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INTRODCUTION

Diabetes mellitus (DM) and cancer associated with lower health outcomes. Free radicals are reactive oxygen species (ROS) and have a tendency to donate oxygen to other substances. Therefore, they are unstable, highly reactive and can generate a second free radical, which then go on to react with a new target. One of the main difficulties is a direct measurement of ROS because of their short lifetime. ROS-induced modification of a purine residue in DNA leads to formation of water- soluble and renally excreted derivative called 8-hydroxydeoxyguanosine (8-OHdG) which is prevalent in cancer cells. Urinary 8-OHdG is now considered to be an important biomarker of cellular oxidative stress in patients with DM and its level increases accordance with severity of diabetic complications . The objective of this study was to evaluate the urinary 8-Hydroxydeoxyguanosine level as a biomarker of disease progression (DM and cancer) before and after chemotherapy administration in diabetic cancer patients.

METHODS

This was a controlled prospective observational study carried out on 100 diabetic patients newly diagnosed with diverse types of cancers eligible for different chemotherapeutic protocols at the oncology unit of Dr. Lütfi Kırdar Kartal Teaching and Research Hospital (Istanbul-Turkey). Patients who candidate to receive a weekly dose of the chemotherapeutic regimen were followed by six cycles (a total duration of 42 days); patients who candidate to receive the chemotherapeutic regimen every 14 days were followed by three cycles (a total duration of 42 days); patients who eligible to receive the chemotherapeutic regimen every 21 days were followed by three cycles (a total duration of 63 days). Urine samples for assessment of the urinary 8- OHdG level were collected from the participants at the baseline (before starting the chemotherapeutic protocol schedule), and the 2nd reading (at the end of the required chemotherapy protocol schedule). Urine samples were stored and frozen at -70°C until analysed. They were centrifuged at 2000 rpm for 10 min to remove the particulate matter and after proper dilution the supernatant was used for the determination of 8-OHdG by a competitive ELISA assay performed according to the manufacturer's instructions. The SPSS 16.0 Package was used for statistical analysis. The results were assumed significant when the $p < 0.05$ threshold reached by all statistical analysis.

RESULTS AND DISCUSSION

The mean age of patients was 61.82 ± 8.62 years. Majority of the patients were females (64%). Breast carcinoma was the most common type of cancer (25%). Most of the participants received chemotherapy regimens every 21 days (67%). The urinary 8-OHdG level is presented in Table (1) and showed that there was a significant increase ($p < 0.05$) between the baseline and 2nd readings at the end of the required chemotherapeutic schedule (27.04 ± 4.33 ng/dl) vs (30.77 ± 4.63 ng/dl). The urinary 8-OHdG level based on chemotherapy protocol schedule is presented in Table (2). There was a significant increase between the baseline and 2nd readings at 7-day course (25.96 ± 4.21 ng/dl) vs (28.16 ± 5.27 ng/dl), at 14-day course (27.76 ± 5.33 ng/dl) vs (31.56 ± 4.47 ng/dl), and at 21-day course (27.22 ± 4.16 ng/dl) vs (31.40 ± 4.24 ng/dl). There was also a significant increase between the 2nd readings of the 7-day and 14-day course (28.16 ± 5.27 ng/dl) vs (31.56 ± 4.47 ng/dl), and of the 7-day and the 21-day course (28.16 ± 5.27 ng/dl) vs (31.40 ± 4.24 ng/dl).

Parameter	Patients n=100 (\pm SD)	p-value
Baseline 8-OHdG Reading (ng/dl)	27.04 ± 4.33	0.0001
2 nd 8-OHdG Reading (ng/dl)	30.77 ± 4.63 *	

Chemotherapy Course	Patients No. (n=)	Baseline 8-OHdG Reading (\pm SD) (ng/dl)	2 nd 8-OHdG Reading (\pm SD) (ng/dl)	p-value
7-day (6 cycles)	n=20	25.96 ± 4.21	28.16 ± 5.27 *	0.029
14-day (3 cycles)	n=13	27.76 ± 5.33	31.56 ± 4.47 * a	0.016
21-day (3 cycles)	n=67	27.22 ± 4.16	31.40 ± 4.24 * a	0.0001

Some of the commonly used anticancer agents such as doxorubicin, cyclophosphamide, can cause production of ROS. Higher levels of 8-OHdG were also detected in blood levels of breast cancer patients majorly those who also suffering from DM. Elevated levels of urinary 8-OHdG as a biomarker of oxidative stress (ROS) are observed in patients with type 1 and 2 DM as well as in cancer. These data were supported by a study of Takeshi Nishikawa et al. who found that hyperglycemia increase urinary 8-OHdG level in patients with DM.

CONCLUSION

The results of this study found that many medical conditions including, DM and cancer were associated with increased oxidative stress based on elevation of the urinary 8-OHdG level and their progression further augmented during chemotherapy administration.

