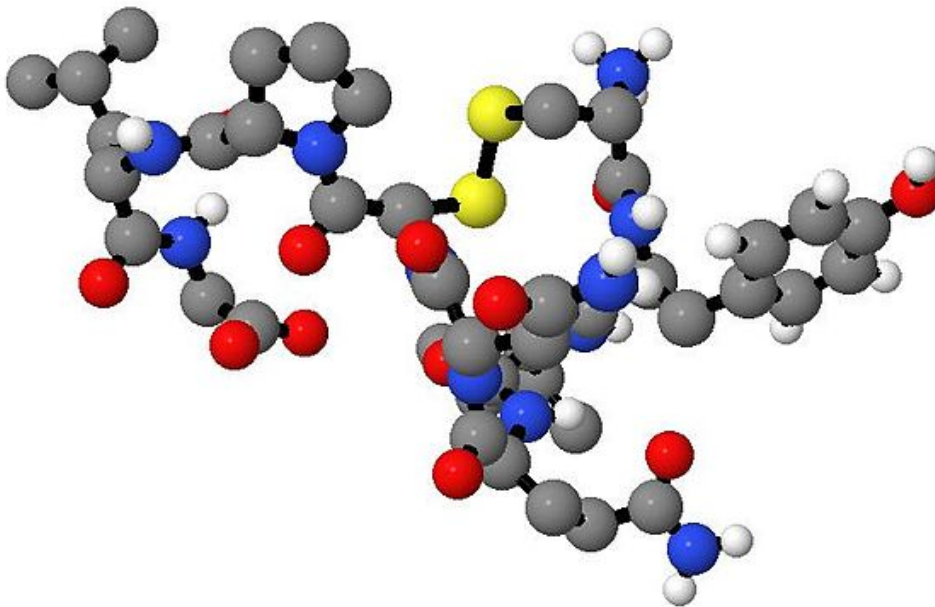


SIADH (Syndrome of Inappropriate Antidiuretic Hormone Secretion) in Children — Signs and Symptoms

[See online here](#)

SIADH is characterized by hyponatremia, serum hypoosmolality, and increased urine osmolality. SIADH is a disease characterized by a decrease of the amount of volume expansion as a consequence of excess renal water reabsorption through excess of antidiuretic hormone secretion. The symptoms of SIADH are mainly due to the effect of hyponatremia on the brain. The diagnosis of SIADH is dependent on the exclusion of other causes of hyponatremia, the confirmation of hyponatremia and the documentation of hypoosmolality. Fluid restriction is the first line therapy for SIADH, followed by an increased solute intake in refractory cases. Loop diuretics might be indicated in patients who do not respond to these measures.



Overview

SIADH is characterized by **hyponatremia and hypoosmolality due to the inadequate and continued secretion of the antidiuretic hormone despite normal plasma volume**. The end-point is impaired water excretion, water retention, and hyponatremia. Hyponatremia happens in SIADH because of excess water not due to absolute sodium deficiency in the blood.

The classic **Bartter-Schwartz criteria** can be used to confirm the diagnosis of SIADH. The patient is expected to have hyponatremia with hypoosmolality, absence of clinical evidence of volume depletion, absence of other causes of hyponatremia, urine that is not maximally diluted i.e .reduced water excretion, and continued excretion of sodium in the urine. The restriction of fluid intake should correct the hyponatremia in a child diagnosed with SIADH.

Epidemiology of SIADH in Children

Incidence and prevalence

The most common cause of hyponatremia in children is SIADH; therefore, the prevalence and incidence of SIADH in this patient's age group can be estimated from the incidence and prevalence of hyponatremia. The estimated prevalence of hyponatremia in patients in the United States can be 2.5 % to **as high as 30 %!** Hyponatremia can also be caused by the administration of large amounts of hypotonic intravenous fluids; therefore, the **diagnosis of SIADH should be made with caution.**

Men and boys are more likely to develop hyponatremia compared to girls. Women tend to develop drug-induced or exercise-induced hyponatremia. Hyponatremia and SIADH are more common in adults as compared to children.

Prognosis

The **prognosis of SIADH is largely dependent on the etiology.** Drug-induced SIADH usually has an excellent prognosis. On the other hand, SIADH due to central nervous system infection is more likely to be associated with permanent neurological deficits and increased morbidity. Rapid correction of hyponatremia in patients with SIADH is associated with central pontine myelinolysis and permanent neurological impairment.

In addition to the central nervous system complications of SIADH, noncardiogenic pulmonary edema has also been described in some patients. Severe hyponatremia is the most important prognostic factor for increased mortality in children with SIADH.

Etiology of SIADH in Children

Causes

SIADH can be caused by either:

- The ectopic production of the antidiuretic hormone or
- By the production of the antidiuretic hormone from the normal hypothalamus.

The most common causes of SIADH that are related to central nervous system disease are:



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- Acute psychosis
- Brain abscess
- Cavernous sinus thrombosis
- Cerebrovascular accident
- Central nervous system lupus
- Encephalitis
- Head trauma
- Multiple sclerosis
- Subarachnoid hemorrhage
- Intracranial hemorrhage
- Epilepsy.

Other causes associated with SIADH:

- Lung carcinoma
- Gastrointestinal cancers
- Adrenocortical carcinoma
- Ureter, bladder or prostate cancer
- Ovarian cancers

The most common pulmonary causes of SIADH in children:

- Bronchitis
- Bronchiolitis
- Asthma
- Pneumonia
- Cystic fibrosis
- Pulmonary abscess
- Tuberculosis
- Sarcoidosis

SIADH can also occur **as a complication to certain drugs**. The most common drugs that have previously been shown to be associated with SIADH are:

- Antineoplastic drugs,

- Barbiturates,
- Carbamazepine,
- Anti-psychotic medication,
- Opiates, and
- Antidepressants.

Metformin, oxytocin, nonsteroidal anti-inflammatory drugs and theophylline potentiate the effects of antidiuretic hormone, but do not cause overproduction of the hormone; therefore, such drugs are said to cause a SIADH-like picture and not true SIADH.

CNS	Lungs	GI	Medications
<ul style="list-style-type: none"> • Tumor • Meningitis • Encephalitis • Hemorrhage • Vasculitis • Surgical Trauma 	<ul style="list-style-type: none"> • Pneumonia • Bronchiolitis • Cystic Fibrosis • Malignancy 	<ul style="list-style-type: none"> • Gastroenteritis 	<ul style="list-style-type: none"> • TCA • SSRI • PPI • ACE inhibitor

Pathophysiology of SIADH

SIADH is characterized by the **over-production of the antidiuretic hormone** which causes water retention. **Excess water will dilute the extracellular sodium and will cause hyponatremia;** therefore, hyponatremia in SIADH is not caused by sodium deficiency.

The symptoms of SIADH are mainly due to the brain's response to hyponatremia. Fortunately, **in most cases, SIADH hyponatremia is mild to moderate and rarely severe.** On the molecular level, brain cells respond to hyponatremia by losing glutamate, creatinine, and potassium. The loss of these intracellular osmolytes is associated with brain cell swelling and eventually brain edema. Extremely severe hyponatremia might cause severe brain cell swelling and fatal brain herniation. Fortunately, this only occurs in a minority of the patients, < 5 %.

Over-secretion of the ADH hormone leads to water retention by stimulating increased water permeability in the renal collecting duct of the kidney. This increases the glomerular filtration rate (GFR) due to volume expansion and vasodilation caused by brain natriuretic peptides (that cause excessive sodium excretion through urine). Natriuretic peptides are secreted because of two reasons, one is ADH stimulation, and another one is increased plasma volume expansion. This blocks the reabsorption of sodium in the collecting duct leading to SIADH.

Clinical Presentation of SIADH in Children

Most of SIADH symptoms are attributed to hyponatremia, its severity and the rate of development. Most cases of hyponatremia in SIADH are mild and are rarely asymptomatic. This explains why most cases of SIADH in children are diagnosed incidentally by **laboratory investigations.**

The most common symptoms

The most common symptoms of mild chronic hyponatremia in children are a cognitive **decline, ataxia, and frequent falls.** It is a bit controversial whether the frequent falls are the cause of SIADH, i.e., repeated minor head trauma, or are the consequence of SIADH. Symptoms of acute hyponatremia include **anorexia, fatigue, and nausea.** Muscle cramps, headaches, drowsiness, confusion, seizures, and even coma can happen

in acute severe hyponatremia.

A mental status examination

A mental status examination in a child with SIADH might show **confusion, disorientation, or delirium**. Tremors, myoclonus, and abnormal deep tendon reflexes might also be evident. Patients with SIADH are usually **normotensive**.

Diagnostic Workup for SIADH in Children

Characteristic laboratory results

SIADH is characterized by hyponatremia ($\text{Na} < 135 \text{ mmol/kg}$) and hypoosmolality (serum osmolality $< 280 \text{ mOsm/kg}$). Urine osmolality is supposed to be high. Urine Na concentration in SIADH is usually above 40 mEq/L and is reflective of a normal renal sodium excretory capability.

Supporting laboratory tests

In addition to the previously-mentioned laboratory tests to confirm the diagnosis of SIADH, other supporting laboratory tests are also indicated to exclude other causes of hyponatremia. **Serum glucose, cortisol and thyroid-stimulating hormone levels** should be checked. For instance, mineralocorticoid deficiency syndromes can cause hyponatremia.

Serum potassium levels should also be checked. Patients with hypokalemia and hyponatremia should receive an **arterial gases test** to confirm the presence of alkalosis. If metabolic alkalosis is present, the patient should be evaluated for the possibility of vomiting-induced hyponatremia before jumping to the diagnosis of SIADH.

Radioimmunoassay for ADH is used for accurate diagnosis of SIADH.

Imaging studies

Imaging studies in SIADH are more tailored towards the **exclusion of other causes of excessive antidiuretic hormone secretion**, i.e., ectopic SIADH. A chest X-ray followed by a computed tomography scan (**CT**) or a magnetic resonance imaging study (**MRI**) of the lungs is a reasonable option in a patient suspected to have a lung nodule who is also considered as high risk for lung carcinoma. Brain computed tomography scanning and magnetic resonance imaging is helpful in **excluding central nervous system tumors, a potential cause of SIADH.**

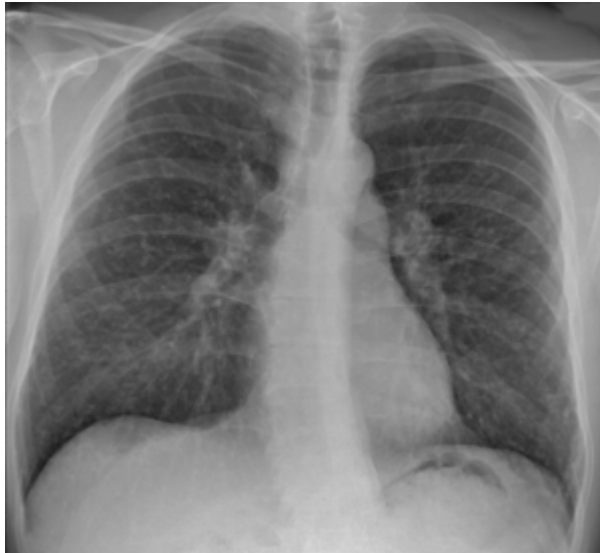


Image: "Chest X-ray of sarcoidosis nodules" by Mikael Häggström.
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Treatment of SIADH in Children

The treatment of SIADH in children includes three main interventions. First, **fluid intake should be restricted**. Restricting fluid intake usually solves SIADH in most patients and that is why it is part of the diagnosis. If that measure fails to correct the serum hypoosmolality, the patient should be instructed to start loop diuretics or to increase their oral sodium chloride intake.

Vasopressin receptor antagonists and lithium should not be used in children with SIADH. The administration of sodium to correct hyponatremia should be a last resort in patients with SIADH. If sodium administration is associated with rapid correction of hyponatremia, the administration of water, 5 % dextrose or desmopressin should be initiated to lower the rate of hyponatremia correction.

References

Thomas, Christie P. 2017. "[Syndrome of Inappropriate Antidiuretic Hormone Secretion Treatment & Management](https://www.medscape.com/article/246650)." Available at: [emedicine.medscape.com/article/246650](https://www.medscape.com/article/246650)

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