



Research article

Association of plasma levels of lipid and polychlorinated biphenyls in Iranian adult

Omid Aminian^a, Zeinab Moinfar^b, Sahar Eftekhari^{a,*}, André Esser^c, Thomas Schettgen^c, Michael Felten^c, Andrea Kaifie^c, Thomas Kraus^c^a Center for Research on Occupational Diseases, Tehran University of Medical Sciences (TUMS), Tehran, Iran^b Community and Preventive Medicine Department, Tehran University of Medical Sciences (TUMS), Tehran, Iran^c Institute for Occupational, Social and Environmental Medicine University Hospital Aachen, RWTH University Aachen, Germany

ARTICLE INFO

Keywords:

Public health
Endocrinology
Biological sciences
Health sciences
Polychlorinated biphenyls
Serum lipid
Body mass index
Triglyceride
LDL
HDL

ABSTRACT

Background: Exposure to Polychlorinated biphenyls (PCBs) continues over the world through seafood consumption and indoor exposure to building materials containing PCB. This study aimed to assess the relationship between plasma level of PCB congeners and lipid profile and Body Mass Index (BMI) as well.**Methods:** The study population consisted of 181 Iranian adults. Data on BMI, plasma concentration of PCB congeners and serum level of lipid profile including Triglyceride, low-density lipoproteins and high-density lipoproteins, recruited from database of a project entitled "Occupational and environmental exposure to PCBs in Iran". Multiple linear regression analysis of associations between different quartiles of PCB congeners and various lipid fractions and BMI have been conducted.**Results:** A linear increase in average serum Triglyceride and low-density lipoproteins (LDL) levels of participants in first, second, third and fourth quartiles of some PCB congeners was obtained. Following adjustment for age, gender, diet and other variables, only the association between different quartiles of PCB 138, PCB 153, PCB 118 and PCB sum and TG remained statistically significant.**Conclusion:** The study showed a significant positive relation between plasma PCBs concentrations and serum level of TG in the study population with normal PCBs levels.

1. Introduction

Polychlorinated biphenyls (PCBs) are organic chlorine compounds which have been used over the world as dielectric fluid in electrical capacitors and transformers due to their resistance to temperature and pressure extremes [1]. PCBs congeners are identified according to the number and position of the chlorine atoms. These compounds are resistant to degeneration and their bioaccumulation in ecosystem and human tissues resulted in continued exposure, in spite of the ban of their production and usage since three decades ago [1, 2, 3]. Many studies have shown that exposure to PCBs continues over the world through seafood consumption and indoor exposure to materials containing PCB, which have been formerly used in construction of concrete buildings [4, 5, 6].

Regarding health outcomes of PCBs, a number of studies have reported that exposure to persistent, fat soluble chlorinated compounds such as PCBs, dioxins and some pesticides is related to higher level of

serum lipids [7, 8, 9, 10, 11, 12, 13]. This association between PCBs and elevated Triglyceride (TG) as well as decreased high-density lipoproteins (HDL) has been shown in different studies [8, 9, 11, 12]. There is still uncertainty about causal relationship between these two, and whether exposure to these compounds is the underlying cause of serum lipid elevation or the increased serum level of PCBs is consequence of hyperlipidemia conversely [14]. However, significant evidences from various studies on animals support the hypothesis that exposure to both mixtures of PCB congeners results in enzyme induction in liver to synthesize more lipids, causing the elevation of the levels of serum cholesterol and TG [8, 15, 16, 17, 18].

Moreover, hyperlipidemia is one of the known predisposing risk factors of cardiovascular diseases (CVDs) with a global burden of 235000 in 2015 which has increased 5.4% since 2005 [19]. Several factors including genetic, diet, lack of exercise, smoking and endocrine factors result in elevated serum lipids. Also, environmental and occupational

* Corresponding author.

E-mail address: s_eftekhari@sina.tums.ac.ir (S. Eftekhari).

exposure to certain agents have been suggested as one of the risk factors [20, 21, 22, 23, 24, 25]. Additionally, overweight and obesity are increasing worldwide and lead to an important challenge in prevention of chronic non-communicable diseases, while raised Body Mass Index (BMI) is among the five leading risk factors of CVDs in both developed and developing countries [26, 27].

Considering the continued PCBs exposure and its possible relation with elevated serum concentration of TG and LDL (low-density lipoproteins) and low concentration of HDL (High-density lipoproteins) as a major risk factor for CVDs on one hand [14], and increasing prevalence of obesity as one of the metabolic syndrome components which increases risk of type 2 diabetes on the other hand [28], this study aimed to assess the relationship between serum level of PCB congeners and lipid profile and BMI as well.

2. Material and methods

The study population consisted of 181 Iranian adults for whom complete data on plasma concentration of 21 PCB congeners, demographic information (gender, age, diet, BMI), serum level of lipid profile (including TG, LDL and HDL) and working type was available. The study population age ranged from 17 to 70 years. This sample recruited from database of a project entitled "Occupational and environmental exposure to PCBs in Iran – a multicenter study", which is described elsewhere [29]. The studied subjects were recruited from workers of different occupational groups located in Tehran and surrounding regions including electrical power distribution company (N = 30, mean age: 36.80 ± 7.74), manufacturers of paint and pesticides (N = 19, mean age: 41.76 ± 6.94 and N = 21, mean age: 35.38 ± 8.76 respectively), turning and casting operations (N = 20, mean age: 39.70 ± 9.30), polymer plastic manufacturing (N = 20, mean age: 29.90 ± 5.57), professional driving (N = 27, mean age: 42.52 ± 9.70) and office work (N = 14, mean age: 38.01 ± 11.57), as well as a number of housewives living in the same area (N = 30, mean age: 37.95 ± 11.17). Housewives that spent most of their live at home, probably had high indoor air exposure to some background pollutants unrelated to occupational exposures as the other groups.

A single interviewer collected data on their demographic information, diet (fat rich habit and see food diet), occupational history and measured patients' heights and weights using standardized devices. The dietary assessment consisted of a last two-week recalls on food frequency questionnaire. The semi-quantitative food frequency questionnaire included 50 food items and for each food item, the interviewer asked about the type of consumption frequency (daily, weekly, monthly or never). The questionnaire was developed considering Iranian population's eating habits.

Height was measured without shoes with a standard stadiometer. The vertical and horizontal placement of the stadiometer was checked using the standardized carpenters' level. Seca medical column scale placed on hard floor. Carpenters level was used to verify that the floor and the scale are in horizontal position. Calibration of the device was done at the beginning of the examination days, using the standardized weights. BMI was calculated as $\text{weight}/\text{height}^2$ (kg/m^2).

All serum samples (obtained from approximately 5 ml venous blood) were sent to one standard laboratory in Tehran for lipid profile measurement. Plasma samples transferred with DHL mailing service to the laboratory of the Institute of Occupational and Social Medicine at RWTH Aachen University in Germany for determining nine non-dioxin-like (28, 52, 66, 74, 99, 101, 138, 153, 180) as well as twelve dioxin-like (77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, 189) PCB-congeners, using gas chromatography coupled with mass spectrometry [29].

Congeners with less than 10% of measurements values above the Lower limit Of Detection (LOD, $0.005 \mu\text{g}/\text{L}$) were excluded and further investigations were applied for PCB 138, 153, 180 and 118. In this study, the cut-off for LOD was considered $0.005 \mu\text{g}/\text{L}$, as LOD = $0.01 \mu\text{g}/\text{l}$ plasma was not reached.

2.1. Statistical tests

IBM SPSS Statistics 22 package was used for statistical analysis. Variables distributions normality was checked with the *Kolmogorov-Smirnov test*. P value less than 0.05 was considered significant for all statistical tests.

Cut-off points of 25th, 50th and 75th percentile values were applied to categorize the serum concentrations of PCBs. If more than 25% of the values of congeners were below LOD, all these values were added to the first quartile and the rest values were divided into three equal parts for building quartiles 2–4 [30]. To assess linear dose–response relationship association, P for trend was estimated.

Also, multiple linear regression modelling was used to evaluate association between outcome variables (serum concentration of total cholesterol, HDL cholesterol, LDL cholesterol, TG) and serum concentrations of various PCB congeners. Each regression model was adjusted for confounders (age, sex, body mass index, diet, and working type).

2.2. Ethical considerations

All participants of the study signed the written informed consents. Participation was voluntary and confidentiality was guaranteed through anonymous data gathering. Indeed, this study has been approved by the Ethics Committee at the Research Division of the Ministry of Health in Tehran (Project number: 93-03-103-26804-144653).

3. Results

Excluding participants that were on any lipid lowering medication which might have obscured the results, 181 out of 200 participants were included in the study. Table 1 shows the demographic characteristics and main metabolic values of the examined participants. The study population ranged from 17 to 70 years in age (mean 37.27 , SD: ± 10.03 years), and 78.5 percent of them were male. According to eating habits of the participants, low seafood and low fat rich diet were prominent (65.2% and 56.9% respectively). In addition, 38.7% of them had sedentary working types. Near 60% of the study population had BMI greater than $25 \text{ kg}/\text{m}^2$ and were categorized in overweight and obese groups. The average plasma TG and LDL cholesterol were $152.02 \pm 94.45 \text{ mg}/\text{dl}$ and $108.50 \pm 29.33 \text{ mg}/\text{dl}$ respectively. The male participants had mean HDL level of $45.15 \pm 8.58 \text{ mg}/\text{dl}$ and the women had mean HDL level of $54.91 \pm 11.57 \text{ mg}/\text{dl}$.

Table 2 shows a linear increase in average serum TG level of participants in first, second, third and fourth quartiles of PCB138, PCB153, PCB180, PCB sum and PCB 118 (P trend <0.001). The highest increase of TG level reached in fourth quartile for all of PCB congeners. According to the results of Table 2, LDL cholesterol level showed a linear increase from 1st to 4th quartiles of PCB138, PCB153, PCB180 and PCB sum, which was statistically significant for PCB 138 and PCB sum (p trend 0.03 and 0.04 respectively). Additionally, the highest increase of HDL cholesterol level was observed in the second quartile of PCB138, PCB180, PCB 118, PCB sum and the first quartile of PCB153. Furthermore, a linear increase in the mean BMI of participants along with the first, second, third and fourth quartiles of PCB138, PCB153 and PCB sum (p trend 0.02, 0.10 and 0.05 respectively) was observed.

Table 3 shows the linear regression model for the relationship between PCB quartiles and lipid profile and BMI. Following adjustment for age, gender, BMI, fat rich diet and working type (active or sedentary), only the association between different quartiles of PCB 138, PCB 153, PCB 118 and PCB sum and TG remained statistically significant.

4. Discussion

In this study, TG level of participants in different quartiles of PCB138, PCB153, PCB sum and PCB118 showed a statistically significant linear increase. This finding is consistent with conclusion of some previous

Table 1. Demographic characteristics and metabolic values of the study population (N = 181).

| Characteristic | Grouping | Number (%) |
|--------------------------|-----------|--------------------|
| Gender | Male | 142 (78.5) |
| | Female | 39 (21.5) |
| Fat rich diet | High | 78 (43.1) |
| | Low | 103 (56.9) |
| Sea food diet | High | 63 (34.8) |
| | Low | 118 (65.2) |
| Working Type | Sedentary | 70 (38.7) |
| | Active | 111 (61.3) |
| Variable | Mean | Standard Deviation |
| Age | 37.27 | 10.03 |
| Triglycerides | 152.02 | 94.45 |
| LDL Cholesterol | 108.50 | 29.33 |
| HDL Cholesterol (Male) | 45.15 | 8.58 |
| HDL Cholesterol (Female) | 54.91 | 11.57 |
| BMI | 26.29 | 3.86 |

studies [7, 8, 9, 13, 31]. A study on residents of Anniston found that PCB concentrations (including PCB 138, PCB 153 and PCB 180) are positively correlated with total cholesterol and TG levels, but not with LDL, HDL levels, while the strongest associations were for three, four or at least eight substituted chlorines PCBs [14]. However, in this study, we excluded results of these PCB congeners from further investigations analysis since less than 10% of measurements values reached the LOD. Another study on US population showed an inverted U shaped association of PCB 138, PCB 153, PCB 170, PCB 180 and PCB 187 with metabolic syndrome, waist circumference and TG, which was most strongly for TG [13]. However, Lee et al did not demonstrate linear increase of TG levels in different quartiles of PCB 138, PCB 153, PCB 180 and PCB 118 in their study. Whilst, they showed HDL decrease from first to second quartile and increase from second to fourth quartile [31]. Likewise, in our study, a linear decrease was not seen in HDL levels. Although the

participants in first and second quartile groups of PCB 138, PCB 153, PCB 180, PCB sum and PCB 118 had higher HDL level comparing to the third and fourth quartiles.

In the current study, we observed a linear increase in mean BMI from 1st to 4th quartiles of PCB138, and PCB sum, but the significance of this association disappeared after adjustment for age, sex, diet and type of working (sedentary or active). This finding was aligned with a previous study which found no statistically significant association between BMI and serum concentration of PCB138, PCB 153, PCB 180 and PCB sum [32]. While Lee et al. reported the highest increase of BMI in the 2nd quartile of PCB 153 and PCB 180, in the current study the individuals in the 3rd and 4th quartiles of PCB 153 and PCB 180 had higher but not statistically significant BMI mean [31].

Although recent epidemiologic data suggested positive association between PCB concentration and type 2 diabetes and metabolic syndrome [13, 33, 34, 35], many studies have shown a negative correlation between BMI (as a key factor in metabolic syndrome and as a known risk factor for development of insulin resistance and diabetes) and PCB concentration [3, 36]. A Belgian cohort study showed as BMI increased, PCB 153, PCB 170, PCB 180 and PCB sum level decreased significantly. These findings might be explained by the fact that PCBs as lipophilic compounds are preferably stored in adipose tissue, and consequently appear with lower levels in serum [2]. This suggests that measurement of serum concentration of PCBs may not provide accurate estimate of body burden of these compounds [37].

Globally, CVD is one of the leading causes of death [19]. Several elements including type 2 diabetes, hypertension, obesity, sedentary life style are CVD's known risk factors [38] as well as Environmental pollutants such as PCB that can contribute to developing CVD directly or indirectly via promotion of associated risk factors. Therefore, identifying and assessment of these modifiable factors is imperious [14]. According to some previous studies, the only common property of PCB congeners that predicts dyslipidemia is their long persistency in body that increases by number of chlorines. In addition, it is stated that long time exposure to low dose of PCBs is required to disturb the lipid metabolism by POPs [31,

Table 2. Mean and Standard deviation of TG, LDL, HDL and BMI according to quartiles of PCBs.

| PCB Congers | Quartiles | Number | Mean (SD) TG | Mean (SD) LDL | Mean (SD) HDL | Mean (SD) BMI |
|-------------|----------------|---------|-----------------|----------------|---------------|---------------|
| PCB 138 | Quartile 1 | N = 53 | 111.15 (51.43) | 103.54 (33.20) | 47.98 (9.68) | 25.39 (3.53) |
| | Quartile 2 | N = 40 | 128.95 (41.54) | 104.84 (25.18) | 50.66 (10.92) | 26.26 (3.99) |
| | Quartile 3 | N = 45 | 161.24 (88.25) | 109.91 (26.70) | 44.79 (7.36) | 26.31 (4.46) |
| | Quartile 4 | N = 43 | 213.67 (135.78) | 116.10 (29.29) | 45.90 (11.62) | 27.40 (3.23) |
| | <i>P trend</i> | | < 0.001 | 0.03 | 0.07 | 0.02 |
| PCB 153 | Quartile 1 | N = 45 | 108.16 (47.02) | 104.38 (35.25) | 49.02 (11.09) | 25.69 (3.57) |
| | Quartile 2 | N = 48 | 148.15 (79.84) | 106.23 (24.02) | 47.46 (9.71) | 26.06 (3.93) |
| | Quartile 3 | N = 46 | 141.50 (64.16) | 108.50 (28.77) | 46.73 (8.87) | 26.44 (4.61) |
| | Quartile 4 | N = 42 | 214.88 (136.38) | 115.02 (27.75) | 45.40 (10.46) | 27.01 (3.11) |
| | <i>P trend</i> | | < 0.001 | 0.10 | 0.10 | 0.10 |
| PCB 180 | Quartile 1 | N = 55 | 122.29 (70.04) | 104.71 (33.12) | 46.69 (7.96) | 25.74 (3.45) |
| | Quartile 2 | N = 36 | 128.09 (44.97) | 105.46 (26.22) | 52.21 (11.34) | 25.54 (4.15) |
| | Quartile 3 | N = 48 | 166.94 (115.96) | 107.33 (29.64) | 45.33 (10.79) | 26.98 (4.26) |
| | Quartile 4 | N = 42 | 193.86 (108.00) | 116.56 (25.16) | 46.32 (9.87) | 26.85 (3.53) |
| | <i>P trend</i> | | < 0.001 | 0.06 | 0.23 | 0.06 |
| PCB Sum | Quartile 1 | N = 46 | 108.02 (49.18) | 102.76 (33.93) | 46.88 (8.55) | 25.41 (3.52) |
| | Quartile 2 | N = 46 | 147.36 (73.85) | 106.95 (26.22) | 51.55 (11.79) | 26.13 (4.12) |
| | Quartile 3 | N = 47 | 160.36 (115.25) | 108.44 (28.86) | 44.33 (7.63) | 26.69 (4.32) |
| | Quartile 4 | N = 42 | 195.88 (106.25) | 116.05 (26.83) | 46.47 (11.04) | 26.96 (3.26) |
| | <i>P trend</i> | | < 0.001 | 0.04 | 0.10 | 0.05 |
| PCB 118 | Quartile 1 | N = 135 | 137.08 (76.37) | 108.29 (28.32) | 47.78 (9.84) | 25.80 (3.90) |
| | Quartile 2 | N = 15 | 172.14 (60.50) | 114.08 (33.80) | 48.46 (12.45) | 27.34 (3.73) |
| | Quartile 3 | N = 17 | 176.18 (80.71) | 103.06 (31.13) | 43.37 (10.39) | 28.13 (3.58) |
| | Quartile 4 | N = 14 | 246.64 (194.60) | 111.92 (33.92) | 45.23 (9.00) | 27.58 (2.93) |
| | <i>P trend</i> | | 0. < 0.001 | 0.99 | 0.18 | 0.08 |

Table 3. Results of multiple linear regression analysis of associations between different quartiles of PCB congeners and various lipid fractions and BMI (n = 181).

| Variable in Model | TG ^a | | LDL ^a | | HDL ^b | | BMI ^c | |
|-------------------|-----------------|---------|------------------|---------|------------------|---------|------------------|---------|
| | B | P value | B | P value | B | P value | B | P value |
| PCB 138 quartiles | 44.98 | 0.001* | 3.21 | 0.50 | -2.01 | 0.17 | 0.64 | 0.27 |
| PCB 153 quartiles | 30.14 | 0.04* | 1.98 | 0.71 | -1.27 | 0.43 | -0.41 | 0.53 |
| PCB 180 quartiles | 20.64 | 0.09 | 0.02 | 0.10 | 0.12 | 0.93 | 0.04 | 0.94 |
| PCB Sum quartiles | 65.82 | 0.006* | 1.78 | 0.84 | 3.32 | 0.22 | -0.02 | 0.99 |
| PCB 118 quartiles | 20.10 | 0.005* | 2.45 | 0.36 | -1.22 | 0.14 | 0.62 | 0.053 |
| Model R square | 0.31 | | 0.06 | | 0.25 | | 0.13 | |

*Statistically significant relationship ($p < 0.05$).

^a TG & LDL adjusted for Age, Gender, BMI, Fat rich diet, Working Type (Active or Sedentary).

^b HDL adjusted for Age, Gender, BMI, Fat rich diet, Working Type (Active or Sedentary) and Seafood diet.

^c BMI adjusted for Age, Gender, Fat rich diet, Working Type (Active or Sedentary).

39]. Iranian population, even those who are employed by high-risk jobs, have relatively low level of PCBs [29] and this provides further support to this hypothesis.

Efforts to prevent CVD have prominently focused on correcting dyslipidemia, because it is modifiable by life style changes and drug therapies [40, 41]. In addition, it is important to find the methods of minimizing the toxicity of environmental pollutants such as PCBs [37]. According to recent studies, healthy life style and a diet rich in antioxidants can be helpful in reducing toxicity of PCB [42, 43, 44].

4.1. Strengths and weaknesses

Selecting the study population from different occupational groups with a wide range of assumed PCB-exposure risks was the major strength of the current study. This led to reduction of selection bias compared to some previous studies on PCB only assessing subjects with known high exposures to various pollutants in occupational settings. Moreover, we excluded individuals on lipid lowering medication and adjusted results for the important confounders.

However, we performed a single measurement of PCBs level and the cross sectional design of the study does not support causality assessment, while small sample size may limit the power of the study as well. The other limitation of the study is that dioxin like PCB congeners except for PCB 118 could only be detected in a small number of the studied population and were excluded from further investigations analysis. Furthermore, none of the low chlorinated PCBs in our study group, had more than 10% of measurements serum values laid above the LOD and we were not able to investigate their effect on lipid profile and BMI.

5. Conclusion

The study showed a significant positive relation between PCBs levels and serum TG in the study population with normal PCBs levels.

Plasma concentration of PCB congeners were significantly associated with elevated levels of TG but not LDL and HDL after adjustment for age, sex and BMI. This finding is consistent with the hypothesis that higher levels of POPs resulted in elevation of serum lipids as one known risk factor of cardiovascular diseases.

Declarations

Author contribution statement

O. Aminian and T.K raus: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

Z. Moinfar, A. Esser and M. Felten: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

S. Eftekhari: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

T. Schettgen: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

A. Kaifie: Analyzed and interpreted the data; Wrote the paper.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

- [1] W.H. Organization, Health Risks of Persistent Organic Pollutants from Long-Range Transboundary Air Pollution, 2003.
- [2] E. Dirinck, P.G. Jorens, A. Covaci, T. Geens, L. Roosens, H. Neels, et al., Obesity and persistent organic pollutants: possible obesogenic effect of organochlorine pesticides and polychlorinated biphenyls, *Obesity* 19 (4) (2011) 709–714.
- [3] A. Agudo, F. Goni, A. Exxeandia, A. Vives, E. Millán, R. López, et al., Polychlorinated biphenyls in Spanish adults: determinants of serum concentrations, *Environ. Res.* 109 (5) (2009) 620–628.
- [4] J. Xue, S.V. Liu, V.G. Zartarian, A.M. Geller, B.D. Schultz, Analysis of NHANES measured blood PCBs in the general US population and application of SHEDS model to identify key exposure factors, *J. Expo. Sci. Environ. Epidemiol.* 24 (6) (2014) 615.
- [5] H.W. Meyer, M. Frederiksen, T. Göen, N.E. Ebbenhøj, L. Gunnarsen, C. Brauer, et al., Plasma polychlorinated biphenyls in residents of 91 PCB-contaminated and 108 non-contaminated dwellings—an exposure study, *Int. J. Hyg Environ. Health* 216 (6) (2013) 755–762.
- [6] T. Schettgen, A. Alt, D. Preim, D. Keller, T. Kraus, Biological monitoring of indoor-exposure to dioxin-like and non-dioxin-like polychlorinated biphenyls (PCB) in a public building, *Toxicol. Lett.* 213 (1) (2012) 116–121.
- [7] J.R.E.L. Baker, P.J. Landrigan, C.J. Glueck, M.M. Zack JR, J.A. Liddle, V.W. Burse, et al., Metabolic consequences of exposure to polychlorinated biphenyls (PCB) in sewage sludge, *Am. J. Epidemiol.* 112 (4) (1980) 553–563.
- [8] F.P. Bell, F. Iverson, D. Arnold, T.J. Vidmar, Long-term effects of Aroclor 1254 (PCBs) on plasma lipid and carnitine concentrations in rhesus monkey, *Toxicology* 89 (2) (1994) 139–153.
- [9] K.H. Chase, O. Wong, D. Thomas, B. Berney, R.K. Simon, Clinical and metabolic abnormalities associated with occupational exposure to polychlorinated biphenyls (PCBs), *J. Occup. Med.* 24 (2) (1982) 109–114, official publication of the Industrial Medical Association.
- [10] J. Martin, Lipid abnormalities in workers exposed to dioxin, *Occup. Environ. Med.* 41 (2) (1984) 254–256.
- [11] P.A. Stehr-Green, E. Welty, G. Steele, K. Steinberg, Evaluation of potential health effects associated with serum polychlorinated biphenyl levels, *Environ. Health Perspect.* 70 (1986) 255.

- [12] S. Tokunaga, K. Kataoka, A longitudinal analysis on the association of serum lipids and lipoproteins concentrations with blood polychlorinated biphenyls level in chronic "Yusho" patients, *Fukuoka Acta Med.* 94 (5; ISSU 980) (2003) 32–39.
- [13] D.-H. Lee, I.-K. Lee, M. Porta, M. Steffes, D. Jacobs, Relationship between serum concentrations of persistent organic pollutants and the prevalence of metabolic syndrome among non-diabetic adults: results from the National Health and Nutrition Examination Survey 1999–2002, *Diabetologia* 50 (9) (2007) 1841–1851.
- [14] Z. Aminov, R.F. Haase, M. Pavuk, D.O. Carpenter, Analysis of the effects of exposure to polychlorinated biphenyls and chlorinated pesticides on serum lipid levels in residents of Anniston, Alabama, *Environ. Health* 12 (1) (2013) 108.
- [15] K. Imstilp, L. Hansen, PCB profiles in mouse skin biopsies and fat from an environmental mixture, *Environ. Toxicol. Pharmacol.* 19 (1) (2005) 71–84.
- [16] M. Boll*, L. Weber, B. Messner, A. Stampfl, Polychlorinated biphenyls affect the activities of gluconeogenic and lipogenic enzymes in rat liver: is there an interference with regulatory hormone actions? *Xenobiotica* 28 (5) (1998) 479–492.
- [17] H. Mochizuki, H. Oda, H. Yokogoshi, Dietary taurine alters ascorbic acid metabolism in rats fed diets containing polychlorinated biphenyls, *J. Nutr.* 130 (4) (2000) 873–876.
- [18] H. Oda, H. Fukui, Y. Hitomi, A. Yoshida, Alteration of serum lipoprotein metabolism by polychlorinated biphenyls and methionine in rats fed a soybean protein diet, *J. Nutr.* 121 (7) (1991) 925–933.
- [19] M.H. Forouzanfar, A. Afshin, L.T. Alexander, H.R. Anderson, Z.A. Bhutta, S. Biryukov, et al., Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015, *Lancet* 388 (10053) (2016) 1659–1724.
- [20] A. Basu, S. Pal, S. Saha, R. Bandyopadhyay, S. Mukherjee, P. Sarkar, Risk factor analysis in ischaemic stroke: a hospital-based study, *J. Indian Med. Assoc.* 103 (11) (2005) 586–588.
- [21] J.N. Cohn, W. Colucci, Cardiovascular effects of aldosterone and post-acute myocardial infarction pathophysiology, *Am. J. Cardiol.* 97 (10) (2006) 4–12.
- [22] M. Kratz, *Dietary Cholesterol, Atherosclerosis and Coronary Heart Disease. Atherosclerosis: Diet and Drugs*, Springer, 2005, pp. 195–213.
- [23] P. Poirier, T.D. Giles, G.A. Bray, Y. Hong, J.S. Stern, F.X. Pi-Sunyer, et al., Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American heart association scientific statement on obesity and heart disease from the obesity committee of the council on nutrition, physical activity, and metabolism, *Circulation* 113 (6) (2006) 898–918.
- [24] T.P. Dalton, J.K. Kerzee, B. Wang, M. Miller, M.Z. Dieter, J.N. Lorenz, et al., Dioxin exposure is an environmental risk factor for ischemic heart disease, *Cardiovasc. Toxicol.* 1 (4) (2001) 285–298.
- [25] A. König, C. Bouzan, J.T. Cohen, W.E. Connor, P.M. Kris-Etherton, G.M. Gray, et al., A quantitative analysis of fish consumption and coronary heart disease mortality, *Am. J. Prev. Med.* 29 (4) (2005) 335–346.
- [26] P.T. James, N. Rigby, R. Leach, I.O.T. Force, The obesity epidemic, metabolic syndrome and future prevention strategies, *Eur. J. Cardiovasc. Prev. Rehabil.* 11 (1) (2004) 3–8.
- [27] L.F. Van Gaal, I.L. Mertens, E. Christophe, Mechanisms linking obesity with cardiovascular disease, *Nature* 444 (7121) (2006) 875.
- [28] A. Adler, Obesity and target organ damage: diabetes, *Int. J. Obes.* 26 (S4) (2002) S11.
- [29] S. Eftekhari, O. Aminian, Z. Moynfar, T. Schettgen, A. Kaifie, M. Felten, et al., Association of plasma PCB levels and HbA1c concentration in Iran, *J. Occup. Med. Toxicol.* 13 (1) (2018) 18.
- [30] A. Esser, T. Schettgen, M. Gube, A. Koch, T. Kraus, Association between polychlorinated biphenyls and diabetes mellitus in the German HELPCB cohort, *Int. J. Hyg Environ. Health* 219 (6) (2016) 557–565.
- [31] D.-H. Lee, M.W. Steffes, A. Sjödin, R.S. Jones, L.L. Needham, D.R. Jacobs Jr., Low dose organochlorine pesticides and polychlorinated biphenyls predict obesity, dyslipidemia, and insulin resistance among people free of diabetes, *PLoS One* 6 (1) (2011), e15977.
- [32] J. Arrebola, M. Cuellar, E. Claire, M. Quevedo, S. Antelo, E. Mutch, et al., Concentrations of organochlorine pesticides and polychlorinated biphenyls in human serum and adipose tissue from Bolivia, *Environ. Res.* 112 (2012) 40–47.
- [33] Y.-M. Lee, K.-S. Kim, S.-A. Kim, N.-S. Hong, S.-J. Lee, D.-H. Lee, Prospective associations between persistent organic pollutants and metabolic syndrome: a nested case–control study, *Sci. Total Environ.* 496 (2014) 219–225.
- [34] D.-H. Lee, I.-K. Lee, K. Song, M. Steffes, W. Toscano, B.A. Baker, et al., A strong dose-response relation between serum concentrations of persistent organic pollutants and diabetes: results from the National Health and Examination Survey 1999–2002, *Diabetes Care* 29 (7) (2006) 1638–1644.
- [35] T. Tanaka, A. Morita, M. Kato, T. Hirai, T. Mizoue, Y. Terauchi, et al., Congener-specific polychlorinated biphenyls and the prevalence of diabetes in the saku control obesity program (SCOP), *Endocr. J.* 58 (7) (2011) 589–596.
- [36] M.S. Wolff, J.A. Britton, S.L. Teitelbaum, S. Eng, E. Deych, K. Ireland, et al., Improving organochlorine biomarker models for cancer research, *Cancer Epidemiol. Prev. Biomark.* 14 (9) (2005) 2224–2236.
- [37] J.T. Perkins, M.C. Petriello, B.J. Newsome, B. Hennig, Polychlorinated biphenyls and links to cardiovascular disease, *Environ. Sci. Pollut. Control Ser.* 23 (3) (2016) 2160–2172.
- [38] A. Alwan, *Global Status Report on Noncommunicable Diseases 2010*, World Health Organization, 2011.
- [39] M.C.C. López, Determination of potentially bioaccumulating complex mixtures of organochlorine compounds in wastewater: a review, *Environ. Int.* 28 (8) (2003) 751–759.
- [40] M.D. Huffman, D.M. Lloyd-Jones, H. Ning, D.R. Labarthe, M.G. Castillo, M. O'flaherty, et al., Quantifying options for reducing coronary heart disease mortality by 2020, *Circulation* 112 (2013), 000769. CIRCULATIONAHA.
- [41] S.S. Martin, M.J. Blaha, R. Blankstein, A. Agatston, J.J. Rivera, S.S. Virani, et al., Dyslipidemia, coronary artery calcium, and incident atherosclerotic cardiovascular Disease: Clinical perspective: implications for statin therapy from the multi-ethnic study of atherosclerosis, *Circulation* 129 (1) (2014) 77–86.
- [42] N.A. Baker, V. English, M. Sunkara, A.J. Morris, K.J. Pearson, L.A. Cassis, Resveratrol protects against polychlorinated biphenyl-mediated impairment of glucose homeostasis in adipocytes, *J. Nutr. Biochem.* 24 (12) (2013) 2168–2174.
- [43] B.J. Newsome, M.C. Petriello, S.G. Han, M.O. Murphy, K.E. Eske, M. Sunkara, et al., Green tea diet decreases PCB 126-induced oxidative stress in mice by up-regulating antioxidant enzymes, *J. Nutr. Biochem.* 25 (2) (2014) 126–135.
- [44] M.C. Petriello, B. Newsome, B. Hennig, Influence of nutrition in PCB-induced vascular inflammation, *Environ. Sci. Pollut. Control Ser.* 21 (10) (2014) 6410–6418.