DISSERTATION ON

"A STUDY OF PITUITARY MACROADENOMA TRANSNASAL ENDOSCOPIC EXCISION"

Dissertation submitted in partial fulfillment of the regulations for the award of the degree of

M.S.DEGREE BRANCH-IV OTORHINOLARYNGOLOGY of

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY



UPGRADED INSTITUTE OF OTORHINOLARYNGOLOGY, MADRAS MEDICAL COLLEGE, CHENNAI.

APRIL 2017

CERTIFICATE

This is to certify that this dissertation **"A Study Of Pituitary Macroadenoma Transnasal Endoscopic Excision"** submitted by **Dr.S.HEMACHANDRAN**, appearing for M.S ENT Branch IV Degree examination in April 2017 is a bonafide record of work done by him under our guidance and supervision in partial fulfillment of the regulations of the Tamilnadu Dr.M.G.R Medical University, Chennai. I forward this to the Tamilnadu Dr.M.G.R Medical University, Chennai, Tamilnadu, India.

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DECLARATION

I solemnly declare that the dissertation entitled "A Study Of Pituitary Macroadenoma Transnasal Endoscopic Excision" is done by me at Madras Medical College, Chennai-3 during June 2015 to September 2016 under the guidance and supervision of Prof DR. R. MUTHUKUMAR M.S, DLO., to be submitted to The Tamil Nadu Dr.M.G.R Medial University towards the partial fulfillment of requirements for the award of M.S DEGREE in OTORHINOLARYNGOLOGY BRANCH-IV.

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ACKNOWLEDGEMENT

I sincerely thank my guide **Prof Dr. R.Muthukumar**, **MS., DLO., DNB.,** Upgraded institute of otorhinolaryngology whose passion for teaching and interest in patient care with active academics has been a great source of inspiration to all the post graduates including me.

I thank my Director, Upgraded institute of otorhinolaryngology, my Chief coordinator **Prof Dr. M.K.Rajasekar, MS., DLO.,** who was instrumental in initiating new ideas and continues to support our endeavors.

I thank my professors **Dr.G.Sankaranarayanan**, **MS.**, **DLO.**, **DNB.**, and **Dr.N.Suresh Kumar**, **MS.**, **DLO.**, and my Assistant Professors **DR.K.Semmanaselvan**, **MS.**, **DLO.**, and **Dr.M.Venugopal**, **MS.**, who were kind enough to support and help me in my project.

I would like to thank my seniors, colleagues, juniors who were of great help throughout the project.

I thank my patients without whose will this would not have been a successful effort. I also thank my family and the Almighty for giving me the opportunity and strength to complete this project.

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INTRODUCTION

The most common pituitary tumour is adenoma, that accounts for 10 -15% of all intracranial tumour that originate from epithelial cells of pituitary. Depending on size of the adenoma it is classified as microadenomas[<10mm] and macro adenomas[>10mm] Pituitary macroadenomas are enclosed/ invasive or expanding [snow man or dumbell shaped]. The various modes of presentation are A) non secretory/non functional type that can be asymptomatic or produce mass effects like headache,visual defects,vomiting etc B)secretory/functional type-producing hormonal imbalance.

The role of imaging techniques has implication in surgery based on the tumour size, extent and consistency that determines the ease of resection, cure and occurence of complication.

The transnasal trans-sphenoidal endoscopic approach recently been applied procedure minimally invasive to ressect pituitary tumours .

By reviewing various surgical techniques for radical/complete exicision of tumour with restoration of vision and preservation of pituitary functions that are fullfilled with minimum morbidity and mortality.

The study also deals with per operative and post operative complications and their management

AIMS AND OBJECTIVES OF THE STUDY

Aim : To Study about the Pituitary Macroadenoma- Transnasal Endoscopic Excision Objectives :

1.To study the modes of presentation of pituitary macroadenoma

2.To evaluate radiological study of the tumour by computed tomography (CT) /magnetic resonance imaging (MRI) and its implications in surgical techniques
3.To review the surgical techniques in complete excision of the macroadenoma
4.To study the per operative and post operative complications and its management

ANATOMY

DEVELOPMENT OF PITUITARY GLAND

From the developing embryo the pituitary originates with two parts 1) dorsal evagination of stomodeum known as Rathke's pouch that is anteriorly immediate to buccopharangeal membrane with a ventral extension caudally to optic chiasma of diencephalon known as infundibulum, both are derivatives of ectoderm.2)The pouch of Sessel is another dorsal evagination of stomodeum arising posteriorly from buccopharyngeal membrane.^{1,2}

MORPHOGENESIS

The glandular epithelium is differentiated from Rathke's pouch and is characteristic of other endocrine organs. The exocrine ductless tissue is formed by infundibulum. The anterior end of notochord situated caudal to stomodeum induces glandular and neural primordial leading to development of hypophysis.

At 3rd week of intrauterine life³, ventral diverticulum in the floor of third ventricle developed from infundibulum leading to infundibular process by extension from median eminence known as infundibular stem.Dorsally an ectodermal placode appear in stomodeum roof and form Rathke's pouch by invagination simultaneously.

By 2nd month of intrauterine life, intergration of Rathke's pouch and infundibulum occurs by flattening of former with anterior and laterl surface of latter. There occurs pass through of chondrification centers of developing presphenoid and basisphenoid skull

bones due to connection between Rathke's pouch and oral cavity.By 6th week ,expansion of sphenoidal mesenchyme leads to regression of this connection.

Remnants of Rathke's pouch during its course if persists in oropharyngeal roof or in sphenoid bone presents as pharyngeal hypophysis or as basipharyngeal canal. The anterior lobe of pituitary (adenohypophysis) is formed by the cellular proliferation of Rathke's pouch's anterior wall-pars distalis. The pars intermedia is of less active walls of posterior Rathke's pouch⁴{cells do not proliferate extensively but differentiated},upward growth of anterior wall forms pars tuberalis. The Rathke's pouch which is incompletely obliterated ieads to remenant to form rathke's cleft/pituitary fissure. The differentiation of neural ectoderm into pars nervosa, infundibular stem and median eminence leads to development of neuro hypophysis

Infundibular stem is surrounded by pars tuberalis together comprises pituitary stalk. The neurohypophysis consists of neuroglial cells(pitucytes) as well as nerve fibres and terminal cells originating from hypothalamic nuclei. Apart from secretion and transport of hormones from neurohypophysis, pituicytes have phagocytic activity.

DEVELOPMENT OF PITUITARY

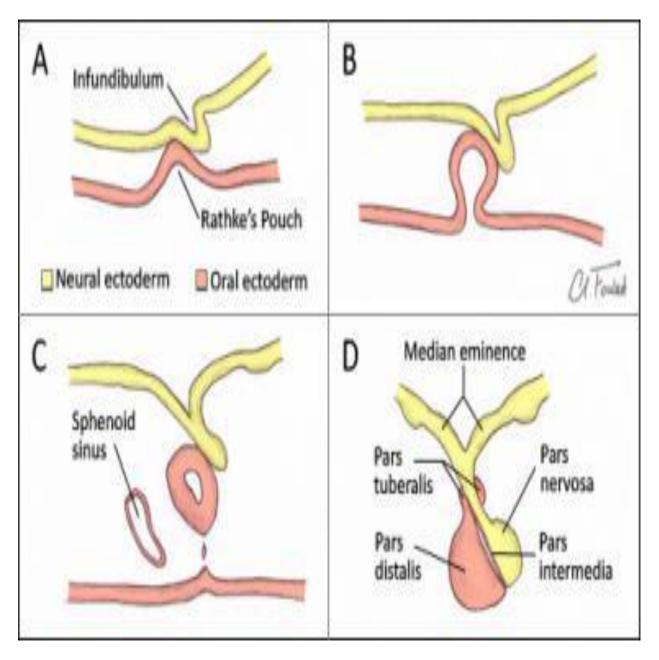


FIG-1

A:Infundibulum and Rathke's pouch develop from neural ectoderm and oral ectoderm, respectively. B: Rathke's pouch constricts at base. C: Rathke's pouch completely separates from oral epithelium. D: Adenohypophysis is formed by development of pars distalis, pars tuberalis, and pars intermedia; neurohypophysis is formed by development of pars nervosa, infundibular stem, and median eminence.

HISTOGENISIS

The third and fourth month of gestation anterior lobe cells arranged cords around blood sinuses with surrounding mesenchyme inducing glandular organisation.By first⁵ trimester the portal blood vessels are fully established.differenciation of anterior lobe cells characterised affinity of cytoplasm into acidophilic basophilic and chromophobes.Basophilic cells concentrated in pars medialis whereas acidophilic cells are concentrated inpars lateralis.the early detected hormones are corticotrophs betaendorphin and leutinising hormone and follicular stimulating hormone.Trh developed in early second trimester .during second half of pregnancy growth hormone and prolactin are synthesised.In late fetal life neurosecretory activity of posterior lobe begins.

ANATOMY OF PITUITARY AND SELLAR REGION

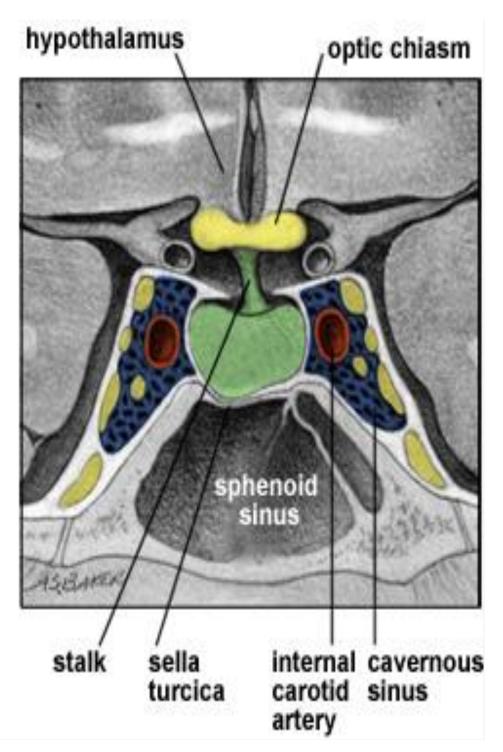


FIG-2

Sellar anatomy- the sphenoid bone is the entry for skull base that is located in the centre of skull base.recently the endoscopic endonasal approach to skullbase iss accesss to the middle of the skull base.the bony constituents of sella turcica forms the limitation of the pituitary fossa anteriorly posteriorly and inferiorly .the average bone thickness is 0.4mm .the average distance from fossa is 14 to 17 cm.anterior boundary of pituitary fossa forms tuberculum sella whereas posterior boundary forms dorsum sella. A minimal groove lie at optic foramen which forms chiasmatic sulcus . The sellar tuberculum lies posterior and sphenoidale planum anterior to the chiasmatic sulcus.

Rounded knob like structures formed by supralateral margins of dorsum sella called as posterior clenoid process. The middle clenoid process are lateral to the tuberculum sella .Anterior clenoid process located in the medial wing of lesser wing sphenoid.

The dorsum sella is continuous as clivus the superior portion of which is formed by bone of sphenoid and inferior portion is formed by bone of occiput. Along lateral surface of the body of sphenoid extends the carotid sulcus. Hypophyseal floor is formed by roof of sphenoid sinus partly/completely.

Sphenoid sinus is subject to considerable variation in size shape and to degree of pneumatisation. Adult sphenoidal sinuses based with pneumatisation are –conchale ,presellar and sellar type.Conchale type - a solid block of bone with out aircavity area below sella.Presella type -penetrtion aircavity doesnot occur beyond vertical plane parallel to anterior sellar wall. Sellar type-aircavity enters extends into body of sphenoid below the sella as posteriorly as the clivus.The septa/bony trabeculae

within sphenoid sinus vary in size, shape, thickness and location and completeness and relation to the sellar flow.Only in 20% of cases inter sinus septum is attatched to midpoint of anterior sella and may be absent altogether.The posterior attatchment of inter sinus septum to serpeginous prominence produced by carotid artery into the sinus wall below the floor and along the anterior margin of the sella.Usually optic canal protrude into supra lateral portion of the sella and infrolateral part of the second division of trigerminal nerve protrudes.

High variability of Sella contour –round/ oval /profile with flattened although .At birth shallow depression at sella dorsum ossification not occurred. By approximately four years of age sella outline appears more rounded .Diaphragma sella forms the incomplete roof of sella turcica covering the pituitary gland except a central opening for transmitting pituitary stalk.The shape of diaphragm sella is more of rectangular and has convexity or concavity.

The anterior lobe of pituitary from overlying optic chiasma is separated by diaphragm sella. The margins of diaphragm are attatched to the tuberculum sella , anterior clinoid process and dorsum sella superior aspect. The lateral wall of pituitsry fossa is by lateral continuation of diaphragm with dural folds. The variable size in central aperture of diaphragm ranging from a small foramen to a large hole surrounded by a tenacious membrane of tissues. A deficiency in diaphragm sella is preconditioned to form empty sella. Though this central opening in diaphragm sella an outpouching arachnoid protrudes in 50% of cases indicates important source of post operative cerebrospinal leak..

PITUITARY GLAND-it is a pea shaped gland situated in fibro osseous compartment within the hypophyseal fossa at the centre of the skull base. It weighs about 100 mg averagely at birth. The size in adults is 10 mm in length ,10-15 mm width and 5 mm height. Female gland is 20% heavier than the male gland. The weight of the gland increases by 12 to 100 % during pregnancy. Accurate size can be measured with MRI. Volume of pituitary gland decreases with aging. The lower part of the pituitary stalk is wrapped by anterior lobe to form pars tuberalis. Compared to anterior lobe posterior lobe is more adherent to sella wall.

In most patients the width of the gland is equal or more in its length / height. The Shape of sella floor is confirmed by inferior surface of the gland .Even the lateral and superior margin ary in shape as the walls are composed of soft tissue rather than bone. The gland tends to be concave superiorly in the area around the stalk if there is a large opening in the diaphragm. As a result of compression of gland laterally and posteriorly by carotid artery the superior surface is triangular. The tendency of pars tuberalis to be retained with posterior lobe as anterior lobe is separated from the posterior lobe. During separation of anterior and posterior lobe the intermediate lobe cysts are frequently encountered.

PARASELLAR/SUPRASELLAR ANATOMY-the lateral wall of hypophyseal fossa formed by folds of duramater contains cavernous sinuses consisting serially arranged compartments of venous channels separated by fibrous trabeculae.

The communication between two cavernous sinuses leads to intercavernous connection named on the basis of relationship to pituitary gland i.e. anterior intercavernous sinus runs anterior to diaphragma sella and posterior intercavernous sinus behind the pituitary stalk. The anterior sinus is usually larger than the posterior sinus but either or both maybe absent if connections coexists forms circular sinuses. The lateral wall of cavernous sinus the occulomotor nerve ,trochlear nerve and first two divisions of trigerminal nerve are embided lying between the dura and the endothelial lining but 6th cranial nerve is present with the sinus. A small portion of the internal carotid artery encircled with sympathetic nerve trunk is enveloped by cavernous sinus. The forward extension cavernous segment of internal carotid artery(ICA) is adjascent to supralateral surface of body of sphenoid bonewith groove known as carotid sulcus. The ICA courses superiorly medial to the anterior clinoid process at the anterior end of carotid sulcus and pierces the dura and enters subarachnoid space. ICA medial limitus approximately 5 mm awayfrom midline whereas lateral limit vary from 13-20 mm from midlineThe Suprasella region- over the hypophysis is hypothalamus and visual pathways.

Depending upon the variations in the development of sphenoid bone just anterior hypophyseal fossa producing inconsistency in the relation between pituitary gland, stalk ,diaphragma sella and sulcus chiasmaticus. The variations are

1.body of sphenoid bone develops so that sulcus chiasmaticus is more inferior than usual known as prefixed chiasma present in 10% of cases.

2.intracranial course of optic nerve is slightly larger than the preceding pattern .Therefore the entire optic chiasma rests above the anterior part of diaphragma sella leading to most vulnerable of optic chiasma to supra sellar extension of pituitary tumour in 12% of cases.3.optic chiasma most posteriorly placed than previous arrangement in 75% of cases.

4.optic chiasma located on and behind dorsal sella leads to vulnerability of the medial aspect of optic nerve when suprasellar extension of intrasellar tumour.

Nerve supply -The anterior pituitary has no direct nerve supply other than autonomic nerves. The posterior lobe, in contrast, is composed almost exclusively of hypothalamic nerve fibres.Hypothalamic projections release hormones and trophic factors by neurosecretion into the median eminence and portal system. There are two principal tracts; the hypothalamo-hypophyseal tract arises in the magnocellular neurones of the supraoptic and paraventricular nuclei and releases vasopressin and oxytocin into the posterior pituitary, the parvocellular neurones of the tubero-infundibular tract originate in multiple hypothalamic nuclei and project to the median eminence.

Circulatory supply The adenohypophysis and hypothalamus share a complex portal blood supply carrying trophic and inhibitory hormones from the hypothalamus, thus regulating systemic release of anterior pituitary hormones. The anterior pituitary has no direct arterial supply.Branches of the superior, middle and inferior hypophyseal arteries supply the median eminence and posterior pituitary. The superior hypophyseal arteries branch into an internal and external plexus. The internal plexus forms glomeruloid structures known as gomitoli. Gomitoli regulate the flow of regulatory hormones in the pituitary paracrine 'biological network' and are the presumed origin of sellar glomangiomas. The inferior arteries supply the pituitary capsule, the neural lobe and the pituitary stalk.The venous drainage of the pituitary gland is to the inferior petrosal sinuses via the cavernous sinus.The capacity of the venous drainage is exceeded by the volume of blood entering the gland, thus forming a reservoir. Reversal of blood flow here results in secretory products from the adenohypophysis entering the neurohypophysis and median eminence. This vascular anatomy is important in the pathophysiology of apoplexy.

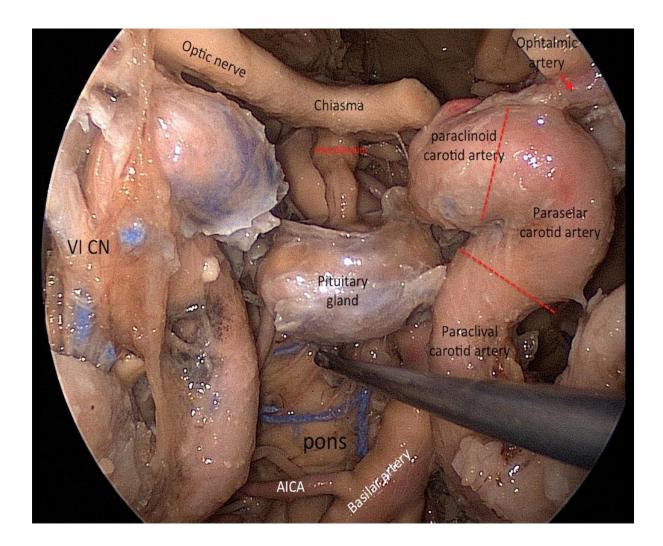


FIG-3

SELLAR AND PARASELLAR REGION

(ENDOSCOPIC AND ENDONASAL ANATOMY)

PHYSIOLOGY OF PITUITARY

Pituitary gland consists of two principle lobes anterior lobe, posterior lobe and intermediate lobe situated between anterior and posterior lobe .Anterior lobe secretes following hormones growth hormone (GH) ,thyroid stimulating hormone(TSH), adenocortico trophic hormone (ACTH) ,gonadotrophic hormone (GnRH)-a)follicular stimulating hormone b)leutinizing hormone prolactin

Secretion of anterior pituitary hormone is governed by hormones from median eminence of hypothalamus .Cortico tropin, prolactin and growth hormone are simple polypeptides whereas leutinizing hormone follicle stimulating hormone ,and thyroid stimulating hormones are glycoproteins .

The glycoproteins are made up of two subunits (heterodimer namely alpha and beta). Alpha subunits hormones reproducts of chromosome 6 of a single gene. Beta subunits varying in structure produced by different genes. Secretions of alpha subunits only describe with the context of non functioning pituitary adenoma.

Serum levels of anterior pituitary hormones along with alpha subunit can be measured by radio immunoassay.Growth hormone-the somatotroph of anterior pituitary secretes peptide hormone known as growth hormone. Growth hormone releasing hormone(GHRH)

Stimulates secretion of growth hormone. Somatomedin-exerts range of wide metabolic actions. Hypoglycemia increase plasma levels of aminoacids ,decrease plasma free fatty

acids ,inhibits uptake of glucose by most of tissues.Glucose is conserved for brain use by anti insulin action,promotes lipolysis-non carbohydrate substrate for ATP generation.

Synthesis of protein is promoted by GH and is crucially needed between the age of three years and puberty for normal skeletal growth. Synthesis of IGF and its secretion stimulated by growth hormone. The cartilage cells derived and deposited at epiphyses (growth plate) is encouraged and enhanced by IGF.

The pituitary gland normally secretes GH with a molecular weight of 22000.Corticotrophic hormones-seccreted by anterior pituitary corticotrophs.The action of corticotrophin for the basal secretion of glucocorticoids and aldosterone as well as hormones produced by various stresses act on the adrenal gland.Rapid atrophy of adrenal cortex occurs after hypophysectomy. It is a polypeptide containing 39 aminoacids with its half life in circulation approximately 10 minutes.participating in rapidly adjustment of circulatory levels of glucocorticoids is due to this half life property .

ACTH regulates the secretion of glucocorticoids steroid hormones and responds to stress.Pituitary glycoprotein hormones-TSH ,FSH ,LH .TSH regulates the secretions of thyroxine (t4) and tri-iodo thyronine.These secretions are regulated by hypothalamic TRH.A triangular peptide in medial part of paraventricular nucleus .

TSH contains 211 aminoacids and biological half life is 60 minutes.TSH secretion is pulsatile and peaks out during midnight.TSH acts on cell receptors and activates adenalyl cyclise through a GTP binding protein.TRH is increased during exposure to cold temperature.By feedback inhibition T3 AND T4 levels are blocked by TSH.

FSH and LH –Regulates the function of gonads.The secretion is influenced by hypothalamic gonadotrophic releasing hormone(GnRH) which is a decapeptide. In females FSH helps preparation for ovulation and secretion of estrogen by growing follicle. LH triggers ovulation and production of progesterone by corpus leuteum.I FSH is needed for spermatogenesis while LH produces testosterone by leydig cells in males.The half life of FSH is 170 minutes that of LH is 60 minutes.

Secretion of GnRH is pulsatile for purpose of reproduction and endocrine function.Inhibin synthesised in gonads of both sexes is a polypeptide inhibits FSH.

PROLACTIN(PRL)-contains 198 aminoacid residues .Half life is 20 minutes similar to growth hormoneand the receptors also resemble growth hormone and undergoes dimerisation before activating several intra cellular enzyme cascades .PRL secretion is usually inhibited by hypothalamic prolactin inhibiting homone or prolactin inhibiting factor called dopamine.Hormonal release is generated in response to sucking inhibits the hypothalamic dopamine release in lactating women .Prolactin inhibits the action of gonatrophin on ovary that prevents ovulation during lactation or those with prolactin secreting tumour.Excessive prolactin in male leads to impotence.

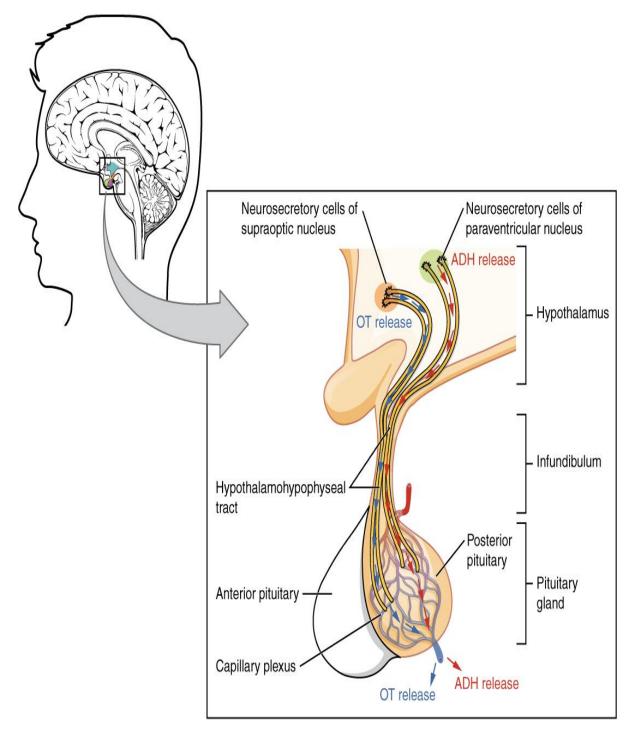
Physiology of intermediate lobe-about 3.5% of glandular mass of pituitary is cells of pars media in human fetus but less than 1% in adults. The pars intermedia synthesise POMC, a large protein precursor .The principal products of POMC hydrolysed to form CLIP,gamma lipoprotein, beta endorphin and melanotrophins. The intermediate lobe form two melanotrophins , alpha –MSH and beta MSH where beta MSH controls migration of pigment molecules.melanin synthesis is due to MSH molecule binded to melanotrophin 1 receptor on melanocytes.

Physiology of posterior pituitary-Oxytocin and Vasopressin are the hormones of posterior lobe.The latter also called as anti diuretic hormone(ADH),as one of its principal physiological effects is retention of water by kidneys.In response to electrical activity at the axon endings posterior lobe hormones are released in to general circulation.Both these hormones contains nonapeptides with a disulfide ring at one end.Synthesis of these hormones occurs in the cell bodies of the magnocellular neurons of supraoptic and paraventricular nuclei of hypothalamus.Supraoptic fibres mostly end in posterior lobe itself whereas paraventricular fibres some end in median eminence as well. Release of stored hormones is trigerred by calcium-dependent exocytosis in response to action potential.

Oxytocin-Action of oxytocin occurs through G-protien-coupled receptors of cell surface, triggering of which increases intracellular calcium in response to activation.Oxytocin casues contraction of myoepitheleal cells lining the breast ducts.Tactile stimulation of nipples leads to flow of milk from alveoli of breast.Contraction of utrine smooth muscles during delivery leads to fetal descent and enhances labour and in non pregnant uterus acts by facilitation of sperm passage in to fallopian canal.In men oxytocin increases at the time of ejaculation that propels sperm towards urethra by contraction of vasdefrens smooth muscle.

Vasopressin (ADH-Antidiuretic hormone)-Vasopressin action through cell surface receptors namely,serpentine,transmembrane and G-protien coupled receptors leads to formation of second messanger and exerts many physiological effects on body.Vasopressin's half life biologically is 18 minutes.

Action on collecting ducts: permea bility of collecting duct is increased by aquaporin water channels translocation from endosomal compartment to luminal side enables entry of water to the hypertonic interstium of renal pyramid. This leads to decrease in urine volume and increase in concentration of urine. Conditions that increases ADH are decreased blood volume, increased plasma osmotic pressure, increased angiotensin II levels, pain , emotion and exercise. ADH secretion is inhibited by alcohol. Vasopressin is potent vascular smooth muscle constrictor and also acts by paracrine action on anterior pituitary and releases corticotrophin hormones.





PHYSIOLOGY OF PITUITARY

REIVIEW OF LITERATURE

HISTORCAL RIVIEW

Scholffer in1906 was first person to succesfully remove the pituitary tumour via trans sphenoidal approach and considered to be safe.In 1909,Hirsch used submucosal resection of septum and endonasal approach.1910-A.E.

Halstead's description of sublabial gingival incision for initial stage of exposure.By 1914,Harvey Cushing combined sublabial incision with submucosal septal approach,preserving nasal functions without an external scar with contemporary to OskarHirsch,operated 231pituitary tumours with mortality of 5.6%.

Cushing got expertise in transcranial surgery and able to verify supra sellar tumour and achived decompression of optic apparatus better, resulting in better recovery of vision and lower reccurrence rate however, the mortality rate is reduced to 4.5%. As Cushing influenced neurosurgery world wide, his shift from the trans sphenoidal to transcranial approach was to influence the destiny of pituitary surgery for many years to come.

At a period of time the trans nasal surgery was abandoned by Cushing himself and all other neurosurgeons went in favour of transcranial approach.Norman Dott , a visiting scholar passed through Edinborough ,Scotland because of his work the lineage that kept the transphenoidal procedure alive where others persued transcranial approach.Dott appreciated the merits of transsphenoidal procedure during his stay in Boston fromNovember 1923 to June 1924.He designed instruments specifically for the transphenoidal procedure. In 1956 Gerad Guiot ,a pupil of the legendary French Neuro surgeon Clovis Vincent visited Normann Dott and had a chance of observing transphenoidal operation.

Guiot introduced intra operative radiographic control and intra operative fluoroscopy during transphenoidal surgery.Guit in 1958 presents its first few papers of pituitary adenoma operated on transphenoidally in front of French society of neuro surgery and revived the interests of many physicians throughout Europe.

Joules Hardy decided to try the transhenoidal route and able to perform hypophysectomies in a dark ,deep and narrow field.He also introduced operating microscope for the refining the procedure.

The concept of microadenoma was introduced by him and demonstrated surgical cue to be possible in case of small hypofunctioning adenomas and significantly increases the efficacy and surgical morbidity.In 1970 the development of endoscopy occurred ,in 1992 Jankowski et al performed endoscopic transnasal transhenoidal approach,then in 1996 Jho et al described entirely endoscopic transnasal transphenoidal approach.



FIG -5:Harvey Williams Cushings



FIG-6 : Normann Dott

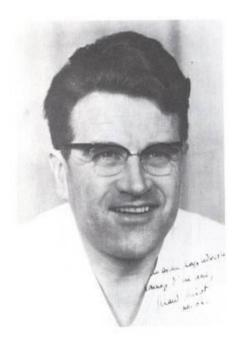


FIG-7: Gerad Guiot

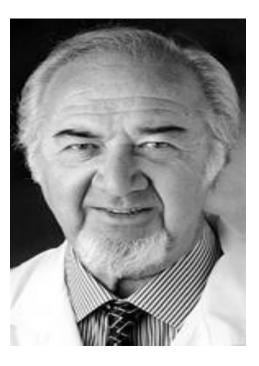


FIG -8: Hardy Jules

"Pituitary macroadenoma-The sellar region is a site of various types of tumors. Pituitary adenomas are the most common. They arise from epithelial pituitary cells and account for 10-15% of all intracranial tumors. Tumors exceeding 10 mm are defined as macroadenomas, and those smaller than 10 mm are termed microadenomas. Most pituitary adenomas are microadenomas".

Pathophysiology "The cause of pituitary macroadenomas is unknown. The most acceptable theory attributes monoclonal neoplastic transformation of pituitary cells leading to tumor initiation and growth. The monoclonal nature of most pituitary tumors and their retention of a response to negative feedback by hormones produced by target organs support this hypothesis."

Pituitary macroadenomas are epithelial tumours , benign in nature and consists of anterior pituitary cells. Primary pituitary tumors that are malignant are not common. The development of pituitary adenoma has irreversible initiation phase followed by tumor promotion phase . Heredity ,hormonal and genetic mutations influence development of pituitary macroadenoma . The monoclonal nature of most pituitary tumors indicates that they arise from a mutated pituitary cell.

A report suggested that patients with pituitary tumors from 4 Irish families share a common mutation with a patient from the 18th century who had pituitary tumor– mediated gigantism indicating the role of genetic mutation.

"Specific immunochemical stains permit differentiation of anterior pituitary cells into somatotrophs (growth hormone; GH), lactotrophs (prolactin), thyrotrophs (thyrotrophin; TSH), gonadotrophs (luteinising hormone and follicle-stimulating hormone; LH and FSH) and adrenocorticotrophs (adrenocorticotrophin; ACTH)." Any of these cell types can give rise to functional or silent adenomas. Mutations in the Ikaros gene and cell cycle proteins are implicated in pituitary tumorigenesis. Pituitary adenomas can be differentiated from normal pituitary tissue by the loss of the nodular reticulin framework and uniform immunohistochemical staining with a single pituitary hormone.

Adenomas may be hormonally inactive, presenting particularly with visual field defects, headaches, nausea and vomiting. Tumours that secrete hormones often produce clinical symptoms corresponding to the systemic effects of the hormone concerned. Adenomas often maintain some degree of hormonal regulation and pituitary carcinomas are rare, supporting the concept of 'reversible plasticity' in pituitary adenomas. Aggressive nature of pituitary adenomas can be predicted by over expression of the cell proliferation marker Ki67 (Mib-1) or increased expression of the p53protien.

Various modes of presentation

"Pituitary tumors can be either secretory or non-secretory, stating to whether they overproduce pituitary hormones. Secretory tumors cause disease because of the excess quantities of hormones which they secrete (release) into the bloodstream. The most common type of secretory pituitary tumor is termed as prolactinoma. Excess prolactin in the blood may lead to irregular or absent periods in women, decreased libido and erections in men and infertility or milk production in men or women. However, there are excellent medicines available to treat this disorder, so surgery is rarely needed. Most patients with prolactinomas are treated by endocrinologists, who are medical specialists in gland and hormone disorders".

"Secretory tumors, that commonly require surgery, include those which cause acromegaly and Cushing's disease. Acromegaly (or gigantism if occurring in a child) results from an too much of growth hormone production". Excess of adrenocorticotropic hormone (ACTH) leads to overproduction of cortisol by the adrenal glands, giving rise to a disorder called Cushing's disease. Surgical removal of these tumors can restore normal hormone production in many cases. "Non-secretory tumors ("non-functioning") do not overproduce hormones, but cause problems due to their size and location. This is because they can compress both the normal pituitary gland and the surrounding structures. Hormone deficiencies may result from compression of the normal pituitary gland. Nonsecreting tumors can also cause vision defects by growing upwards and compressing the optic nerves and chiasma, nerves which are essential for vision. This pressure can lead to loss of peripheral vision. Surgical removal such tumors relieves the pressure on structures surrounded by"

Symptoms:

"Tumors in asymptomatic patients may be discovered when imaging the head for unrelated medical conditions. The frequency of diagnosis of pituitary tumors has increased with widespread use of computed tomography (CT) and magnetic resonance imaging (MRI) scans."

"Pituitary hormone effects depend on the hormones involved. Panhypopituitarism may present with a deficiency of all the pituitary hormones, but often some are spared. The larger the tumor, the more likely it is to involve most hormones. Anterior pituitary cells are not equally sensitive to mass effects. The most sensitive are the somatotrophs and the gonadotrophs, whereas corticotrophs and thyrotrophs tend to be more resistant. Distinct clinical syndromes, specifically the following, are the result of the hormonal activity of the tumor". Hyperprolactinemia manifests as hypogonadism, infertility, amenorrhea, and galactorrhea. due to increased hormone production by a prolactinoma, or due to stalk compression by the tumour. Cushing disease occurs due to corticotropin excess .Corticotropinomas are rarely macroadenomas. Compression of the normal corticotrophs causes corticotropin suppression and leads to glucocorticoid insufficiency. secondary hyperthyroidism arises with thyrotropin excess. Thyrotropinomas are uncommon and frequently present as macroadenomas. Biologically inadequate thyrotropin presents with secondary hypothyroidism.

Excess growth hormone result in acromegaly due to somatotropinoma. Failure to thrive in children is seen in GH insufficiency but not so in adults.

Gonadotropinomas most often are asymptomatic and are macroadenomas resulting in hypopituitarism. Testicular enlargement in men and ovarian hyperstimulation in women are its uncommon features. Hypogonadism and infertility occur due decrease of gonadotropins.

Visual defects, headache, raised intracranial pressure, or intracranial bleed are due to pressure effects of the macroadenoma..

Pituitary apoplexy results from infarction of a pituitary tumor or sudden hemorrhage within. It is a medical emergency. It presents with headache, sudden collapse, shock, and death if not treated emergently. This tends to occur in macroadenomas. Administration of TSH, GnRH, and insulin-hypoglycemia, increases the metabolic needs by the macroadenoma, leading to necrosis. Presenting symptom of a gonadotropinoma in an elderly men receiving GnRH agonist therapy for prostate cancer may be apoplexy.

Nelson syndrome results from treatment of Cushing disease with bilateral adrenalectomy. Lack of negative glucocorticoid feedback leads to excessive tumor growth which are aggressive in nature.

Signs

Mostly patients associated with macroadenomas are asymptomatic. Physical findings are due to mass effects or hormonal disruption. Visual field defects appear when tumour extends on to optic chiasma . Sudden enlargement in tumor size, due to hemorrhage, may lead to raised intracranial pressure. Hyperthyroidism, Cushing syndrome, or hyperprolactinemia are manifestation of target organ stimulation in secretory tumours .

Mirian Cabral et al⁶ reported that most prevalent tumour was the producer of GH(7.6%), followed by prolactinoma(6.9%), and adrenocorticotropic hormone(6.2%). Thyrotrophic hormone producing tumour was very less (0.7%).

Omar López Arbolay etal⁷ reported that among 238 patients with macroadenomas and 40 with microadenomas were operated on using the EEA technique. 92 were functioning tumors and 186 non-functioning. Headache and visual field defects were the most common complaints in patients with non-functioning adenomas. In patients with secreting tumors modes of presentation depended on the increased hormone.

Role of imaging techniques and surgical implication

In adults most common suprasellar mass is pituitary macroadenoma that is responsible for trans sphenoidal hypophysectomy in majority of cases. Solid tumours with attenuation similar to brain (30-40 hounse field with moderate contrast enhancement) in MRI T1 and T2 weighted images show isointense to the grey matter , these attenuation and signal characters however vary significantly depending on tumour components such as hemorrage , cystic transformation and necrosis.⁸

In CT scan contrast attenuation cannot vary on hemorrhage, cystic mass and necrosis. pituitary adenomas are isodense to adjasceent brain parenchyma on unenhanced CT. They demonstrate intense contrast enhancement after injection of contrast material. Bony erosion and expansion of sella turcica are well demonstrated on bone window images. Calcification is less common in 5% of cases. Hemorrahge within pituitary tumour is rare that can be detected as focal hyper density. Solid adenomas without hemorrhage typically have attenuation similar to brain and demonstrate isodense on enhancement⁹.

MRI is the most powerful modality for delineating the mass and also visualise the optic chiasma, central vessels and cavernous sinus.Over all signal characters depend on component of the tumour whether cystic hemorrahage or necrosis.T1 shows isointense to grey matter typically after heterogenous with larger lesion and due to areas cystic changes ,hemorrahage and necrosis that vary in signal.T1C +Gd (gadolinium)-solid component shows moderate to high enhancement .T2 isointense to grey matter typically .Heterogenesity after with larger lesions and vary with signal due cystic hemorrhage and necrosis.Calcification is rare and excluded with CT.

T2 gradient with echo is more sensitive for delineation of hemorrhagic components with areas of signal loss . Pituitary macroadenomas preoperative evaluation of consistency with DW MRI¹⁰ the transnasal approach is contraindicated in tumour extension into 1.sphenoid sinus; 2.ectactic midline carotid artery (kissing carotid) ;3.significant lateral suprasellar extension.

Based on tumour consistency -Most of the macroadenoma are easily resectable due to soft consis tency.Only 10% are fibrous and shows increase in consistency.Clinical Knowledge of macroadenoma consistency helps to plan the surgical technique well before the surgery properly.¹¹Role of conventional MRI in relationship to consistency of macroadenoma is controversial.In one study macroadenoma of lower T2weighted signal intensity (SI) image shows enhancement more homogeneously with the mass are fibrosis/more collagen.¹² Another study suggested that no particular correlation between MRI and tumour consistency.DW MRI measure diffusion of water and affected by the size and strength

of structures normally restricts brain diffusion.¹³ Tumour consistency at time of surgery blinded to DW MRI finding evaluated by neurosurgeon.Based on the apparent diffusion coefficient the tumours were classified on three groups -1.soft consistency tumour that are easily removable through suction ,2.intermediate consistency tumour that has difficulty in removal with suction 3.hard consistency that are not able to be removed by suction but by excision enbloc.¹⁴

DW imaging with generator of apparent diffusion coefficient (ADC map useful method for prediction of consistency of pituitary macroadenomas with respect respectability of tumour with endoscopic technique.Mass arising from pituitary fossa that is hypointense on T1 MRI images and hyperintense and heterogenous in T2 weighted images.¹⁵

On conventional MRI tumour consistency and signal intensity on T2 weighted MRI shows soft tissue tumours displays lower SI than intermediate and hard groups.Fibrous tissue in macroadenoma with high cellularity with a nucleus to cytoplasm ratio is low

indicates lower signal intensity whereas extracellular space may cause larger increase in SI on T2 weighted MRI because of free increase in water.¹⁶ No relation between tumour consistency on SI T1 weighted MRI and contrast enhanced but cyst and haemorrhages are easily depicted by conventional MRI and easily found in Macroadenoma.^{17,18}

DW MRI images provide information about consistency of macroadenoma during surgery more than 50% of macroadenoma which is softer consistency allowed complete removal through suction .Therefore the ADC is relatively low.In intermediate consistency the ADC is slightly higher than the soft growth.In hard consistency solid tumours cannot be aspirated and excision done by enbloc.ADC significantly higher than those of intermediate and soft type of tumours. Therefore the preoperative detection of tumour check with DW MRI and ADC map as a relationship with tumour resectability.

In a study conducted by Alberto Pierallini he reported the tumor consistency at surgery was soft in 12 (55%) patients, intermediate in six (27%) patients, and hard in four (18%) patients. In two patients, cystic components were evident with conventional MR imaging sequences and were confirmed at surgery.

Of the twenty nine patients, peroperative tumor consistency was classified as hard macroadenoma in 17% and soft macroadenoma in 83% of the cases according to J. Yamamoto etal.¹⁹ In the surgical management of pituitary macroadenomas the transsphenoidal approach has become the preferred operation because of its low morbidity and mortality.^{21,22,23} The factors determining a complete excision are cavernous sinus invasion, size and consistency of the tumor. Radical excision of the tumor with restoration of vision and preservation of pituitary function are the goals of surgery for

pituitary adenomas. The transsphenoidal approach fulfills these goals with minimal morbidity and mortality. ²³

Hardy's classification of the suprasellar extension of pituitary adenomas

Type-A **T**umour with sellar extension, not reaching the optic chaiasma

Type-B Tumour reaches the floor of 3^{rd} ventricle obliterating the anterior recess of 3^{rd} ventricle

Type-C Tumour indents the floor of 3rd ventricle

Type-D Tumour with intradural extension

Type-E Tumour invading the cavernous sinus

"The grade A and B tumors were considered easier to excise while the removal of grade C and D tumors, those that had a superior margin more than 20 mm above the jugum sphenoidale, was more difficult (40% had residual tumor on the postoperative CT scan). The coronal images provided additional information regarding asymmetric lateral expansion of the tumor (grade D) that made a complete excision technically more difficult. Wilson's modification of Hardy's system²⁴ introduced a 'stage E' when there was a direct lateral extension into the cavernous sinus and subsets to the 'stage D' when there was extension into the anterior, middle and posterior fossae."

The transsphenoidal surgical line of vision on a sagittal MRI is useful in assessing the ease of resectability of pituitary adenomas, especially in Grade C tumors. Depending on the clinical course, it may be possible to plan either a second stage transsphenoidal surgery or a craniotomy when more than 50% of the tumor is above the line of vision.

KNOSP classification of parasellar extension

Knosp et al²⁵ offered a grading system for showing invasion of cavernous sinus by pituitary macroadenoma. Briefly, the much laterally adenoma grows and surrounds the ICA, the more grade level is. The grading defined by the relation of carotid lines with the limits of invasion. These lines passes through supra- and intra-cavernous parts of ICA in coronal view. There are medial, median and lateral carotid lines

Grade 0 –Adenoma did not encroach the cavernous sinus space,not crossingthe medial aspect of intra and supra cavernous ICA

Grade 1- Tumour crosses medial tangent but does not extend beyond inter carotid line

Grade 2- Tumour crossed beyond intercarotid line but does not cross beyond lateral tangent of intra and supra cavernous ICA

Grade- 3 - Tumour extends beyond lateral line

Grade-4- Total encasement of intra cavernous ICA by tumour

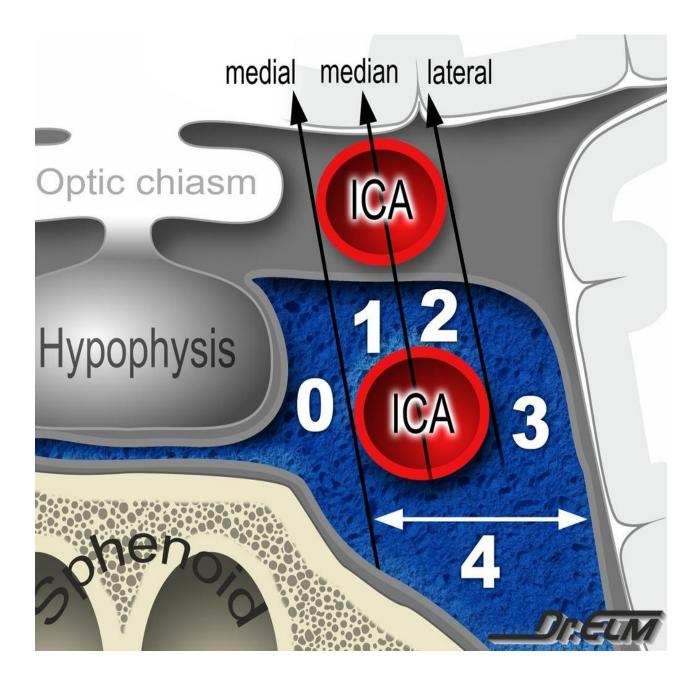


FIG-9 KNOSP CLASSIFICATION OF PARASELLAR TUMOUR

a Hardy classification system

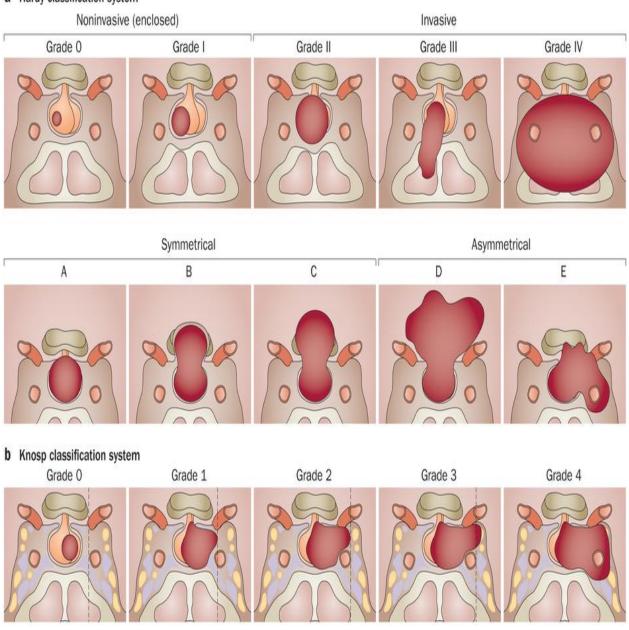


FIG -10

a) HARDY CLASSIFICATION AND b) KNOSP CLASSIFICATION

a) Hardy classification system. "

Sella turcica tumours can be

1.noninvasive :grade 0- intact with normal contour; grade I-intact with bulging floor; or grade II- intact, enlarged fossa or

2.invasive :grade III- localized sellar destruction; or grade IV-diffuse destruction. Suprasellar tumours can be

1.symmetrical :grade A- suprasellar cistern only; grade B- recess of the third ventricle; or grade C- whole anterior third ventricle or

2. asymmetrical :grade D- intracranial extradural; or grade E- extracranial extradural (cavernous sinus).

b) Knosp classification system used to quantify invasion of the cavernous sinus, in which only grades 3 and 4 define true invasion of the tumour into the cavernous sinus. Grade 0, no cavernous sinus involvement; grades 1 and 2, the tumour pushes into the medial wall of the cavernous sinus, but does not go beyond a hypothetical line extending between the centres of the two segments of the internal carotid artery (grade 1) or it goes beyond such a line, but without passing a line tangent to the lateral margins of the artery itself (grade 2); grade 3, the tumour extends laterally to the internal carotid artery.

Recent imaging techniques, especially MRI, has high sensitivity in detecting aggressive pituitary tumors which are usually macroadenomas, but currently there are no reliable features distinguishing aggressive from apparently 'benign' adenomas in the series of atypical adenomas reported by Zada et al.²⁶ Chatzellis E etal ²⁷

described 94% atypical adenomas were macroadenomas, and radiological invasion was evident in 83% compared to 45% of typical adenomas (p = 0.004). Ten lesions (56%) showed infrasellar invasion with clival or sellar floor erosion, nine (50%) showed suprasellar invasion and six (33%) invaded at least one cavernous sinus; in five patients (28%), invasion of all three regions was noted.

Surgical techniques in complete excision

Indications for surgery •Tumour with mass effect(Macroadenoma: >1cm) – Chiasmalcompression and objective visual field defect –Raised intracranial pressure •Pituitary dependant Cushing's disease •GH secreting tumour •Prolactinoma –Failure of medical of treatment –Intolerance of medical management –Pt preference •TSHoma – Thyrotoxicosis

Endoscopic assisted transphenoidal surgery

This procedure is performed using Hopkins rod a 0 deg telesscope, length of 18 cm and diameter 0.4 cm, as the sole visualizing instrument of the surgical field; sometimes angled scope are used to further explore the suprasellar area after the lesion removal. Appropriate surgical instruments with different angled tips are needed for permiting movements in all the visible corners of the surgical field.^{28,29} A thorough preoperative planning by three dimensional reconstructed MRI and/or CT scans, is a road map of surgery.

An image-guided system (neuronavigator) is needed when the classic landmarks are unidentifiable.

Bipolar endonasal foreceps of different diameters and lengths can be easily introduced and maneuvered in the nasal cavity,. High-speed lengthy low-profile drills are useful to open bony structures to reach dural space.Finally, the important use of micro doppler probe to protect the major arteries .For increasing the work space and the handling of the instruments is achieved by a)middle turbinate on one side to be removed; b) lateralization

of the middle turbinate in the other nostril; and c) removal of the posterior part of the nasal septum. An anterior sphenoidotomy widely done.

Positioning of the patient

The patient is placed supinely or in slight Trendelenburg's position with turning of head $10^{\circ}-15^{\circ}$ on the horizontal plane, towards the surgeon. The endoscopic equipment and the neuro image guiding system are placed behind the head of the patient

and in front of the surgeon.^{30,31,32}

An altered combination endoscopic transseptal/transnasal binostril approach in Patients with a narrow Space in nasal cavity for pitiuitary lessions. This uses a two-surgeon, four-handed technique can provide a single, wide surgical field by a combination of septoplasty and nasoseptal flap (NSF) harvestation, that proved to be a genuine and acceptable method for that prevents postoperative cerebrospinal fluid (CSF) leakage However, standard pituitary surgery does not usually require either the NSF or the twosurgeon, four-handed technique. Meantime this technique not only provides dynamic endoscopic movement by an ENT(ear,,nose,,throat)surgeon, that offers a clear and pseudo-three dimensional visual area, but also allows manipulation of instruments which is smooth and comfortable.

Modified Stamm's approach has following advantages. 1) suitable for pituitary lesions associated with narrow nasal spaces 2) Handling of instruments in and out through the transseptal route cannot be prevented by the nasal turbinates and/or septal mucosa, 3) the harvested flap can be used for sellar reconstruction in case of csf leak. Finally, it can collaterally improve patients' symptoms due to chronic nasosinusal diseases. The disavantages are time consumption for septal mucosa dissection and can lead to a septal perforation , transient dental pain or hyperesthesia. Nasal packing is done to prevent hematoma formation and promote mucosal healing, leading to patient suffering. The three different binostril approaches for the pituitary lesions are common binostril approach, original Stamm's approach and modified Stamm's <u>approach</u>.

Transseptal-Transnasal 1. Killian incision 2.Bilateral flaps 3.Resect posterior septum 4. Elevate unilateral SN flap 5. Enter sphenoid as in transseptal approach 6. Advantages 7.Two surgeon ability 8.SN flap reconstruction 9. Preserves contralateral mucosa Incision is made and through a minimal invasive procedure endoscopically.Lengthy instruments are passed via the nostril while visualising the monitor. Nasal septum that divides the left and right nostril is partly removed.The front wall of the sphenoid sinus is opened with the help of bone-biting instruments.

Behind the posterior wall of sphenoid sinus is the bone overlying the pituitary gland, known as sella. The dura is exposed by removing thin bone of the sella which exposes the tumor and pituitary gland.

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The tumor is removed by the neurosurgeon / ENT surgeons via a small hole in the sella, in pieces with special instruments called curette, by coring out the from its centre all the tumor margins were let to fall inward towards the reach of surgeon. Once all removal of visible tumor is done, the endosope is advanced into the sella for inspection of hidden tumor.

The sella floor closed by replacing with bone graft from the septum. Tissue glue is applied over the graft in the sphenoid sinus.

Peroperative photograph showing, (a) exposed sphenoid sinus and of sellar floor (SF), tuberculum sellae (TS), planum sphenoidale (PS), lateral and medial carotid recesses, optic and carotid prominences, and clivus (b)dural exposure of SF, TS, and PS with superior intercavernous sinus (c) sellar cavity tumour , and (d) covering suprasellar part of the tumor with its pseudocapsule and arachnoid . (e) endosellar or extraarachnoid approach for intracapsular removal of intrasellar pituitary adenoma (f) intraarachnoid or extracapsular removal of suprasellar adenoma (g and h) panoramic (g) and focus view (h) views of the operative areas after complete tumor removal.

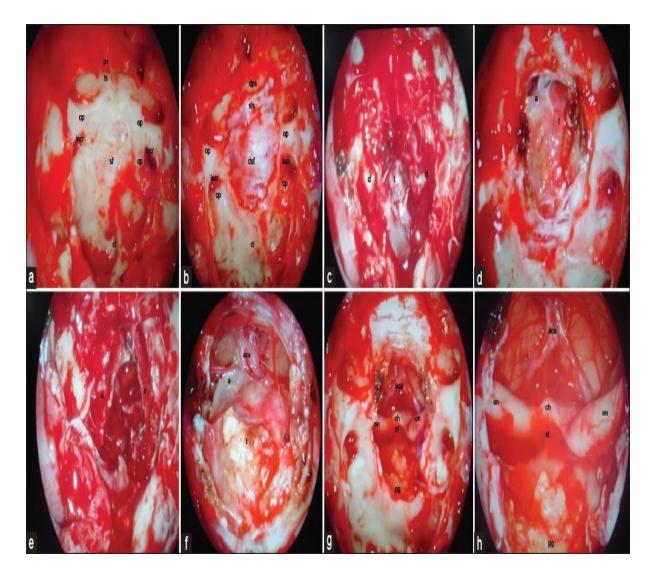


FIG -11

ENDOSCOPIC TRANS SPHENOIDAL EXCISION OF PITUITARY

MACROADENOMA PER OPERATIVELY

Endoscopic transsphenoidal approach has evolved considerably in the last 10-15 years and is now the commonly used surgical procedure for most pituitary adenomas. Recent studies with this approach have shown increased tumor resection rates with minimal complications . However, certain adenomas, such as those with dumbbell configuration, firm or fibrous consistency, or pure suprasellar components, and some large recurrent tumors are difficult to remove by the conventional endoscopic approach. As a result, alternative surgical procedures like staged-transsphenoidal, transcranial, or combination of transsphenoidal-transcranial approaches having been used for management of these subtypes of pituitary tumors. With growing experience in the endoscopic surgery for various skull base lesions, it has now become possible to remove a wide variety of anterior and middle fossa tumors safely and more effectively.

The advantages of EEEA are many and are mainly because of the wider exposure that it provides after removal of SF and the bone of the TS and PS. The intradural exposure achieved by this approach offers a simultaneous and direct endosellar and extraarachnoidal (intracapsular) access to the tumor in the sellar region, and a suprasellar and intraarachnoidal (extracapsular) access to the suprasellar part of the tumor. The intracapsular tumor removal is carried out via the endosellar route, and using the suprasellar corridor at the same time, the tumor capsule is dissected from overlying suprasellar cistern, OPs and chiasm, and the anterior cerebral arteries under direct vision. The basic technique of pituitary macroadenoma surgery involves tumor removal by curettage and suction method. Although it works well for the majority of pituitary tumors, the maneuver is totally ineffective when the tumor is firm and fibrosed. A blind curettage to remove suprasellar mass from the endosellar route has been found potentially dangerous and is associated with a high incidence of incomplete tumor removal from the suprasellar region. The standard transsphenoidal surgery for pituitary adenomas also relies mainly on spontaneous descent of the suprasellar portion of tumor into sellar cavity after initial tumor debulking by endosellar route.Occasionally, the suprasellar tumor does not fall into the sella and causes a large tumor mass to remain in the suprasellar region as a residue. The EEEA provides different corridors, endosellar and suprasellar, to dissect the tumor safely from the surrounding structures under direct vision. It also provides direct visualization and accessibility to suprasellar, subchiasmal, retrochiasmal, and retrosellar regions which are generally poorly visible in the standard transsphenoidal surgery.

In cases of dumbbell tumors, a narrow diaphragma opening prevents descent of the suprasellar portion of tumor into the sellar cavity. The fibrous tumors, recurrent tumors after initial surgery or irradiation, and some medically treated large tumors fail to fall into the sellar cavity because of their firm consistency and are, therefore, less likely to be removed totally by the routine transsphenoidal route. The EEEA is advantageous in these cases because it offers larger tumor exposures through two different routes, endosellar or extraarchnoidal, and suprasellar or intraarachnoidal, which facilitates entire tumor removal in a single-stage surgery. Purely suprasellar tumors and some giant tumors with large midline extensions in the subfrontal regions are not adequately visualized via the endosellar route and are, therefore, clearly unsuitable for the standard transsphenoidal approach. By adding a transtubercular-transplanum extension to the regular

transsphenoidal endosellar approach, the possibility of tumor removal from these areas can be increased considerably. Both patients in our series with primary suprasellar residual tumors and one of the two patients, who had giant pituitary tumors with large subfrontal extensions, had a complete resection of their adenomas.

After endoscopic surgery duration for hospital stay is for one or two days. During this period, nurses will change dressings and helps the patient in bathroom needs. Patient will be able to return to a normal diet as long as they take fluids well. Patients are encouraged to get out of bed and walk as soon as they are able. While in the hospital, patient will be asked to help your nurses keep track of the amount of fluids they drink and their urine output to evaluate pituitary function.

Home care may include:

- Analgesics to control headaches, the most common complaint after surgery
- Lifting weights or straining for stools are allowed until clear advice given by the doctors.
- Follow-up visits with your endocrinologist and surgeons
- MRI has to be repeated
- Eye testing
- It is important to let your doctors know about:
- Any headache that doesn't go away with medication
 - 44

- Nausea and vomiting
- Fever
- epistaxis
- Watery discharge from the nose
- Increase in frequency of urination

At first Jankowski³³ and his colleagues reported tumour removed successfully via endoscopy in 3 pituitary adenomas." "Further on, many more surgeons committed themselves to endoscopic transphenoidal pituitary surgery. Many successful cases were also reported in China."^{34,35}

In a study by Yun-ping Fan etal ³⁶ total resection was demonstrated in 16 patients; subtotal resection (the extent of removal was greater than 90%) was in 8 patients; partial resection was in 3 patients. Only biopsy was done in one patient (GH secreting tumor) owing to unexpected excessive bleeding intra-operatively and hard quality of the tumor. Among 3 cases with partial resection, 2 had tumor growth seen on CT in the 6 months follow-up period; one resorted to radiotherapy, but the other refused and eventually lost to follow-up.

Junko et al ³⁷ reported that transsphenoidal approach is safe procedure even in giant pituitary adenomas, as it allows rapid and appropriate decompression of the optic nerves and chiasm with low morbidity rates.

Peroperative and postoperative complications and their management

General complications are due to haemorrhage, infection and anesthesia. Specific complications are

Visual loss- peroperative damage to optic chiasm can be damaged during surgery. If vision problems existed preoperatively, decompression may not restore normal vision. The nerve would have been permanently damaged by the tumor.

- Pituitary gland damage- Hormone are given post operatively.
- diabetes insipidus (DI): neurohypophysis damage. DI leads to polyuria and polydipsia because the kidneys inability to concentrate the urine and is mostly temporary, lasting 1 to 3 days. Desmopressin acetate (DDAVP) in nasal spray or pillform are used for control of DI.
- cerebrospinal fluid (CSF) rhinorrhea : identified as wash out sign.treated with multiple layer of patching.
- meningeal irritation
- CVA- due to peroperative injury of carotid and cavernous sinus leading to decreased blood supply to the brain.
- Nasal congestion

- Epistaxis
- Nasal deformity

According to Yadav etal ³⁸ no intraoperative csf leak but higher incidence of post operative csf leak in the endoscopic group was because of large lesions with higher proportions of suprasellar tumors and also due to initial learning curve but Leng Lz etal ³⁹ repoted low CSF leak in the endoscopic group.

Gondim *et al* ⁴⁰ observed 26.9% complications in their series. Post-operative CSF leaks-2.6%, delayed nasal bleeding-1.9%, sphenoid sinusitis -1.6%, carotid artery injury-0.9%, and meningitis occurred in 0.6%. Endocrinological complications were observed in 17.9% cases out of which anterior lobe insufficiency was seen in 11.6% and diabetes insipidus in 6.3% cases. Nasal complications occurred in 29.6% of the operated cases according to Yadav etal According to Mirian Cabral Morieade Castero etal no nasal complications observed.

MATERIALS AND METHODOLOGY

The study was conducted in Rajiv Gandhi Government General Hospital and Madras Medical College in the Upgraded Institute Of Oto-Rhino-Laryngology, Chennai from June 2015 to September 2016. The study was a retrospective and prospective study .The study population comprised of patients who were diagnosed to have pituitary macroadenoma. Cases of pituitary macroadenoma attending neurology opd ,surgical endocrinology opd and cases referred from these opd's to Upgraded Institute of Otorhinolaryngology, Rajiv Gandhi Government General Hospital, who satisfy the inclusion criteria were studied. The inclusion criterias- for selection of the study group were all cases fit for surgery ,newly diagnosed cases and recurrent cases. The exclusion criterias were the cases of extreme age groups and poor general conditions and cases having comorbid conditions that are not fit for surgery. The sample size for this study was 28 .CT scan and MRI was done. Instituitional Ethical clearance and informed consent was obtained.

Data regarding patient age ,sex ,type of tumour, modes of presentation , tumour consistency ,tumour intensity and tumour extension based on MRI T2 weighted images, peroperative findings, tumour excision, peroperative complications, post operative complications ,management of complications and post operative

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recurrences was collected.data was entered as codes in excel sheet and analysis was done using statistical software EPI INFO version 7.

Descriptive statistics like mean ,standard deviation and proportion were used to express the study characteristics.Chi square test was used to find association between the MRI T2 weighted images based consistency and tumour extension with surgical.Implication.A p-value <0.05 was considered as significant.

RESULTS AND OBSERVATIONS

A total number of 28 cases were studied. The details of all the cases are given in the master chart. the following observations were made and analysed. The age range of the study population was from from 24 to 58 years. Their mean age of the was 40.39 years and standard deviation 10.76.

AGE IN YEARS	NUMBER OF INDIVIDUALS	PERCENTAGE
<u>20-30</u>	07	25.00%
31-40	07	25.00%
41-50	09	32.14%
51-60	05	17.86%
TOTAL	28	100.00%

TABLE 1 : AGE DISTRIBUTION OF STUDY POPULATION

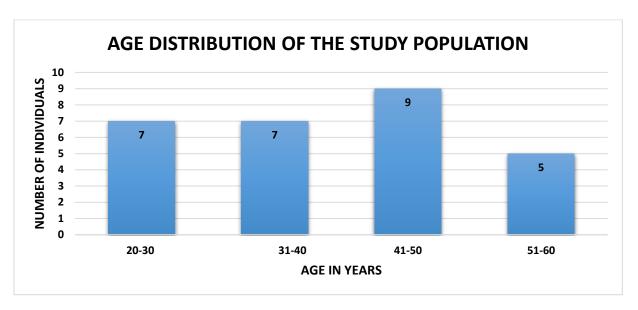


FIG-12 Majority of the pituitary macroadenomas were seen in the age group 41-50 year(32.14%).

TABLE 2 :SEX DISTRIBUTION OF THE STUDY POPULATION

SEX	NUMBER OF INDIVIDUALS	PERCENT
MALE	13	46.4%
FEMALE	15	53.6%
TOTAL	28	100.00%

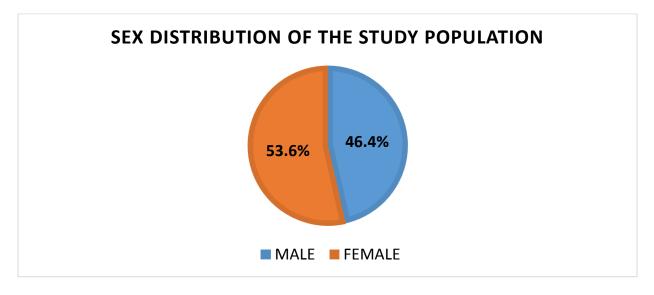
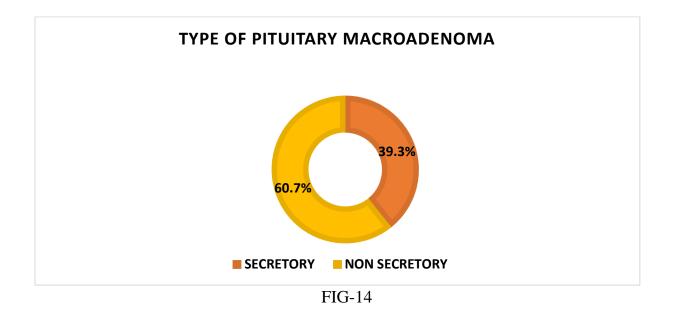


FIG-13

The total number of females were 15(53.6%) and males were 13(46.4%).

TABLE 3: TYPE OF PITUITARY MACROADENOMA

TYPE OF PITUITARY MACROADENOMA	NUMBER OF INDIVIDUALS	PERCENT
SECRETORY	11	39.3%
NON SECRETORY	17	60.7%
TOTAL	28	100.00%



All the pituitary macroadenomas were divided into non secretory and secretory group. Among the 28, nonsecretory were 17(60.7%) and secretory were 11(39.3%).

	TYPE OF PITUITAR		
AGE GROUPS IN YEARS	SECRETORY N(%)NON SECRETORY N(%)		TOTAL(%)
20-30	5(71.4)	2(28.6)	7(100)
31-40	2(28.5)	5(71.4)	7(100)
41-50	3(33.3)	6(66.7)	9(100)
51-60	1(20.0)	4(80.0)	5(100)
TOTAL(%)	11(39.3)	17(60.7)	28(100)

TABLE 4: Age Wise Distribution Of Types Of Pituitary Macroadenoma

Among the secretory type and non secretory type of tumour majority were present in the age groups 20-30 years and 51-60 years respectively.

TABLE 5:SEX WISE DISTRIBUTION	OF TYPES OF PITUITARY
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	TYPE OF PITUIT		
SEX	SECRETORY N(%)	TOTAL	
MALE	7(53.8)	6(46.1)	13 (100.00%)
FEMALE	4(26.7)	11(73.3)	15 (100.00%)
TOTAL	11(39.3)	17(60.7)	(100.00%)

Secretory type of tumours were more predominant in males (53.8%) and nonsecretory type of tumours were predominant in females 11(73.3%).

TABLE 6:NEW / RECURRENT CASES

NEW /RECURRENT CASES	NUMBER OF INDIVIDUAL	PERCENTAGE
RECURRENT CASES	3	10.7%
NEW CASES	25	89.3%
TOTAL	28	100.00%

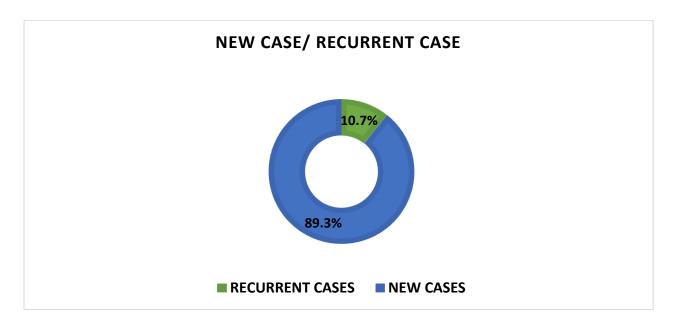


FIG-15

Among the study population 25 (89.3%) were new cases and 3 were recurrent

cases(10.7%)

TABLE 7: MODES OF PRESENTATION OF PITUITARY MACROADENOMA

MODES OF PRESENTATION*	NUMBER OF INDIVIDUAL N=28	PERCENTAGE	
HEAD ACHE	20	71.4%	
PROLACTINOMA	05	17.8%	
APOPLEXY	01	3.5%	
VISUAL DEFECTS	12	42.8%	
ACROMEGALY	05	17.8%	
CUSHINGS SYNDROME	01	3.5%	
*multiple response	01	3.3%	

*multiple response

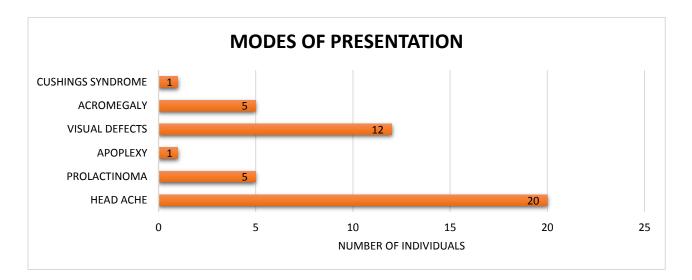


FIG-16

In our study the predominant symptoms were headache (71.4%) and visual defects (42.8%).Out of 5 cases of prolactinoma 3 cases presented with galactorrhoea and 2 cases presented with gynaecomastia and loss of libido. 2 cases presented with head ache and galactorrhoea ,5 cases presented with head ache and acromegaly,5 cases presented with head ache and visual defects and 1 case presented with head ache, galactorrhoea,visual defect and apoplexy.

TABLE 8:TUMOUR CONSISTENCY BASED ON MRI WEIGHTED IMAGES

TUMOUR CONSISTENCY	NUMBER OF INDIVIDUAL	PERCENTAGE
CYSTIC	5	17.9%
SEMISOLID	10	35.7%
SOLID	13	46.4%
TOTAL	28	100.00%

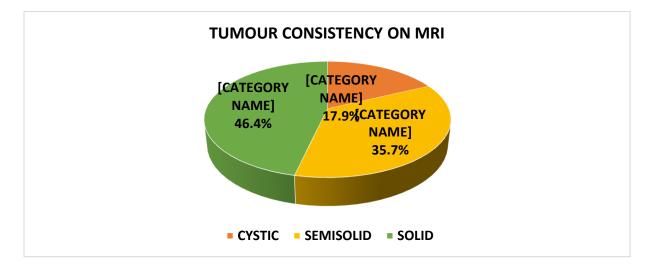


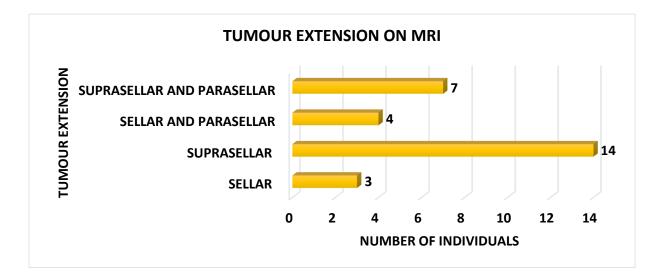
FIG-17

MRI weighted images showed 46.4% ,35.7% and 17.9% of the tumours were solid

,semisolid and cystic respectively.

TABLE 9: TUMOUR EXTENSION BASED ON MRI WEIGHTED IMAGES

TUMOUR EXTENSION	NUMBER OF INDIVIDUAL (N=25)	PERCENTAGE	
SELLAR	03	10.7%	
SUPRASELLAR	14	50.00%	
SELLAR AND PARASELLAR	04	14.3%	
SUPRASELLAR AND			
PARASELLAR	07	25.00%	
TOTAL	28	100.00%	





Majority of tumour extension was to the suprasellar region (50%) and in 25% the tumour extension was seen in both suprasellar and parasellar region.Tumour was limited to sellar region in 3 cases (10.7%)

TABLE 10: SURGICAL IMPLICATION OF CONSISTENCY BASED ON MRI WI

	TUMOUR CONSISTENCY PER OPERATIVE				Chi squre	P value
CONSISTENCY BASED ON MRI	CYSTIC	FIRM	SOFT	Total	value	
SEMISOLID	0(0.0%)	4(40.0%)	6(60.0%)	10(100.0%)		
SOLID	0(0.0%)	12(92.31%)	1(7.69%)	13(100.00%)	36.89	< 0.05
CYSTIC	5(100.0%)	0(0.0%)	0(0.0%)	5(100.0%)		(signif icant)
TOTAL	5(17.8%)	16(57.1%)	7(25.0%)	28(100.0%)		

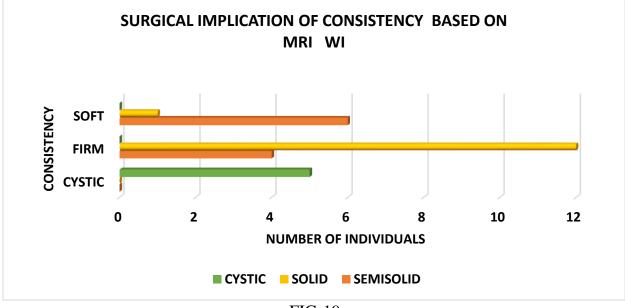
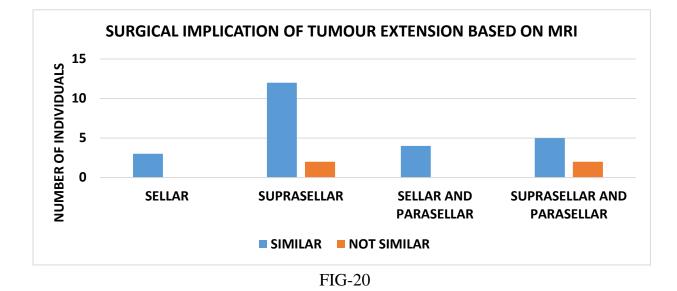


FIG-19

On MRI based images , consistency of 10 tumours were semisolid of which on peroperative findings 6(60%)were soft and 4(40%) were firm. 92.3% of the tumours having solid consistency on MRI weighted based images were firm and the remaining 7.6%% were found to be soft on per operative finding. Cystic consistency based on MRI images were similar with the peroperative findings.Cystic tumours were removed by suction.

TABLE 11 :SURGICAL IMPLICATION OF TUMOUR EXTENSION BASED ON MRI WI

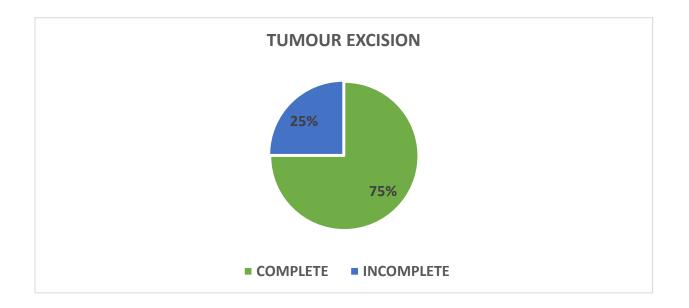
	TUMOUR EXTENSION -PER OPERATIVE				
TUMOUR EXTENSION ON MRI	SIMILAR	NOT SIMILAR	Total		P value
SELLAR	3(100%)	0(0.0%)	3(100.0%)		
SUPRASELLAR	12(85.7%)	2(14.2%)	14(100.0%)		
SELLAR AND PARASELLAR	4(100.0%)	0(0.0%)	4(100.0%)	2.333	0.506
SUPRASELLAR AND PARASELLAR	5(71.4%)	2(28.5%)	7(100.0%)		(not significant)
TOTAL	24(85.7%)	4(14.2%)	28(100.0%)		



Suprasellar extension on MRI was s similar in 12 cases peroperatively and 2 cases showed extension of tumour laterally (parasellar) without carotid encasement or cavernous sinus invasion.Suprasellar and parasellar extension on MRI were similar only in 5 cases whereas 2 cases were not similar with the peroperative findings.

TABLE 12: TUMOUR EXCISION

TUMOUR EXCISION	NUMBER OF INDIVIDUAL	PERCENTAGE
COMPLETE	21	75.00%
INCOMPLETE	7	25.00%
TOTAL	28	100.00%





Complete excision was done in75% of the cases and the remaining 25% was incomplete excision of the tumour .

TABLE 13: PEROPERATIVE COMPLICATION

PEROPERATIVE COMPLICATION	NUMBER OF INDIVIDUAL	PERCENTAGE
NIL	22	78.57%
CSF LEAK	6	21.43%
TOTAL	28	100.00%



FIG-22

CSF leak was the only peroperative complication found in 6 cases(21.4%).

POST OPERATIVE COMPLICATION*	NUMBER OF INDIVIDUAL N=28	PERCENTAGE
NIL	20	71.400%
DIABETES INSIPIDUS	3	42.8.00%
PNEUMOENCEPHALOCOEL	1	3.5%
CVA	2	7.1%
CSF LEAK	1	14.2%

TABLE 14: POST OPERATIVE COMPLICATION

*multiple response.

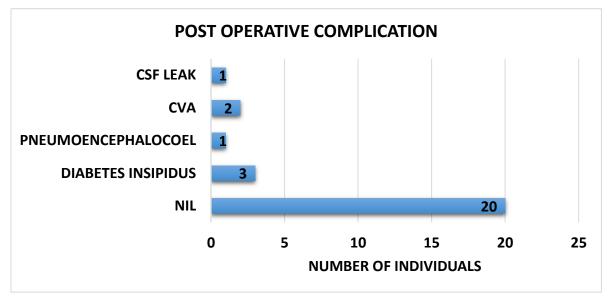


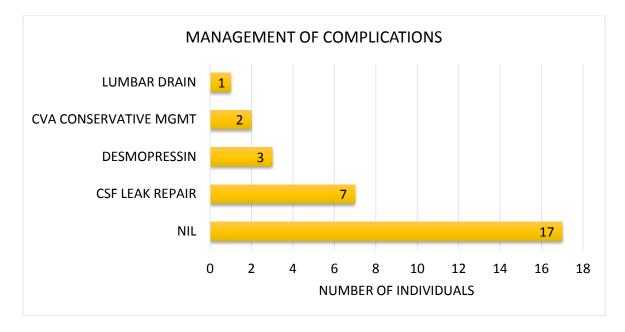
FIG- 23

The most common post operative complication was diabetes insipidus in 3 cases .In one case pneumoencephalocoel along with CSF leak and in another case CVA with diabetes insipidus was noted.

TABLE 15:MANAGEMENT OF COMPLICATIONS

MANAGEMENT OF COMPLICATIONS*	NUMBER OF INDIVIDUAL N=28	PERCENTAGE
NIL	17	60.7%
CSF LEAK REPAIR	7	25.0%
DESMOPRESSIN	3	10.7%
CVA CONSERVATIVE		
MGMT	2	7.1%
LUMBAR DRAIN	1	3.5%

*multiple response.





Peroperative CSF leak repair was done for 6 cases and for 1 case post operative CSF leak repair done and lumbar drain was kept. Post operative diabetes insipidus was treated with intranasal desmopressin in 3 cases.CVA was managed conservatively in 2 cases.

TABLE 16: RELATIONSHIP BETWEEN TUMOUR EXTENSION AND HEAD ACHE.

	HEAD ACHE		
TUMOUR EXTENSION ON MRI	PRESENT	ABSENT	TOTAL
SELLAR	2(66.6%)	1(33.3%)	3(100.00%)
SUPRASELLAR	10(71.4%)	4(28.5%)	14(100.00%)
SELLAR AND PARASELLAR	4(100.0%)	0(0.0%)	4(100.00%)
SUPRASELLAR AND PARASELLAR	4(57.1%)	3(42.8%)	7(100.00%)
TOTAL	20(71.4%)	8(28.5%)	28((100.00%)

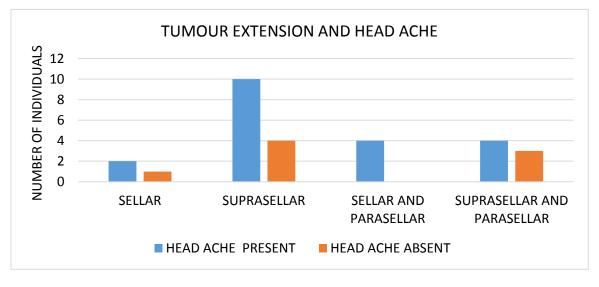


FIG-25

Among 14 cases with suprasellar extension 10(71.4%) presented with head ache and all 4 cases with sellar and parasellar extension presented with headache.

TABLES 17: RELATIONSHIP BETWEEN TUMOUR EXTENSION AND VISUAL DEFECT.

	VISUAL		
TUMOUR EXTENSION ON MRI	PRESENT	ABSENT	TOTAL
SELLAR	0(0%)	3(100%)	3(100%)
SUPRASELLAR	6(42.8%)	8(57.1%)	14(100%)
SELLAR AND PARASELLAR	1(25.0%)	3(75.0%)	4(100%)
SUPRASELLAR AND PARASELLAR	5(71.4%)	2(28.5%)	7(100%)
TOTAL	12(42.8%)	16(57.1)%	28(100%)

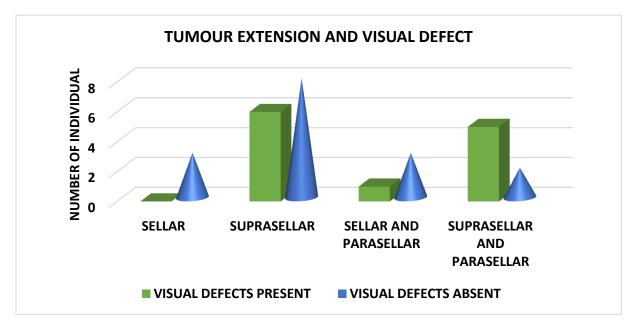


FIG-26

Visual defects were present in 5(71.4%) cases among the 7 cases having sellar and parasellar extension.

MRI – SUPRASELLAR EXTENSION

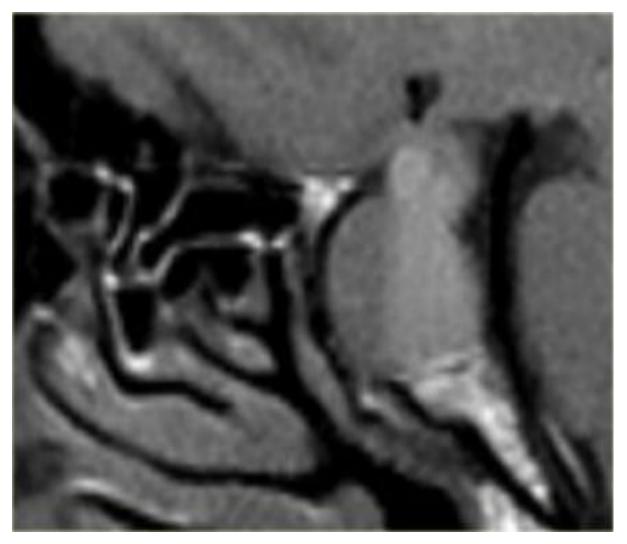


FIG-27

The enlarged lesion starts in the sella, and extends into the suprasellar cistern. The classic dumbbell shaped (snowman appearance) observed is caused by constriction by the diaphragma sellae. The blood-fluid level indicates hemorrhage.

MRI – SELLAR AND PARASELLAR



Pituitary macroadenoma with bilateral cavernous sinus extension with hemorrhagic foci .

MRI – SUPRASELLAR AND PARASELLAR

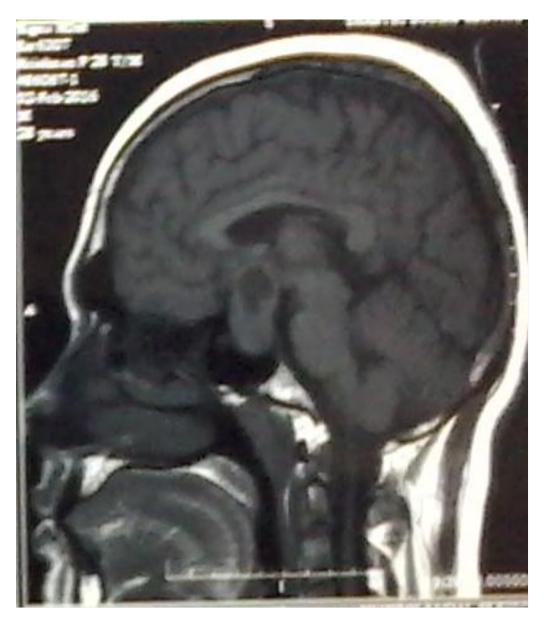


FIG -29

A large suprasellar mass compresses optic chiasma and optic nerves causing significant mass effect and mild extension towards cavernous sinus.

MRI – RECURRENT/RESIDUAL PITUITARYMACROADENOMA

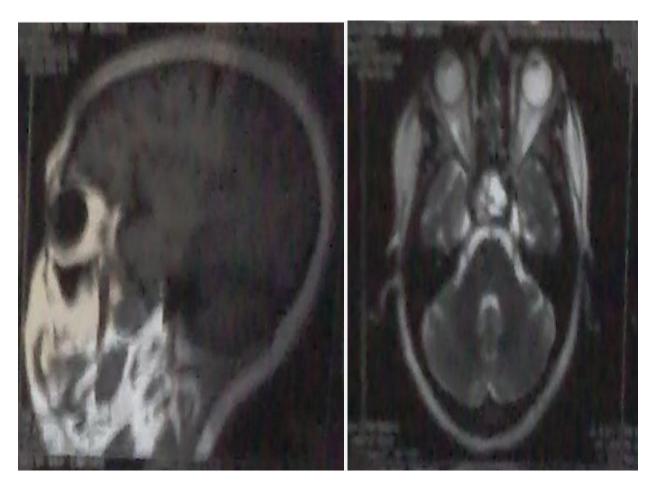


FIG-30

Well defined isointense mass causing compression of optic chiasma and lateral displacement of cavernous segment of bilateral internal carotid artery.

MRI – PITUITARY APOPLEXY

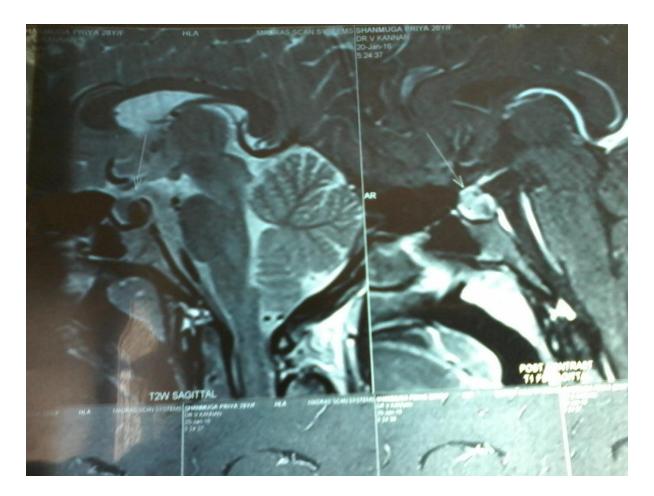


FIG -31

MRI Sella with contrast- pituitary appears enlarged .The posterior pituitary hyperintense lesion with central hypointensity and anterior pituitary appears isointense.On IV contrast lesion shows peripheral enhancement with central non enhancing component.



FIG -32

A CASE OF PITUITARY MACROADENOMA WITH ACROMEGALY

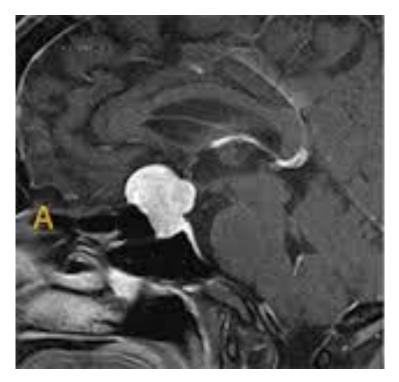


FIG -33: MRI – BEFORE SURGERY

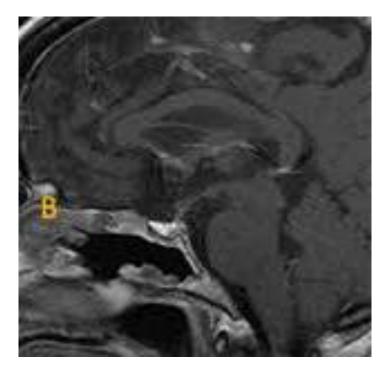


FIG -34: MRI – AFTER SURGERY

DISCUSSION

The present study was undertaken on 28 patients who sought treatment in department of ENT ,Rajiv Gandhi government hospital and Madras Medical College.

In our study the mean age of the study population was 40.39 years and standard 10.76. Majority of the pituitary macroadenomas were seen in the age group 41-50 year(32.14%). Cawich S et al⁴¹ found in his study the mean age was 45.4 years (SD +/-14.8). The females constituted 60% and males 40% in our study which was similar to a study conducted by Cawich S et al.⁴¹

Non secretory type of pituitary macroadenomas were predominant (60.7%) than the secretory type(39.3%) in our study .According to Cawich S et al 55% were non secretory and 44.4% were secretory type .**Castro** MC⁶ et al in his study found nonsecreting type in 96 (74.42%) and secreting in 33 patients (22.58%).In our study the predominant symptoms were headache (71.4%) and visual defects (42.8%) whereas Cawich et al⁴¹ reported visual defects as the predominant symptom followed by headache. Castro MC etal ⁶ reported acromegaly and galactorrhoea in their study while Junko³⁷ in his study found visual defects as predominant symptom followed by head ache , galactorrhoea and acromegaly.

Modes Of Presentation	Castro MC et al (6)	Cawich S et al (41)	Junko et al (37)	Our Study
Head Ache	-	72.3%	12.8%	71.4%
Galactorrhoea	6.9%	19.3%	18.0%	10.7%
Apoplexy	-	05%	-	3.5%
Visual Defects	-	80.7%	71.7%	42.8%
Acromegaly	7.6%	-	5.1%	3.5%
Cranial Nerve Palsy	-	16%	-	-
Amenorrhoea	-	26%	-	-

TABLE 18: COMPARATIVE STUDIES ON MODES OF PRESENTATION

Signal Intensity of MRI based on T2 weighted images was 40% hyperintense,33% isointense and 27% hypointense according Heck A et al.⁴²

Yamato et al¹⁹ reported 62 .06% tumours were solid and 37.93% semisolid in a comparative study of solid and semisolid types of pituitary macroadenoma. In contrast our study found 60% were semi solid and 40% were solid tumours. Out of 15 semisolid tumour on MRI T2 WI 13 were soft and 2 cases hard peroperatively and among 14 solid tumour on MRI T2 WI only 3 were found to be hard and the remaining 11 were soft per operatively according to Yamato et al and he also found that there was no significant correlation between tumor consistency at the time of surgery and T2WI.

On MRI based images , consistency of 10 tumours were semisolid of which on peroperative findings 6(60%)were soft and 4(40%) were firm. 92.3% of the tumours having solid consistency on MRI weighted based images were firm and the remaining 7.6%% were found to be soft on per operative finding. Cystic consistency based on MRI images were similar with the peroperative findings.

Ramakrishnan VR^{43} in his study found that of the 106 patients included in the study, seventy one (67%) showed suprasellar extension of their tumor. Various studies revealed parasellar invasion by a pituitary adenoma is clinically significant and occurs in 6 to 10% of cases.⁴⁴

Majority of tumour extension was to the suprasellar region (50%) and in 25% the tumour extension was seen in both suprasellar and parasellar region. Suprasellar extension on MRI was similar in 12 cases peroperatively and 2 cases showed extension of tumour laterally (parasellar) without carotid encasement or cavernous sinus invasion. Suprasellar and parasellar extension on MRI were similar only in 5 cases whereas 2 cases were not similar with the peroperative findings.

The assessment of parasellar extension of a macroadenoma is important in the evaluation of the preoperative MRI study. There are few indicators of parasellar involvement, since clinical features occur late and subsequent examination of both histologic and molecular tumor markers is inconsistently correlated with parasellar invasion. ⁴⁵

According to Hardys' classification the grade A and B tumors were considered easier to excise while the removal of grade C and D tumors, those that had a superior margin more

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than 20 mm above the jugum sphenoidale, was more difficult (40% had residual tumor on the postoperative CT scan).

Knosp et al offered a grading system for showing invasion of cavernous sinus by pituitary macroadenoma. Briefly, the much laterally adenoma grows and surrounds the ICA, the more grade level is. The grading defined by the relation of carotid lines with the limits of invasion.

Thereby enmasse dissection is possible only when tumour lies with minimal or no suprasellar extension and also lies between the carotid.

Arbolay Omar⁷ in his study noted gross removal of tumour is seen in 92.4% and subtotal resection in 7.8%. by endonasal endoscopic trans sphenoidal surgery.

Fan YP etal ³⁶ reported among 28 patients ,total resection was done in 16 patients , subtotal resection (the extent of removal was > 90%) in 8 patients , partial resection in 3 patients and biopsy in 1 due to excessive bleeding and hard nature.

Complete excision was done in75% of the cases and the remaining 25% was incomplete excision of the tumour . Among the incompletely removed 5 cases underwent subtotal removal and 2 cases partial removal. Complete resection is done in all cases where there is proper plane of dissection with no or minimal suprasellar extension and enmasse resection is also possible only when tumour lies with in the carotid . Intra operative carotid doppler monitoring had been used that prevents from encountering the carotid artery . Incomplete excision was done in 7 cases of which subtotal resection was done (>90% of tumour removed) in 5 cases. Among these 5 cases in which subtotal resection

was done, in three cases extension was found to suprasellar and parasellar region involving right cavernous sinus with further extension into the sphenoid sinus while in other two cases the tumour had suprasellar extension with encasement of carotid laterally. One among these two cases which encased carotid laterally had galactorrhoea who developed pituitary apoplexy leading to sudden headache and ,visual defects along with galactorrhoea. This patient was taken for surgery immediately and per operatively blood clotted sellar could not be identified easily. These 5 tumours were found to be very hard in consistency and was removed in piece meal.

In our study CSF leak was the only peroperative complication found in 6cases (21.4%) and the most common post operative complication noted was diabetes insipidus in 3 cases .In one case pneumoencephalocoel along with CSF leak and in another case CVA with diabetes insipidus was noted.

Castro MC et al^6 found the main complication found in patients were CSF fistulas in 8.5%, meningitis in 3.1% and one death due to major intracerebral hemorrhage in the postoperative period.

As complications ,transient diabetes insipidus in 13 cases(33.3%), cerebrospinal fluid leakage in 3 cases(7.7%), subarachnoid hemorrhage in 1 case (2.6%) were observed by Junko et al.³⁷

The low rate of complications depends on several factors such as the extension of the tumoral resection, the type of tumor, and the preservation of the structures around the injury (hypophysis, cavernous sinus, suprasellar space).

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Junko et al³⁷ in his study observed CSF fistulas, that occurred in eleven patients were cured by conservative treatment in seven cases (5.53%), and four patients (3.1%) were reoperated through the endoscopic approach to close the fistula. Meningitis complication was managed with antibiotics therapy.

In our study peroperative CSF leak repair was done for 6 cases by multilayer closure done by sealing with fat, cartilage ,naso septal flap , surgicell and tissue glue followed by nasal packing done with meurocell and kept insitu for one week. The post operative period was uneventful and pack was removed after a week and by doing diagnostic nasal endoscopy in our operation theatre under aseptic condition no leak was observed in those cases. For 1 case, which was a recurrent case, after incomplete removal of the tumour patient developed csf rhinorrhoea on second post operative day followed by which patient developed pneumoencephalocoel that manifested as severe head ache ,vomiting and giddiness .The patient was on higher antibiotics ,osmotic diuresis and anti seizure drugs The patient was kept in Fowlers position at 30 degrees and lumbar drain was kept for a week.CSF leak stopped and symptoms of pneumoencephalocoel subsided.This was followed by subsequent surgery for closure of the defect. Post operative period was uneventful. Post operative diabetes insipidus presented with polyuria, nocturia and polydipsia abruptly with in first 24-48 hours of surgery in 3 cases .Thirst was prominent and constant symptom. The biochemical analysis of post operative diabetes insipidus was established by increased osmolarity and hypernatremia in the presence of hyposmolar urine .Urine specific gravity was checked routinely every 12 hours and urine output was carefully monitored. Fluid replacement was done based on input output chart where input is increased to that of the output loss and patient was with manifestation was treated with oral and intranasal desmopressin. All these 3 patients improved well with in a week to 10 days.

Two cases who had hypertension as comorbid condition developed cerebro vascular accident (CVA)post operatively due to persistent elevation of blood pressure leading to anterior cerbral artery infarction.CVA was perse not due to surgical intervention as carotid artery was monitored with carotid Doppler preoperatively. CVA was managed conservatively.

CONCLUSION

In our study pituitary macroadenoma is predominant in 5th decade.Non secretory tumours are more than secretory tumours with female preponderance but secretory tumours are common in male.

Headache is common and early symptom that to with suprasellar extension followed by visual defects. In sellar tumours the manifestations are less common.

Among secretory macroadenoma acromegaly is most common manifestation followed by prolactinoma and least is ACTH producing tumour.

MRI is a reasonable tool to predict the consistency of pituitary macroadenoma.T2 weighted MRI that is hyperintense without contrast characterizes the nature of the tumour.

The transsphenoidal endoscopic surgical approach is adequate for total removal of pituitary macroadenoma with cystic and soft consistency. A well formed circumscribed capsule confined to sella allows for extracapsuler centrepetal dissection which leads to total resection of macro adenoma.

In solid tumours with extensive suprasellar extension and parasellar encasement of carotids, the trans sphenoidal endoscopic approach may not be adequate for complete resection.

The incidence of per operative complications like csf leak, haemorrhage and post operative diabetes insipidus is very less if meticulous dissection technique is carried out with tissue respect and minimal injury.

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ANNEXURES

PROFORMA

Serial number	MRD N	O:	IP/OP NUMBER:
Name:	Age:		Sex:
Address			
Occupation			Income:
Chief complaints:			
History of presentir	ng illness:		
1. head ache	2.galactorrhoea	3. acromegaly	4. visual defects
5.vomiting	6. cushingoid features	7.impotence 8.lo	ss of libido
8.any history	of ear ,nose ,throat sympt	coms	
Past history: h/o dia	abetes mellitus ,hyperter	nsion ,TB,Asthma	,epilepsy ,

h/o irradiation for similar disease,h/o previous surgery

Family history: h/o similar history among family members

Personal history: h/o smoking ,alcohol,

dietary habits,

CLINICAL EXAMINATION

General examination-conciousness , orientation, built

Pallor, icterus, cyanosis, clubbing, oedema,

Vitals :pulse ,blood pressure ,temperature ,respiratory rate

Anthropometry:height,weight

Systemic examination

1.central nervous system:level of consciousness

Higher functions

Signs of meningeal irritation

Cranial nerve tests:olfactory ,optic ,occulomotor

,trochlear,trigerminal,abducent, facial ,vestibulocochlear ,glossopharyngeal ,vagus

, cranial spinal accessory and hypoglossal.

2.Respiratory system		
3. Cardiovascular system		
4.Gastrointestinal system		
Local examination		
Ear nose throat examination:		
Ear –	Right	Left
Pinna		
Preauricular region		
Post auricular region		
Tragal tenderness		
External auditory canal		
Tympanic membrane		
Mastoid tenderness		
Facial nerve		
Fistula sign		
Tuning fork test		
Rinnie		
Weber		
ABC		
Vestibular and cerebellar func	tion test	

Nose :external contour

Anterior nasal examination

Paranasal sinus tenderness

Post nasal examination

Throat

Oral cavity

Oropharynx

Indirect Laryngoscopy

Neck

Investigation:

MRI :

Size of the tumour :

consistency of tumour- 1.semisolid 2.solid 3.cystic

intensity of the tumour-1.hyperintense 2.hypointense 3.isointense

Extension of tumour - 1.Sellar 2.suprasellar 3.sellar parasellar

4.suprasellar and parasellar

PER OPERATIVE FINDING:

Consistency: 1.soft 2.firm 3.cystic

Extension of tumour :1.similar to MRI findings 2.not similar to MRI findings

Tumour excision- 1.complete 2.incomplete

Peroperative complication: 1.csf leak 2.bleeding 3.damage to

internal carotid artery 4.0thers 5.no complication

POST OPERATIVE COMPLICATIONS: 1.csf leak 2.diabetes insipidus 3.meningitis

4.pneumoencephalocoel 5.CVA 6.others

7.nil complications

MANAGEMENT OF COMPLICATION: 1.Leak repair 2.desmopressin 3. Antibiotic

4.conservative management of CVA 5.lumbar

drain 6. Others

INFORMATION SHEET

We are conducting a retrospective prospective study "A Study Of Pituitary Macroadenoma Transnasal Endoscopic Excision"

- at the Upgraded Institute of Otorhinolaryngology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai – 600003
- At the time of announcing the results and suggestions, name and identity of the patients will be confidential.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator

Signature of Participant

Date

PATIENT CONSENT FORM

Title of the Project : A Study Of Pituitary Macroadenoma Transnasal Endoscopic Excision

Institution	Upgraded Institute of Otorhinolaryngology, Madras Medical College, Chennai – 600003.
Name :	Date :
Age :	IP No.:
Sex :	Project Patient No. :

The details of the study have been provided to me in writing and explained to me in my own language.

I confirm that I have understood the above study and had the opportunity to ask questions.

I understood that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected.

I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

I have been given an information sheet giving details of the study.

I fully consent to participate in the above study.

Name of the subject

Signature

Date

Name of the Investigator

Signature

Date

ABBREVIATIONS

- MRI- magnetic resonance imaging
- CT-Computed tomography
- GH- growth hormone
- TSH-thyroid stimulating hormone
- ACTH- adenocortico trophic hormone,
- GnRH-gonadotrophic hormone
- FSH-follicular stimulating hormone
- LH-leutinizing hormone
- ADH-anti diuretic hormone
- DW MRI- diffusion weighted magnetic resonance imaging
- ADC-apparent diffusion coefficient
- NSF-naso septal flap
- CSF-cerebrospinal fluid
- EEEA- extended endoscopic endonasal approach
- DI- diabetes insipidus
- CVA-Cerebrovascular accidents

INSTITUTIONAL ETHICS COMMITTEE MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013 Telephone No.044 25305301 Fax: 011 25363970

CERTIFICATE OF APPROVAL

To Dr.S.Hemachandran, Post Graduate in MS(ENT) – Post ELO Madras Medical College/RGGGH Chennai 600 003

Dear Dr.S.Hemachandran,

The Institutional Ethics Committee has considered your request and approved your study titled **"A STUDY OF PITUITARY MACROADENOMA TRANSNASAL ENDOSCOPIC EXCISION"** - NO.19022016.

The following members of Ethics Committee were present in the meeting hold on **02.02.2016** conducted at Madras Medical College, Chennai 3

:Chairperson
:Deputy Chairperson
: Member Secretary
: Member
: Member
: Member
1-3: Member
3: Member
: Member
: Lay Person
: Lawyer
:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee MEMBER SECRETARY INSTITUTIONAL ETHICS COMMITTEE MADRAS MEDICAL COLLEGE CHENNAL-600 003

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MASTER CHART

S. No	Name	Age	Sex	Recurrent /new case	Head ache	Prolact inoma	Acro megaly	Visual Defect	Apo Plexy	Cushing Syndrome	Type of Tumour	Mass Effect	Tumour Size (Cms)
1	indra	43	f	new case	yes	no	no	no	no	no	non secretory	yes	1.7*1.1
2	krishnan	28	m	new case	yes	no	no	no	no	no	non secretory	yes	3.2*1.9
3	shanmugapriya	27	f	new case	yes	yes	no	yes	yes	no	secretory	yes	1.2*1.2
4	margandeyan	49	m	new case	no	no	yes	no	no	no	secretory	yes	1.3*1.5
5	Lakshmi	27	f	new case	yes	yes	no	no	no	no	secretory	yes	1.3*1.5
6	Singaravel	49	m	new case	yes	no	yes	no	no	no	secretory	yes	3.6*2.8
7	Kadharkhan	38	m	new case	yes	no	no	no	no	no	secretory	yes	2.8*3.1
8	hariff nisha	43	f	new case	yes	no	no	yes	no	no	non secretory	yes	2.5*1.5
9	selvi	48	f	recurrent	yes	no	no	no	no	no	non secretory	yes	1*3.2
10	selvendran	32	m	new case	no	no	no	yes	no	no	non secretory	yes	3.1*2.2
11	Ramu	49	m	new case	yes	no	yes	no	no	no	secretory	yes	2.1*1.2
12	mohanasundari	24	f	new case	yes	yes	yes	no	no	no	secretory	yes	1.2*1.3
13	sivagami	58	f	recurrent	yes	no	yes	no	no	no	secretory	yes	2.2*3.1
14	gunasekaran	55	m	recurrent	yes	no	no	yes	no	no	non secretory	yes	2.3*2.5
15	kasthuri	43	f	new case	no	no	no	yes	no	no	non secretory	yes	2.1*1.3
16	parvathi	58	f	new case	yes	no	no	no	no	no	non secretory	yes	1.8*3.1
17	mufeeda	32	f	new case	yes	no	no	yes	no	no	non secretory	yes	2.1*1.6
18	ramasamy	55	m	new case	no	no	no	yes	no	no	non secretory	yes	2.8*3.2
19	rajalakshmi	54	f	new case	no	no	no	yes	no	no	non secretory	yes	3.2*2.6
20	sadasivam	40	m	new case	no	no	no	yes	no	no	non secretory	yes	2.6*1.8
21	geethalakshmi	45	f	new case	no	no	no	yes	no	no	non secretory	yes	2.2*2.3
22	kamala	28	f	new case	yes	no	no	yes	no	no	non secretory	yes	1.6*1.8
23	anbukarasi	32	f	new case	yes	no	no	yes	no	no	non secretory	yes	2.2*3.2
24	selvi	45	f	new case	yes	no	no	no	no	no	non secretory	yes	1.8*2.7
25	marimuthu	38	m	new case	yes	no	no	no	no	no	non secretory	yes	1.7*2.3
26	mani	25	m	new case	yes	yes	no	no	no	no	secretory	yes	2.5*3.1
27	jeevan	28	m	new case	yes	yes	no	no	no	no	secretory	no	2.1*3.3
28	balasubramani	38	m	new case	no	no	no	no	no	yes	secretory	no	1.3*1.8

S.		Consistency-MRI	Tumour	Tumour	Consistency	Tumour	Tumour
no		Consistency-wiki	Intensity-MRI	extention-MRI	per operative	Extension- peroperative	Excision
1	indra	cystic	hyperintense	sellar	cystic	similar	Complete
2	krishnan	semisolid	hyperintense	sellar parasellar	soft	similar	Complete
3	shanmugapriya	semisolid	hyperintense	suprasellar	firm	not similar	incomplete
4	margandeyan	semisolid	hyperintense	sellar	soft	similar	Complete
5	Lakshmi	semisolid	hyperintense	suprasellar	soft	similar	Complete
6	Singaravel	semisolid	hyperintense	suprasellar	firm	similar	Complete
7	Kadharkhan	semisolid	hyperintense	suprasellar	firm	not similar	Complete
8	hariff nisha	solid	hypointense	sellar parasellar	firm	similar	Complete
9	selvi	cystic	isointense	sellar parasellar	cystic	similar	Complete
10	Selvendran	solid	hypointense	supra sellar parasellar	firm	similar	incomplete
11	Ramu	semisolid	hyperintense	suprasellar	soft	similar	Complete
12	mohanasundari	cystic	hyperintense	sellar	cystic	similar	Complete
13	sivagami	solid	hypointense	suprasellar	firm	similar	incomplete
14	gunasekaran	solid	hyperintense	supra sellar parasellar	firm	similar	incomplete
15	kasthuri	semisolid	hyperintense	suprasellar	soft	similar	Complete
16	parvathi	solid	hypointense	suprasellar	firm	similar	Complete
17	mufeeda	cystic	isointense	suprasellar	cystic	similar	Complete
18	ramasamy	solid	hypointense	supra sellar parasellar	firm	similar	Complete
19	rajalakshmi	semisolid	hyperintense	suprasellar	firm	similar	Complete
20	sadasivam	solid	hypointense	suprasellar	firm	similar	Complete
21	geethalakshmi	cystic	isointense	supra sellar parasellar	cystic	not similar	Complete
22	kamala	semisolid	hyperintense	suprasellar	soft	similar	Complete
23	anbukarasi	solid	isointense	supra sellar parasellar	soft	not similar	Complete
24	selvi	solid	isointense	supra sellar parasellar	firm	similar	incomplete
25	marimuthu	solid	isointense	suprasellar	firm	similar	Complete
26	mani	solid	hyperintense	supra sellar parasellar	firm	similar	incomplete
27	jeevan	solid	isointense	sellar parasellar	firm	similar	incomplete
28	balasubramani	solid	isointense	suprasellar	firm	similar	Complete

				Post operative			
s.no	Name	peroperative complication	csf leak	diabetes insipidus	pneumoencephalocoel	cva	Management of Complications
1	indra	nil	no	no	no	no	Na
2	krishnan	nil	no	no	no	no	Na
3	shanmugapriya	nil	no	no	no	no	Na
4	margandeyan	nil	no	yes	no	no	Desmopressin
5	Lakshmi	Csf leak	no	no	no	no	Leak repair
6	Singaravel	csf leak	no	no	no	no	Leak repair
7	Kadharkhan	nil	no	no	no	no	Na
8	hariff nisha	nil	no	no	no	no	Na
9	selvi	nil	no	no	no	no	Na
10	selvendran	csf leak	no	yes	no	yes	Leak repair, cva mgmt and desmopressin
11	Ramu	nil	no	no	no	no	Na
12	mohanasundari	nil	no	no	no	no	Na
13	sivagami	Nil	yes	no	yes	no	lumbar drain and leak repair
14	gunasekaran	csf leak	no	no	no	no	leak repair
15	kasthuri	csf leak	no	no	no	no	Leak repair
16	parvathi	Nil	no	no	no	no	Na
17	mufeeda	Nil	no	no	no	no	Na
18	ramasamy	nil	no	yes	no	no	desmopressin
19	rajalakshmi	nil	no	no	no	yes	cva conservative mgmt
20	sadasivam	nil	no	no	no	no	Na
21	geethalakshmi	nil	no	no	no	no	Na
22	kamala	nil	no	no	no	no	Na
23	anbukarasi	csf leak	no	no	no	no	leak repair
24	selvi	nil	no	no	no	no	Na
25	marimuthu	nil	no	no	no	no	Na
26	mani	nil	no	no	no	no	Na
27	jeevan	nil	no	no	no	No	Na
28	balasubramani	nil	no	no	no	no	Na