

## Chemotherapy-induced amenorrhea in patients suffering from breast cancer in the Northwest of Iran

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Dear Editor,

Breast cancer (BC) was ranked number one among malignancies of Iranian women, comprising 24.4% of all neoplasms with a crude incidence rate of 17.81 and an age-standardized rate of 23.65 in 2006.<sup>[1]</sup>

The peak incidence of age for BC is 10 years earlier in Iran compared with Western countries,<sup>[1,2]</sup> and hence we have many premenopausal patients who have an indication for receiving adjuvant chemotherapy for BC.

Therefore, recognizing menopause in women with chemotherapy-induced amenorrhea (CIA) is critical.<sup>[3]</sup>

This retrospective study was conducted to assess the onset and duration of CIA in relation to age and chemotherapy protocols by employing statistical analysis.

The study included newly diagnosed stages I to III premenopausal (menstrual periods in the preceding 6 months) BC patients who had an indication for adjuvant chemotherapy at the Hematology Oncology Research Center in Iran, Tabriz University of Medical Sciences between January 1, 2007 and June 11, 2013.

Postmenopausal patients, patients with the history of tamoxifen taking, chemotherapy or gonadotropin-releasing hormone agonist administration or hysterectomy/bilateral oophorectomy or ovarian radiation histories, patients with metastasis or those who had comorbid diseases not indicated for chemotherapy were excluded.

We defined CIA as the cessation of menses for at least 3 months during the chemotherapy.

All patients received four to eight cycles of systemic chemotherapy (including anthracycline-based or taxane-based regimens or cyclophosphamide, methotrexate and fluorouracil protocol) and/or radiotherapy according to NCCN guideline.

Because doxorubicin + cyclophosphamide (CTX) were used in the first four cycles in AC, AC-Taxol, AC-Docetaxel, CAF, TAC, ACx6 and ACx4 protocols, we divided the protocols to two groups: which had AC in the first 4 cycle or AC(S)x4, and the others such as ECF or EC-Taxol, with other drugs in the first four cycles. Data were analyzed using descriptive studies, *t*-test, ANOVA, univariate and Mann–Whitney U-test using SPSS 16 software package (IBM Company) comparing patients below and over 40 years and different protocols including AC(S)x4.

Table 1 surveys the ages and durations of CIA. Two hundred and thirty-seven patients had study criteria, the mean, median and mode of our patient's ages were 42.38 (27–54), 43, and 46 years, respectively. About 34.7% of patients were ≤40 years old. The majority of patients (99.6%) had ≤52 years, only one patient (0.4%) had 54 years.

Mann–Whitney U-test revealed that duration of amenorrhea is longer in patients over 40 years ( $P < 0.001$ ). Furthermore, it was statistically significant in “continuous” group ( $P < 0.001$ ), but not in <3 months or >3 months ( $P > 0.05$ ).

**Table 1: Patients ages and relation to duration of amenorrhea**

Age	Frequency (%)	Amenorrhea		
		<3 months (%)	>3 months (%)	Continuous (%)
<40	82 (34.7)	21 (26.6)	61 (73.4)	32 (40.5)
>40	154 (65.3)	10 (6.6)	144 (93.6)	122 (80)
<i>P</i>	<0.001	0.132	0.376	<0.001

AC(S)x4 had a significant relation with beginning of CIA in patients >40 ( $P = 0.033$ ) but there was no relation between various protocols, including AC(S)x4 and duration of amenorrhea in treated patients (including <40 and/or >40 years) by Kruskal–Wallis test.

Twenty-three out of 237 patients (9.7%) did not have amenorrhea while 90.3% had (60.6% after three cycles and 77.9% after four cycles).

Of these patients CIA (duration of amenorrhea more than 3 months), was detected in 86.8% of patients.

Adriamucin + CTX are the drugs used in the first four cycles of AC, AC-Taxotere and AC-Taxol protocols including 66.6% of patients. This means that Adria + CTX could be responsible for at least 66.6% of CIA of our patients.

Like other studies, duration of CIA was longer in patients over 40 in Iranian patients. AC protocol caused about 66.6% of CIA in this study. Further studies are needed to determine the

recovery period of menses after BC therapy.

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