Biochemistry examinations and health disorder evaluation of Taiwanese living near incinerators and with low serum PCDD/Fs levels

Hsiu-Ling Chen, Huey-Jen Su, Yue-Liang Guo, Pao-Chi Liao, Chung-Feng Hung, Ching-Chang Lee

Abstract

The main objective of this study was to establish background levels of serum PCDD/Fs and biochemistry of residents living near municipal waste incinerators (MWIs) which had been operating between 1 and 8 years, and also to examine the association between the serum PCDD/Fs levels and health outcomes of interest. Information on medical history, lifestyle, and dietary habits was obtained by questionnaire interview. Significantly elevated levels of glucose and blood urea nitrogen (BUN) were found in those with low to high serum PCDD/Fs levels (p<0.05), and PCDD/Fs levels were found to be positively associated with glucose levels, and marginally with GGT levels even after adjusting for age, sex, BMI and smoking status. Although no conclusive findings on health disorder were associated with the accumulation of serum PCDD/Fs in our study participants, we suggest that the current biochemistry examinations only reflect partially the physiological change in glucose modulation and liver function. However, the low serum PCDD/Fs level does not seem to be sufficient in eliciting pathological process for diabetes or liver-related diseases. The findings suggest that the human body’s biochemistry functions such as liver and glucose modulation were affected by PCDD/Fs exposure at even these low serum PCDD/Fs levels found in the general population. Other biochemical functions therefore should be further analyzed, especially for hormone-related and immune functions.

Keywords: PCDD/Fs; Dioxin; Incinerator; Glucose; GGT; Biochemistry examination

1. Introduction

Rich information on the toxic effects resulting from exposure to polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) has become available, including immune deficiency, liver damage, human carcinogenesis, and enhanced neuromotor maturation of children (Becher and Flesch-Janys, 1998; Eskenazi and Kimmel, 1995; Ilsem et al., 1996; McGregor et al.,...
A national health assessment (Kitamura et al., 2000) for workers with highly PCDF-contaminated municipal waste incinerators (MWIs) in Japan reported significantly positive correlations between PCDF levels and GGT, total protein, uric acid, and calcium, but these correlations were no longer valid after adjustment for age, smoking status, and alcohol drinking. Odds ratios for a history of hyperlipidemia or allergy also significantly increased. Another study (Pelclova et al., 2001) reported the results of examinations for biochemical, neuropsychological, and neurological abnormalities in 13 workers following exposure to 2,3,7,8-TCDD during 1974–1996 at a herbicide production plant. A positive correlation was found between plasma levels of 2,3,7,8-TCDD in 1996 and levels of cholesterol and plasma lipid that had existed since 1974. A survey (Hoffman et al., 1986) showed no consistent variations in medical history, physical examination, serum and urinary chemistry studies, and neurological tests between groups living in 2,3,7,8-TCDD contaminated areas and unexposed groups. Another study (Michalek et al., 2001) also showed that mean corpuscular volume was slightly (1%) higher and platelet count was 4% higher in the highest TCDD levels in veterans of the U.S. Air Force than those sprayed Agent Orange in Vietnam. On the contrary, Webb et al. (1989) reported no pattern of clinical abnormalities related to TCDD levels of 41 persons with a history of TCDD exposure.

Though correlations had been found at medical histories and laboratory tests from a herbicide production plant between human exposure to 2,3,7,8-TCDD and liver function, lipid metabolism, immune system function, and thyroid function (Pelclova et al., 2001), there was still no distinct association between this exposure and the above mentioned specific health disorders from other studies (Hoffman et al., 1986; Webb et al., 1989). In addition, most studies were focused on occupational exposure with higher PCDD/Fs concentration, and there was only limited information at the general populations with lower PCDD/Fs levels.

Since Taiwan government set and enforced the strict PCDD/Fs emission standard at 0.1 pg I-TEQ/Nm³, the residents living near these incinerators were assumed to have the lower PCDD/Fs intakes from ambient exposure than workers with high occupational exposure in other studies. PCDD/Fs, however, are highly persistent in human, and several of those congeners are known to induce a wide range of adverse effects. In Taiwan, 19 MWIs have been operated for 1 to 8 years, and the Taiwan EPA (The Taiwan Environmental Protection Agency) conducted a long-term program to periodically monitor serum PCDD/Fs levels and evaluate the health disorders of the general population living in the vicinity of 19 MWIs since 1999. Up to now, the monitoring of serum PCDD/Fs levels and health disorders of the residents near 12 MWIs in Taiwan had been completed.

Therefore, the main objective of this study was to build up the background levels of serum PCDD/Fs and biochemistry of residents living near MWIs, and also to examine the association between the health outcomes and serum PCDD/Fs levels.

2. Materials and methods

2.1. Participant selection

Twelve MWIs in Taiwan were surveyed at this study. In the beginning of this study, 2 MWIs had been operating for about 7–8 years, and 10 for less than 3 years. Volunteers of 1129 living near the 12 MWIs were recruited between 2000 and 2001. At first, the number of subject in each area was determined based on age, sex ratio, and the population distribution of each administrative district. To improve the participation rate, the heads of the districts were asked to invite the residents to participate this study. Participants had to sign and confirm that they have lived within 5 km of one of the 12 MWIs for at least 5 years; they also required to have no occupational exposures to PCDD/Fs, such as having worked in MWIs, pesticide manufacturing factory, ferrous and nonferrous metal smelting plants and others before this study (Chen et al., 2003). At the end, 1034 participants completed all examinations (1034 from 1129 participants who had signed the consensual letters, 95.58%), and the other 95 selected subjects were not eligible for this study because they were unable to provide 20 mL serum for PCDD/Fs analysis or they did not complete any one of the questionnaire interviews. The examinations included health and dietary questionnaires, a blood biochemistry test, and a serum PCDD/Fs analysis. All selected participants were grouped by age: group 1, 18 to 35 years old; group 2, 36 to 55 years old; and group 3, 56 to 65 years old. To prevent unexpected incidents during the blood drawing, only those with no history of cardiac diseases or angiopathy were selected, and only those who agreed to provide blood sample at least 60 mL were included. The serum from each blood sample was obtained by centrifugation and stored at −70 °C until analysis.
2.2. Serum cleanups and HRGC/HRMS analysis of PCDDs and PCDFs

The serum sample enrichment and clean-up procedures used in this study were similar to those reported by Chang et al. (1993). Each serum sample was spiked with a mixture containing fifteen $^{13}$C$_{12}$-labeled PCDD and PCDF standards as defined in USEPA Method 1613. The amount of each spiked congener was 0.5 ng, except that $^{13}$C$_{12}$-OCDD which was 1.0 ng. Serum samples were enriched and fractionated by C18, SCX (SPE Cartridges—Silica Ion Exchange purchased from Varian Inc.), silica, and Florisil cartridges before HRGC/HRMS analysis. Each analytical run consisted of a method blank, a quality control sample, and seven unknown samples. The quantification of PCDD/Fs was performed with high-resolution gas chromatography/high-resolution mass spectrometry (Hewlett-Packard Model 6890 plus/Micromass AutoSpec Ultima EBE tri-sector mass spectrometer) with a Rtx-5MS column (60 m, 0.25 mm i.d., 0.25 μm film thickness) (Chen et al., 2003). Seventeen toxic 2,3,7,8-substituted congeners were quantified. The peaks were quantified when the criteria were met: (1) isotope ratio within ± 15% of theoretical values and (2) signal/noise ratio ≥ 2.5. Recoveries of $^{13}$C$_{12}$-labeled PCDD/Fs internal standards in samples ranged 30–120%. The detection limit of 2,3,7,8-TCDD for the analysis was 0.03 pg/column-injection or 0.007 pg/mL-serum. Quality assurance and quality control protocols conforming to those defined in USEPA Method 1613 were established in our laboratory to ensure positive identification and the quality of the measurements. All PCDD/Fs levels were adjusted to the lipid content analyzed from the corresponding samples.

2.3. Interviewer-administered questionnaire

Information obtained from the questionnaire including demographic characteristics (sex, age, occupational history, neighborhood geography, and others), life style (alcohol intake and tobacco usage), frequencies of dietary intakes over the previous decade, and medical histories, including physician-diagnosed high blood pressure, arrhythmia, coronary disease, skin allergy, gout, liver cirrhosis, calculus of the liver, anemia, hemicrania, diabetes, hyperthyroidism, hypothyroidism, and goiter during the past 10 years. Trained interviewers administered the questionnaires according to standard operating procedures prepared in advance.

2.4. Blood biochemistry examination

Blood biochemistry tests for glucose (GLU), total protein (TP), albumin (ALB), blood urea nitrogen (BUN), serum creatinine (CREA), uric acid (UA), cholesterol (CHOL), triglycerides (TG), glutamyl oxaloacetic transaminase (GOT), glutamyl pyruvic transaminase (GPT), $\gamma$-glutamyl transpeptidase (GGT), total bilirubin (T-BIL), and alkaline phosphatase (ALP) were analyzed in our medical center’s pathology laboratory by technicians who blind to the participants’ characteristics and their serum PCDD/Fs levels.

2.5. Statistical methods

PCDD/Fs concentrations were reported as pg I-TEQ/g lipid (international toxic equivalent concentration). The sum of the TEQ concentrations represented an equivalent toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). In addition, the body mass index (BMI, kg/m$^2$) was calculated based on height and weight of the individual. JMP commercial statistical software (SAS Institute, Inc., Cary, NC) was used for data management and statistical analysis. Standard descriptive statistics were conducted to describe the characteristics of participants. We applied Student’s $t$ test and ANOVA

<table>
<thead>
<tr>
<th>Groups</th>
<th>No. (%)</th>
<th>PCDD/Fs level*</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>525 (50.8)</td>
<td>15.8±8.3</td>
<td>0.006$^\dagger$</td>
</tr>
<tr>
<td>Female</td>
<td>509 (49.2)</td>
<td>17.6±7.8</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–35 years old</td>
<td>184 (17.7)</td>
<td>13.1±7.3</td>
<td>&lt;0.0001$^\dagger$</td>
</tr>
<tr>
<td>36–55 years old</td>
<td>572 (55.3)</td>
<td>16.8±8.0</td>
<td></td>
</tr>
<tr>
<td>&gt;55 years old</td>
<td>278 (27.0)</td>
<td>18.9±8.0</td>
<td></td>
</tr>
<tr>
<td>BMI (mean)</td>
<td></td>
<td></td>
<td>0.075</td>
</tr>
<tr>
<td>&lt;25% (&lt;20.23)</td>
<td>259</td>
<td>15.7±7.6</td>
<td></td>
</tr>
<tr>
<td>≥25%, &lt;50% (&lt;23.10)</td>
<td>258</td>
<td>17.0±8.0</td>
<td></td>
</tr>
<tr>
<td>≥50%, &lt;75% (&lt;25.37)</td>
<td>259</td>
<td>17.0±8.6</td>
<td></td>
</tr>
<tr>
<td>≥75% (&lt;29.15)</td>
<td>258</td>
<td>17.2±8.1</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td>&lt;0.0001$^\dagger$</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>385 (37.2)</td>
<td>16.7±7.9</td>
<td></td>
</tr>
<tr>
<td>Current smokers</td>
<td>303 (29.3)</td>
<td>15.1±7.6</td>
<td></td>
</tr>
<tr>
<td>Passive smokers</td>
<td>346 (33.5)</td>
<td>18.1±8.4</td>
<td></td>
</tr>
</tbody>
</table>

*pg I-TEQ/g-lipid; data are mean±standard deviation. $^\dagger$ p<0.05 (Student’s $t$ test or ANOVA test).
test to analyze the differences of PCDD/Fs levels among the different demographic groups, as well as for results of biochemistry tests among low to high serum PCDD/Fs groups. Multivariate regression models were used to estimate the associations between the PCDD, PCDF, and PCDD/Fs levels

Fig. 1. The relationship between serum PCDD/Fs level and biochemistry tests (Glucose, ALB, BUN, CREA, CHOL, T-BIL) in the 3 age groups.
and results of blood biochemistry tests and illnesses from the questionnaire interview, after adjusting for age, sex, and BMI. In addition, we used logistic regression models to estimate the adjusted odds ratios (ORs) of the serum PCDD/Fs-level-related health outcomes of residents.
3. Results

3.1. Participant characteristics

No significant difference in age, sex ratio was shown between responders and general population. The demographic characteristics and serum PCDD/Fs concentrations of the participants are presented in Table 1. These study participants represent the general population with lower PCDD/Fs exposure than the occupational groups or victims of accidental exposure to higher PCDD/Fs contamination in other studies (Michalek et al., 2001; Neubert et al., 1995; Neubert et al., 2000). Number of men to women was equal, but varied in each age group. Significantly higher concentration of PCDD/Fs was found in women than in men, and also in elder groups than those in the two younger ones. Higher levels of serum PCDD/Fs were observed in those with a BMI $\geq 21.87$ when participants were divided into 4 groups by BMI level. All participants were further divided into 3 groups by smoking status: Group 1—never smokers and reporting no passive smoke exposure; group 2—active smokers (including ex-smokers) and with possible exposures to passive smoke; group 3—passive smokers who had never been a smoker but often exposed to second-hand smoke. The levels of serum PCDD/Fs were higher in nonsmokers and passive smokers than smokers.

3.2. Serum biochemistry findings

Higher abnormal rates for glucose, blood urea nitrogen, cholesterol, and ALP were seen in subjects over 55 years old than the younger. Fig. 1 showed positive trends between PCDD/Fs levels and glucose, and cholesterol levels for subjects older than 55 years of age. Table 2 showed the distributions of biochemistry data among subjects with different serum PCDD/Fs levels. Significantly elevated levels were found in glucose and BUN levels for those with low to high serum PCDD/Fs levels ($p<0.05$). In addition, statistical differences of albumin, serum creatinine, and uric acid levels were found among subjects with different serum PCDD/Fs levels ($p<0.05$).

3.3. Relationship between serum PCDD/Fs levels and biochemistry examinations

Multivariate regression analysis was used to evaluate the association between serum biochemistry tests and serum PCDD/Fs (Table 3). In the liver function test, all participants with liver illness (cirrhosis of liver, hepatitis, calculus of liver and gall bladder) were excluded in the analysis. After adjusting for age, sex, BMI and smoking status, PCDD/Fs levels were found to be positively associated with glucose levels, and marginally with GGT levels, whereas negatively associated with ALP levels.

Table 2

Levels of serum PCDD/Fs and biochemical findings in the study population

<table>
<thead>
<tr>
<th>Serum PCDD/Fs in 4 quartile$^i$</th>
<th>GLU, mg/dl</th>
<th>TP, IU/L</th>
<th>ALB, mg/dl</th>
<th>BUN, mg/dl</th>
<th>CREA, mg/dl</th>
<th>UA, mg/dl</th>
<th>CHOL, mg/dl</th>
<th>TG, mg/dl</th>
<th>GOT, IU/L</th>
<th>GPT, IU/L</th>
<th>GGT, IU/L</th>
<th>T-BIL, mg/dl</th>
<th>ALP, IU/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&lt;$25% $N=258$</td>
<td>92.7(21.0)</td>
<td>7.4(0.9)</td>
<td>4.44(0.55)</td>
<td>14.2(3.3)</td>
<td>0.93(0.18)</td>
<td>6.5(1.7)</td>
<td>190.2(39.4)</td>
<td>136.0(133.9)</td>
<td>24.5(17.2)</td>
<td>25.9(20.3)</td>
<td>33.6(48.0)</td>
<td>0.8(0.3)</td>
<td></td>
</tr>
<tr>
<td>25–50% $N=259$</td>
<td>94.1(24.9)</td>
<td>7.3(0.8)</td>
<td>4.33(0.48)</td>
<td>15.0(4.4)</td>
<td>0.91(0.27)</td>
<td>6.2(1.7)</td>
<td>194.0(39.5)</td>
<td>134.1(128.5)</td>
<td>23.9(24.7)</td>
<td>23.1(19.6)</td>
<td>30.5(35.8)</td>
<td>0.8(0.3)</td>
<td></td>
</tr>
<tr>
<td>50–75% $N=259$</td>
<td>97.0(33.3)</td>
<td>7.2(0.6)</td>
<td>4.24(0.38)</td>
<td>15.3(3.9)</td>
<td>0.85(0.20)</td>
<td>6.1(1.7)</td>
<td>195.9(40.1)</td>
<td>117.8(90.7)</td>
<td>22.0(9.9)</td>
<td>23.8(17.8)</td>
<td>29.2(36.7)</td>
<td>0.7(0.3)</td>
<td></td>
</tr>
<tr>
<td>$&gt;$75% $N=257$</td>
<td>102.2(40.8)</td>
<td>7.6(4.3)</td>
<td>4.29(0.43)</td>
<td>15.8(3.8)</td>
<td>0.88(0.21)</td>
<td>6.2(1.8)</td>
<td>195.8(40.1)</td>
<td>129.6(111.0)</td>
<td>23.1(11.0)</td>
<td>24.4(15.0)</td>
<td>33.9(37.2)</td>
<td>0.8(0.3)</td>
<td></td>
</tr>
<tr>
<td>$p$ value</td>
<td>$\leq0.05$</td>
<td></td>
<td>$\leq0.05$</td>
<td></td>
<td>$\leq0.05$</td>
<td></td>
<td>$\leq0.05$</td>
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<td>$\leq0.05$</td>
<td></td>
<td>$\leq0.05$</td>
<td></td>
<td>$\leq0.05$</td>
</tr>
</tbody>
</table>

Bold data entries represent the significant differences or significant correlations ($p<0.05$) found.

*Data are mean (standard deviation).

$^i$1(1) $<$25%: serum PCDD/Fs level $<11.13$ pg I-TEQ/g lipid, (2) 25–50%: 11.13 $\leq$ serum PCDD/Fs level $<15.29$ pg I-TEQ/g lipid, (3) 50–75%: 15.29 $\leq$ serum PCDD/Fs level $\leq21.08$ pg -TEQ/g lipid, (4) $>$75%: serum PCDD/Fs level $>21.08$ pg I-TEQ/g lipid.
3.4. Relationship between serum PCDD/Fs levels and medical histories

Table 4 listed findings from logistic regression analysis between physicians-diagnosed illness and serum PCDD/Fs levels. The odds ratio of reporting hypertension was significantly elevated with increased PCDD/Fs levels, and only marginal elevation was seen for diabetes. However, an intriguing reverse relationship was identified for skin allergy. After adjusting for age, sex, and BMI, the trend of risk was eliminated or reduced. Finally, in order to confirm the association between physicians-diagnosed medical conditions and serum PCDD/Fs levels, the highest and lowest 10% participants based on PCDD/Fs levels were selected for further analysis. Table 5 showed a marginally significant decrease in the OR of skin allergy with increasing PCDD/Fs levels. In addition, the increased OR was found in anemia (OR = 3.15, 95%CI: 0.28–40.19), diabetes (OR = 3.10, 95%CI: 0.26–55.89), unfortunately with wide confidence intervals, results were not to be further interpreted.

4. Discussion

4.1. Subject characteristics affect distribution of serum PCDD/Fs levels and health outcomes

We found that sex and age were associated with the distribution of serum PCDD/Fs, a conclusion similar to those from other studies (Patterson et al., 1994;...
Schuhmacher et al., 1999). Beside the above factors, literature also showed higher PCDDs levels in non-smokers than active smokers (Deml et al., 1996). In the current study, subjects with a higher BMI showed greater PCDD/Fs levels than others. The prevalence of overweight and obesity in women compared with men has also been demonstrated (Chiu et al., 2000), and higher levels of dioxins in women than in men might be explained by the greater quantity of adipose tissue in obese women (Gonzalez et al., 1998). In addition, it has been proved in other investigations that an increasing percentage of body fat is associated with an increased half-life of PCDD/Fs (Flesch-Janys et al., 1996; Michalek et al., 1992). Therefore, the accumulation of PCDD/Fs in human could be due partly to an increasing percentage of body fat. Another investigation showing the distributions of physiological variables and blood biochemistry from a large population of 1738 people concluded that blood pressure and blood biochemistry variables were positively associated with age (Chou et al., 1992). In addition, elevating BMI also showed to be related to high serum uric acid concentrations and triglyceride levels (Chang et al., 1995). Age, sex, BMI, and smoking status might be associated with either PCDD/Fs accumulation or health outcomes, therefore the above factors should be considered when examining the relationship between serum PCDD/Fs levels and other health-outcome variables (Chang et al., 1995; Flesch-Janys et al., 1996; Michalek et al., 1992; Patterson et al., 1994; Schuhmacher et al., 1999).

4.2. Serum biochemistry examinations

The aim of this study was to investigate the possible associations between serum PCDD/Fs levels and any disorder implied by biochemistry tests and questionnaire-based interviews. Therefore, the abnormal rates of biochemistry examinations were categorized into groups by age ranges and found that most renal- and liver-function results were different between the older and younger groups.

Most other similar studies assessing the relationship of PCDD/Fs exposure and health outcomes used job categories (Hoffman et al., 1986), blood 2,3,7,8-TCDD analysis (pg/g fat or pg/g serum), or extrapolations of the serum concentrations over a long-term period to define the exposure levels (Calvert et al., 1998, 1996; Michalek et al., 2001; Pelclova et al., 2001). In current study, we collected blood for analysis of serum PCDD/Fs levels and biochemistry tests. Also, we used the toxic equivalent concentration (TEQ), indicating the biological and toxic responses of 17 PCDD/Fs congeners via Ah receptor (AhR) in the human body.

In addition, we evaluated serum liver functions, renal functions, glucose levels, and body lipids, because there were considerable evidences from other laboratories and epidemiological investigations suggesting that impaired liver function, possible changes in cholesterol and triglycerides, and a higher prevalence of diabetes mellitus after TCDD exposure (Calvert et al., 1998, 1996; Hoffman et al., 1986; Pelclova et al., 2001; Triebig et al., 1998). We found an increase in serum glucose and GGT levels correlated with rising PCDD/Fs levels. Such findings were identical to the trends of abnormalities rates associated with hepatic enzymes, and elevating transaminases in veterans of Operation Ranch Hand with prior dioxin exposures (Michalek et al., 2001). The other study showed that the significant elevated multivariate-adjusted OR of diabetes among veterans with the highest quartile serum TCDD levels as compared to those in the first quartile (Longnecker and Michalek, 2000). In addition, another study also showed workers in the chemical plant manufacturing 2,4,5-trichlorophenol over 15 years had a significantly increased adjusted mean serum glucose concentration compared with that of referents with no occupational exposure to TCDD (Calvert et al., 1999), and experimental data suggested that the mechanism resulted from the decreasing uptake of cellular glucose (Enan et al., 1992). Therefore, we concluded that glucose metabolism would be affected even the subjects merely exposed to the background dioxin level. However, others studies results showed oppositely to ours report that TCDD-exposed workers in the USA had higher mean triglyceride concentrations, and one also reported a positive correlation for cholesterol ($p=0.063$) (Calvert et al., 1996; Martin, 1984; Triebig et al., 1998). In addition, Hoffman et al. reported significant differences between group means for serum triglycerides, cholesterol, and bilirubin levels between exposed and unexposed groups (Hoffman et al., 1986). The rationale for each study was schemed as follows: first, it should be noted that the above studies did not control for age and our study did not control for diabetes mellitus. Second, our study used lipid-adjusted serum PCDD/Fs concentrations, but the Calvert study did not. Third, the above studies focused on occupational groups and the current was designed for the general population. Therefore, we suggested that the low serum PCDD/Fs level was not sufficient to elicit the modulation of triglycerides, and cholesterol.
4.3. Medical histories

We observed higher positive relationships between PCDD/Fs levels and goiter than for other illnesses. Two major mechanisms might plausibly explain the effect of thyroid interference. Firstly, the microsomal enzyme UDP-glucuronosyl transferase catalyses the formation of T4-gluconeuronic acids, which are then excreted into the bile (Barter and Klaassen, 1992). Additionally, PCB and phenobarbital have been reported to be associated with increase of T4 clearance in bile, which may be related to decreasing serum T4. Secondly, in an in vivo study, the distribution of thyroid hormone after treatment with PCBs and related compounds may have a direct effect on the thyroid gland and then on the proteolysis of thyroglobulin before releasing thyroid hormone (Beetstra et al., 1991). One epidemiological study found an adverse result in highly exposed workers—they had a significantly highly adjusted mean free thyroxine index (T4) compared with references—but no evidence was found for an increased risk of thyroid disease (Calvert et al., 1998). Another study found 138 individual workers who also had the higher increased prevalence of pooled thyroid disorders, including goiter, thyrotoxicosis, hypothyroidism, and thyroid adenoma, than unexposed reference groups (Ott et al., 1994). One cross-sectional study found serum PCDD/Fs not to be associated with thyroid hormone in PCDD/Fs-exposed workers (Triebig et al., 1998). Higher positive association, however, non-statistical significance of serum PCDD/Fs levels and thyroid related illness was found in the current study, and we suggested that thyroid related examination should be further assess for evaluating their association in future.

Many biochemistry tests had shown to be confounded by other factors such as age. In a logistic regression model adjusted for age indicated that large BMI values might be related to high serum uric acid concentrations and triglyceride levels (Chang et al., 1995). It also found that serum cholesterol levels, cigarette smoking and gender were significantly associated with leg vessel disease and with the development of ischemic heart diseases. Therefore, we used adjusting logistic regression analysis to examine the association between the PCDD/Fs body burden and health outcomes. Though the multivariate-adjusted ORs of hypertension and arrhythmia was eliminated, however, the previous study showed the highest relative risk for ischemic heart diseases in 1189 male workers with PCDD/Fs exposure in chemical plant (Flesch-Janys et al., 1995). Another study did a cohort mortality analysis of 5132 chemical workers at 12 plants in the USA, and 69% of the cohort had adequate work history data on TCDD contaminations (Steenland et al., 1999). The standardized mortality ratio (SMR) for heart disease showed a weakly increasing trend with higher exposure. A cross-sectional study had found no significant association between TCDD exposure and any cardiovascular outcomes, including myocardial infarction, angina, cardiac arrhythmias, hypertension, and abnormal peripheral arterial flow (Calvert et al., 1998). Comparison across these several studies, although our study presented lower serum PCDD/Fs levels than Calvert et al. did, and a non-significant result did not justify definitive conclusions, a causal contribution from low PCDD/Fs exposure could not be wholly dismissed.

The study found a negative association for skin allergy. Some studies have proved that PCDD/Fs exposure might cause immune dysfunction in in vivo and in epidemiological studies (Badesha et al., 1995; Ernst et al., 1998), such as dissociation of antigen-specific T-cell while the cell exposed to TCDD, however, very limited data has been observed that PCDD/Fs exposure might cause skin allergy. In sum, our findings suggested that lower PCDD/Fs burden than previously believed could indicate dysfunction in biochemistry tests of the liver and affect glucose levels. Therefore, we might suggest that the current biochemistry examinations only reflect partially the physiological change in glucose modulation and liver function. However, the low serum PCDD/Fs level does not seem to be sufficient in eliciting pathological process for diabetes or liver-related diseases. In addition, examinations of the immune function, liver function, and other hormone related functions such as thyroid and other diabetes related tests in long-term and lower exposure groups should be further warranted.

5. Conclusion

The biochemical analysis supports that glucose and GGT levels are associated with serum PCDD/Fs levels. In addition, increased risks presented for reporting arrhythmia, hemicrania, diabetes, and hypothyroidism though no significant association offer convincing evidences for the PCDD/Fs exposure and health effects. We therefore suggest that the human body’s biochemistry functions such as liver and glucose modulation were affected by PCDD/Fs exposure at even these low serum PCDD/Fs levels found in the general population, but the low serum PCDD/Fs level does not seem to be sufficient in eliciting pathological process for diabetes
or liver-related diseases. Additional biochemistry analysis should be warranted for immune function, liver function, and other hormone related functions. Complete results are hoped to serve as reference values for the population exposed to long-term and low PCDD/Fs contaminations.

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