Evaluation of sister chromatid exchange in patients with breast cancer in relation to clinical stage

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Abstract
High levels of sister chromatid exchanges (SCE) in patients with breast cancer reflects a genomic instability that may be operative in carcinogenesis. The frequency of sister chromatid exchanges in peripheral blood lymphocytes was analyzed in patients with breast cancer in relation to clinical stage in 12 stage II and 5 Stage IV untreated breast cancer patients. Moreover, SCE baseline values in patients were compared with a control group of 12 healthy women. A significant difference emerged between patients and control (P<0.01). SCE increased significantly in stage IV breast cancer patients compared with those patients of stage II (P<0.05). The results reveal that SCE frequency increases with the progression of clinical stage of breast cancer.
Introduction
Breast cancer dramatically impact the lives of affected women and further place a significant economic burden on both their families and the health care system (1). Sister chromatid exchange (SCE) can be used as a preclinical marker for early detection of cancer (2,3). High levels of SCE in breast cancer patients reflect a genomic instability that may be operative in carcinogenesis (4). In this study, the frequency of SCE was analyzed in patients with breast cancer in relation to disease stage.

Materials and Methods
Twelve untreated breast cancer patients in stage II (age: 30-65 years) and five untreated breast cancer patients stage IV (age: 32-60 years), in addition to twelve healthy women (age: 26-82) as a control were the subjects of this study. Patients were admitted to Baghdad teaching hospital and their clinical stages were determined according to TMN system. The samples collected during summer 2008. Whole blood was cultured in RPMI-1640 medium for SCE analysis. 0.25 ml of heparinized blood was inoculated in 2 ml of RPMI-1640 medium (Serva) containing phytohemagglutinin (PHA) and 10% fetal calf serum (Sigma). Cultures were incubated at 37 for 72 hours. Colchicine 0.1 ml (Serva) was added to each culture tube for the final two hours of incubation to harvest the cells. Cells then treated with hypotonic solution (0.075 KCl) for 20 minutes and fixed with methanol-acetic acid (3:1 vol/vol). Cells were dropped onto clean slides (5). SCE were scored using fluorescence plus Giemsa modified staining technique (6). SCE were scored in 25 well-spread second metaphase. Results were analyzed statistically using t-test.

Results and Discussion
Table 1 shows SCE (mean ±SE) of this study. The frequency of SCE in stage II and stage IV breast cancer patients revealed marked increase in their cells. The mean of SCE was higher in lymphocytes of stage II patients (5.62 ±0.89 SCE/cell versus 3.12 ±0.15 in control P<0.01). The mean of SEC of stage IV patients showed high significant value compared with control (6.89 ±87 SCE/cell versus 3.12 ±0.15 P<0.01).
Table 1: SCE (mean ±SE) in stage II, Stage IV and control groups.

<table>
<thead>
<tr>
<th>Study groups</th>
<th>SCE (Mean±SE)</th>
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<tbody>
<tr>
<td>Control</td>
<td>3.12±0.15</td>
</tr>
<tr>
<td>Stage II</td>
<td>5.62±0.89$^a$</td>
</tr>
<tr>
<td>Stage IV</td>
<td>6.89±87$^{a,b}$</td>
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</tbody>
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$^a$ P$<0.01$ vs. control group  
$^b$ P$<0.05$ vs. stage II group

High levels of SEC in those patients reflects impairment of DNA systems and repair (7). Furthermore, BRCA1 and BRCA2 play important roles in the mechanisms that lead to the repair of DNA - double strand breaks (8). Thus, those patients may have mutated BRCA genes.

The results of this study reveal an increase in SEC/cell in patients with breast cancer with progression of disease. The SEC in stage IV patients was higher than SCE in patients with stage II disease. The significance difference was not highly (P$<0.05$), this may be due to the sample size. Our results were in agreement with Aristei et al., 2009 that their results showed increase in SEC frequency in 20 stage II breast cancer patients.

According to the results of this study, we conclude that SCE levels increase with progression of clinical stage of breast cancer.

References


8. Aristei Cynthia; Stracci Fabrizio; Guerrieri Paola; Anselmo Paola; Arnellini Rossana; Rulli Antonio; Barberini Francesco; Latini Paolo; Menghini Anna Rita (2009): Frequency of sister chromatid exchanges and micronuclei monitored over time in patients with early-stage breast cancer: results of an observational study. Cancer genetics and cytogenetics; 192:24-9.

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