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### RESEARCH ARTICLE

#### HYPOPITUITARISM

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#### Abstract

Hypopituitarism is defined as deficiency of one or more hormones of the pituitary gland which can result from diseases of the pituitary gland or from diseases of the hypothalamus causing diminished secretion of hypothalamic releasing hormones, thereby reducing secretion of the corresponding pituitary hormones. Clinical manifestations depend on the extent of hormone deficiency and may be non-specific, such as fatigue, hypotension, cold intolerance, or more indicative such as growth retardation or impotence and infertility in GH and gonadotropin deficiency.

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#### Introduction:-

##### Case history:

Mr. Senthil Kumar 38 years, known case of hypopituitarism, he came for regular follow up in a government hospital with fatigue, hypotension, headache cold intolerance, or more indicative such as impotence and infertility in GH and gonadotropin deficiency, respectively. Investigations reveals Blood pressure 100/70, pulse 120b/mts, RR 22b/mts, Hb 7.7g/dl, WBC 6.67, Eosinophil 0.1, HbA1C 5.7, total protein 4.7mg/dl, Albumin 2.4g/dl, sodium 133mg/dl. He is treated by Cap. Cernos 40mg, Tab. Thyrox-50mg, Tab. Shelcal HD, Tab. Osteofos-70mg, Cabergoline 0.25mg, Minirin 0.1mg.

##### Brief view:

Hypopituitarism is defined as deficiency of one or more hormones of the pituitary gland which can result from diseases of the pituitary gland or from diseases of the hypothalamus causing diminished secretion of hypothalamic releasing hormones, thereby reducing secretion of the corresponding pituitary hormones. However, when one hormone is deficient, it is usually called isolated deficiency, e.g. isolated GH deficiency or isolated ACTH deficiency. Deficiency of a single pituitary hormone occurs less commonly than deficiency of more than one hormone. The deficiency of all anterior pituitary hormones is termed panhypopituitarism, and less than all is often termed partial hypopituitarism. The hypothalamus regulates pituitary secretion by the production of releasing hormones and posterior pituitary hormones, and hence its dysfunction can also lead to hypopituitarism.

##### Introduction:

The pituitary gland is found at the base of the brain. It produces several important hormones that control the production of other hormones made by glands in the body. In panhypopituitarism, the gland produces an insufficient number of hormones. Inadequate or absent production of the anterior pituitary hormones due to various causes. The anterior pituitary produces the hormones thyrotropin (thyroid-stimulating hormone [TSH]), corticotropin (adrenocorticotrophic hormone [ACTH]), luteinizing hormone (LH), follicle-stimulating hormone (FSH), growth

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hormone (GH), and prolactin (PRL). Also known as hypopituitarism. The condition may occur at birth or may be acquired later in life. Acquired hypopituitarism is more common than the congenital (present at birth) form. Symptoms include fatigue, weight loss, decrease in sex drive, infertility, sensitivity to cold, decreased facial or body hair in men, and puffiness of the face.

#### **Definition:**

Hypopituitarism is defined as diminished production of one or more anterior pituitary hormones.

#### **Etiology and classification:**

##### **Primary hypopituitarism:**

1. Postpartum vascular insufficiency of anterior pituitary (Sheehan's syndrome)
  - a) Seen in postpartum patients with history of hemorrhage at delivery or in the immediate postpartum period.
  - b) Suspect in any post-partum patient who fails to resume menses or does not lactate.
2. Ischemic necrosis of pituitary secondary to sickle cell anemia, vasculitis, diabetes mellitus
3. Neoplasms (primary or metastatic)
4. Granulomatous diseases (sarcoidosis, Wegener's granulomatous)
5. Cavernous sinus thrombosis)
6. Infections (tuberculosis, mycoses, syphilis, meningitis)
7. Empty Sella syndrome

Primary empty sella syndrome: protrusion of the third ventricle (subarachnoid cistern) in the sellaturica; it is difficult to diagnose by conventional CT scan because the cerebrospinal fluid in the empty sella has the same density fluid from a cystic pituitary tumor, but it can be readily diagnosed by MRI.

1. Secondary empty sella syndrome: decrease in size of the pituitary from various causes (irradiation, surgery)
2. Aneurysmal dilation of internal carotid artery
3. Radiation therapy for neck and head tumors
4. Other: surgical destruction, lymphocytic hypophysitis, hemochromatosis, chronic renal failure, familial (genetic defects), autoimmune

##### **Secondary hypopituitarism:**

Hypothalamic abnormalities: tumors, inflammation, (sarcoidosis, tuberculosis), trauma, radiation, subarachnoid hemorrhage, infections (encephalitis, meningitis), lipid-storage diseases.

Lesions of pituitary stalk: trauma, surgery, aneurysms, or tumor, compression.

#### **Risk Factors:**

Factors that may increase your chance of hypopituitarism include:

1. Damage to the pituitary gland, which may occur from trauma, radiation therapy, cancer spread, bleeding after childbirth (postpartum hemorrhage)
2. Tumor of the pituitary gland
3. Symptoms
4. Compression of the Tumor
5. Compression of the tumor on local structures, especially the nerves of the eyes, can cause:
6. Blurred vision
7. Loss of visual field
8. Poor temperature control
9. Insufficient Hormones
10. Insufficient levels of gonadotropins can cause:
11. In premenopausal women—missed menstrual cycles, infertility, osteoporosis, vaginal dryness, loss or reduction in female characteristics

#### **Pathophysiology:**

Total or partial hypopituitarism may occur in patients with pituitary adenomas, parasellar disease, or hypophysitis; after pituitary surgery or radiation (including head and neck radiation for malignancy); or after head injury. Pituitary apoplexy resulting from into an existing adenoma is also commonly associated with hypopituitarism. This also can occur in the postpartum setting when the pituitary is markedly enlarged, after a complicated delivery with a large

amount of bleeding and hypotension. In a recent retrospective chart review of patients with classic pituitary apoplexy over a 20- year period, approximately 90% of the patients had permanent hypopituitarism, independent of whether they underwent surgical decompression. Deficiency of any or all of the six major hormones (LH, FSH, GH, thyrotropin, corticotropin, prolactin) can occur. The most common symptom is hypogonadism due to LH and FSH deficiency.

**Clinical presentation:**

1. Symptoms secondary to mass effect (uncommon)
2. Visual disturbances
3. Bitemporal hemianopia: most common defect; caused by compression of the optic chiasm
4. Superior bitemporal defect: earliest defect
5. Loss of central vision: caused by pressure on the posterior part of the chiasm (location of the papillomacular bundle of fibers)
6. Headaches
7. Seizures (rare)

**Other symptoms:**

1. Stomach pain, decreased appetite, nausea and vomiting, and constipation
2. Excessive thirst and urination
3. Fatigue and/or weakness
4. Anemia, meaning weakness from not having enough red blood cells
5. Headache and dizziness
6. Sensitivity to cold
7. Weight loss or weight gain
8. Stiffness in the joints
9. Hypophysitis (inflammation of the pituitary gland)
10. Histiocytosis

**In women:**

1. Loss of armpit or pubic hair,
2. Decreased sex drive,
3. Infertility,
4. Problems with breast feeding,
5. Irregular or no menstrual periods, and hot flashes

**In men:**

1. Loss of hair (on the face, or in the armpits or pubic area),
2. Decreased sex drive, infertility

**In children,**

1. Problems with growth (including height) and
2. Sexual development

**B. Hormonal deficiencies:**

1. Growth Hormone (GH) deficiency: initial hormonal deficiency; manifests with a lack of vigor, decreased exercise tolerance
2. Gonadal dysfunction: amenorrhoea in menstruating women, impotence in men; hypogonadotropic hypogonadism is the earliest and most frequent presentation.
3. often mistaken for depression
4. Adrenocorticotrophic hormone (ACTH) deficiency (Addison's disease): develops in later stages of hypopituitarism; can manifest with an Addisonian crisis during a period of stress, such as surgery or infection.

**Diagnosis:**

The diagnosis of hypopituitarism relies on the measurement of basal and stimulated secretion of anterior pituitary hormones and of the hormones secreted by pituitary target glands. MR imaging of the hypothalamo-pituitary region may provide essential information.

**Endocrine tests:**

1. Demonstration of target gland deficiency (e.g., measurement of testosterone levels in an important man)
2. Measurement of pituitary hormones (e.g., decreased plasma follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels in an impotent man with low testosterone levels indicate hypogonadism caused by central defect (secondary hypogonadism).
3. Tests of pituitary reserve: cortisol and GH levels fluctuate widely in response to stress or diurnal variation, but their deficiency can be demonstrated by using the following provocative testing methods.

**Metypapone test:**

1. Metypapone competitively inhibits the adrenal enzyme 11- $\beta$  hydroxylase necessary for the conversion of 11-deoxycortisol to cortisol. The resulting low cortisol level stimulates the normal pituitary to release ACTH, thereby increasing adrenal production of 11-deoxycortisol.
2. An elevated plasma 11-deoxycortisol level following a 30 mg/kg, maximum 2g PO dose of metypapone overnight is proof of adequate ACTH reserve.

**Insulin tolerance test:**

1. An insulin infusion is started at 0.1U/kg/h and continued until the blood sugar levels falls to half the control value or until the patient becomes symptomatic.
2. The induced hypoglycemia should result in rise in cortisol ( $>7\text{mg/dl}$ ) and GH ( $>7\text{mg/dl}$ ) in a patient with an intact hypothalamic-pituitary-adrenal axis.
3. Cosyntropin stimulation test helps distinguish pituitary from adrenal causes of adrenal insufficiency

**Imaging studies:**

1. Perform an MRI scan of brain with gadolinium contrast.
2. CT scan of brain with coronal views and contrast enhancement if MRI is contraindicated or not available.

**Treatment options include:****Hormone replacement therapy:**

It is the sum of the treatments of each of the patient pituitary hormonal deficiencies detected. Replacement of the hormones are required lifelong. L-thyroxine (100-150  $\mu\text{g}$ ) can be given once daily empty stomach in morning, because there is little, if any, variation in its secretion. The goal of therapy should be a normal serum T4 value.

**Corticosteroids:**

These drugs, such as hydrocortisone or prednisone replace the adrenal hormones that aren't being produced because of an adrenocorticotrophic hormone (ACTH) deficiency. Levothyroxine treats the low thyroid hormone levels (hypothyroidism) that a thyroid-stimulating hormone (TSH) deficiency can cause.

**Sex hormones:**

These include testosterone in men and estrogen or a combination of estrogen and progesterone in women.

**Growth hormone:**

It is also called somatotropin growth hormone is administered through an injection beneath your skin. Adults with symptoms of growth hormone deficiency also may benefit from growth hormone replacement, but they won't grow taller.

**Fertility hormones:**

If person is infertile, gonadotropins can be administered by injection to stimulate ovulation in women and sperm production in men.

1. Tumor removal—done if the cause of the damage is a tumor
2. Radiation therapy—done if the cause of the damage is a cancer or a tumor that cannot be removed with surgery

**Conclusion:-**

The pituitary gland produces a number of hormones or chemicals which are released into the blood to control other glands in the body. If the pituitary is not producing one or more of these hormones, or not producing enough, then this condition is known as hypopituitarism. Hypopituitarism is most often caused by a benign (i.e. not cancerous) tumour of the pituitary gland, or of the brain in the region of the hypothalamus. Pituitary underactivity may be

caused by the direct pressure of the tumour mass on the normal pituitary or by the effects of surgery or radiotherapy used to treat the tumour.

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