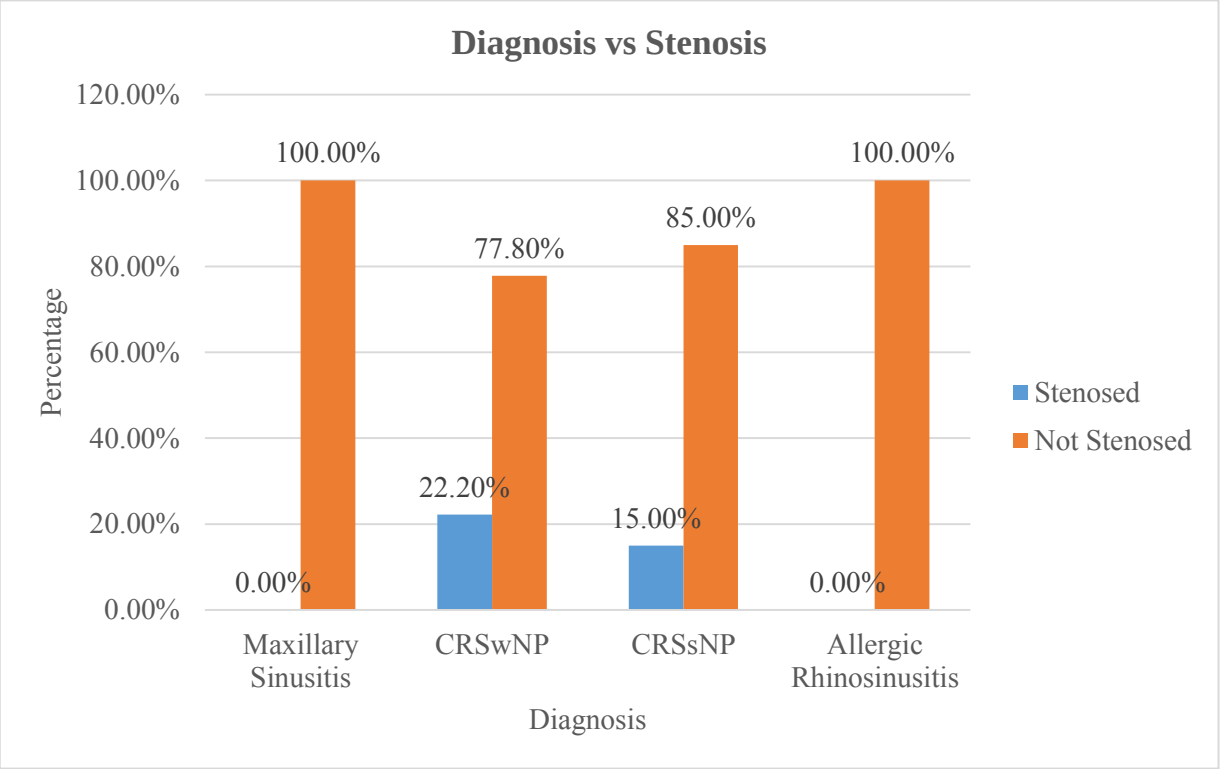


Figure 10: Bar diagram showing Association between Diagnosis and Stenosis

DISCUSSION

DISCUSSION

CRS is an inflammatory disease of the PNS that produces long term inflammation of the mucous lining of the sinuses causing significant decrease in the quality of life. Most cases of chronic rhinosinusitis are sequelae of unresolved acute sinusitis and the known risk factors are allergic rhinitis, non-allergic rhinitis, anatomic obstruction in the osteo-meatal complex, and immunologic disorders.[51]

The prevalence of chronic rhinosinusitis in India varies between 20-30 % and there is increase in prevalence of chronic rhinosinusitis due to a greater number of people adopting urban lifestyle and an increased exposure to various forms of air pollution. Patients with –Chronic Rhinosinusitis" suffer from combination of cardinal symptoms which gives rise to profound effects on functional wellbeing and general health thereby affecting the quality of life. Severe fatigue and poor sleep quality are the two most commonly reported complains by patients with CRS resulting in lack of productivity and relatively poor cognitive function. [51]

Similar studies quote that quality of life of patients with CRS is worse than that of patients with Congestive Heart failure, Chronic obstructive pulmonary disorder and Parkinson's disease. Another noteworthy factor that impacts overall quality of life and wellbeing which has been recently researched in patients with CRS is the presence of depression, with the prevalence rate ranging from 11-40%. [51]

As per the 2003 amended Rhinosinusitis Task Force's criteria for the diagnosis of CRS, confirmatory radiographic or nasal endoscopic or physical examination findings are essential in addition to suggestive history. CRS may manifest as one of three major clinical syndromes: CRS without nasal polyp, CRS with nasal polyp, or allergic fungal rhinosinusitis. This classification is central to the management of each of these.[52,53]

The initial management is by medical therapy which is directed to enhance muco-ciliary clearance, reduce edema of sinus tissues (in order to improve the access for topical medications), facilitate the drainage of sinus secretions and treat concomitant infections. If the medical line of management fails, surgery becomes the main modality of treatment. Selected patients not responding to first-line medical therapy with a history suggestive of other comorbidities (e.g., vasculitis, granulomatous diseases, cystic fibrosis, immunodeficiency) should be referred to an allergy specialist or pulmonologist.[54,55]

The primary objective of FESS is to restore paranasal sinus function by re-establishing the physiologic pattern of ventilation and muco-ciliary clearance. The goal is to remove irreversibly diseased mucosa and bone, preserve normal tissue, and judiciously widen the true natural ostia of the sinuses. The "Osteo-meatal complex" (OMC) is most often the primary target of FESS, because minimal inflammation in this area can lead to disease in the maxillary, anterior ethmoid, and frontal sinuses. Aggressive removal of mucosa is inappropriate and unnecessary and it causes postoperative problems with healing. The mucosal lining of the skull base, lamina papyracea, and sinus cavities should be preserved, and uninvolved sinuses should be left alone. In spite of adequate surgery with widened Ostia, development of postsurgical stenosis of middle meatal antrostomy often occurs resulting in anatomical obstruction leading to failure of Primary sinus surgery. [55,56]

More extensive surgery may be necessary for complicated acute rhinosinusitis or for extensive fungal or polyp disease.

Kennedy et al.18 described the natural size of the maxillary ostium to be 5 mm by 5 mm, considering >5mm*5mm to be patent and < 5mm*5mm to be narrowed.[56]

In a study, **Ramadan** estimated the rate of surgical failure at the time of revision surgery, 30% were because of remanent ethmoidal air cells and 27% due to stenosis of maxillary sinus ostia, were the most common cause of surgery failure. Studies carried out by **Hinohira** et al observed that the most common cause for surgical failure was stenosis of maxillary sinus ostia. and **Chambers** et al noticed that the only endoscopic finding is the scarring of middle meatal antrostomy and at the ethmoid labyrinth. Similarly, **Murray and Kountakis** reported the most common anatomical finding in revision endoscopic surgery was a stenosed osteo-meatal complex and specifically a stenosed middle meatal antrostomy -39%[59,60,61,]

Despite advancements in surgical instruments and technique, postoperative adhesions and the formation of synechiae still occur in up to 27 percent of cases. Adhesions requiring surgical intervention occur in 1-2 percent of patients (10) With a reported incidence of 1–36 percent, synechia formation and ostial stenosis are common after FESS. The first step in preventing adhesions and synechia is to prevent them from forming in the operating room. Avoiding formation of stenosis and synechiae can be achieved by carefully removing bone splinters and avoiding mucosal stripping. The use of modern micro-debriders also helps to preserve the mucosa and reduce the presence of bone fragments and remnant tissues.[62,63,64]

In our study, 50 patients of Chronic Rhinosinusitis underwent middle meatal antrostomy, the ostia size was made 1cm*1cm following which mitomycin C was applied in order to prevent post operative complication of stenosis formation.

In the process of scar formation, fibroblasts play a crucial role. Their proliferation, migration and extracellular matrix production are the most important step in collagen synthesis by inhibiting the synthesis of DNA, cellular RNA and protein. MMC has helped in reduction of clinical scar formation.[65,66,67]

Mitomycin –C" as a topical agent has shown clinical efficacy in the reduction of clinical scar formation. It is derived from stepromyces caesitosus strain of actinomyces for its antibacterial properties. It acts by disrupting the base pairing of DNA molecules in G1 phase of cell cycle, inhibits formation of RNA, protein synthesis and cellular mitosis. Hence, it inhibits proliferation of epithelial cells and fibroblasts. Additional function is promotion of apoptosis in fibroblasts and blockage of angiogenesis.[68,69]

Mitomycin C has been widely utilised to prevent scarring during ophthalmologic surgery, particularly glaucoma filtration surgery, to keep the patency of the draining fistula there by improving surgical outcome [10]. MMC's propensity to decrease fibrosis and vascular ingrowth has been credited with its ability to reduce scar formation during these treatments. Topical MMC has also been studied for otolaryngological operations in recent investigations.[70]

The synechia and scar formation which occurs due to raw areas lying in vicinity, tends to heal with regenerating epithelium and fibrous tissue growing between them. If the adhesions are of adequate size and proper location, it can lead to re-obstruction of the adjoining sinus ostium and hence recurrence of disease. [71,72,73]

Stammberger observed varying degrees of synechia between head of middle turbinate and lateral wall of nose in 8% (243/500) of his patients during follow up. He made use of a small piece of silastic in the nose following excision of synechiae and scar tissue but he concluded that recurrence of synechiae could not always be prevented. **Weymullar** et al suggested prolonged packing of the operative site such that middle turbinate was medialized towards the nasal septum. However, this may result in airway obstruction and diminished olfaction. **Brennan** described a device made of medical grade polyurethane which isolated the middle turbinate from both the

Septum of nose and lateral nasal wall. This boomerang turbinate glove was used in 234 successive intranasal sinus surgical procedure for 10-14 days with no major adhesions observed. [74,75,76,77]

Ingrams et al. [5], who were the first to investigate the outcome of MMC on the normal sinus mucosa of rabbits, found that a 5 min application of 0.4 mg/ml MMC to rabbit maxillary antrostomies delayed their closure from 1 to 4 weeks while antrostomies of the untreated control group were closed around postoperative 1 week. However, their results were obtained from pathogen-free rabbits. Because FESS is a procedure mainly for sinusitis, it may be more practical to examine the outcome of topical MMC for inflamed sino-nasal mucosa. Furthermore, it is still unpredictable how inflamed mucosa will respond to the application of MMC. Studies on cultured fibroblasts with MMC has demonstrated an antiproliferative effect at the concentration of 0.04 mg/ml and cytocidal effect at higher concentration. A 5 minutes single Topical application has a measurable effect on cell proliferation and cellular morphology for up to 36 hours.[78]
Recently, **Hu** et al examined the result of MMC on cultured Human nasal mucosa and found the short term exposure to MMC inhibits fibroblast proliferation and increase fibroblast apoptosis.[79]

The concentration of MMC that we have used in our study is 0.5mg/ml for 3 minutes, this particular specification has been decided upon, after weighing the advantages and side effect of it. In our study, the application of MMC was done meticulously after middle meatal antrostomy, taking care not to touch the other region of nasal mucosa. A thorough normal saline wash after the procedure was given in order to remove blood clots from the antrostomy site, as it could affect the absorption of drug and result in poor outcome. Hence, application was done after strict hemostasis and over a clean antrostomy site.

The size of the middle meatal antrostomy was made to be –1cm X 1cm" intra-operatively in all cases because a larger ostium can disrupt the drainage of anteriorly draining sinuses and a smaller ostium could be predisposed to stenosis.

Antrostomy more than –1cmX1cm" can predispose to anteriorly draining sinuses draining into maxillary antrum itself and resulting in recurrent sinusitis and need for revision surgery.
Based on the measurement of ostium size, we observed in our study that the ostium did not significantly stenose for 3 weeks after surgery. However, 3 months post surgery, the ostium size started stenosing with 84% of patients showing Grade 2, 16% Grade 3 and 6% Grade 4 stenosis.

Various clinical studies have shown, a short term effect of Mitomycin C in antrostomy stenosis. Few authors have suggested 70% of the fibroblasts survive after 5 minutes of Mitomycin C application (0.04mg/ml) with the evidence of regrowth with 2-3 days. [71]

The effects of MMC on anterostomy size were studied in **Kim et al**. (2009) study, which comprised 20 patients with bilateral CRS refractory to treatment. MMC was found to be effective only in the first month following surgery. However, after a six-month (long-term) follow-up, MMC had no influence on the incidence of antrostomy narrowing or obstruction. This discovery is consistent with our findings, as the MMC groups showed no crustration or synechia after 3 weeks, however synechia began to resurface after 6 months in the MMC group.[81]

Venkatraman et al. (2012) Observed that using topical - MMC at the end of FESS reduced the incidence of synechiae and improved patients' symptoms scores in the early postoperative period in a prospective, randomised controlled trial involving 50 patients with chronic bilateral rhinosinusitis. This partially corroborates our findings.[82]

A prospective hospital-based interventional trial in 2014, observed that 3.1 percent of patients with CRS who underwent FESS and topical administration of MMC, at the completion of FESS/ESS had absence of adhesion formation, which is consistent with our findings.[83]

Yamaoka et al. (2012) discovered a decrease in synechia formation. After 3 months, **Ramalingam** et al (2018) found that 38.7% of patients in the MMC group experienced synechia, whereas 61.22 percent of patients were synechia-free, compared to 21.43 percent [84,85]

The role of MMC in reducing synechiae formation and ostial stenosis during FESS was investigated by **Venkatraman et al (2011) and Singh et al (2011).** They found that topical MMC administration reduced the occurrence of adhesions, improved symptoms, and reduced adverse tissue reactions (such as discharge, polypoidal mucosa, and crusting) while increasing the concentration of MMC.[86]

The results of our study demonstrate that the topical use of MMC is beneficial in decreasing adhesion formation after endoscopic nasal surgery. It also proved to be safe with regards local or general complications. MMC has a wide range of applications in the field of rhinology and in the future, it may play an important role after endoscopic sinus surgery based on further researches like our study.[88,89]

As observed in our study, short term application of Mitomycin C inhibits the growth of Fibroblast but there are other mechanisms also contributing to other aspects of wound healing or scar formations. The narrowing of ostium 3 months after surgery in our study could also be due to regeneration of fibroblasts.

We observed that the narrowing and stenosis of the ostia are found to be higher amongst the patient with chronic rhinosinusitis with Polyposis and chronic rhinosinusitis along with allergic

According to various studies in literature, the success rate of FESS can be as high as 90% in Chronic Rhinosinusitis patients without polyps (CRSsNP) and as low as 30% in CRS patients with nasal polyps (CRSwNP). Surgical technique, adhesions and synechiae formation, residual disease, anatomic blockage, and inadequate postoperative care are all variables that contribute to the need for revision endoscopic sinus surgery (RESS). When medical therapy fails, revision surgery must concentrate on improving quality-of-life results.,[90,91,92,93]

Larger multi-institutional studies incorporating other agents to minimize scaring in addition to MMC may facilitate effective prevention of middle meatal antrostomy in future. The causes for higher incidence of antrostomy stenosis in patients having chronic rhinosinusitis with polyp need to be investigated.

SUMMARY

SUMMARY

Chronic Rhinosinusitis (CRS) represents a significant disease burden, which produces long-term inflammation of the mucous lining of the sinuses and affects at least 11% of the population worldwide.

Functional endoscopic sinus surgery (FESS), as described by Messerklinger and Stammberger in the 1980s has become a fully accepted technique for treating chronic sinus disease with the assumption that restoration of sinus ventilation and correction of mucous apposition will allow restoration of the muco-ciliary clearance system.

One major sequel following FESS is the post-operative adhesion occurring between the raw surfaces on the middle turbinate and the lateral nasal wall. At the same time due to the subjective nature of the symptoms experienced by the patient Outcome studies are difficult to perform following FESS.

Various surgical approaches, systemic drugs and site-specific barriers, have been used to minimize inflammation and injury during surgery in order to reduce the risk of adhesion formation.

In our study, upon completion of FESS, a cotton wick impregnated with mitomycin C was applied to one of the middle meatal antrostomy sites, and the other side acted as control. The test site was followed up at three weeks, three months and six months interval and patients were evaluated based upon the subjective and objective improvements of their symptoms.

At 3 weeks among cases and controls, compared to ostia size made intra-operatively, not much difference was seen whereas at 3 months and 6 months a significant difference was present in the Ostia sizes, between cases and controls.

Hence Mitomycin C may be topically applied to the Middle meatal antrostomy sites following FESS to reduce adhesion formation and hence the need for revision surgery.

The narrowing of ostium 3 months after surgery in our study could also be due to regeneration of fibroblasts.

CONCLUSION

CONCLUSION

1. Stenosis of Middle meatal antrostomy following endoscopic Sinus Surgery is fairly common particularly when blood clots, cautery burns or remanent bony spicules are left behind. This can lead to Recurrent sinusitis requiring Revision sinus surgery.
2. An antrostomy measuring 5mmX5mm or more in its diameter is mandatory to have effective drainage of maxillary antrum.
3. Fibroblast suppressive action of Mitomycin C along with its effect on cell cycle has been known to prevents scarring and soft tissue stenosis. However, excessive or prolong use of Mitomycin C can have cytotoxic effect.
4. Topical Application of Mitomycin C for 5 minutes after Middle meatal antrostomy can prevent stenosis at least for a period of 3 months.
5. Mitomycin C and other substances which delay or prevent scarring hold promise in preventing Antrostomy stenosis in endoscopic procedure in Rhinology in future.

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ANNEXURE

ANNEXURE

PERFORMA

Name: **Date:**

Age: **UHID**

OP No: **IP No:**

Address:

Diagnosis at presentation:

Reason for performing tracheostomy:

Duration of tracheostomy:

Type of tracheostomy tube:

History of smoking: + / -

Duration

Pack index:

TASK FORCE CRITERIA

MAJOR CRITERIA	**DURATION**	**MINOR CRITERIA**	**DURATION**
FACIAL PAIN/ PRESSURE		HEADACHE	
FACIAL CONGESTION/ FULLNESS		HALITOSIS	
NASAL OBSTRUCTION/ BLOCKAGE		FATIGUE	
HYPOSMIA/ ANOSMIA		DENTAL PAIN	
PURULENT NASAL DISCHARGE		COUGH	
		EAR PAIN/PRESSURE/FU	

		LLNESS	
		FEVER	

Nose:

External frame work: Normal / Abnormal

Vestibule and columella:

Anterior Rhinoscopy:

Septum: Central / Deviated: (R/L)/ Spur

Turbinates:

- **Atrophy**
- **Hypetrtrophy:**

Mucosa:

- **Normal / congested / dry / crusts**
- **Discharge: + / -**

Inferior meatus and middle meatus: Polyps: + / -

Floor:

Roof:

Cold spatula test:

Posterior rhinoscopy:

Post nasal discharge: +/ -

Mass:

PNS tenderness: + / -

DNE findings:

Mucosal edema: + / -

Polyps: + / -

Discharge in middle meatus: + / -

Obstruction of middle meatus: + / -

Others Findings:-

Examination:

GPE:

Vitals:

Systemic examination:

CVS: **P/A:**

RS: **CNS:**

Lund Mackay Score:

Throat:

Oral cavity: **Lips, teeth, gingiva, buccal mucosa:**

Tongue:

Soft palate, uvula:

Oropharynx: **Anterior and posterior pillar:**

Tonsils:

Posterior pharyngeal wall:

Lund-Mackay CT scan assessment
Paranasal sinuses
Maxillary (0, 1, 2)
Anterior ethmoid (0, 1, 2)
Posterior ethmoid (0, 1, 2)
Sphenoid (0, 1, 2)
Frontal (0, 1, 2)
Ostiomeatal complex (0, 2)*
Total
0 - With no abnormalities
1 - Partial opacification
2 - Total opacification
* 0: Without obstruction; 2: Obstructed.

LUND AND KENNEDY ENDOSCOPIC CLASSIFICATION

Criteria of assessment/ endoscopic observation	Scores		
	0	1	2
Polyps in the middle meatus	Absent	Restricted to middle meatus	Beyond the middle meatus
Discharge in the middle meatus	Absent	Thin and clear discharge	Thick and purulent
Edema of the middle meatus	Absent	Mild-moderate	Moderate-severe
Crusting in the middle meatus	Absent	Mild-moderate	Moderate-severe

PATIENT INFORMATION SHEET

I am Dr.KARNIKA R.K post graduate in the department of otorhinolaryngology Sri Devaraj Urs medical college Kolar. Conducting a study on –POST OPERATIVE RESPONSE OF MIDDLE MEATAL ANTROSTOMY OF MAXILLARY SINUS WITH AND WITHOUT MYTOMYCIN C APPLICATION" at R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar aiming to study whether application of Mitomycin C on the meatus will keep the meatus patent.

Study details: Chronic rhinosinusitis is currently a global problem and re-occurrence of the disease and undergoing revision surgeries are major issue in spite of undergoing the definitive surgical treatment available. Our study aims to determine the outcome of patency of middle meatal antrostomy site with or without after application of Mitomycin C after functional endoscopic sinus surgery to avoid re-occurrence of the disease and chances of needing revision surgeries.

Purpose: As application of mitomycin C on the meatus after middle meatal antrostomy will help keep the meatus patent in order to maintain aeration and proper drainage of the sinus. Our study aims to compare the outcome of the meatal patency after surgery as it will help avoid re-occurrence of the disease and further avoid revision surgeries.

Type of research intervention: This is a Prospective Comparative study.

Participant selection: selected after diagnosing chronic rhinosinusitis which is after failure of conservative treatment for 12 weeks for the same disease.

Voluntary participation: There is no compulsion to participate in this study. The care you will get will not change if you do not wish to participate.

Information on the trial: 50 patients who will be diagnosed as chronic rhinosinusitis will be

subjected to study after obtaining informed written consent. Patients will be counselled to undergo surgical procedure that is Middle meatal antrostomy (FESS) followed Mitomycin C for the patency of the meatus.

INFORMED CONSENT

I have read or have been read to me and understand the purpose for study, the procedure being Functional endoscopic sinus surgery (FESS) for middle meatal antrostomy of maxillary sinus and management of the patency of the meatus with application of Mitomycin C on one side as a part of research program and the possible associated complications and need for the intervention in a language I understand. I understand the risk and benefits associated with my involvement in the study and nature of information that will be collected and disclosed during the study.

I have had the opportunity to ask my questions regarding various aspects of the study and my questions are answered to my satisfaction.

I understand that I remain free to withdraw from the study at any time and this will not change my future care.

I the undersigned agree to participate in this study and authorize the collection and disclosure of my personnel information for dissertation.

Parents/ guardians name/ thumb impression.

MASTER CHART

CASES	UHID	AGE/SEX	DATE	DIAGNOSIS	OPERATIVE PROCEDURES	INTRA-OP MEASUREMENTS		3 WEEKS		3 MONTHS		6 MONTHS	
CASE1	827091	25/M	2/15/2020	B/L MAXILLARY SINUSITIS+ ALLERGIC RHINITIS+ DNS TO RIGHT	FESS+ Septplastry+ Planectomy	1	1	2	2	3	3	3	3
CASE 2	836790	36/F	2/24/2020	B/L MAXILLARY SINUSITIS	FESS	1	1	2	2	2	2	LOSS FOLLOW UP	
CASE 3	829751	28/M	3/2/2020	CRSsNP	FESS+ Septoplasty	1	1	2	2	2	2	2	2
CASE 4	830550	30/F	3/5/2020	CRSsNP	FESS+ Septoplasty	1	1	2	2	2	2	3	3
CASE 5	828072	37/F	3/5/2020	CRSwNP + RIGHT DNS	FESS+Septoplasty	1	1	2	2	2	3	3	3
CASE 6	45878	58/F	2/24/2020	CRSwNP+DNS TO LEFT	FESS+Septoplasty	1	1	2	2	2	2	2	2
CASE 7	829499	37/F	1/31/2020	CRSwNP+DNS TO RIGHT	FESS+Septoplasty	1	1	2	2	3	3	3	3
CASE 8	831394	20/F	2/2/2020	CRSwNP	FESS	1	1	2	2	2	2	2	2
CASE 9	829006	26/M	3/15/2020	CRSsNP +DNS WITH SPUR LEFT	FESS+ Septoplasty	1	1	2	2	2	2	2	3
CASE 10	830638	34/M	2/5/2020	CRSwNP	FESS	1	1	2	2	2	2	2	2
CASE 11	797754	48/M	1/26/2020	CRSwNP	FESS	1	1	2	2	2	3	3	4
CASE 12	805386	20/M	1/31/2020	CRSsNP	FESS	1	1	2	2	2	2	2	2
CASE 13	806929	20/M	3/15/2020	CRSsNP	FESS+ Septoplasty	1	1	2	2	2	4	3	4
CASE 14	819591	65/M	3/2/2020	CRSsNP	**FESS**	1	1	2	2	2	2	LOSS FOLLOW UP	
CASE 15	818126	32/M	2/24/2020	B/L MAXILLARY SINUSITIS	FESS	1	1	2	2	2	3	2	3
CASE 16	785797	52/M	3/20/2020	CRSsNP	FESS	1	1	2	2	2	3	2	4
CASE 17	880742	25/M	3/16/2020	BILATERAL MAXILLARY SINUSITIS	MIDDLE MEATAL ANTROSTOMY	1	1	2	2	2	2	2	2
CASE 18	880123	55/M	12/10/2020	CRS + NASAL RHINOSPORIDIOSIS	**FESS+ Septoplasty**	1	1	2	2	2	2	LOSS FOLLOW UP	
CASE 19	879117	57/M	12/14/2020	CRSwNP	FESS	1	1	2	2	2	2	2	3
CASE 20	880742	43/F	1/14/1900	CRSwNP+DNS TO LEFT	FESS+ Septoplasty	1	1	2	2	3	4	3	4
CASE 21	883394	23/m	1/6/2021	CRSsNP	FESS	1	1	2	2	2	2	2	3
CASE 22	883664	43/F	1/12/2021	CRSwNP	FESS	1	1	2	2	2	3	2	3
CASE 23	565266	20/m	1/16/2021	CRSsNP + DNS TO RIGHT	FESS+ Septoplasty	1	1	2	2	2	2	2	2
CASE 24	885648	21/m	1/18/2021	CRSsNP	FESS	1	1	2	2	2	2	2	2
CASE 25	880742	25/M	1/20/2021	BILATERAL MAXILLARY SINUSITIS+ DNS TO LEFT	FESS+ Septoplasty	1	1	2	2	2	2	2	2
CASE 26	8966235	23/F	1/20/2021	CRSsNP	FESS	1	1	2	2	3	3	3	3
CASE 27	888538	47/M	1/24/2021	CRSwNP	FESS	1	1	2	2	2	2	3	4
CASE 28	839955	34/F	2/1/2021	CRSsNP + DNS TO RIGHT+ ALLERGIC RHINITIS	FESS+ Septoplasty	1	1	2	2	3	3	3	3
CASE 29	827142	20/F	2/10/2021	CRSwNP+ S SHAPED DNS	FESS+Septoplasty	1	1	2	2	2	3	2	3
CASE 30	886677	43/F	2/13/2021	CRSwNP	FESS	1	1	2	2	2	2	2	4
CASE 31	885637	30/M	2/13/2021	CRSsNP+ DNS TO RIGHT	FESS+ Septoplasty	1	1	2	2	2	2	2	2
CASE 32	883728	65/M	2/13/2021	CRSwNP	FESS	1	1	2	2	2	3	3	3
CASE 33	892637	39/F	2/16/2021	BILATERAL MAXILLARY SINUSITIS	FESS	1	1	2	2	2	2	2	2
CASE 34	890328	24/M	2/24/2021	CRSsNP+ DNS R	FESS+ Septoplasty	1	1	2	2	2	2	2	2
CASE 35	892738	34/F	2/23/2021	CRSwNP+DNS TO LEFT	FESS+Septoplasty	1	1	2	2	3	3	3	4
CASE 36	892823	36/F	2/26/2021	ALLERGIC RHINOSINUSITIS	FESS	1	1	2	2	2	3	3	3
CASE 37	812345	67/M	2/26/2021	CRSwNP	FESS	1	1	2	2	3	3	3	3
CASE 38	891123	36F	3/1/2021	CRSsNP+ DNS TO RIGHT	FESS+ Septoplasty	1	1	2	2	2	2	2	2
CASE 39	892563	35/M	3/7/2021	CRSsNP	FESS	1	1	2	2	2	3	2	4
CASE 40	892738	34/F	3/13/2021	CRSsNP+ DNS TO RIGHT	FESS+ Septoplasty	1	1	2	2	LOSS FOLLOW UP	2	LOSS FOLLOW UP	
CASE 41	891727	24/F	3/16/2021	BILATERAL MAXILLARY SINUSITIS +DNS R	FESS	1	1	2	2	2	2	2	3
CASE 42	891783	23/M	3/20/2021	BILATERAL MAXILLARY SINUSITIS +DNS L	FESS	1	1	2	2	2	2	2	2
CASE 43	862636	19/F	3/20/2021	CRSsNP+ DNS TO RIGHT	FESS+ Septoplasty	1	1	2	2	3	3	3	3
CASE 44	808335	26/F	3/23/2021	CRSsNP+ DNS TO RIGHT	FESS+ Septoplasty	1	1	2	2	2	2	2	4
CASE 45	976532	55/M	3/28/2021	CRSwNP	FESS	1	1	2	2	2	4	2	4
CASE 46	978654	54/F	3/31/2021	ALLERGIC RHINOSINUSITIS	FESS+ Septoplasty	1	1	2	2	2	2	2	3
CASE 47	976754	34/M	4/11/2021	CRSsNP	**FESS**	1	1	2	2	2	3	3	3
CASE 48	976854	44/M	4/11/2021	BILATERAL MAXILLARY SINUSITIS + DNS R	FESS	1	1	2	2	2	2	LOSS FOLLOW UP	
CASE 49	978765	23/F	4/18/2021	CRSsNP + DNS TO LEFT	FESS+ Septoplasty	1	1	2	2	2	3	2	3
CASE 50	976584	48/M	4/18/2021	ALLERGIC RHINOSINUSITIS	FESS+ Septoplasty	1	1	2	2	2	2	2	2
CASE 51	986531	26/F	4/20/2021	CRSwNP+ DNS TO LEFT	FESS+ Septoplasty	1	1	2	2	2	2	2	4
CASE 52	986725	28/F	4/22/2021	CRSwNP+ DNS TO RIGHT	FESS+septoplasty	1	1	2	2	2	2	2	3

CASE 53	988672	37/M	4/25/2021	BILATERAL MAXILLARY SINUSITIS +DNS R	FESS	**1**	**1**	**2**	**2**	2	2	2	2
CASE 54	989179	30/F	4/28/2021	CRSsNP+ DNS TO RIGHT	FESS+ Septoplasty	**1**	**1**	**2**	**2**	2	2	2	2
CASE 55	989971	35/M	4/30/2021	ALLERGIC RHINOSINUSITIS	FESS+ Septoplasty	**1**	**1**	**2**	**2**	2	2	2	3

Legends :

MEASUREMENTS OF OSTEA SIZES:

1 - 1cm*1cm

2 - >5mm*5mm

3 - <5mm*5mm

4 - Stenosed.