

*Original Article*

## The prevalence and risk factors of the Syndrome of Inappropriate Anti-Diuretic Hormone secretion (SIADH) following spinal surgery

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**Abstract**

**BACKGROUND:** The Syndrome of Inappropriate Anti-Diuretic Hormone (SIADH) secretion is the most common etiology of normovolemic hyponatremia, which occurs following non-physiologic release of antidiuretic hormone (ADH) from the posterior pituitary, or an ectopic source. SIADH has been reported as a complication of cardiothoracic, brain, and spinal surgeries. This study was conducted to assess the prevalence of SIADH following spinal surgeries and to identify the underlying risk factors.

**METHODS:** Samples were patients undergoing any spinal surgery at the Hospitals of Shafa Yahyaian and Rasoul Akram, Tehran, Iran in a 2-year period. Blood and urine sodium concentrations and osmolarity were measured before and after surgery. The amount of hemorrhage, as well as the patients' fluid input and output during surgery were recorded. Fluid input and output was also recorded on the first postoperative day.

**RESULTS:** The prevalence of SIADH following spinal surgeries was 60.3%. Mean duration of surgery in SIADH patients was longer than in others. Mean amount of hemorrhage and total fluid loss during surgery were significantly higher in SIADH patients than in healthy individuals.

**CONCLUSIONS:** SIADH is the principal cause of hyponatremia following spinal surgeries; the reported prevalence rates vary widely from 5 to 100%. SIADH following surgery has been attributed to stress, and in spinal or neurological surgeries to dural damage or traction of neuronal pathways. Time is of the essence in the treatment of hyponatremia and prevention of complications that may increase the mortality and morbidity of spinal surgeries.

**KEYWORDS:** Inappropriate ADH Syndrome, spinal surgeries, hyponatremia.

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The Syndrome of Inappropriate Anti-Diuretic Hormone (SIADH) was originally described in 1975 in patients with bronchogenic carcinoma.<sup>1</sup> SIADH is the most common cause of normovolemic hyponatremia, which occurs due to non-physiologic ADH release from the posterior pituitary or an ectopic source such as carcinoma of the bronchi, stomach, prostate or the ovaries, sinonasal neuroendocrine carcinoma, agenesis of the corpus callosum, cleft lip, closed or open head

trauma, infections including abscess and/or tuberculosis of the lungs or the brain, viral and bacterial encephalitis or meningitis, pulmonary nocardiosis, ophthalmic herpes zoster, congenital insufficiency of anterior pituitary gland, asthma, the Gillan-Barre syndrome, multiple sclerosis, hydrocephalus, treatment with diuretics, use of amiodarone, citalopram, haloperidol, venlafaxine, quitipin, selective serotonin reuptake inhibitors (SSRIs), cerebral vascular occlusion, cavernous sinus

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thrombosis and marathon runners.<sup>2-23</sup> SIADH has been reported as a complication following cardiothoracic, brain and spinal surgeries<sup>24</sup>. SIADH results in water retention, sodium loss, and production of concentrated urine with normal or increased extracellular fluid volume without any physiologic or pharmacologic stimulation of ADH secretion.<sup>24</sup> The symptoms of SIADH are varied and range from mild pain, muscle cramps, and anorexia to nausea, vomiting, confusion, coma, convulsion and death. Low urinary output and increased specific gravity of the urine are usually the early signs of SIADH.<sup>25,26</sup> Previous studies have reported prevalence rates of 5%, 33%, and 100% for SIADH following spinal surgeries.<sup>3,25,27,28</sup> There are two surgical approaches to repair scoliosis, posterior spinal fusion (PSF) and anterior spinal fusion (ASF).<sup>24</sup> The second one is mostly used for severe cases of scoliosis and is done through laparotomy and Thoracotomy; so intraabdominal organ manipulation in this method is more than in PSF. It is estimated that bleeding and length of surgery are also much more prominent in this type of surgery. These may lead to higher chance of SIADH occurrence. Most of the studies done in this area, evaluated PSF approach, while there is a lack of data on ASF approach and its effect on the occurrence of SIADH. This study was conducted to assess the prevalence of SIADH following the above two types of spinal surgeries and to identify the underlying risk factors.

## Methods

All patients undergoing spinal surgery for correction of congenital abnormalities of the spine, scoliosis, herniated disc, spinal stenosis, and listhesis at the Hospitals of Shafa Yahyaian and Rasoul Akram, Tehran, Iran, from November 2006 to June 2007 were included in this cross-sectional analytical study. Urine and blood samples were taken 24 hours before and after the surgery. The sodium concentration of blood and urine samples was checked. Blood and urine osmolarity were measured using osmometer based on ion selective electrode method. The amount of hemorrhage, as well as

the patients' fluid input and output during surgery were recorded. Fluid input and output was also recorded on the first postoperative day. Also, lost fluid volume was calculated adding patient blood loss volume during the surgery to patient urine output both measured in cubic centimeter. The diagnosis of SIADH was made based on the above measurements. The criteria for diagnosis of SIADH are presented in table 1. Demographic information including age and sex, as well as data on the type of abnormality and type and duration of operation was collected using data collection forms. Patients who received hypotonic serum before or during surgery were excluded.

**Table 1.** Criteria for laboratory evaluation and diagnosis of SIADH

Serum Na < 155 meq/L
Urine Na > 40 meq/L
Serum Osmolarity < 275 mosm/kg
Urine Osmolarity > 100 mosm/kg

## Results

Of 63 patients who underwent surgery for correction of congenital spinal abnormalities, scoliosis, herniated disc, spinal stenosis, and listhesis, 29 (46%) were male and 34 (54%) were female. The patients had a mean age of 20.21 ± 12.01 years. Based on laboratory diagnostic criteria presented in table 1, 38 patients (60.3%) developed SIADH following spinal surgery and 25 patients (39.7%) did not. Table 2 presents the frequency distribution and relative frequency of SIADH according to sex. Chi-square test yielded a P value greater than 0.05. Patients with and without SIADH had mean ages of 15.74 ± 4.26 and 27 ± 00 years, respectively, with t-test revealing a significant difference (P < 0.05). Patients underwent procedures including ASF, PSF, discectomy or a combination of ASF and PSF. Table 3 presents the frequency distribution and relative frequency of SIADH according to the type of surgical procedure. Chi-square test yielded a P value less than 0.05. Mean duration of surgery in SIADH

and non-SIADH patients was  $306.39 \pm 135.45$  and  $222.48 \pm 122.15$  minutes, respectively, with a significant difference as determined by t-test ( $P < 0.05$ ) (figure 1). Mean lost fluid volume

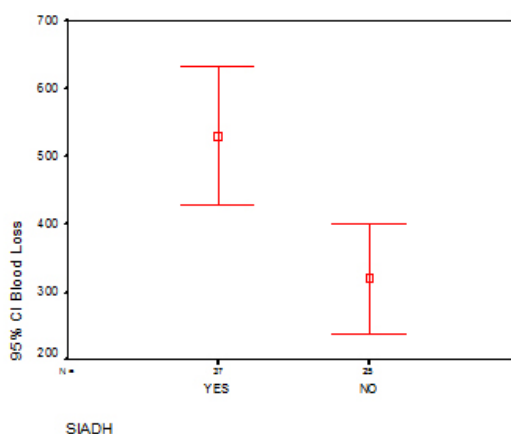
during surgery was  $2319.19 \pm 1311.07$  and  $1639 \pm 996.44$  milliliters in SIADH and non-SIADH patients, respectively, with t-test revealing a significant difference ( $P < 0.05$ ) (figure 2).

**Table 2.** Frequency distribution and relative frequency of SIADH according to sex.

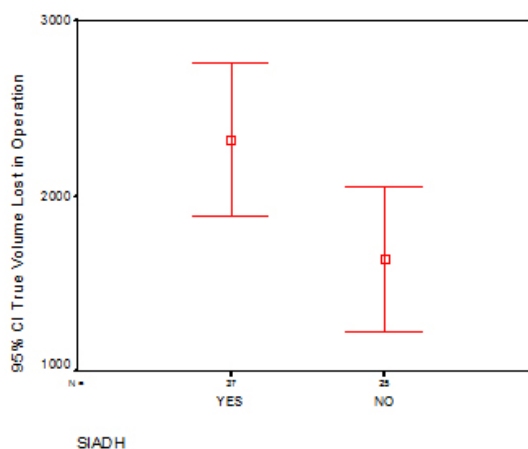
	Men	Women	Total
SIADH	20 (69%)	18 (52.9%)	38
No SIADH	9 (31%)	16 (47.1%)	25
Total	29	34	63

**Table 3.** Frequency distribution and relative frequency of SIADH according to the type of surgery.

	Type of surgery				Total
	ASF	PSF	Discectomy	ASF & PSF	
SIADH	17 (68.0%)	19 (70.4%)	0 (0.0%)	2 (100.0%)	38
No SIADH	8 (32.0%)	8 (29.6%)	9 (100.0%)	0 (0.0%)	25
Total	25	27	9	2	63



**Figure 1.** Mean and 95% confidence interval of the volume of blood lost during surgery in SIADH and non-SIADH patients.



**Figure 2.** Mean and 95% confidence interval of total fluid volume lost during surgery in SIADH and non-SIADH patients.

## Discussion

SIADH following spinal surgery has been widely reported.<sup>3,27,28</sup> Elster reported the prevalence of SIADH at 5% in a retrospective study of 161 patients who had undergone spinal surgery.<sup>27</sup> Callewart reported a prevalence of 6.9% in a study of 116 patients who had undergone spinal surgery.<sup>3</sup> Lieh-Lai reported a prevalence of 33% in a prospective cross-sectional study of 30 patients following spinal surgery.<sup>25</sup> In a prospective study of 10 patients, Bell and colleagues reported the prevalence of SIADH at 100% following spinal surgeries.<sup>28</sup> Burrow and colleagues reported the prevalence of SIADH at 81% in their study of 24 patients who underwent spinal fusion surgery.<sup>29</sup> Callewart reported SIADH in patients who had undergone revision surgery or their hemorrhage had exceeded 10%.<sup>3</sup> Lieh-Lai, however, reported no correlation between hemorrhage or type of spinal surgery, and the development of SIADH.<sup>25</sup> SIADH following surgery has been attributed to stress, and in spinal or neurological surgeries to dural damage or traction of neuronal pathways.<sup>25,30</sup> Lieh-Lai found that ADH levels rise immediately and also 6 hours after surgery but return to preoperative levels after 12 hours. He found that serum osmolarity drops to subnormal levels within 6 hours post-surgery; these findings suggest that SIADH develops immediately following surgery and that careful evaluation of patients for decreased urinary output and serum sodium levels may contribute to early detection of SIADH.<sup>25</sup> It is worth noting that ADH levels may rise in a physiologic response to hypovolemia or hyponatremia; this can be

differentiated from SIADH using the guidelines set forth by Schwartz and colleagues (emphasizing on low serum sodium levels, low serum osmolarity, high serum sodium levels, and high urinary osmolarity in SIADH).<sup>1</sup> SIADH following spinal surgery is self-limiting, usually resolving within 2-3 weeks; nonetheless, while a stop in ADH secretion is to be anticipated, the severity of hyponatremia should mandate appropriate intervention for timely correction of water and electrolyte imbalance.<sup>24</sup> Hypotonic fluids increase the odds of SIADH and should be avoided prior to spinal surgery.<sup>31</sup> In mild minimally symptomatic hyponatremia, reducing free water intake and increasing oral intake of salt may prove sufficient. However, in patients with marked hyponatremia (sodium concentration < 120 meq/L) and central nervous system-pulmonary symptoms, sodium correction at a rate of 0.5 meq/L per hour, not exceeding a total of 12 meq/L and 18 meq/L in the first 24 and 48 hours, respectively, should be performed to preclude demyelinating central pontine and extrapontine myelinolysis, a condition that can increase morbidity and mortality.<sup>21,32-35</sup> Treatment of SIADH with vasopressin receptor antagonists including conivaptan hydrochloride and tolvaptan and also intravenous contrast media is being investigated.<sup>36-39</sup> SIADH is the principal cause of hyponatremia following spinal surgeries. Early detection of SIADH and prompt treatment of the resultant hyponatremia is of critical importance in reducing the mortality and morbidity associated with surgeries of the spine.

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