HIGH SERUM CALCIUM IN HUMAN BRUCELLOSIS: A CASE-CONTROL STUDY

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Abstract. In a retrospective case-control study of 58 cases of human brucellosis, adjusted mean serum calcium levels were found to be significantly higher in patients with brucellosis compared with controls: mean (95% confidence interval) = 2.39 (2.35–2.42) mmol/L versus 2.30 (2.26–2.34) mmol/L (P = 0.0012). The possible mechanisms underlying the cause of hypercalcemia in human brucellosis are discussed.

Demographic data, protein, albumin, phosphate, and adjusted calcium levels of brucellosis patients and control subjects were compared. In patients with brucellosis, the mean adjusted serum calcium level was significantly higher than in the control group. There was no significant difference in total serum calcium levels between the groups although the total calcium × phosphate product levels were higher in the patients with brucellosis.

DISCUSSION

This case-control study has shown that adjusted serum calcium levels are higher in patients with brucellosis compared with the controls.

Table 1 shows the demographic data and laboratory test results of both patients with brucellosis and the control group. There was no significant difference in total serum protein or phosphate levels between the groups although the total calcium × phosphate product levels were higher in the patients with brucellosis.

**RESULTS**

Table 1 shows the demographic data and laboratory test results of both patients with brucellosis and the control group. There was no significant difference in total serum protein or phosphate levels between the groups although the total calcium × phosphate product levels were higher in the patients with brucellosis. The adjusted mean (95% confidence interval [CI]) serum calcium level was significantly higher in the patients with brucellosis compared with the controls: 2.39 (2.35–2.42) mmol/L versus 2.30 (2.26–2.34) mmol/L (P = 0.0012). The mean (95% CI) albumin level was significantly lower in patients with brucellosis compared with the controls: 35.26 (26.34–44.47) g/L versus 38.97 (33.02–40.18) g/L (P = 0.0008). Figure 1 shows the adjusted mean (95% CI) serum calcium levels in patients with brucellosis and the controls.

**DISCUSSION**

This case-control study has shown that adjusted serum calcium levels are higher in patients with brucellosis compared with the controls. To minimize bias, the patients and controls

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>Brucellosis group [N]</th>
<th>Control group [N]</th>
<th>P (by unpaired t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of subjects</td>
<td>58</td>
<td>58</td>
<td>0.2956</td>
</tr>
<tr>
<td>Mean age in years (95% CI)</td>
<td>26.48 (20.98–31.99) [58]</td>
<td>27.85 (21.99–33.69) [58]</td>
<td>0.3052</td>
</tr>
<tr>
<td>Males</td>
<td>32 [58]</td>
<td>32 [58]</td>
<td>0.0008†</td>
</tr>
<tr>
<td>Females</td>
<td>26 [58]</td>
<td>26 [58]</td>
<td>0.0008†</td>
</tr>
<tr>
<td>Mean total protein in g/L (95% CI)</td>
<td>73.50 (66.98–79.02) [52]</td>
<td>70.00 (64.50–75.10) [38]</td>
<td>0.1349</td>
</tr>
<tr>
<td>Mean albumin in g/L (95% CI)</td>
<td>35.26 (26.34–44.47) [58]</td>
<td>38.97 (33.02–40.18) [58]</td>
<td>0.1349</td>
</tr>
<tr>
<td>Mean phosphate in mmol/L (95% CI)</td>
<td>1.22 (1.01–1.86) [20]</td>
<td>1.07 (0.58–1.69) [27]</td>
<td>0.1277</td>
</tr>
<tr>
<td>Mean adjusted calcium in mmol/L (95% CI)</td>
<td>2.39 (2.35–2.42) [58]</td>
<td>2.30 (2.26–2.34) [58]</td>
<td>0.0012†</td>
</tr>
<tr>
<td>Mean calcium × phosphate product level (total) in mmol/L (95% CI)</td>
<td>3.07 (2.43–3.70) [8.0]</td>
<td>2.54 (1.56–3.51) [8.0]</td>
<td>0.3004</td>
</tr>
</tbody>
</table>

* CI = confidence interval.
† Significant P value.
controls were matched for age and sex. Cases with known abnormal calcium metabolism were not included in both groups. The patients and controls were admitted to the hospital during the same period; therefore, the laboratory techniques used in the assessment were applicable to both. The mechanisms causing higher serum calcium levels in patients with brucellosis are likely to be similar to those seen in other granulomatous diseases, including tuberculosis and sarcoidosis, mainly through vitamin D hypersensitivity. Activated macrophages in the granulomas of patients with these diseases have been shown to have 1-alpha-hydroxylase activity, which converts 25-hydroxy-vitamin D3 to 1,25-dihydroxy-vitamin D3. Bone involvement in tuberculosis has been described as a possible cause contributing to hypercalcemia. Brucellosis is known to involve the bones and joints. However, it is difficult in this retrospective study to assess the possible role of bone involvement in brucellosis in causing higher serum calcium levels. The hypoalbuminemia observed in patients with brucellosis is consistent with results from previous studies, which have shown involvement of the liver in brucellosis, leading to abnormal liver function test results. It is worth noting the higher phosphate levels and the higher total calcium x phosphate product levels in patients with brucellosis compared with controls, although these differences are not statistically significant. The higher calcium x phosphate product levels could explain tissue calcification, which is known to complicate brucellosis granulomas.

In conclusion, this case-control study has provided evidence of higher serum calcium levels in patients with brucellosis. However, prospective studies are needed to investigate the possible role of macrophages and vitamin D metabolites or bone involvement in this hypercalcemia and to ascertain the clinical significance of these higher serum calcium levels.

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REFERENCES