Urinary chromium excretion during pregnancy and its relationship with intravenous glucose loading\textsuperscript{1,2}

\textit{Güny Saner\textsuperscript{3}}

\textbf{ABSTRACT} This study was conducted to investigate the changes in urinary chromium excretion in the different stages of pregnancy and the effect of intravenous glucose tolerance test on urinary excretion of chromium in late pregnancy. Urine samples were collected from pregnant women cross-sectionally and longitudinally in different stages of pregnancy. Urinary chromium excretion before and after intravenous glucose tolerance test was also determined in nine women in their 3rd trimester of pregnancy. The results can be summarized as: 1) mean chromium/creatinine ratio in urine increased significantly with advancing pregnancy, 2) in late pregnancy, with the exception of one subject, urinary chromium/creatinine ratio showed a decrease after intravenous glucose tolerance test. The results obtained in this study have led us to conclude that the habitual dietary intake does not meet the increased chromium requirement and that prophylaxis may be of benefit and appears to be advisable in pregnancy. \textit{Am. J. Clin. Nutr.} 34: 1676-1679, 1981.

\textbf{KEY WORDS} Pregnancy, urine, chromium, effect of intravenous glucose tolerance test on urinary chromium

\textbf{Introduction}

The impairment of glucose tolerance during pregnancy and the decrease in hair chromium content reported in multiparous women and in the last stage of pregnancy indicate that pregnancy may lead to chromium deficiency (1-5; G. Saner, unpublished observations). The diagnosis of chromium deficiency is rather difficult and there is no general agreement as to the method of choice. Available data indicate that correction of impaired glucose tolerance in response to chromium is the most dependable criterion in the determination of the deficiency state. Urinary chromium/creatinine (Cr/Cre) ratio in single samples and the changes in this ratio after glucose tolerance tests (GTT) are also reported as reliable criteria in the evaluation of chromium nutrition (6, 7).

This present study was designed to investigate the changes in urinary chromium excretion in the different stages of pregnancy and the effect of IV GTT on urinary excretion of chromium in late pregnancy.

\textbf{Materials and methods}

The study was carried out on 145 Turkish pregnant women. Their ages varied from 16 to 40 yr and parity of the group ranged from 1 to 6. None of the subjects showed clinical evidence of nutritional deficiency. No subject had received iron or vitamin supplements during pregnancy. Morning single urine samples were collected from the subjects cross-sectionally in the different stages of pregnancy. In 19 women, urine samples were also collected longitudinally for every consecutive trimester. Collected urine samples in polyethylene bottles were kept at $-20^\circ$C until analysis. All equipment used in the collection procedure was checked for chromium contamination before use.

Nine subjects in their 3rd trimester of pregnancy were subjected to an IV GTT after a 10 to 12 hr fasting period. The glucose (25 g) was given as a 30\% solution by a peripheral vein over a period of 2 to 4 min (4). Venous blood samples were taken initially and at 15, 30, 45, and 60 min after the administration of glucose. Four-hour urine samples were collected from these women before and after IV GTT.

Plasma glucose was measured in duplicate by the glucose oxidase method (8). Glucose removal rate (K)

\textsuperscript{1} From the Department of Pediatrics, University of Istanbul, Capa, Istanbul, Turkey.

\textsuperscript{2} Supported in part by funds provided by Turkish Scientific and Technical Research Council.

\textsuperscript{3} Professor of Pediatrics.
was calculated on the increments observed in the blood glucose level (9).

Chromium concentration of urine was determined by flameless atomic absorption technique using a Perkin-Elmer 503 double-beam atomic absorption spectrometer equipped with both a HGA-2100 graphite furnace and a model 56 recorder (10).

Triplicate urine samples of 500 μl were placed in a vacuum oven and kept at 60°C for 4 to 6 h until all samples were dried. All samples were ashed for 2 h (1 mm O2 pressure, RF power 400 watts forward, 3 to 5 watts reflected) in a Low Temperature Asher (Trapel LTA 505, LFE Corp. Waltham, MA). The ashed samples were treated with 500 μl of 0.25 N HCl, redried and reashed for 1 additional h. Samples were then dissolved in 500 μl of 0.5 N HCl and 50-μl aliquots injected into graphite furnace for analysis (drying for 30 sec at 100°C, charring for 60 sec at 1150°C, and atomization for 12 s at 2600°C). The sample response was compared to that of inorganic chromium as potassium chromate (Fisher Scientific Co.). The analytical procedure was verified by the use of the NBS Brewer’s yeast, certified for chromium.

Urinary creatinine levels were measured by the Jaffé reaction (11). Urinary chromium excretion was expressed as Cr (ng)/Cre (mg) ratio.

**Results**

The mean Cr/Cre ratio was found to be 7.75 ± 0.55 (mean ± SEM) in 32 women in the 1st trimester, 10.81 ± 0.51 in 51 women in the 2nd trimester, and 13.94 ± 0.62 in 62 women in the 3rd trimester of pregnancy. A significant increase was noted in Cr/Cre ratio between the 1st and 2nd, as well as between the 2nd and 3rd trimesters (t = 3.9646, p < 0.001; t = 3.7713, p < 0.001). The longitudinal data also support the results of the cross-sectional study (Fig. 1). The mean creatinine value in urine was found to be 88 ± 30 mg/dl in the 1st trimester, 89 ± 38 mg/dl in the 2nd trimester, and 85 ± 41 mg/dl in the 3rd trimester of pregnancy.

The urinary Cr/Cre ratio of nine pregnant women in late pregnancy before and after IV GTT are listed in Table 1. As indicated in Table 1, the mean Cr/Cre ratio in urine was found to be 11.75 ± 1.75 and 8.73 ± 1.23 before and after IV GTT, respectively. The difference between the mean values for the whole group before and after IV GTT was not statistically significant (t = 2.1305, 0.05 < p < 0.10). When the results for each case were analyzed individually, with the exception of one subject (subject 2), Cr/Cre ratios decreased after IV GTT. The mean glucose removal rate in these women was found to be 3.85 ± 0.46% min.

**Discussion**

Alterations in carbohydrate and chromium metabolism in normal human pregnancy have been demonstrated by several investigators (1–5, 12). However, these observations have not been validated by adequate, longitudinal data on urinary chromium excretion during pregnancy.

To eliminate errors due to fluctuations in urine volume and the diurnal fluctuations which are known to occur in the excretion of chromium in random urine samples (6), in this study, urinary Cr/Cre ratio was taken as the index in the expression of the chromium nutritional state.

The mean Cr/Cre ratio in urine for the 1st trimester of pregnancy did entirely agree with the values obtained in normal Turkish adults of comparable ages (6). Thereafter, this ratio showed a significant increase with advancing pregnancy. Since the creatinine values in urine remained constant in all groups, the differences observed in Cr/Cre ratio were not related to urinary creatinine excretion. These results indicate that a state of relative deficiency of chromium or one of increased chromium requirement develops during pregnancy.

Davidson and Burt (13) investigated the effect of GTT on plasma chromium levels in nonpregnant women and also in pregnant women of similar ages. In this study, fasting plasma chromium levels for pregnant women were found to be significantly lower than those of nonpregnant subjects. A prompt and persisting decrease was noted in plasma chromium levels in nonpregnant women with either intravenous or oral glucose loading, whereas this decrease did not occur in women in late pregnancy. Immunoreactive insulin response to GTT was also found to be more exaggerated in the pregnant group (13). Hammond (12) also demonstrated that the serum chromium response to glucose loading in women during the last month of gestation was impaired in 71% of the group, whereas in normal nonpregnant women and in pregnant women of less than 36 wk gestation the
Urine collected cross-sectionally

Urine collected longitudinally

FIG. 1. Urinary chromium excretion (Cr/Cr ratio) in different stages of pregnancy. Cr/Cr ratio: 1st versus 2nd trimester, \( t_{\text{exp}} = 3.9646, p < 0.001 \) (cross-sectional), \( t_{\text{exp}} = 8.1858, p < 0.001 \) (longitudinal); 2nd versus 3rd trimester, \( t_{\text{exp}} = 3.7713, p < 0.001 \) (cross-sectional), \( t_{\text{exp}} = 4.3315, p < 0.001 \) (longitudinal).

TABLE 1
Urinary chromium excretion (Cr/Cr ratio) of pregnant women in late pregnancy before and after IV GTT*

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Age</th>
<th>Before IV GTT</th>
<th>After IV GTT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>yr</td>
<td>ng/mg</td>
<td>ng/mg</td>
</tr>
<tr>
<td>1</td>
<td>30</td>
<td>15.90</td>
<td>6.96</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>8.69</td>
<td>12.07</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>7.35</td>
<td>6.87</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>16.79</td>
<td>8.04</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>6.28</td>
<td>5.23</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>9.77</td>
<td>4.53</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
<td>10.93</td>
<td>10.46</td>
</tr>
<tr>
<td>8</td>
<td>27</td>
<td>21.81</td>
<td>16.29</td>
</tr>
<tr>
<td>9</td>
<td>33</td>
<td>8.23</td>
<td>8.08</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td></td>
<td>11.75 ± 1.75</td>
<td>8.73 ± 1.23</td>
</tr>
</tbody>
</table>

* Urinary chromium excretion (Cr/Cr ratio): before IV GTT versus after IV GTT, \( t_{\text{exp}} = 2.1305, 0.05 < p < 0.10 \).
healthy Turkish men and women has shown that these subjects do respond to a standard oral GTT with increased chromium excretion (7).

In our group of pregnant women in late pregnancy, IV GTT did not result in the expected increase in urinary chromium excretion, and further, with the exception of one subject, Cr/Cr ratios showed a decrease after IV glucose loading.

The absence of a urinary chromium response to IV GTT, increased chromium excretion with advancing pregnancy, and the reduction of chromium in hair can be considered as indicators that the habitual dietary intake does not meet the increased chromium requirement in pregnancy. Therefore, the prophylactic administration of organic chromium compound, so-called glucose tolerance factor prophylaxis, may be of benefit and appears to be advisable during pregnancy. 

The technical assistance of Mr. Sirri Çağdem is deeply appreciated.

References