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Serum levels of Organochlorine Pesticides and Breast Cancer Risk in Iranian Women

Parisa Paydar[1,2] · Gholamreza Asadikaram[2,3] · Hossein Fallah[2,4] · Hamid Zeynali Nejad[5] · Hamed Akbari[6] · Moslem Abolhassani[2] · Vahid Moazed[7] · Payam Khazaeli[8] · Mahmoud Reza Heidari[8]

Abstract

Breast cancer is a multifactorial disease and its etiology is linked to multiple risk factors. There are shreds of controversial evidence that exposure to organochlorine pesticides (OCPs) are important in the etiology of breast cancer. The present study aimed to determine the circulating levels of OCPs in patients with breast tumors in Southeastern of Iran. This case–control study included 27 patients with malignant breast tumors (MBT), 31 patients with benign breast tumors (BBT), and 27 healthy women as a control group. Serum OCPs levels, including α-hexachlorocyclohexane (α-HCH), β-HCH, γ-HCH, 2,4-dichlorodiphenyltrichloroethane (2,4-DDT), 4,4-DDT, 2,4-dichlorodiphenyldichloroethylene (2,4-DDE), and 4,4-DDE, were measured using gas chromatography. Our data revealed significantly higher concentrations of 2,4-DDT in MBT and BBT groups compared with control ones ($P < 0.001$ for both comparisons). Patients with breast cancer suffered significantly higher accumulation levels of 4,4-DDE compared with control subjects ($P = 0.04$). Significant correlations were found among organochlorine compounds with each other in both patients' groups. There was a significant positive correlation between body mass index and serum levels of 2,4-DDT in BBT group ($r = 0.407$, $P = 0.02$). The present findings suggest that the serum levels of 4,4-DDE and 2,4-DDT are associated with an increase in the risk of breast cancer in Southeastern women of Iran.

✉ Gholamreza Asadikaram
asadi_ka@yahoo.com; Gh_asadi@kmu.ac.ir

1 Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman, Iran

2 Department of Clinical Biochemistry, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

3 Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran

4 Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

5 Department of Surgery, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

6 Student Research Committee, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

7 Department of Hematology and Oncology, Faculty of Medicine, Kerman University of Medical Sciences, Kerman, Iran

8 Department of Toxicology and Pharmacology, School of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer death in women worldwide (Siegel et al. 2018). In Iran, 24.4% of all diagnosed cancers are breast cancer, which is responsible for more than 1063 deaths each year (Farhood et al. 2018). Although breast cancer etiology is not fully understood, some hereditary and nonhereditary factors can contribute to the development of this malignancy, including age, sex, race, familial history of cancer, lower age of menarche, late childbearing, not lactating, later menopause, obesity, alcohol consumption, inactivity, hormone replacement therapy (HRT), and environmental chemicals (Kamińska et al. 2015; Rodgers et al. 2018).

Among environmental chemicals linked to breast cancer, preceding studies have revealed a significant association between organochlorine pesticides (OCPs) and an increase in breast cancer risk (He et al. 2017; Romieu et al. 2000). Pesticides are a group of chemical compounds used for destructing and/or controlling different kinds of pests, including insects, weeds, fungi, bacteria, etc. (Jayaraj et al. 2016). OCPs are organic compounds with heterogeneous structures composed predominantly of carbon, hydrogen, and chlorine atoms (Mrema et al. 2013). There are three main groups of OCPs, including DDT and its derivative

products, hexachlorocyclohexane (HCH) and chlorinated cyclodiene (Pirsaheb et al. 2015). These chemicals belong to the persistent organic pollutants (POPs) group, which persist in the environment because of their resistance against various types of degradation and might be accumulated in animal and human food chains for a long time (Wong et al. 2012). Serious concerns about POPs are attributed to their adverse health effects in humans, including immunosuppressive, oxidative, proinflammatory, neurotoxic, hormone-disrupting, metabolic, and carcinogenic effects (Carpenter 2013; Porta 2012). Accumulating evidence given by epidemiological and agricultural health studies disclosed that OCPs exposure could be associated with the risk of cancers, such as breast, prostate, lung, stomach, colorectal, bladder cancer, etc. (Abolhassani et al. 2019; Jayaraj et al. 2016; Mortazavi et al. 2019). OCPs may interfere with female hormonal functions and affect breast cell proliferation by acting as estrogen mimics, interfering with hormone transport and disrupting hormone synthesis, thereby increasing breast cancer risk (Bretveld et al. 2006). Despite the application of OCPs was banned in the 1980s, they can accumulate in the human body due to its lipophilicity and persistence for many years (Bayat et al. 2011; He et al. 2017).

Exposure to OCPs has been studied in the Iranian population and the results have revealed a high degree of contamination by OCPs (Arzi et al. 2009; Behrooz et al. 2012; Cok et al. 1999; Hashemy-Tonkabony and Soleimani-Amiri 1978). Therefore, the possible presence of OCPs in our environment still causes concerns. Because Kerman province is considered as one of the most important regions for agricultural activities and regarding the alarming mortality rate of breast cancer among Iranian women, we sought to determine whether breast cancer risk is associated with serum levels of OCPs in Southeastern women of Iran.

Materials and Methods

Subjects

This case–control study involved 27 female patients with malignant breast tumor (MBT) and 31 female patients with benign breast tumor (BBT) who underwent surgical resection at Shahid Bahonar and Afzalipour hospitals from March 2015 to November 2016 as described elsewhere (Paydar et al. 2018). Detection of breast cancer from benign breast diseases was performed based on clinical and pathological documents following surgery. Among patients with breast cancer, 24 had ductal carcinoma (invasive, infiltrative, and in situ ductal carcinoma) and 3 had invasive lobular carcinoma. Among patients with benign breast diseases, 17, 9, 2, 2, and 1 had fibroadenoma, fibrocystic disease, chronic

granulomatous mastitis, glandular adenosis, and hydradenoma respectively.

In addition, 27 healthy women were enrolled as controls (CON) in this study. According to inclusion criteria in the current study, all patients were new cases and patients who had any treatments, such as surgery, radiotherapy, and chemotherapy, were excluded from the study. All the studied patients previously had no history of alcohol consumption and smoking. The control group was women who had no acute and chronic diseases and known cancer as well as they were not smoking or consuming alcohol. Moreover, all the participated women in this study were local inhabitant (Kerman, Iran) for more than 40 years. Written, informed consent was obtained from all the subjects participating in the study before enrollment. The study was conducted in accordance with the principles of the revised *Declaration of Helsinki* and approved by the Ethics Committee of Kerman University of Medical Sciences, Kerman, Iran (IR.KMU.REC.1394.315). Because surgery may change the blood levels of OCPs, blood specimens were obtained from studied patients before surgery. Blood samples were collected from the participants in the morning after overnight fasting and immediately centrifuged and serum samples kept frozen at −70 °C in preparation for OCPs detection.

Chemicals

The standards of OCPs include α-HCH, β-HCH, γ-HCH, 2,4-DDT, 4,4-DDT, 2,4-DDE, and 4,4-DDE and internal standard (4,4-dichlorobenzophenone, DBP) were purchased from Ehrenstorfer company (Germany). *N*-hexane, anhydrous sodium sulfate, and ethyl acetate were obtained from Merck (Germany), and sulphuric acid was purchased from Scharlab (Spain).

OCPs Extraction from Serum Specimens

Serum OCPs residues of all subjects were identified and quantified using a gas chromatographic analyzer (Agilent 7890A, USA) coupled to flame ionization detector (GC-FID). Identification of OCPs residues was performed by a slightly modified version of the method as described by Zumbado et al. (2005). Briefly, the internal standard (IS) was added to 0.5 ml of serums. Samples were extracted twice with 2 ml of hexane. Then, with adding 200 μL of concentrated sulphuric acid to combined extracts, organic part of it became separated. We dehydrated this organic part using 100 mg of anhydrous sodium sulfate. Followed by centrifugation, the transferred organic layer was completely concentrated at room temperature. Finally, we added 100 μL of ethyl acetate to each sample for solving extracted OCPs.

GC Condition and OCPs Analysis

An HP5 capillary column (30-m length, 0.22-mm ID, 0.25-μm film thickness) was utilized with nitrogen as carrier gas at a flow rate of 1.5 ml/min. The initial temperature of the oven was maintained at 50 °C for 2 min and then elevated by 30 °C/min to 200 °C and finally programmed to increase at 5 °C/min to 280 °C. Injector and flame ionization detector temperatures were set to 320 °C and 350 °C respectively. A volume of 1 μL of samples and standards were injected into the gas chromatograph with a 5-μL syringe. Under this condition, the seven OCPs were successively detected within a very reasonable time (Fig. 1). The measurement of OCP levels was performed by determination of the retention time and peak area with an internal standard method that are qualitative and quantitative analysis respectively. In this regard, a set of pesticides' standards solutions with known concentrations (0.78, 1.56, 3.12, 6.25, 12.5, 25, 50, 100, 200, and 400 μg/ml) was prepared, and 100 μg/ml of IS was added to each standard solution. Peak areas of OCP standards and IS were measured and standard curves of OCPs separately constructed by plotting the analyte-to-IS ratio versus the known concentrations of analyte in each sample. The analytical limit of detection (LOD) was estimated 0.7 μg/ml for α-HCH, β-HCH, γ-HCH, 2,4-DDE, and 4,4-DDE and 3 μg/ml for 2,4-DDT and 4,4-DDT.

Statistical Analysis

All continuous and categorical variables were presented as mean ± standard deviation (SD) and numbers (percentages) respectively. Kolmogorov–Smirnov test was utilized to determine the distribution of data. The differences among groups were analyzed using one-way analysis of variance (ANOVA)/Kruskal–Wallis with post hoc Tukey/Mann–Whitney U tests as well as Chi-square/Fisher's exact tests. Correlations between continuous variables were evaluated using Pearson and Spearman correlation of coefficients. The statistical analyses were performed using SPSS software version 23.0 for Windows (SPSS Inc., Chicago, IL). P values < 0.05 were considered statistically significant.

Results

Participants' demographic and clinical characteristics are listed in Table 1. No significant differences were found in age, body mass index (BMI), residence, menopause status, and clinical stages of the three studied groups ($P > 0.05$ for all comparisons).

Comparison of serum levels of OCPs (ng/L) is presented in Fig. 2 and Table 2. The chromatograms of serum OCPs from a breast cancer patient and the matched normal subject are shown in Figs. 3 and 4. The most prevalent OCPs were 2,4-DDT and 2,4-DDE, which were detected
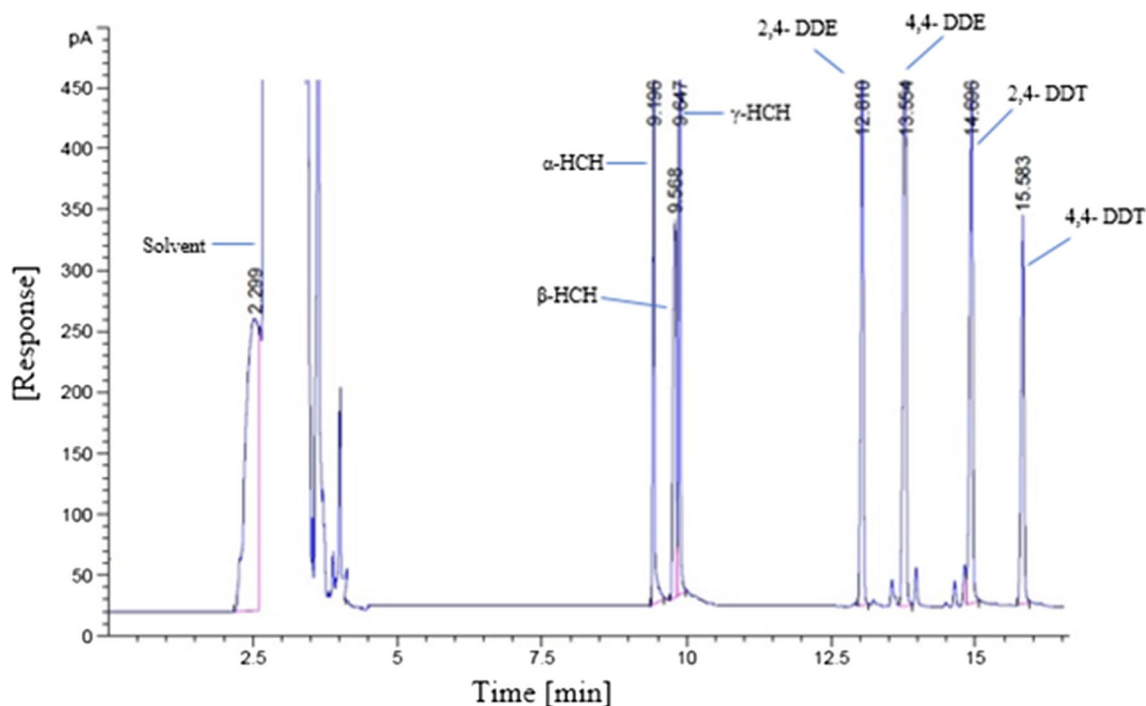
Fig. 1 The chromatogram of seven kinds of OCPs. Under the condition of gas chromatography, these pesticides were detected successively

Table 1 Clinical and demographic characteristics of MBT, BBT and CON groups

		MBT (n=27)	BBT (n=31)	CON (n=27)	*P*-value
Age (Year)		49.48±7.25	47.26±6.48	45.74±4.26	0.086[a]
BMI (Kg/m^2)		23.50±2.93	22.47±2.67	22.89±2.57	0.277[b]
Residence	**Urban**	6 (22)	8 (22)	3 (11)	0.468[c]
	Rural	21 (78)	28 (78)	24 (89)	
Menopause	**Yes**	24 (89)	28 (90)	23 (85)	0.914[c]
	No	3 (11)	3 (10)	4 (15)	
Stages	**I**	2 (8)			
	II	17 (63)			
	III	8 (29)			
Histological grade	**I**	4 (14.8)			
	II	5 (18.5)			
	III	18 (66.7)			

MBT, malignant breast tumor; BBT, benign breast tumor; CON, control; BMI, body mass index; Continuous and categorical values are expressed as Mean±SD and number, respectively. Significant at <0.05 levels.
a; ANOVA followed by post-hoc Tukey test.
b; Kruskal-Wallis followed by post-hoc Mann-Whitney U-test
c; Chi-Square test.

in almost all the samples (Table 2). α-HCH was only found in few patients with breast cancer and 4,4-DDT detected in none of three groups. Nevertheless, β-HCH and γ-HCH were detected in the serum of both MBT and BBT groups. Both serum levels of α-HCH and β-HCH showed no significant differences between both MBT and BBT groups ($P = 0.40$ and $P = 0.52$, respectively). The serum levels of 2,4-DDT were remarkably different in patients with MBT and BBT compared with healthy women ($P < 0.001$). The mean serum concentrations of 2,4-DDT were significantly higher in patients with MBT (547.38±480.59 ng/L) and BBT (488.43±453.53 ng/L) than the control group (68.00±29.44 ng/L) ($P < 0.001$ for both comparisons). It should be noted that the mean serum levels of 2,4-DDT were not significantly different between MBT and BBT groups ($P = 0.64$).

The mean serum levels of 2,4-DDE in MBT, BBT, and CON groups were 640.86±348.06, 634.63±295.55, and 643.29±359.68 ng/L, respectively (Table 2). There were no significant differences in 2,4-DDE levels among the three groups ($P = 0.99$). Furthermore, two by two comparisons did not reveal any considerable differences between groups [$P = 0.99$ (MBT vs. BBT), $P = 1$ (MBT vs. CON), and $P = 0.99$ (BBT vs. CON)].

No significant differences were found in the mean serum levels of 4,4-DDE among the three groups ($P = 0.052$; Table 2). Nonetheless, the post hoc Tukey test demonstrated significant higher levels of 4,4-DDE in patients with MBT (110.65±48.00 ng/L) compared to healthy (72.42±23.98 ng/L) women ($P = 0.04$). Likewise, the Tukey test showed higher levels of 4,4-DDE, but not significant, in patients with BBT (83.07±33.28 ng/L) compared
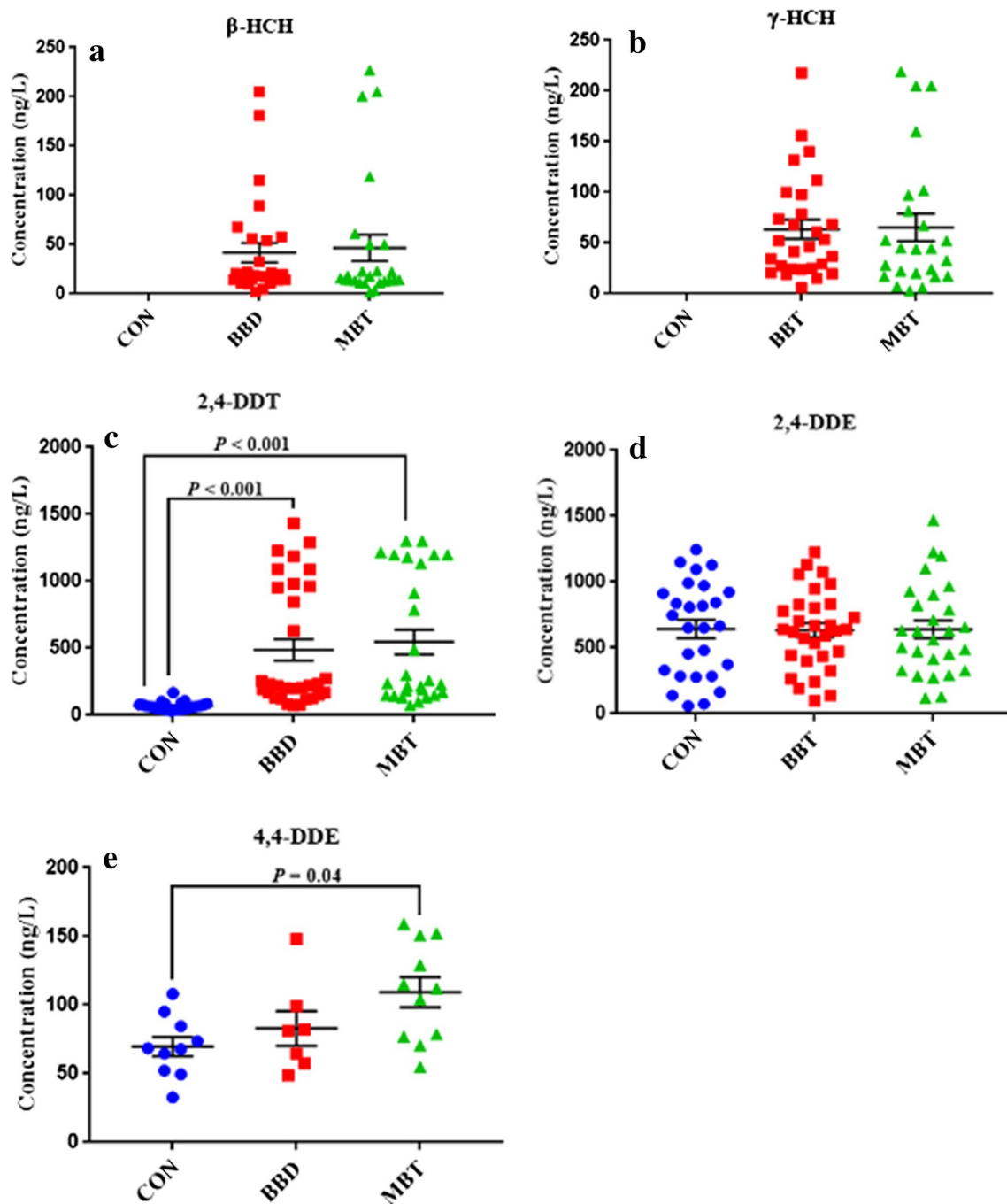
Fig. 2 The scatter dot plot of five kinds of OCPs in patients with MBT, BBT and control subjects. No significant differences were observed in the mean serum levels β-HCH, γ-HCH and 2,4-DDE pesticides among the three studied groups ($P > 0.05$ for all comparisons) (**a**, **b** and **d**). However, statistically significant differences were found in the mean levels of 2,4-DDT in MBT and BBT groups compared to control group ($P < 0.001$ for both comparisons) (**c**) and there was also a significant difference in 4,4-DDE levels between the MBT and control groups ($P = 0.04$) (**e**). P values < 0.05 were considered statistically significant. *OCPs* Organochlorine pesticides, *MBT* malignant breast tumor, *BBT* benign breast tumor, *CON* control

with control group ($P = 0.73$). In addition, it was shown that mean serum levels of 4,4-DDE were not markedly different between MBT and BBT patients ($P = 0.27$). The serum levels of OCPs were independent of the demographic characteristics of the participants (data are not shown). Tables 3 and 4 illustrate the correlations among age, BMI, and OCPs within MBT and BBT groups. A significant positive correlation was found between BMI and serum 2,4-DDT

Table 2 Detectable serum levels of OCPs (ng/L) in the studied groups

	MBT ($n=27$)		BBT ($n=30$)		CON ($n=27$)		P value
	Mean ± SD	D (%)	Mean ± SD	D (%)	Mean ± SD	D (%)	
α-HCH	53.10 ± 34.81	4 (14.8)	–	–	–	–	n.a
β-HCH	48.55 ± 67.36	24 (88.8)	61.73 ± 116.17	28 (90.3)	–	–	0.402[a]
γ-HCH	65.53 ± 66.46	24 (88.8)	63.73 ± 50.60	28 (90.3)	–	–	0.521[a]
2,4 –DDT	547.38 ± 480.59*	27 (100)	488.43 ± 453.53*	31 (100)	68.00 ± 29.44	25 (92.5)	< 0.001[b]
2,4-DDE	640.86 ± 348.06	27 (100)	634.63 ± 295.55	31 (100)	643.29 ± 359.68	27 (100)	0.995[c]
4,4-DDE	110.65 ± 48.00*	6 (22.2)	83.07 ± 33.28	7 (22.5)	72.42 ± 23.98	6 (22.2)	0.052[c]

Continuous and categorical values are expressed as mean ± SD and number, respectively

MBT malignant breast tumor, *BBT* benign breast tumor, *CON* control, *SD* standard deviation, *D* detected compound, *n.a.* not applicable
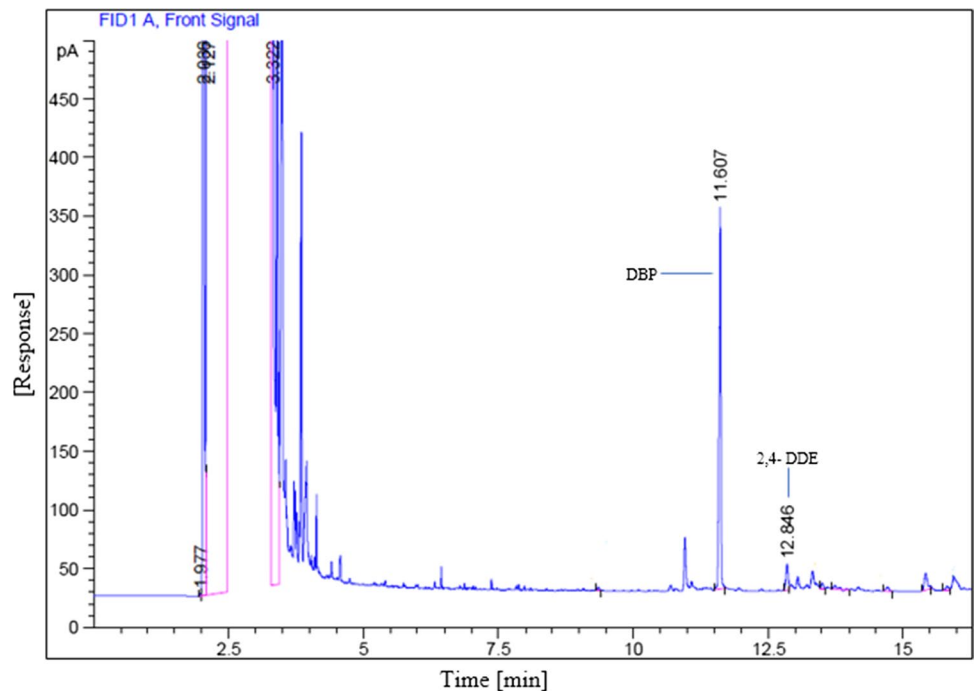
[a]Independent sample *t* test

[b]Kruskal–Wallis followed by post hoc Mann–Whitney *U* test

[c]ANOVA followed by post hoc Tukey test

*Significant difference with CON group ($P<0.05$). As Table 3 illustrates, the mean serum levels of 2,4-DDT were significantly higher in MBT and BBT groups than those control women ($P<0.001$ for both comparisons). Moreover, a significantly higher level of 4,4-DDE was witnessed in MBT women compared with control women ($P=0.04$)

Fig. 3 The chromatogram of OCPs and internal standard (DBP) in a normal subject. DBP and 2,4-DDE were detected in the serum sample of this subject. *OCPs* organochlorine pesticides, *DBP*, *4,4*-dichlorobenzophenone

Discussion

Breast cancer, a recognizable major public health problem, is one of the common malignant tumors among women worldwide. Although the precise cause of breast cancer

concentrations in the BBT group ($r=0.40$, $P=0.02$). Furthermore, the mean serum levels of all OCPs were positively correlated with each other.

development is not fully understood, some possible risk factors are related to its occurrence, including genetic, reproductive, lifestyles, and environmental factors (Paydar et al. 2019). It has been suggested that OCPs can act as endocrine disruptors and increase the risk of developing breast cancer through an estrogen-like effect (Bretveld et al. 2006). In general, some research groups in various countries have investigated the presence of OCPs in different diseases, particularly breast cancer, but until now, the results were still controversial. Several lines of evidence support our hypothesis

Fig. 4 The chromatogram of OCPs and internal standard (DBP) in a patient with MBT. The OCPs such as α-HCH, β-HCH, γ-HCH, 2,4-DDT, 2,4-DDE and 4,4-DDT were detected in the serum sample of the patient. *OCPs* organochlorine pesticides, *DBP*, *4,4*-dichlorobenzophenone, *MBT* malignant breast tumor
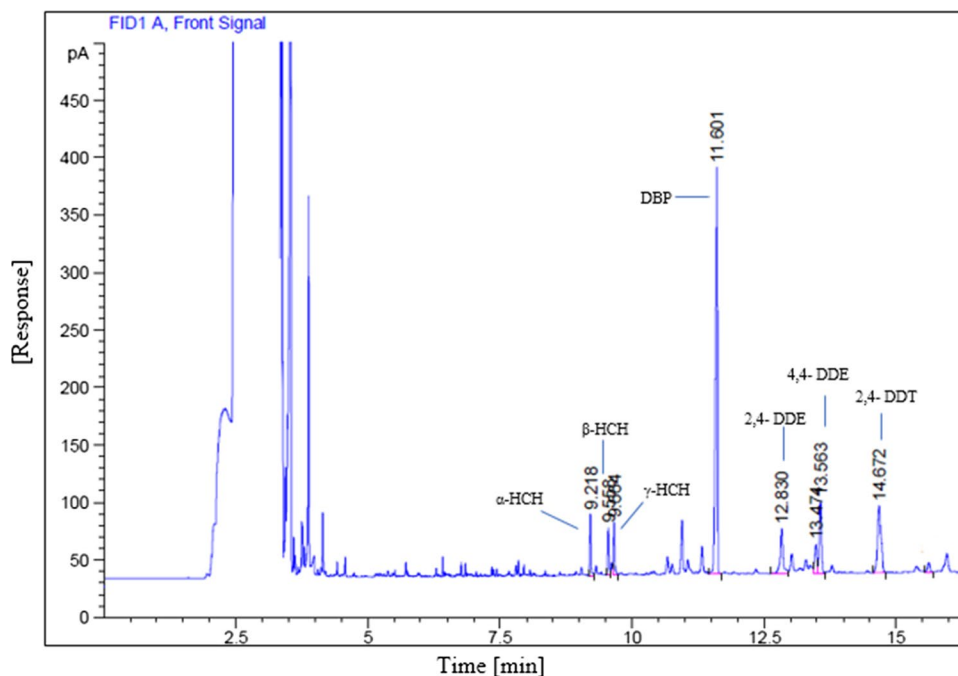
Table 3 Correlations among age, BMI, β-HCH, γ-HCH, 2,4-DDT, 2,4-DDE, and 4,4-DDE within MBT group

	Age	BMI	β-HCH	γ-HCH	2,4-DDT	2,4-DDE	4,4-DDE
Age		− .071	− .137	− .284	− .236	− .357	− .771
BMI			− .149	− .131	− .205	− .087	− .406
β-HCH				.713**	.531**	.741**	.600
γ-HCH					.757**	.774**	.812
2,4-DDT						.671**	.829*
2,4-DDE							.867*
4,4-DDE							

This table illustrates that there are good positive correlations between β-HCH versus γ-HCH, β-HCH versus 2,4-DDE and a moderate positive correlation between β-HCH versus 2,4-DDT. There are good positive correlations between γ-HCH versus 2,4-DDT, γ-HCH versus 2,4-DDE. There is a strong positive correlation between 2,4-DDTversus 4,4-DDE and a good positive correlation 2,4-DDTversus 2,4-DDE

**Correlation is significant at the 0.01 level (2-tailed)

*Correlation is significant at the 0.05 level (2-tailed). Pearson and Spearman correlation tests were used

Table 4 Correlations among age, BMI, β-HCH, γ-HCH, 2,4-DDT, 2,4-DDE, and 4,4-DDE within BBT group

	Age	BMI	β-HCH	γ-HCH	2,4-DDT	2,4-DDE	4,4-DDE
Age		.453*	.056	.043	.132	.106	.224
BMI			.334	.331	.407*	.325	.600
β-HCH				.671**	.466*	.561**	.750
γ-HCH					.665**	.783**	.857*
2,4-DDT						.808**	.750
2,4-DDE							.607
4,4-DDE							

This table illustrates that there are positive moderate correlations between age versus BMI and BMI versus 2,4-DDT. There are moderate positive correlations between β-HCH versus 2,4-DDT, β-HCH versus 2,4-DDE and a good positive correlation between β-HCH versus γ-HCH. There are good positive correlations between γ-HCH versus 2,4-DDT, γ-HCH versus 2,4-DDE and a strong positive correlation between γ-HCH versus 4,4-DDE. There is a strong positive correlation between 2,4-DDT and 2,4-DDE

**Correlation is significant at the 0.01 level (2-tailed)

*Correlation is significant at the 0.05 level (2-tailed). Pearson and Spearman correlation tests were used

about the association between body burden of OCPs and breast cancer risk. In the present study, we demonstrated that serum levels of 2,4-DDT and 4,4-DDE may enhance the risk of breast cancer development. In exploring of OCPs in three studied groups, we found that the higher levels of 2,4-DDT and 4,4-DDE residues were accumulated in the serum of patients with MBT compared with normal subjects. Moreover, elevated serum levels of 2,4-DDT were detected in patients with BBT as compared to the control group.

In agreement with current result, He et al. found an association between p,p′-DDE and breast cancer risk. They showed the presence of p,p′-DDE in breast tissues of more than 90% breast cancer cases (He et al. 2017). In the study conducted by Mathur et al. blood OCPs, including DDT and its metabolites DDD and DDE, heptachlor, dieldrin, and HCH, were found significantly higher in the breast cancer patients than normal participants (Mathur et al. 2002). Romieu et al. indicated that serum levels of DDE are positively related to breast cancer risk and this association is more apparent among postmenopausal women. Based on their report, no association was found between serum levels of DDT and breast cancer risk (Romieu et al. 2000). Attaullah et al. (2018) reported higher serum levels of 4,4-DDE in breast cancer cases compared with controls that are consistent with our result. Taken together, the high levels of 2,4-DDT and 4,4-DDE in the serum of patients with MBT are remarkable findings, which suggest the possible involvement of OCPs in the development of breast cancer. On the other hand, high levels of serum 2,4-DDT in breast cancer patients describe the presence of this pesticide in Iran, which is consistent with a study conducted by Behrooz et al. (2012) that revealed the presence of organochlorine contaminants in the hair of Iranian pregnant women.

Based on present results, β-HCH and γ-HCH were found in the serum specimens of patients with MBT and BBT and the levels of these pesticides were not statistically significant between two groups. Furthermore, α-HCH was detected in the serum samples of the small numbers of patients with MBT. In line with current findings, Lopez and coworkers revealed no relationship between β-HCH and breast cancer risk (Lopez-Carrillo et al. 2002). Moreover, Itoh et al. reported the lack of association of breast cancer risk with the serum concentration of β-HCH in the Japanese population (Itoh et al. 2009). In contrast, Yang et al. demonstrated the higher levels of β-HCH in serum and adipose tissue of breast cancer patients with positive estrogen receptor than those with negative estrogen receptor, suggesting that OCPs can disturb endocrine pathways (Yang et al. 2015).

According to our result, no significant difference was observed in the serum concentrations of 2,4-DDE in three studied groups, and none of the participants had detectable levels of 4,4-DDT. Contrary to our results, Boada and coworkers indicated that the organochlorine pesticide mixtures,

such as aldrin, DDE, and DDD, may play a relevant role in the development of breast malignancy (Boada et al. 2012). Apart from these human studies, multiple research on animal models and cell culture supports our result regarding the involvement of OCPs in breast cancer development. Johnson et al. (2012) demonstrated p,p′-DDE exposure at concentrations relevant to human exposure in adipose tissue surrounding mammary epithelium promotes mammary tumorigenesis in mice. It is noteworthy that we also found higher concentrations of 4,4-DDE in serum samples of breast cancer patients compared with control subjects. Furthermore, Bratton et al. (2012) indicated that o,p-DDT is able to stimulate genes expression in breast cancer cells through initiating crosstalk between MAPK signaling pathways and transcriptional coactivators. Interestingly, we observed the higher serum levels of 2,4-DDT in patients with breast tumors compared with healthy individuals.

Although some studies have shown the roles of OCPs in the development of breast cancer, two meta-analysis studies in 2013 and 2014 explained that exposure to OCPs, such as DDT and DDE, could not be associated with human breast cancer risk (Ingber et al. 2013; Park et al. 2014). These contraries may be due to the delay time between exposure to pesticides and cancer diagnosis, age exposed to pesticides, the effect of susceptible populations, and combined exposure with other environmental carcinogens (Park et al. 2014).

Based on the correlation analysis in our study, the concentrations of β-HCH, γ-HCH, 2,4-DDT, 2,4-DDE, and 4,4-DDE were correlated with each other in MBT and BBT groups. This is consistent with previous reports, which suggested the presence of correlations among OCPs with each other (Lind et al. 2018; Yang et al. 2012). These correlations support the concept that the collective effects of OCPs may increase breast cancer risk and affect clinical outcomes of cancer.

In this study, we also observed a significant relationship between BMI and serum 2,4-DDT concentrations in BBT group. This finding emphasizes that OCPs levels are directly related to the fat content in view of the lipophilic nature of OCPs. In agreement with this data, a study showed a correlation between p,p-DDE, but not 2,4-DDT, and BMI in breast cancer patients (Ellsworth et al. 2018).

Generally, the present findings warrant further analysis and consideration of possible exposure routes. Because carcinogenesis is considered as a multifactorial event, it is substantial to try to clarify the role of environmental chemicals in the development of cancer.

Some limitations of our study warrant mention. Because the sampling process was demanding and time-consuming, the sample size is rather small. In our study, serum levels of OCPs were strongly correlated with each other, thus they also can be correlated with unmeasured other OCPs and environmental substances. Hence, the current findings

might not have represented the direct effect of studied OCPs in the development of breast tumors. The present study, however, enjoys a strong point including the presence of a link between exposure to OCPs and risk of breast cancer. In addition, the status of serum OCPs due to their biological persistence reflects long-term cumulative exposure to these environmental compounds in our study. Moreover, the present research is the first study that has explored the presence of serum OCPs in patients with breast cancer in Iran. Therefore, the outcome of our study opens a new avenue for understanding the possible causes of the rapid growth of breast cancer in Iran.

Conclusions

The results of the present study support the hypothesis that exposure to OCPs, particularly 2,4-DDT and 4,4-DDE, may be associated with breast cancer risk. We demonstrated that exposure to 2,4-DDT may increase the risk of benign breast diseases. Because significant correlations were found among the different OCPs in the serum samples of MBT and BBT groups, it could be concluded that total body burden of OCPs may mediate the involvement of these pesticides in development of different malignancies. Moreover, the presence of a correlation between BMI and the levels of 2,4-DDT obviously suggests that obese women may bear higher levels of OCPs compared with nonobese in the same condition.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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