

# Gallstones and biliary sludge in Greek patients with complete high spinal cord injury: an ultrasonographical evaluation

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## ABSTRACT

**Introduction:** We used ultrasonography to detect the presence of biliary sludge or gallstones in Greek patients with complete high spinal cord injury (SCI) above the seventh thoracic segment (T7), within the first six months from injury onset, in order to evaluate the effects of neurological instability and dysfunction of the sympathetic nervous system (SNS) on the gallbladder function in the early post-SCI phase.

**Methods:** We evaluated 78 asymptomatic patients (57 males, 21 females; mean age 34.8 (range 19–56) years) with complete high SCI located above the T7 segment, and 78 healthy subjects (59 males, 19 females; mean age 35.2 (range 21–59) years) matched for age, gender and race, for a total period of 39 months. All the participants underwent ultrasonographical examination of the gallbladder and common bile duct within the first six months from the injury, in order to investigate the development of biliary sludge and gallstones.

**Results:** The incidence of biliary sludge was significantly higher in patients with SCI compared with the control group. The incidence of biliary sludge and gallstones was also significantly higher in patients with SCI patients in comparison with the healthy subjects. In male SCI patients, the incidence of biliary sludge was significantly increased in comparison with healthy subjects. No significant difference was revealed between the two groups in detection of gallstones.

**Conclusion:** Our study indicates that the detection of gallbladder sludge and gallstones are significantly higher in Greek patients with complete high SCI above the T7 segment, as compared with healthy control subjects within the first six months of the injury onset.

The complete disruption of the SNS and the neurological instability in the early post-SCI phase is probably responsible for the biliary sludge and gallstone formation. Our results suggest that ultrasonography should be performed in these patients at the first 3–6 months from the injury for the early diagnosis of the lithogenic bile.

**Keywords:** biliary sludge, gallstones, spinal cord injury, ultrasonography

*Singapore Med J 2009; 50(9): 889-893*

## INTRODUCTION

Spinal cord injury (SCI) is a pathological condition characterised by nervous system dysfunction due to the disruption of motor and sensory functions below the level of injury. Patients with SCI may present with multiple gastrointestinal complications.<sup>(1)</sup> It has been established that 30% of the gastrointestinal symptoms in patients with SCI result from cholelithiasis<sup>(2-5)</sup> with a high prevalence.<sup>(6-8)</sup> Recent studies have suggested that SCI is a risk factor for the development of cholelithiasis<sup>(2,9)</sup> and sludged bile, especially during the first months after SCI.<sup>(6,10)</sup> This is due to a dysfunction of the spinal sympathetic system. The sympathetic innervations originate from the seventh to tenth spinal segment<sup>(6)</sup> and inhibit gallbladder contraction.<sup>(11-13)</sup> In SCI patients, the sympathetic nervous system (SNS) dysfunction alters gallbladder motility<sup>(6,14)</sup> and predisposes to cholelithiasis and biliary sludge formation,<sup>(9)</sup> while the parasympathetic innervations that provide stimulating impulses by vagal trunks remain intact.<sup>(2,6,15)</sup> In a recent study, Xia et al found that SCI predisposes to gallstone disease and that cholelithiasis formation was not associated with the age and body weight of patients, the severity and the duration of the disease.<sup>(16)</sup>

The dysfunction of the autonomic nervous system establishes within six months of SCI,<sup>(17)</sup> therefore neurological instability effects on gallbladder function are more prominent within that period. To the best of our knowledge, the effect of a completely damaged SNS, such

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**Table I. Characteristics of spinal cord injury patients and age-, race- and gender-matched controls.**

| Characteristics  | No. of SCI patients | No. of controls | p-value |
|------------------|---------------------|-----------------|---------|
| Gender           |                     |                 |         |
| Male             | 57                  | 59              | > 0.05  |
| Female           | 21                  | 19              | > 0.05  |
| Total            | 78                  | 78              |         |
| Mean age (years) | 34.8                | 35.2            | > 0.05  |

SCI: spinal cord injury

as spinal cord injury above the seventh thoracic segment (T7), on the gallbladder function in the early post-SCI phase has not been extensively evaluated. Additionally, the clinical diagnosis of cholelithiasis in the early post-injury phase is difficult and delayed due to significant sensory disturbances below the level of injury in these patients. The aim of this study was to detect by ultrasonography the presence of biliary sludge or gallstones in Greek patients with complete high paraplegia or tetraplegia within the first six months from injury onset, in order to evaluate the effects of neurological instability on the gallbladder function in the early post-SCI phase.

## METHODS

The study population consisted of 78 asymptomatic adult patients (57 males, 21 females; mean age 34.8 [range 19–56] years) with SCI above T7. The level of SCI was determined by neurological and radiological investigations. All patients had complete neurological damage of the motor and sensory functions with no movement or sensation below the lesion (ASIA A) according to the classification of the American Spinal Injury Association (ASIA). According to ASIA, the impairment scale of the international standards for the neurological and functional classifications of spinal cord injury patients is as follows: ASIA A: motor and sensory functions complete with no movement or sensation below the lesion; ASIA B: incomplete sensory function, but no motor function preserved through S4–5; ASIA C: motor and sensory functions incomplete with strength < grade 3 (of 5) for most of muscles below the lesion; ASIA D: motor and sensory function incomplete with strength  $\geq$  grade 3 (of 5) for most muscles; ASIA E: normal motor and sensory functions.<sup>(18)</sup>

The control group consisted of 78 healthy subjects (59 males, 19 females; mean age 35.2 [range 21–59] years) matched for age, gender and race with the patient population (Table I). In all individuals, the body weight was within or slightly below normal limits. Risk factors for the development of gallstones, such as obesity, diabetes

mellitus, biliary infection, alcoholic cirrhosis, haemolytic anaemias and oral contraceptives, were not reported in either group. 42 patients with complete high SCI above the T7 segment and 42 controls were admitted to the Radiology Imaging Department of Athens General Hospital “G. Gennimatas”, Greece, and 36 patients with complete high SCI above T7 as well as 36 controls were admitted to the Second Radiology Department of University General Hospital “Attikon”, Greece, during a period of 39 months, from September 2004 to December 2007.

All subjects underwent ultrasonographical examination of the gallbladder and common bile duct during the study period. The SCI patients were examined  $108 \pm 25$  days after the trauma, and all cases within the six months from the injury onset. Ultrasonographical examinations were performed using two echo units (HDI 5000 and HDI 3500, ATL Ultrasound Inc, Bothell, WA, USA) equipped with a high-resolution 2–5 MHz curved transducer. The examinations were carried out by three independent experienced radiologists blinded to the patients’ identities, and the images were interpreted in consensus. For each ultrasonographical session, the transducer was placed over the right upper abdominal quadrant. Biliary sludge was defined as non-shadowing low-amplitude echoes layering in the dependent portion of the gallbladder or common bile duct and forming a fluid-fluid level with changes in the patient position.<sup>(19)</sup> Gallstones were defined as echogenic intraluminal filling defects of the gallbladder or common bile duct with an accompanying posterior acoustic shadow, moving freely with gravity.<sup>(20)</sup> In cases of lithiasis, the size of the gallstones was measured. The gallbladder wall thickness and echogenicity, as well as the bile duct width were registered in all subjects.

## RESULTS

The chi-square test was used for the statistical analysis. We obtained a raw comparison of the frequencies of the biliary sludge or lithiasis between patients and healthy subjects based on gender, i.e. male patients and male controls, and female patients and female controls. A p-value < 0.05 was regarded as significant. Of 78 SCI patients, 21 (26.92%) demonstrated ultrasonographical findings of gallstones or biliary sludge in the gallbladder, 15 (19.23%) developed gallbladder sludge compared with none of the control group, and six (7.69%) developed gallstones compared with three (3.85%) of the control population. All the patients who developed gallstones had a post-injury duration of longer than four months.

No simultaneous presence of biliary sludge and lithiasis was identified during the examinations. The statistical analysis revealed a significantly higher

**Table II. Chi-square test results for incidences of biliary sludge and gallstones between spinal cord injury patients and normal subjects of both gender.**

| Studied variable  | No. (%) of cases (n = 78) | No. (%) of controls (n = 78) | p-value ( $\chi^2$ ) |
|-------------------|---------------------------|------------------------------|----------------------|
| <b>Sludge</b>     |                           |                              |                      |
| Male              | 12 (21.05)                | 0                            | < 0.0001             |
| Female            | 3 (14.29)                 | 0                            | 0.135                |
| Total             | 15 (19.23)                | 0                            | < 0.0001             |
| <b>Stones</b>     |                           |                              |                      |
| Male              | 5 (8.77)                  | 2 (3.39)                     | 0.205                |
| Female            | 1 (4.76)                  | 1 (5.26)                     | 0.73                 |
| Total             | 6 (7.69)                  | 3 (3.84)                     | 0.247                |
| Sludge and stones | 21 (26.92)                | 3 (3.84)                     | < 0.0001             |

incidence of cholelithiasis or biliary sludge in the SCI patients compared with the healthy individuals ( $p < 0.001$ ). In addition, the detection of biliary sludge without cholelithiasis was significantly higher in SCI patients than in controls ( $p < 0.001$ ); however, the incidence of gallstones was not different between the two groups (Table II). Gallbladder biliary sludge was found in 12 (21.05%) male patients and in three (14.29%) female patients (Figs. 1 & 2). Five (8.77%) male patients had gallstones compared with two (3.39%) males in the control group. Only one (4.76%) female patient (and one [5.26%] female control) presented with gallstones. There was no significant difference in the incidence of gallstones between males and females, both in SCI patients and healthy subjects. The number of male patients with biliary sludge was statistically significantly higher ( $p < 0.0001$ ) compared with the male controls, but no significant difference was observed between the respective female groups (Table II).

No patient developed sludge or lithiasis in the common bile duct. All the gallstones were small in size, with a diameter  $< 0.5$  cm, not strongly echogenic, and were associated by an acoustic shadow (Figs. 3 & 4). In all subjects of the study, the gallbladder wall was thin ( $< 0.3$  mm) and with normal echogenicity. The common bile duct measured  $< 0.3$  mm in width in all patients and controls.

## DISCUSSION

Previous studies have shown the efficacy of ultrasonography in the diagnosis of biliary sludge and lithiasis in SCI patients.<sup>(6,10,16,21,22)</sup> The method is rapid and inexpensive; however, the main disadvantage is that it depends on the skills and experience of the operator. In this study, we used ultrasonography to evaluate patients with complete SCI (ASIA A) above the T7 segment within the first six months of the injury, in order to investigate the effects of neurological instability and SNS dysfunction in the gallbladder and common bile duct within the early post-SCI phase. The T7 segment was chosen as SCI patients injured above this level have a complete

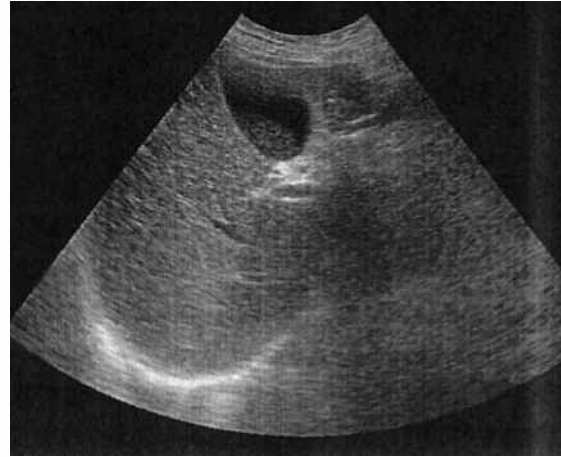
disruption of the SNS. The disruption of the sympathetic innervations reduces normal gallbladder motility after an injury,<sup>(23,24)</sup> which leads to gallbladder stasis<sup>(16)</sup> and probably predisposes to an increased incidence of biliary sludge and gallstones development in the above patients.<sup>(25-27)</sup> According to previous investigations, disturbances of intestinal motility following SCI could also promote bile stasis and lithogenic bile development,<sup>(15,28)</sup> although this hypothesis has not been widely accepted.<sup>(29)</sup>

Our results showed that the incidence of biliary sludge was significantly higher in patients with complete high SCI compared with controls ( $p < 0.001$ ). This is in accordance with previous studies which exhibited a high frequency of sludge bile formation particularly in high SCI patients during the early phase after an injury.<sup>(6)</sup> On the other hand, our data demonstrated the development of gallstones in six out of the 78 complete SCI patients during the early post-injury period; however, the above finding was not significantly different compared with the control subjects. Development of cholelithiasis was not reported in the study of Tandon et al,<sup>(6)</sup> a finding which was probably due to the limited number of study subjects ( $n = 18$ ) with SCI above the T10 segment. Additionally, gallstone formation in our population could be attributed to factors such as different diet and ethnic characteristics.

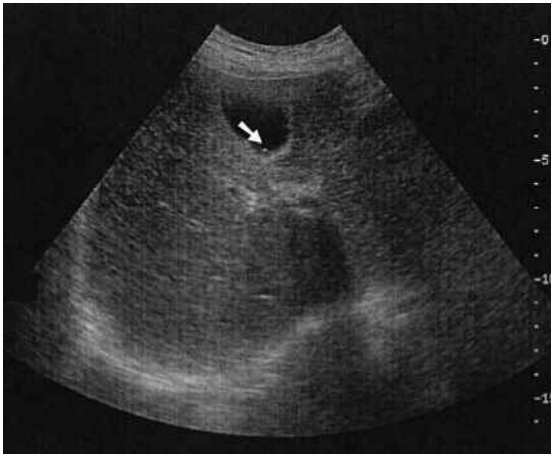
In previous studies, the incidence of cholelithiasis in SCI patients ranged from 29% to 49%;<sup>(2,9)</sup> however, our data showed a lower incidence of gallstones (7.69%), possibly due to differences of level, duration and completeness of the SCI. The above investigations were performed in patients with long-standing SCI. Moonka et al demonstrated an increased prevalence of cholelithiasis in patients with complete SCIs.<sup>(9)</sup> In contrast, we prospectively studied patients within six months post-injury in order to evaluate the effect of complete SNS damage to the gallbladder in the early post-SCI phase. The reported incidence of gallstones in Greek cadaveric males and females is 4.52% and 8.86%, respectively.<sup>(30)</sup> However, in our study, the incidence was 8.77% in male patients, a finding that surpasses the normal



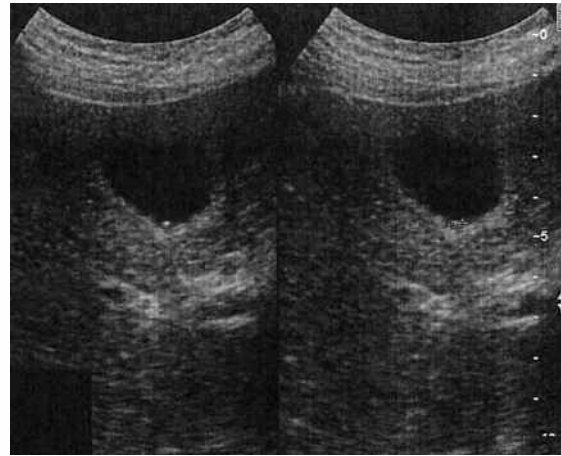
**Fig. 1** Transverse US image of the gallbladder in a male high-SCI patient shows a smooth ovoid relatively-high hyperechoic mass within the gallbladder lumen representing a tumefactive biliary sludge.



**Fig. 2** Longitudinal real-time US image of the gallbladder in a female high-SCI patient shows a fluid-fluid level with the denser component (biliary sludge) posteriorly.



**Fig. 3** Sagittal US image of the gallbladder in a male high-SCI patient shows a slightly echodense gallstone (arrow) in the dependent portion of the gallbladder.



**Fig. 4** Left lateral decubitus axial US image in a male high-SCI patient shows a small gallstone with a diameter of 0.27 cm, moving to the dependent portion of the gallbladder. An acoustic shadowing is seen deep in the gallstone.

Greek male cadaveric population. In contrast, the incidence of gallstones in SCI females was lower than the normal Greek cadaveric female population, possibly due to the small number of female participants included in the study. In our study, the total number of patients with gallstones and biliary sludge was significantly higher compared with the control group (Table II). The above finding is in accordance with the results of Shin et al,<sup>(21)</sup> although their number of SCI patients with gallstones was higher than those with biliary sludge, probably due to the longer post-injury duration of the study (11.1 months) and different levels of injury.

Two interesting observations were derived from our study. First, in all cases of cholelithiasis, the development of gallstones was observed after four months of injury. Second, all gallstones were small in diameter (<5.0 mm) and not strongly echogenic, a finding which has not been previously reported (Figs. 3 & 4). The above observations

imply that interference with the neurological instability to the gallbladder in the early post-SCI phase may play an important role in the development of lithogenic bile. It is speculated that in patients with complete damage of the SNS, such as above the T7 segment, biliary sludge formation might be a prefatory stage for the development of gallstones during the first six months from the injury onset (tumefactive biliary sludge, Fig 1). In addition, our results showed a significantly higher number of male patients with biliary sludge compared to the healthy male controls within the first six months of the injury onset. No significant difference in the incidence of gallstone formation was observed between males and females, both in patients and controls. A recent study revealed a higher prevalence of biliary sludge and lithiasis, as a late SCI phase complication in male SCI patients.<sup>(22)</sup> It is hypothesised that there is probably a gender predilection of biliary sludge formation in SCI patients, which is

independent to the post-injury duration.

Our study has certain limitations. Firstly, we were unable to follow up our SCI patients on a tactical basis during the first six months of the injury onset, because of the limitations of the National Health System and the distance of the patients' residence from the hospital. If they were followed up, biliary sludge and gallstones might have been detected simultaneously in some cases. Secondly, the number of male SCI patients was significantly higher than female SCI patients, possibly due to the elevated number of males involved in automobile accidents.

In conclusion, diseases associated with SCI require an early diagnosis, as the clinical signs are attenuated by motion and sensory disruption. Our study indicates that gallbladder sludge and lithiasis are significantly more common in Greek patients with a complete high SCI above T7, compared with healthy controls, within the first six months from the injury onset. This is probably due to the complete disruption of the gallbladder sympathetic innervation and neurological instability in the early post-SCI phase. According to our results, ultrasonography should be performed in these patients and particularly in males, within the first 3–6 months from time of injury, for the early diagnosis of lithogenic bile and for the selection of the appropriate therapeutic option.

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