

# Sheehan syndrome; experience from a tertiary care center from Central India

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## ABSTRACT

**INTRODUCTION:** Sheehan Syndrome (SS) though not uncommon is identified as a consequence of ischemic pituitary necrosis due to severe postpartum hemorrhage leading to various manifestations due to varying degree of anterior pituitary hormone deficiency.

**AIM:** The aim of our study was to determine the clinical and biochemical characteristics of Sheehan's syndrome in our patients.

**MATERIAL AND METHODS** – It was the retrospective cohort study in which we identified the patients who visited our endocrine department and were diagnosed with SS. The various clinical, biochemical and radiological findings of these patients were recorded and analyzed.

**RESULTS:** Mean age of our patients was 36.65 years. 16 patients had history of blood transfusion during peri-partum period but only 11 patients had history of massive bleeding at delivery. 19 patients reported lactation failure and 12 patients reported loss of menstruation following delivery while rest all reported amenorrhea within 2-3 years following delivery. On anterior pituitary hormonal analysis 19 patients had secondary hypothyroidism, 13 had adrenal insufficiency, 21 had low gonadotropin levels, 9 had low prolactin levels. On radiological examination by Magnetic Resonance Imaging (MRI) complete or partial empty Sella was recorded in 23 patients.

**CONCLUSION:** Thus in our cases early menopause and lactational failure were the most common clinical findings and early clue to suspect for SS and do necessary work up for further management.

**Key Words:** Sheehan Syndrome; Postpartum Hemorrhage; Pituitary Necrosis; lactation failure; Amenorrhea; Empty Sella.

## INTRODUCTION

Sheehan Syndrome (SS) though not an uncommon clinical condition, it is identified as a consequence of ischemic pituitary necrosis due to severe postpartum hemorrhage leading to various manifestations due to varying degree of anterior pituitary hormone deficiency. In 1937 SS was first published by described by H. L. Sheehan as report in 1937 describing as pituitary necrosis at the time of autopsy in women who died from obstetric hemorrhage. It is one of the common causes of hypopituitarism in underdeveloped or developing countries. The exact pathogenesis of Sheehan's syndrome is not yet well understood. However, increased pituitary size during pregnancy can make the pituitary weaker against ischemia because of compression of the superior hypophyseal arteries [1]. Autoimmunity, small Sella size and disseminated intravascular coagulopathy may also have role in the pathogenesis [2, 3].

Clinical manifestation may vary from patient to patient, ranging from non-specific symptoms to coma due to varying degree of anterior pituitary hormone deficiency. Patients may present with amenorrhea, lactation failure, weakness, weight loss, dry skin, loss of axillary and pubic hair, breast atrophy, and psychiatric disturbance. The diagnosis of SS is usually difficult as symptoms can be subtle and confused with the symptoms of new motherhood [4].

Thus, we undertook this study to identify the various clinical, biochemical and radiological findings in our patients diagnosed with SS which may help in early diagnosis of SS and early intervention.

## MATERIALS AND METHODS

This was a retrospective observational cohort study performed at our Endocrine department in which 25 patients who attended our department from January 2017 to January 2020 and diagnosed with Sheehan syndrome were enrolled after proper consent.

The clinical history of the patient was taken in detail which included the number of pregnancy regularity of menstrual cycles after the postpartum period, last delivery at home or at hospital, any bad obstetric history, and history of hemorrhage during and/or after delivery, history of blood transfusion, breastfeeding in the postpartum period, history of regression

of secondary sexual character and history of symptoms suggesting of adrenal failure and hypothyroidism.

Other causes of hypopituitarism, such as cranial radiotherapy, head trauma and head surgery, were excluded by history. Clinical examination including breast atrophy, diminished hairs in pubic and axillary regions were noted. In biochemical examination measurement of anterior pituitary hormone levels was done, radiological investigation included MRI (magnetic resonance imaging).

## RESULTS

The patients were aged between 24 to 46 years with mean age of  $36.65 \pm 3.36$  years and mean duration between last delivery and diagnosis at our center was  $11.21 \pm 3.43$ . The baseline clinical characteristics are described in Table 1.

The number of pregnancies ranged from 1 to 7, but history of massive hemorrhage and blood transfusion was present in 11 and 16 cases respectively. 15 women never breast fed after delivery while 4 had breast fed their baby for few weeks but had to start top feed within weeks because of insufficient milk production.

12 patients never menstruated following last delivery while rest of 13 had few menstrual cycles which ceased within 2-3 years. Loss of secondary sexual characteristics was identified as breast atrophy and loss of sexual hair in 9 and 11 patients respectively. 21 patients had nonspecific complains like generalized body ache, weakness while 3 patients presented to emergency with altered consciousness.

On MRI empty sella and partial empty sella was identified in 16 and 7 patients respectively.

Details of clinical and radiological findings are described in Table 2.

Hyponatremia was identified in 9 patients and severe hyponatremia was identified in 2 patients. 2 patients presented with hypoglycemia in which one had severe hypoglycemia. Details of biochemical characteristics are described in Table 3.

Baseline anterior pituitary hormone analysis is described in Table 3. 19 patients had secondary hypothyroidism identified with low T4 and low

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**TABLE 1**  
**Baseline Characteristics**

	Mean $\pm$ SD	range
Age	36.65 $\pm$ 3.36	24-46
Number Pregnancies	2.54 $\pm$ 1.27	1-7
Duration between last delivery and diagnosis	11.21 $\pm$ 3.43	1-19

**TABLE 2**  
**Clinical and Radiological Characteristics**

	N=25	Percentage (%)
Post-partum hemorrhage	11	44
Blood transfusion	16	64
Lactational Failure		
Immediate	15	60
Delayed	4	16
Amenorrhea		
Immediate	12	48
Delayed	13	52
Loss of Axillary or Pubic hair	11	44
Breast Atrophy	9	36
Loss of Consciousness	3	12
Somatic complains like lethargy, weakness, generalized body ache	21	84
Pre-Existing Diseases		
Diabetes	1	4
Hypertension	1	4
Hypothyroidism	2	8
Radiological Findings on MRI		
Total Empty Sella	15	60
Partial Empty Sella	7	28
Normal Pituitary	3	12

**TABLE 3**  
**Biochemical Characteristics of our patients**

Parameter (Normal range)	Mean $\pm$ SD	Range	Low Levels recorded	High Level recorded
Hemoglobin (12 – 14 g/dl)	9.8 $\pm$ 1.91	6- 16	17	4
Serum Sodium (135 - 145meq/L)	131.3 $\pm$ 4.14	114 - 142	9	2
Serum Potassium (3.5 – 5.5meq/L)	4.1 $\pm$ 0.46	3.5 – 5.8	4	3
Random Blood Sugar (70 – 200 mg/dl)	121.3 $\pm$ 34.33	59 - 231	2	1
TSH (0.45 – 4.5 UIU/mL)	3.7 $\pm$ 1.61	0.01 – 8.8	12	3
T4 (6.5 – 12.5 mcg/dl)	6.7 $\pm$ 2.14	0.5 – 14.1	19	2
T3 (0.6 – 1.8 ng/ml)	0.8 $\pm$ 0.21	0.1 – 1.7	21	1
LH (mIU/ml)	5.1 $\pm$ 1.13	0.01 – 4.1	20	1
FSH ( mIU/ml)	6.8 $\pm$ 1.96	0.01 - 13	21	2
Prolactin (1.5 – 24 ng/ml)	14.3 $\pm$ 8.13	0.5 – 41.2	9	2
Cortisol (8 am) (5.5 – 18.6 mcg/dl)	8.5 $\pm$ 2.34	0.1 – 16.5	16	1
Cortisol (Post Acton Prolongatium Stimulation) (> 18.6 mcg/dl) ( N =16)	11.8 $\pm$ 7.76	0.8 – 36.4	13	3

or normal TSH. Hypogonadotropic hypogonadism was identified by low levels of LH and FSH in 19 patients by pooled morning samples. 16 patients had low morning baseline serum cortisol of which only 9 had inadequate response to Post Acton Prolongatium Stimulation.

## DISCUSSION

Simmonds in 1914 first described hypopituitarism as a clinical syndrome consisting of four characteristics: weight loss, loss of sexual function, asthenia, and low basal metabolic rate [4]. More than 20 years later, Sheehan described SS a type of hypopituitarism characterized by pituitary necrosis after postpartum hemorrhage and hypovolemia, which may cause hypopituitarism and present either immediately or after several years with various manifestations, depending on the amount of tissue destruction. He suggested that the pituitary gland is especially vulnerable in the third trimester of pregnancy and is easily damaged during parturition [4-6].

The spectrum of clinical presentation of SS is very huge and may vary from non-specific presentations like weakness, fatigue to severe pituitary

insufficiency resulting in coma and death.

In our patients mean duration between last delivery and subsequent manifestation and diagnosis was 11.21 years which ranged from 1 to 19 years while Huang et al described the range of 2-33 years and Dokmetas et al described the range of 1-40 years between post-partum hemorrhage and clinical manifestation [6, 7].

In our patients mean hemoglobin was 9.8 g/dl and ranged from 8-16 g/dl. 17 (68%) patients had anemia of which 2 had severe anemia with hemoglobin less than 7 mg/dl. Hypopituitarism is a rare cause of anemia thus in patients with anemia resistant to treatment SS could be suspected [8].

In our study group, 12 (48%) patients never menstruated following last delivery and in remaining 13 (52%) patients menstrual ceased within 2- 3 years. Though all patients had early menopause the baseline LH and FSH in our patients was not significantly raised suggesting hypogonadotropic hypogonadism. Dokmetas et al described early menopause with low gonadotropin levels in 70% cases [6]. Similarly, Halit Diri et al in their review article described low gonadotropin levels in SS ranged from 75% to 100% in various studies [9].

In our case series 19(76%) patients had difficulty in lactation but only 9 (36%) patients had low baseline prolactin levels. Similar findings were described by Dokmetas et al in their study in which 70% patients had lactational failure but low prolactin levels were identified in 20% cases only. Dokmetas et al in their study described that all patients with lactation failure had failed prolactin response on TRH stimulation suggesting that lactation failure might be due to lack of prolactin surge [6].

In our study group 19 (76%) patients had secondary hypothyroidism identified with low T4 and low or normal TSH. Dokmetas et al in their study described secondary hypothyroidism in 90% cases [6], and Halit Diri et al in their review article described secondary hypothyroidism in SS ranged from 57% to 90% in various studies [9]. Before starting the treatment of hypothyroidism the work up for adrenocortical insufficiency should be done to prevent adrenal crisis in adrenal insufficient patients post levothyroxine replacement.

Adrenocortical insufficiency is one of the most dreaded manifestation of SS. It's presentation may vary from non-specific presentations like weakness, fatigue to hypotension, and sometimes adrenal crisis. It is also a main cause of hypoglycemia and hyponatremia which may be the presenting finding in some patients. In our case series 16 (64%) patients had low baseline morning cortisol and of which 13 (52%) had inadequate response to Acton Prolongatium Stimulation suggesting of adrenal insufficiency. 2 patients had hypoglycemia of which 1 had severe hypoglycemia and presented with altered consciousness. 9 patients had hyponatremia of which 2 patients had severe hyponatremia with serum sodium levels less than 120 meq/L and presented with altered consciousness. Dokmetas et al in their study described adrenal insufficiency in 55% cases [6], and Halit Diri et al in their review article described adrenal insufficiency in SS ranged from 53% to 96% in various studies [9]. Thus, SS must be considered in the differential diagnosis in patients presenting with hypoglycemia, hyponatremia or altered consciousness particularly in regions where it is common.

Partial or total empty sella is a characteristic finding of Sheehan's syndrome [5]. In our study group 15 (60%) had total empty sella and 7 (28%) had partially empty sella while 3 (12%) had normal pituitary findings on MRI scan. Dokmetas et al in their study described total empty sella in 75% cases and partial empty sella in 25% cases. [6] In our series we found normal pituitary findings in 3 patients with classical clinical and biochemical features of SS. Thus, possibility of SS should not be ruled out in presence of normal radiological finding of pituitary if clinical and biochemical features are suggestive of SS.

## Limitation of Study

Possibility of sample Bias cannot be ruled out as patients were from one center with small sample size. Growth hormone assay and dynamic pituitary hormone assay for few hormones was not done due to financial constraints. However, these limitations might not affect the diagnosis and management of SS.

## CONCLUSION

The SS is not an uncommon condition and increases the risk of morbidity and mortality if not diagnosed early. It is therefore important to identify these patients early for proper management and clinical history of post-partum hemorrhage, lactation failure and early menopause are very important clues in early diagnosis.

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