Hypopituitarism: A Rare but Often Neglected Condition

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ABSTRACT
Pituitary insufficiency is an uncommon disorder. The most common cause is compression due to a pituitary mass. Other causes include inflammatory damage and vascular injury like postpartum pituitary apoplexy. Postpartum pituitary apoplexy, also known as Sheehan's syndrome, leads to hormonal deficiencies and causes postpartum amenorrhea, lactational failure, chronic hyponatremia, hypoglycemia, and loss of secondary sexual characters. Here we are discussing the clinical course of 15 female patients of panhypopituitarism. Most of them had a history of postpartum hemorrhage. Knowledge about this entity is essential as it is a treatable condition and ignorance could prove to be fatal.

Keywords: Lactation failure, Panhypopituitarism, Recurrent hyponatremia, Secondary amenorrhea.

INTRODUCTION
Hypopituitarism is defined as deficiency of one or more hormones secreted from the anterior pituitary gland. Vascular injury is an important cause after sellar and parasellar mass compression. Postpartum pituitary apoplexy, as a result of postpartum hemorrhage, is an endocrine emergency, which is not uncommon to find in developing countries where facility of institutional deliveries is still in the struggling phase. Pituitary is a highly vascularized organ and its size and vascularity increases in pregnancy. Lack of institutional deliveries, postpartum hemorrhage (PPH), and unavailability of blood and blood products are common culprits for increased incidence of Sheehan's syndrome in developing countries. The effect of acute deficiency of pituitary hormones may persist for long and causes much morbidity to the patients in long-term.¹ The long-term effects of deficient hormones cripple the patient for years and may even lead to death. Here we are presenting 15 cases of the Sheehan's syndrome of which two succumbed to their illness.

AIMS AND OBJECTIVES
• To know the different presentations of pan-hypopituitarism.
• To know the prevalence of undiagnosed Sheehan's syndrome in our part of the world.
• To assess the improvement with treatment in diagnosed hypopituitarism patients.

MATERIALS AND METHODS
The present study was done at a tertiary care center of Eastern India, catering mainly to rural and semiurban population. The study duration was five years (2013–2018).

Inclusion Criteria
All females presented with seizures, unconsciousness, hypotension, hyponatremia, and hypoglycemia, which on further evaluation were found to have pituitary hormone deficiency, may or may not be Sheehan's syndrome.

Exclusion Criteria
• Male hypopituitarism
• Any alternative diagnosis that was presented with same clinical profile

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hypothyroidism, the condition remained undiagnosed and patients
demographic profile of patients described in Table 1.

We diagnosed 15 cases of panhypopituitarism in last 5 years.
Most of them (n = 12) presented in emergency department due to
one of the fatal complication of this illness (Fig. 1). Age of patients
ranged from 31 to 61 years (mean = 42 years). The average time
between last postpartum amenorrhea and present complaints was
20 years. Most of them (n = 10) had a history of excessive PPH. Five
of them had home delivery, and rest had hospital deliveries. There
was a history of blood transfusion during the postpartum period
in four cases. No patient was diagnosed to be having pituitary
insufficiency during her postpartum period. Two of these patients
were diagnosed about pituitary insufficiency in the recent past, but
they left the treatment by their own. Patients with history of PPH
had a history of postpartum amenorrhea and lactational failure,
except one who had excessive bleeding after second-trimester
abortion. Presenting symptoms were extreme lethargy, recurrent
hyponatremia causing decreased sensorium, hypoglycemia,
and weight loss in decreasing frequency (Table 2). Clinically all
patients had low normal blood pressure except one who presented
with refractory shock. The mean pulse rate at presentation was
64 minutes. All had loss of secondary sexual characters like loss of
pubic and axillary hair and breast atrophy. Most of them had fine
facial wrinkling especially at corner of eyes (Fig. 2A).

Indications for admissions from the emergency department
(n = 12) were hyponatremia, altered sensorium, hypoglycemia,
seizure, and refractory shock in decreasing order (Fig. 1). All of them
got admitted to the intensive care unit. On investigation, mean
hemoglobin, total leukocyte count, and platelet count were 11.2 g%  
(range 8–11.9), 4300 cumm (2,350–10,180), and 84,000 cumm (range
10,000–201,000) respectively. Mean blood urea and creatinine
were 49.5 mg% and 1.6 mg%, respectively. Two patients had acute
kidney injury at presentation. Mean serum sodium, potassium, and
glucose were 123 mEq/dL, 5.1 mEq/dL, and 84 mg%, respectively.
There was one patient who had history of hyponatremia and
rapid correction of which causes extrapontine myelinolysis. On
6 month follow-up her limb movements improved but dysarthria
persisted. One patient with recurrent hyponatremia and vomiting
found to have autoimmune pancreatitis. We investigate her for
infiltrative diseases like IgG4-related disease and sarcoidosis, but
all investigations were negative.

Mean serum TSH, FT4, and FT3 were 2.32 IU/mL, 0.20 ng/dL, and
1.01 pmol/L, respectively. Low in FT4 and FT3 along with low, normal,
or slightly high TSH is suggestive of secondary hypothyroidism
inappropriate setting. Mean serum cortisol (morning fasting)
was 2.1 μg/dL (Table 3). Serum LH, FSH, and prolactin were below
normal range in all except one who presented post-abortion. It may

Table 1: Demographic profile of patients. All patient’s age range between
31 years and 61 years with mean age of patients was 42 and interval
since last child birth was 20 years

| Parameter                  | No. of patients (n = 15) | Percentage |
|----------------------------|--------------------------|------------|
| Age                        |                          |            |
| 20–30 years                | 1                        | 6.7        |
| 30–40 years                | 5                        | 33.3       |
| 40–50 years                | 5                        | 33.3       |
| >50 years                  | 4                        | 26.7       |
| Interval since last delivery|                          |            |
| <10 years                  | 5                        | 33.3       |
| >10 years                  | 10                       | 66.7       |
| Residence                  |                          |            |
| Rural                      | 11                       | 73.3       |
| Urban                      | 4                        | 26.7       |

Table 2: Symptoms of patients (total no of patients: 15)

| Symptoms                                  | n (no. of patients) |
|-------------------------------------------|---------------------|
| Lethargy                                  | 13                  |
| Recurrent hospital admission              | 10                  |
| Postpartum amenorrhea                     | 10                  |
| Lactational failure                       | 10                  |
| Decreased secondary sexual characters     | 13                  |
| Alopecia                                  | 7                   |
| Weight loss                               | 8                   |
| Weight gain                               | 4                   |
| Emotional slowness                        | 6                   |
| Recurrent hyponatremia                    | 8                   |
| Recurrent hypoglycemia                    | 3                   |

Fig. 1: Presenting symptoms of the admitted patients through
emergency room

Figs 2A and B: (A) Patient at admission diagnosed to have hypopituitarism,
had facial wrinkling, emotional liability; (B) 2 months after treatment
be due to partial deficiency of hormones. The MRI of all patients showed empty sella. Two patients did not survive: one who had resistant shock and another, acute renal failure leading to anuria, metabolic acidosis, and death (Table 4). Rest all survived well and are in regular follow-up. There is marked improvement in general activity, blood pressure, dyselectrolytemia, and facial coarsening of patient (Fig. 2B).

**Table 3: Investigations of all patients**

| Parameter                  | Range          | Mean |
|----------------------------|----------------|------|
| Mean arterial pressure (mm Hg) | 40–110         | 94   |
| Serum sodium (mEq/L)       | 101–132        | 123  |
| Serum TSH (IU/mL)          | 1.04–6.47      | 2.32 |
| Serum FT4 (ng/dL)          | 0.08–1.4       | 0.20 |
| Serum cortisol (μg/dL)     | 1.19–3.1       | 2.1  |

**Table 4: Patient's outcome with treatment**

| Parameter                  | No. of patients (n = 15) | Percentage |
|----------------------------|--------------------------|------------|
| Improvement in symptoms    | 13                       | 86.7       |
| Did not survive            | 2                        | 13.3       |

In our study, only one patient presented with pancytopenia who recovered fully on replacing glucocorticoid and thyroid hormone. Important causes of mortality are shock, cardiovascular events, hypoglycemia, and acute renal failure.

Treatment includes supplementation of hormones required for sustaining life. This includes thyroid and cortisol replacement. Cortisol replacement should be done before thyroid because otherwise adrenal crisis can precipitate. Replacing sex steroid is essential if fertility is desired. Treatment with recombinant GH is not recommended to all patients. The exact mortality rate is not known, but if diagnosis or treatment delayed, then mortality can occur.

**Conclusion**

We should screen patients for pituitary insufficiency who are presenting with recurrent hyponatremia, hypoglycemia, low blood pressure, and extreme lethargy.

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