

Effect of GSTM1 and GSTT1 Polymorphisms on Genetic Damage in Humans Populations Exposed to Radiation From Mobile Towers

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Abstract All over the world, people have been debating about associated health risks due to radiation from mobile phones and mobile towers. The carcinogenicity of this nonionizing radiation has been the greatest health concern associated with mobile towers exposure until recently. The objective of our study was to evaluate the genetic damage caused by radiation from mobile towers and to find an association between genetic polymorphism of *GSTM1* and *GSTT1* genes and DNA damage. In our study, 116 persons exposed to radiation from mobile towers and 106 control subjects were genotyped for polymorphisms in the *GSTM1* and *GSTT1* genes by multiplex polymerase chain reaction method. DNA damage in peripheral blood lymphocytes was determined using alkaline comet assay in terms of tail moment (TM) value and micronucleus assay in buccal cells (BMN). There was a significant increase in BMN frequency and TM value in exposed subjects (3.65 ± 2.44 and 6.63 ± 2.32) compared with control subjects (1.23 ± 0.97 and 0.26 ± 0.27). However, there was no association of *GSTM1* and *GSTT1* polymorphisms with the level of DNA damage in both exposed and control groups.

The effect of radiofrequency electromagnetic radiation (RF-EMR) from mobile phone base stations on human health is subject of recent interest due to the enormous increase in mobile phone use throughout the world (as of May 2014 there was more than 938 million wireless users in India). Our study focuses on the effect of electromagnetic radiation from mobile phone base stations or towers that provides links to and from mobile phones. Compared with mobile phone handsets, these links are emitted continuously and are more powerful in close quarters.

A concern associated with cellular phone use is the sitting of cellular phone–transmitting antenna and their base stations. These are appearing at an alarming rate across the country, some even installed on the rooftops of building, with numerous base stations installed on towers. Cell towers and antennas are popping up everywhere including residential areas, near schools and hospitals, etc. In the West, as a precautionary measure, towers are built at a height of 30 m above the building whereas in India the height is just 2–3 ms.

There are many studies in the literature about the biological interactions with electromagnetic fields (EMFs) and the direct biological effects that such exposure could cause (Mild et al. 2003; Lönn et al. 2004). Biomarkers can be employed as end points for the assessment of human–genotoxic interactions from exposure to effects as well as individual host susceptibility (Albertini et al. 2000).

During the last few decades, single-cell gel electrophoresis, or the comet assay, has been introduced as a sensitive and useful biomarker in human biomonitoring studies (Singh et al. 1988; Valverde and Rojas 2009; Collins et al. 2014). It is a straightforward visual method for the detection of DNA damage in interphase cells. This technique is especially sensitive in detecting DNA single-

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strand breaks, alkali-labile damage, and excision repair sites in individual cells (Speit and Hartmann 2005).

The micronucleus test (MNT) has been used in cytogenetic studies to detect chromosomal changes such as acentric chromosome/chromatid fragments induced by clastogen or chromosome lagging at anaphase produced by aneugens. The noninvasive nature of the MNT in exfoliated cells makes it an attractive candidate for the biomonitoring of human populations (Stich et al. 1982; Fenech and Morley 1985; Blaszczyk and Mielzynska-Svach 2014; Natalí Bernardi et al. 2015).

It is increasingly clear that genetic differences among individuals in the ability to modulate the metabolism of the carcinogens may play a primary role in their susceptibility to environmentally induced diseases (Hirvonen 1995, 1997; Sun et al. 2001; Zhang 2010). Because not all exposed individuals develop cancer, genetically determined host factors may contribute predisposition to DNA damage (Pastorelli et al. 1998) and therefore modulate the risk of cancer. The large interindividual variability in the capacity to activate and inactivate potential genotoxic and carcinogenic agent is probably influenced by polymorphism of the genes encoding the metabolism enzymes. Among the most studied genotypes is the human glutathione S-transferase (GST) phase II detoxifying enzyme. It is not surprising that biomarkers of oxidative and antioxidative processes are influenced by GST genotypes. Intracellular glutathione (GSH) bioavailability levels do not only affect genetic damage by competition between oxygen and thiol, they may also have an effect on enzymatic repair, which would account for radiosensitivities (Vos et al. 1986). In conjunction with GST enzymes, GSH can conjugate with numerous harmful electrophilic endogenous compounds and foreign chemicals, thus resulting in their detoxification and cellular elimination (Rinaldi et al. 2002). Genetic polymorphisms in *GSTM1* and *GSTT1* genes have been examined extensively to evaluate the possible role they play in DNA damage and cancer promotion (Agundez 2004; Salinas-Sanchez et al. 2012).

The potential genotoxicity of RF-EMR has been assessed in human epidemiological studies that have shown both positive (Gadhia et al. 2003; Markova et al. 2005; Gandhi and Anita 2005b) and negative reports (Garson et al. 1991; Maes et al. 2006). Therefore, there is a need to evaluate different exposed populations with a variety of genotoxic parameters. Only a few studies have reported the genetic effects of exposure from mobile-tower radiation (Simko et al. 1998; Khalil and Qassem 1991).

In the current investigation, the genotoxic effect of RF-EMR exposure was evaluated in mobile phone base station—exposed individuals using alkaline comet assay in

terms of TM value and BMN assay. The effect of genetic polymorphisms of *GSTM1* and *GSTT1* genes on DNA damage was also investigated.

Methods and Materials

Subject and Sampling

The studied population included 116 individuals residing near mobile towers and 106 healthy control volunteers residing far away (>800 m) from the mobile towers. All of the subjects were informed about the study before consent was informed. The research protocol was approved from the Institutional Human Ethics Committee of Kurukshetra University, Kurukshetra (Haryana). A standard questionnaire was used to assess standard demographic characteristics such as age, sex, consumption habits (smoking, tobacco, and drinking habits, etc.), and different health symptoms (hair loss, insomnia, depression, memory status, etc.). Subjects undergoing medical treatment, X-ray exposure, radiography, or vaccination ≤ 3 months before sampling were not included.

Blood Sampling

Blood samples (approximately 5 mL) were collected from subjects exposed to radiation from mobile towers and control subjects in disposable presterilized and K₂EDTA-coated vacutainer tubes with the help of a trained technician. The blood samples were brought to the laboratory in a well insulated ice box taking care to avoid freezing of samples. Assays were performed under low-temperature conditions immediately after samples were brought to laboratory, and the remaining blood samples were stored at 4 °C.

Alkaline Comet Assay

Alkaline comet assay was performed according to Singh et al. (1988) and Tice et al. (2000) with minor modifications. Slides were prepared in duplicate per sample. Dust-free, plain slides were covered with a layer of 150 μ L of 1 % normal-melting agarose (prepared in distilled water) and allowed to dry for 10 min in a hot air oven. This layer served as an anchor for additional layers to prevent slippage. The blood sample (5 to 10 μ L) was mixed with 90 μ L of warm 0.5 % low-melting agarose (LMA) (prepared in phosphate buffer saline), and this mixture was layered as second additional layer and gelled at 4 °C for 15 min. A third additional layer of 150 μ L of 0.5 % LMA was added on top and gelled again at 4 °C for 15 min. The slides were treated for 2 h in freshly prepared, chilled

lysis buffer solution (25 mM sodium chloride, 100 mM sodium ethylene diamine tetra acetic acid (EDTA), 10 mM Tris, 1 % Triton X-100, and 10 % DMSO added before use [pH adjusted to 10]) at 4 °C. The slides were removed from the lysis solution, incubated in alkaline electrophoresis buffer (10 N NaCl and 200 mM EDTA [pH adjusted to 13]) for 20 min followed by electrophoresis (25 V and 300 mA) for 30 min in the same buffer. The slides were then neutralized with Tris buffer (0.4 M Tris [pH adjusted to 7.5]) and rinsed with distilled water, and every slide was stained by 80 to 100 μ L ethidium bromide (20 μ g mL⁻¹) for 5–8 min under dim or dark conditions.

Comet Scoring

A total of 50 cells from each of the duplicate slides were examined randomly under a fluorescence microscope. The extent of DNA damage was measured quantitatively as TM value using Lucia comet assay software, Czech Republic. The TM is defined by the percentage of DNA in the tail multiplied by the length between the centre of the head and tail (Olive et al. 1990).

BMN Analysis

Buccal cells originate from a multilayered epithelium that lines the oral cavity. Before buccal cell collection, the exposed individuals and control subjects were advised to rinse their mouth thoroughly with water to remove unwanted debris. A sterile wooden spatula was used to obtain cell samples from buccal mucosa. The buccal smears on glass slides were transported to the laboratory in an insulated ice box and processed within 3–4 h of sample collection. The samples were air dried and hydrolysed for 8 min in 1 N HCl at 60 °C. After a rinse in tap water, slides were stained in aceto-orcein (HiMedia, India) for 10 min at room temperature and briefly washed in ethanol and distilled water. Counter-staining was performed with fast green solution for 12 min followed by a final rinse in ethanol and distilled water. Slides were air dried and screened in a double-blind manner to analyse the presence of MN. At least 1000 cells were scored for the presence of MN in exfoliated buccal cells at 1000 $\times$ magnification under a bright-field microscope. The scoring of micronuclei was performed according to the criterion of Tolbert et al. (1991).

GSTM1 and GSTT1 Genotyping

Genomic DNA was isolated from 200 μ L of whole blood by Spin column kit (Bangalore Genei, India). A single assay using multiplex PCR was performed for

simultaneous gene amplification of GSTM1 and GSTT1 genes (Abdel-Rahman et al. 1996). Briefly, 50–100 ng of DNA was amplified in a 25- μ L multiplex reaction mixture containing 20 pmol μ L⁻¹ of each of the following GSTM1 primers (G1 - 5' GAA CTC CCT GAA AAG CTA AAG C 3' and G2 - 5' GTT GGG CTC AAA TAT ACG GTG G 3') and GSTT1 primers (T1 - 5' TTC CTT ACT GGT CCT CAC ATC TC 3' and T2 - 5' TCA CCG GAT CAT GGC CAGCA 3'). As internal control, exon 7 of the CYP1A1 gene was also amplified (5' GAA CTG CCA CTT CAG CTG TCT 3' and 5' CAG CTG CAT TTG GAA GTG CTC 3') in a mixture consisting of 1.5 mM MgCl₂, 200 μ M dNTPs, 2.5 μ L of 10 $\times$ PCR buffer (50 mM KCl and 10 mM Tris-HCl), and 0.7 U Taq DNA polymerase (Bangalore Genei, India). The PCR protocol included an initial denaturation temperature of 94 °C (5 min) followed by 35 cycles of amplification (denaturation at 94 °C for 1 min, annealing at 59 °C for 1 min and, extension at 72 °C for 1 min). A final 10-min extension step (72 °C) terminated the process. The final PCR products were visualized on an ethidium bromide-stained 2.0 % agarose gel. The size of the GSTM1 and GSTT1 genotypes was visualized as 215- and 480-bps fragments, respectively, and the CYP1A1 internal control was a 312-bps fragment.

Mobile Tower Radiation Measurement

The power density of radiation was measured from selected mobile towers at different locations of Kurukshetra city in Haryana state of India using handheld an RF spectrum analyzer HF-4060, Aaronia AG, Germany (frequency range 100 MHz to 6 Hz). Measured values were compared with safe limits recommended by Bioinitiative reports [2012 (0.5 mW/m²)], Salzburg resolution [2000 (1 mW/m²)], European Union Scientific and Technological Options Assessment [2001 (0.1 mW/m²)], and International Council of Nonionizing Radiation Protection (ICNIRP) [2014 (0.9 W/m²)].

Statistical Analysis

Student *t* test was used for comparison of different variables between studied groups. Distribution of GSTM1 and GSTT1 among studied population was determined by χ^2 test. The influence of genetic polymorphisms of *GSTM1* and *GSTT1* genes and confounding factors on studied biomarkers among multiple subgroups was performed by post hoc analysis and Tukey Honestly Significant Difference (HSD) test using multivariate analysis of variance. All tests were performed using statistical package system SPSS 16.0. The level of significance was set at 0.05.

Results

Demographic Characteristics of the Studied Population

The demographic characteristics of studied population have been summarized in Table 1. We collected data from 116 exposed individuals and 106 unexposed control subjects. The distribution of sex was not significantly different in both groups ($p > 0.05$). The exposed population had an average age of 32.87 ± 12.95 years, and average

age of the control population was 33.79 ± 14.46 years. The percentage of smokers, alcohol users, and tobacco chewers among exposed individuals was 25.9, 26.7, and 8.6, respectively, whereas it was found to be 15.1, 27.4, and 9.4, respectively, in the control group. No significant difference in age, sex, and consumption habits was observed between the two studied groups (Table 1). Different health problems, such as blood pressure, depression, memory status, insomnia, and hair loss, were found to be significantly associated with exposed individuals (Table 2).

Table 1 Demographic characteristics of control and exposed groups

Variables	Control group	Exposed group	<i>p</i>
All <i>N</i> (%)	106 (100.0)	116 (100.0)	
Mean ($\pm$ SD) age (years)	33.79 $\pm$ 14.46	32.87 $\pm$ 12.95	0.446
<25	48 (45.3)	43 (37.1)	0.147
25–45	32 (30.2)	55 (47.4)	
>45	26 (24.5)	18 (15.5)	
Sex			
Male	63 (59.4)	68 (58.6)	0.086
Female	43 (40.6)	48 (41.4)	
Diet			
Vegetarian	61 (57.5)	78 (67.2)	0.208
Nonvegetarian	45 (42.5)	38 (32.8)	
Smoking			
Nonsmokers	90 (84.9)	86 (74.1)	0.409
Smokers	16 (15.1)	30 (25.9)	
Alcohol users			
Nonalcoholic	77 (72.6)	85 (73.3)	0.530
Alcoholic	29 (27.4)	31 (26.7)	
Tobacco-chewing			
Non-tobacco-chewers	96 (90.6)	106 (91.4)	0.395
Tobacco chewers	10 (9.4)	10 (8.6)	
Mean ($\pm$ SD) mobile-phone use (h)	1.43 $\pm$ 0.87	1.79 $\pm$ 1.14	0.977
Distance from mobile-phone towers (m)			
50	–	26 (22.4)	–
100	–	41 (35.3)	
150	–	31 (26.7)	
250	–	10 (8.6)	
400	–	8 (6.9)	
Exposure duration (years)			
≤ 8	–	93 (80.17)	–
≥ 9	–	23 (19.83)	
Exposure/d (h)			
≤ 12	–	30 (25.36)	–
≥ 13	–	86 (74.14)	

Student *t* test was applied for comparing mean value of age and mobile usage among the control and exposed groups. χ^2 test was applied for difference in age, sex, diet, and consumption habits among the control and exposed groups

Table 2 Comparison of health symptoms between control and exposed groups

Health symptoms	Control group	Exposed group	<i>p</i>
Blood pressure			
Low	6 (5.66)	20 (17.24)	0.000*
Normal	65 (61.32)	27 (23.28)	
High	35 (33.02)	69 (59.48)	
Depression			
No	105 (99.1)	47 (40.5)	0.000*
Yes	1 (0.9)	69 (59.5)	
Memory status			
Good	100 (94.3)	46 (39.7)	0.040*
Poor	6 (5.7)	70 (60.3)	
Cancer			
No	106 (100.0)	115 (99.1)	0.338
Yes	0 (0.0)	1 (0.9)	
Respiratory diseases			
No	106 (100.0)	111 (95.7)	0.081
Yes	0 (0.0)	5 (4.3)	
Heart impairment			
No	105 (99.1)	116 (100.0)	0.294
Yes	1 (0.9)	0 (0.0)	
Insomnia			
No	104 (98.1)	48 (41.4)	0.000*
Yes	2 (1.9)	68 (58.6)	
Hair loss			
No	106 (100.0)	58 (50.0)	0.000*
Yes	0 (0.0)	58 (50.0)	

* χ^2 test was applied for difference in health symptoms among the control and exposed groups

BMN Frequency and TM Value

The effect of RF-EMR on DNA damage was analysed in exposed and control groups. The exposed group had a significantly high level of BMN frequency and TM value

Table 3 TM value and BMN frequency in the control and exposed groups

TM and BMN	Control group	Exposed group	<i>p</i>
TM (μ M)	0.26 $\pm$ 0.27	6.63 $\pm$ 2.32	0.000*
BMN frequency (%)	1.23 $\pm$ 0.97	3.65 $\pm$ 2.44	0.000*

* Student *t* test was applied for comparing mean values among the control and exposed groups

compared with the control group (Table 3). Maximum BMN frequency and TM values were observed at a 150-m distance. It was found that with an increase in RF-EMR exposure level, there was an increase in BMN frequency and TM values (Table 4).

Mobile-Tower Radiation Measurement

The power density of RF-EMR from the selected mobile towers was measured at different locations of Kurukshetra city. The highest measured power density value of RF-EMR was found to be 12.2 mW/m². Most of the measured values are higher than that of the safe limits recommended by Bioinitiative reports [2012 (0.5 mW/m²)], the Salzburg resolution [2000 (1 mW/m²)], and the European Union [2001 (0.1mW/m²)]. However, the measured values were lower than the safe limits recommended by the ICNIRP and adopted by the Department of Telecommunication, India [2014 (0.9 W/m²)]. Maximum RF-EMR was measured at a 150-m distance from the tower. The measured values of power density at different distances are given in Table 4.

Distribution of GST Genotypes

The distribution of GST genotypes among both the exposed and control groups is summarized in Table 5. The GSTM1 and GSTT1 non-null genotypes were found to be more prominent than their counterpart GSTM1 and GSTT1 null genotypes. The distribution of both genotypes was not found to be significantly different among both groups ($p > 0.05$).

Effect of Age, Sex, Consumption Habits, and Exposure Duration on TM Values and BMN Frequency

It was observed that in both control and exposed subjects, consumption habits such as smoking, alcohol intake, tobacco chewing, and diet did not significantly affect BMN frequency and TM values (Table 6). There was no significant effect of consumption habits both in control and exposed subjects, although TM values and BMN frequency were found to be high in vegetarians, nonsmokers, non-alcoholics, and non-tobacco chewers in exposed group. However, a significant increase in BMN frequency and TM value was found in individuals the in age group >45 years and in females in the exposed group. Individuals who were exposed for ≥ 9 years were found to have significantly high BMN frequency compared with individuals having <9 years of exposure.

Table 4 TM value and BMN frequency at different distances from a mobile tower

Distance (m)	Mean ($\pm$ SD) power density (mW/m ²) at 1800 MHz	Mean ($\pm$ SD) TM value (μ M)	Mean ($\pm$ SD) BMN frequency (%)
50	1.185 $\pm$ 0.64	5.46 $\pm$ 1.79	2.35 $\pm$ 1.23
100	8.842 $\pm$ 2.04	7.45 $\pm$ 2.63 ^a	3.95 $\pm$ 2.88 ^c
150	12.20 $\pm$ 2.36	7.31 $\pm$ 1.72 ^b	4.90 $\pm$ 2.21 ^d
250	1.245 $\pm$ 0.71	5.65 $\pm$ 1.64	3.50 $\pm$ 1.93
400	0.037 $\pm$ 0.06	4.81 $\pm$ 2.13	2.00 $\pm$ 1.33

* Significant at $p < 0.05$. Multivariate analysis of covariance tests for the differences in TM value and BMN frequency at different distances from mobile towers with adjustment for other factors among the control and exposed groups

^a $p = 0.003$, Tukey HSD test with 50-m subgroup as the reference

^b $p = 0.01$, Tukey HSD test with 50-m subgroup as the reference

^c $p = 0.04$, Tukey HSD test with 50-m subgroup as the reference

^d $p = 0.00$, Tukey HSD test with 50-m subgroup as the reference

Table 5 Frequency distribution of GSTM1 and GSTT1 genotypes among the control and exposed groups

Variables	Control group	Exposed group	OR	95 % CI	<i>p</i>
GSTM1 genotype					
Non-null	67 (63.2)	63 (54.3)	1.445	0.844–2.475	0.179
Null	39 (36.8)	53 (45.7)			
GSTT1 genotype					
Non-null	67 (63.2)	70 (60.3)	1.129	0.656–1.942	0.661
Null	39 (36.8)	46 (39.7)			

OR odds ratio, CI confidence interval

χ^2 test was used for comparison of GSTM1 and GSTT1 genotype distribution among the control and exposed groups

Influence of GST Genotypes on BMN Frequency and TM Value

We observed that although GSTM1 and GSTT1 non-null genotypes had high BMN frequency and TM value, there was no significant difference in BMN frequency and TM value between individuals with GSTM1 and GSTT1 non-null and null genotypes (Table 7). Results of linear regression analysis adjusted for model factors, such as age, sex, consumption habit, exposure level, and duration, are given in Table 8.

Discussion

The electromagnetic environment consists of natural radiation and man-made EMFs that are produced either intentionally or are by products of the use of electrical devices and systems. People are constantly exposed to low levels of naturally occurring radiation called “background radiation.” The everyday use of devices and systems emitting radiofrequency EMFs is continuously increasing. Effects of extremely low-frequency EMFs or nonionizing

radiation on biological systems have been studied for >30 years. There is a great concern over the harmful effects of electromagnetic and radiofrequency waves as well as microwaves generated by mobile phones and their telecommunication stations on human health (Vijayalaxmi and Obe 2004).

Our results indicated that TM value and BMN frequency were higher in an exposed population compare with a control group and the difference is significant. Recent in vitro and in vivo studies observed the occurrence of DNA damage (Zmyeolony et al. 2000; Wolf et al. 2005) as well as micronucleus (BMN) generation, which is a well-accepted index for genotoxicity evaluation after RF-EMR exposure (Tice et al. 2002; Trosic et al. 2004).

There are controversial findings regarding the findings in vitro and in vivo genotoxicity studies of RF-EMR exposure. Several studies (Juutilainen et al. 2010; Hintzsche and Stopper 2010) came to the conclusion that nonionizing radiation exposure could not be related to any genotoxic action, although several studies have reported effects with different genotoxic end points such as sister chromatid exchange (Gadhia et al. 2003), micronuclei (Gandhi and Singh 2005a; Gandhi and Anita 2005b; Yadav

Table 6 Influence of age, sex, consumption habits, and exposure duration on TM value and BMN frequency

Variables	Control group			Exposed group		
	N	TM value (μM) Mean $\pm$ SD	BMN frequency (%) Mean $\pm$ SD	N	TM value (μM) Mean $\pm$ SD	BMN frequency (%) Mean $\pm$ SD
Age (years)						
<25	48	0.18 $\pm$ 0.19	1.17 $\pm$ 0.88	43	6.99 $\pm$ 2.42	4.21 $\pm$ 2.42 ^b
25–45	32	0.33 $\pm$ 0.30	1.13 $\pm$ 0.98	55	6.04 $\pm$ 2.06	2.87 $\pm$ 2.06
>45	26	0.33 $\pm$ 0.34	1.46 $\pm$ 1.10	18	7.57 $\pm$ 2.44 ^{*a}	4.67 $\pm$ 2.89 ^{*c}
Sex						
Male	63	0.27 $\pm$ 0.30	1.21 $\pm$ 1.02	68	6.20 $\pm$ 2.26	2.96 $\pm$ 1.93
Female	43	0.25 $\pm$ 0.27	1.26 $\pm$ 0.90	48	7.23 $\pm$ 2.28 [*]	4.63 $\pm$ 2.75 [*]
Diet						
Vegetarian	61	0.28 $\pm$ 0.30	1.25 $\pm$ 1.03	78	6.80 $\pm$ 2.12	3.10 $\pm$ 2.41
Nonvegetarian	45	0.24 $\pm$ 0.24	1.20 $\pm$ 0.89	38	6.28 $\pm$ 2.67	2.71 $\pm$ 2.24
Smoking						
Nonsmokers	90	0.27 $\pm$ 0.27	1.26 $\pm$ 0.97	86	5.89 $\pm$ 2.23	2.98 $\pm$ 2.43
Smokers	16	0.22 $\pm$ 0.28	1.06 $\pm$ 1.00	30	5.86 $\pm$ 2.43	2.67 $\pm$ 2.20
Alcohol user						
Nonalcoholic	77	0.27 $\pm$ 0.27	1.25 $\pm$ 0.91	85	5.93 $\pm$ 2.26	3.08 $\pm$ 2.50
Alcoholic	29	0.26 $\pm$ 0.29	1.17 $\pm$ 1.14	31	5.81 $\pm$ 2.30	2.45 $\pm$ 1.77
Tobacco						
Non-tobacco-chewers	96	0.28 $\pm$ 0.28	1.27 $\pm$ 0.96	107	6.75 $\pm$ 2.33	1.81 $\pm$ 2.44
Tobacco-chewers	10	0.14 $\pm$ 0.16	0.80 $\pm$ 1.03	9	5.17 $\pm$ 1.64	1.66 $\pm$ 1.22
Exposure (8)						
≤ 8	–	–	–	93	6.72 $\pm$ 2.09	3.40 $\pm$ 2.32
≥ 9	–	–	–	23	6.97 $\pm$ 3.09	4.65 $\pm$ 2.69 [*]

* Significant at $p < 0.05$. Multivariate analysis of covariance tests was used for the comparison of TM value and BMN frequency in multiple subgroups among exposed and control groups separately

^a $p = 0.04$, Tukey HSD test with age subgroup 25–45 years as the reference

^b $p = 0.1$, Tukey HSD test with age subgroup 25–45 years as the reference

^c $p = 0.03$, Tukey HSD test with age subgroup 25–45 years as the reference

Table 7 Influence of GST genotypes on TM value and BMN frequency

Biomarkers	Control group			Exposed group		
	N	TM value (μM) Mean $\pm$ SD	BMN frequency (%) Mean $\pm$ SD	N	TM value (μM) Mean $\pm$ SD	BMN frequency (%) Mean $\pm$ SD
GSTM1						
Non-null	67	0.20 $\pm$ 0.20	1.09 $\pm$ 0.77	63	5.55 $\pm$ 2.14	2.50 $\pm$ 2.06
Null	39	0.17 $\pm$ 0.18	0.87 $\pm$ 0.86	53	5.15 $\pm$ 1.67	2.06 $\pm$ 1.47
GSTT1						
Non-null	67	0.28 $\pm$ 0.29	1.32 $\pm$ 0.99	70	6.87 $\pm$ 2.43	3.87 $\pm$ 2.73
Null	39	0.23 $\pm$ 0.25	1.05 $\pm$ 0.92	46	6.27 $\pm$ 2.11	3.30 $\pm$ 1.88

* Significant at $p < 0.05$. Multivariate analysis of covariance tests was used for the differences in tail moment value (TM) and BMN frequency adjusted with age, sex, consumption habits and exposure duration among exposed and control groups separately

Table 8 Association of GST genotypes with TM value and BMN frequency per linear regression analysis

Genotype	Comet assay (mean $\pm$ SD)			BMN frequency (mean $\pm$ SD)		
	β^a	R^2	p^b	β^a	R^2	p^b
Control group ($n = 106$)						
GSTM1	−0.078	0.007	0.429	−0.118	0.031	0.231
GSTT1	−0.079	0.991	0.441	−0.132	0.093	0.166
Exposed group ($n = 116$)						
GSTM1	−0.119	0.014	0.221	−0.178	0.061	0.061
GSTT1	−0.018	0.022	0.818	−0.036	0.044	0.640

^a Unstandardized coefficient^b Model p value. Regression analysis was used for the differences in TM value and BMN frequency adjusted for age, sex, exposure level, duration, and consumption habits

and Sharma 2008), CAs (Lalic et al. 2001; Othman et al. 2003), and DNA strand breakage or comet assay (Sun et al. 2006a, b, c; Garaj-Vrhovac and Orescanin 2009).

Diem et al. (2005) found induced single- and double-strand breaks in cultured human skin fibroblasts and SV-40-transformed rat granulosa cells after exposure to 1800 MHz RFR. In another study describing the effects of 1950 MHz UMTS-like EMFs, increased DNA damage was found (as was an increased frequency of centromere-negative micronuclei) in human cultured fibroblasts. This occurred in dose- and time-dependent ways (Schwarz et al. 2008).

Franzellitti et al. (2010) provided data suggesting that high-frequency EMFs with a carrier frequency and modulation scheme typical of the GSM signal may affect DNA integrity in the human trophoblast HTR-8/SVneo cell line evaluated with the alkaline comet assay.

Studies from Croatian research group have reported increased frequencies of chromosomal aberrations (CAs), micronuclei, or DNA damage as investigated by alkaline comet assay (Kopjar and Garaj-Vrhovac 2001). Some studies from India have also reported increased CAs in peripheral blood lymphocytes and micronuclei in capillary blood (Vijayalaxmi et al. 2001) and DNA damage and micronuclei in buccal mucosal cells (Lai and Singh 1995). Gandhi and Anita (2005b) reported an increase in DNA strand breaks and micronucleation in lymphocytes obtained from cell-phone users. Markova et al. (2005) reported that GSM signals affected chromatin conformation and H2AX foci that colocalized in distinct foci with DNA double-strand breaks in human lymphocytes.

Several studies have reported no genotoxic damage. The absence of genotoxicity was found in mice with MNT and in rats with comet assay (Lagroye et al. 2004a; Görlitz et al. 2005). McNamee et al. (2002) found no significant increase in DNA breaks and MN formation in human leukocytes exposed for 2 h to a 1.9-GHz field at SAR ≤ 10 W/kg. Zeni et al. (2005)

reported that a 2-h exposure to 900-MHz GSM signal at 0.3 and 1 W/kg did not significantly affect levels of DNA strand breaks in human leukocytes. Sakuma et al. (2006) exposed human glioblastoma A172 cells and normal human IMR-90 fibroblasts from fetal lungs to cell-phone radiation for 2 and 24 h. No significant changes in DNA strand breaks were observed up to a SAR of 800 mW/kg. Stronati et al. (2006) showed that 24 h of exposure to 935-MHz GSM basic signal at 1 or 2 W/kg did not cause DNA strand breaks in human blood cells. Maes et al. (2006) used alkaline comet assay as well as the test of sister chromatid exchange and chromosome aberration to investigate genetic damage in the lymphocytes of radio field engineers and other occupationally exposed subjects. They found no evidence for RFR-induced cytogenetic effects.

In our study, we found high TM value and BMN frequency at 100- and 150-m distances from mobile towers that could be correlated with more power density at these distances due to the influence of high antenna positions with maximum values shifted to larger distances. Santini et al. (2002) and Navarro et al. (2003) surveyed people living ≤ 300 m from GSM base stations and found statistically significant correlations between distance from the base stations and health problems. Despite exposure to radiation far below recommended levels (max. 4.1 mW/m²), effects on well-being and performance on cognitive tests were observed in a study of 365 subjects living within 20–600 m from mobile-phone base stations (Hutter et al. 2006).

Regarding sex, a significant increase in TM value and BMN frequency was found in females compared with males. This may be due to more exposure time at home. In our study, DNA damage was high in the age group <25 years and the group >45 years compared with the age group 25–45 years. Ilhan et al. (2004) observed that older people must be more cautious for EMR-induced oxidative damage.

Our findings showed that consumptions habits, such as smoking, alcohol intake, tobacco-chewing, and diet, did not have a significant effect on TM value and BMN frequency in both groups. Maes et al. (2006) also observed that smoking habit had no significant effect on the induction of genotoxicity in an investigation of subjects professionally exposed to RFR.

In our study, we found that different health symptoms, such as depression, memory status, insomnia, and hair loss, were significantly associated with exposure to EMR. Similar to our findings, Al-Khaliwi and Meo (2004) observed symptoms such as headache, fatigue, dizziness, tension, and sleep disturbances in subjects exposed to mobile-phone emissions in Saudi Arabia. According to a French study, people living <300 m from a base station have an increased incidence for tiredness (within 300 m), headache, sleep disturbance, discomfort, etc. (200 m) for irritability, depression, loss of memory, dizziness, and decreased libido decrease, etc. (100 m). Women complained significantly more often than men of headache, nausea, loss of appetite, sleep disturbance, depression, discomfort, and visual perturbations (Santini et al. 2002). A study on inhabitants living near or under a cell-phone base station antenna reported health complaints such as headache (23.5 %), memory changes (28.2 %), dizziness (18.8 %), tremors (9.4 %), symptoms of depression (21.7 %), and sleep disturbances (23.5 %) (Abdel-Rassoul et al. 2007).

Damaging effects of nonionizing radiation result from the generation of reactive oxygen species (ROS) and subsequent radical formation and from direct damage to cellular macromolecules including DNA. Phase II drug-metabolizing enzymes play an important role in the biotransformation of endogenous compounds and free radicals to more easily excretable forms as well as in the metabolic inactivation of pharmacologically active compounds. The adverse effects of nonionizing radiation are partially reduced by molecular defense mechanisms including GSH and enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, which are involved in quenching excessive levels of ROS and other free radicals (Behrendt et al. 2010). GSTs are multi-gene families of enzymes involved in the metabolism of a wide range of electrophilic compounds of both exogenous and endogenous origin. These catalyse the conjugation of reduced GSH with a wide variety of electrophiles, which includes known carcinogens as well as various compounds that are products of oxidative stress due to nonionizing radiation including oxidised DNA and lipids. Indeed, several lines of evidence suggest that certain of these isoenzymes play a pivotal role in protecting cells from the consequences of such stress (Rinaldi et al. 2002).

Deletion of *GSTM1* and *GSTT1* genes, which are important isoenzymes of GST, leads to complete lack of activity of their enzymes. It was therefore suggested that these isoenzymes could serve as a genetic marker for susceptibility to certain forms of cancers (Abdel-Rahman et al. 1996; Bajpai et al. 2007; Cha et al. 2007; Ouerhani et al. 2006). In the present study, it was found that *GSTM1* and *GSTT1* polymorphisms were not significantly associated with DNA damage in the mobile-phone tower-exposed human population. Edvardsen et al. (2007) studied long-term cutaneous radiotherapy effects in breast cancer patients and reported a significant association between long-term pleural thickening and *GSTP1* polymorphisms, whereas no associations were found for *GSTM1* and *GSTT1* deletion polymorphisms.

Although many of the investigations on the genetic and cytogenetic effects of RF-EMR indicated that these EMFs are not capable of inducing any kind of genetic effect, the literature available remains sufficiently controversial to exclude any potential RF-EMR genetic hazard. It is assumed that only large-scale research under well-controlled conditions and allowing the generation of results with sufficient statistical power may lead to a better risk estimate.

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Compliance with Ethical Standards

Conflict of Interest No conflict of interest.

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