



A Retrospective Mid- and Long-term Follow-up Study on the Changes in Hematologic Parameters in the Highly Exposed Residents of the Hebei Spirit Oil Spill in Taean, South Korea

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Objectives: This study aimed to analyze changes in hematologic parameters in the residents of the areas highly contaminated by the Hebei Spirit Oil Spill in 2007 and those who participated in the clean-up activities.

Methods: According to demographic characteristics, health status and behavior, and level of exposure to oil, we compared the hematologic results in 2009 and 2012 among 701 residents. The hematologic parameters were composed of white blood cell (WBC) count, and levels of hemoglobin, hematocrit (Hct), aspartate aminotransferase (AST), alanine aminotransferase (ALT), glucose, glycosylated hemoglobin (HbA1c), blood urea nitrogen (BUN), creatinine (Cr), total cholesterol (T-chol), high-density lipoprotein (HDL), and triglyceride (TG).

Results: Paired *t*-test revealed that the WBC count and levels of Hct, AST, ALT, glucose, and HbA1c significantly increased, whereas the BUN, Cr, HDL, and TG levels significantly decreased. Multiple linear regression modelling showed a relationship between the level of exposure to oil and temporal changes in Hct, glucose, HbA1c, and BUN levels.

Conclusion: Our results suggest a relationship between level of exposure to oil and changes in hematologic parameters over 3 years. Further studies should be conducted to determine the impact of oil spill on health such as the occurrence of diseases.

Key Words: petroleum pollution, hematologic tests, environmental exposure, follow-up studies, Republic of Korea

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INTRODUCTION

On December 7, 2007, Hebei Spirit, a Hong Kong-registered oil tanker, was rammed by a crane-carrying barge of Samsung Heavy Industries tugboats. Approximately 10,900 tons of oil spilled into the sea, which contaminated 1,052 km of coastline in Taean county, Korea [1]. This accident, named the Hebei Spirit Oil Spill, was the largest oil spill accident in South Korea.

The spilled oil contained volatile organic compounds (VOCs), benzene, toluene, ethylbenzene, and xylene (BTEX), polycyclic aromatic hydrocarbons (PAHs), and heavy metals [2]. Exposure to these components of crude oil increases the risk of many health problems such as respiratory symptoms, nervous symptoms, dermatologic symptoms, and cancer [3–7]. During the 7 months after the Hebei Spirit Oil Spill, more than 2 million volunteers, including 556,323 Taean residents, participated in clean-up activities [2]. Many participants wore insufficiently ap-



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appropriate personal protective equipment [8] and reported several health problems, including respiratory, dermatologic, and ophthalmic symptoms [9].

After oil spill accidents abroad, many studies have been conducted to investigate the health impact such as acute symptoms [6,7,10,11]; mental health, including anxiety, posttraumatic stress syndrome (PTSD), and depression [12,13]; pulmonary function testing [14]; and blood tests, including liver function, renal function, and hematologic profile [15–17].

Various studies were also conducted to investigate the health impact after the Hebei Spirit Oil Spill [18–20]. However, most of the previous studies on the oil spill incident in Hebei Spirit were cross-sectional studies related to acute physical symptoms or mental health, or exposure to oil. No studies have been conducted on the mid- to long-term effects of oil toxicants, including the effects on hematologic, liver, and renal functions. Therefore, this study aimed to analyze mid- to long-term changes in hematologic and biochemical parameters, and related factors among residents of the highly exposed areas after the Hebei Spirit Oil Spill accident.

MATERIALS AND METHODS

1. Study subjects

The study subjects were 701 adults who responded to the first survey and monitoring of health impacts in 2009 and participated in the follow-up monitoring in 2012. The first survey was conducted among 9,246 residents of Taean county from January 2009 to June 2010 by using structured questionnaires. Of these participants, 7,971 underwent blood tests for investigating their hematologic profile, liver function, and renal function. In 2012, a follow-up monitoring was conducted among 891 adults who were living in the area most polluted by the oil spill accident from February to March 2012. Residents living in Sowon-myeon, Wonbuk-myeon, Iwon-myeon, Geunheung-myeon, which were exposed to the coasts contaminated by the thick oil layer at the initial stage of the accident, were classified as highly exposed subjects to oil. Of these residents, 701 adults participated in the first survey and the clean-up work (Figure 1).

This study was approved by the Dankook University Hospital Institutional Review Board (DKUH201406013-HE003).

2. Independent variables

The independent variables were demographic characteristics, health status and behavioral characteristics, and oil exposure characteristics. Independent variables were classified into three categories, namely demographic, health behavior, and the level of

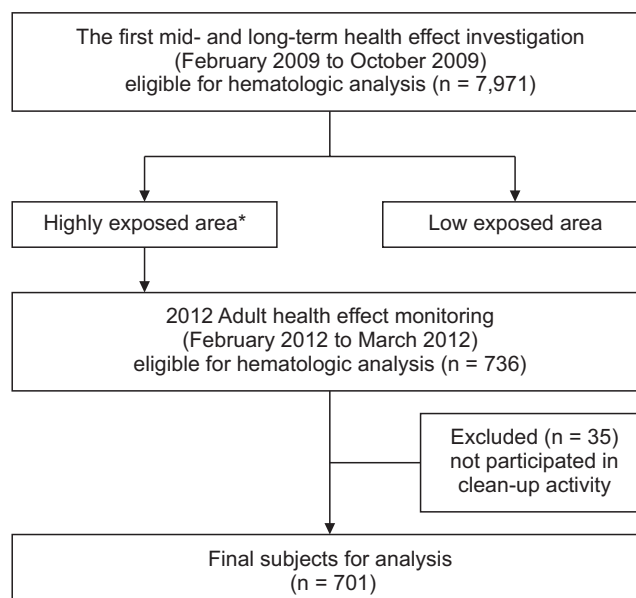


Figure 1. Selection process for study subjects. *Highly exposed area: the area that had seashores covered with thick crude oil in Sowon-myeon, Wonbuk-myeon, Iwon-myeon, Geunheung-myeon in the beginning of the Hebei Spirit Oil Spill accident.

exposure to oil.

The demographic characteristics included sex, age, educational attainment, marital status, type of health insurance, monthly household income, religion, and occupation. The age variable was divided into age groups of 26–49, 50–59, 60–69, and 70–81 years, respectively. Educational attainment was classified as below elementary school graduation, elementary school graduation, and above middle school graduation. Marital status was classified as married and other. The types of health insurance were national health insurance and Medicaid. Monthly household income was divided into < 500,000, 500,000–999,999, 1,000,000–1,999,999 and > 2 million KRW. Religion was divided into presence or absence of a religion. Occupation was divided into farmer-fisherman and others.

Health behavior variables included body mass index (BMI), presence of chronic disease, smoking status, drinking status, and frequency of weekly exercise. BMI was divided into three subgroups: normal, overweight, and obese. Smoking was classified into three groups, namely nonsmokers, ex-smokers, and current smokers. The numbers of weekly exercises were divided into 1 or 2 times, 3 or 4 times, and 5 or 6 times.

The levels of exposure to spilled oil were categorized according to the days of acute-phase clean-up work, the days of total clean-up work, the distance from the accident point to the residence, the distance from the initial pollution shore to the residence, respiratory symptoms, skin symptoms, and risk of

Table 1. General characteristics and health behaviors of the subjects according to sex

Variable	Male	Female	Total
Age (y)			
26–49	24 (9.2)	47 (10.7)	71 (10.1)
50–59	61 (23.5)	119 (27.0)	180 (25.7)
60–69	104 (40.0)	181 (41.0)	285 (40.7)
70–81	71 (27.3)	94 (21.3)	165 (23.5)
Educational attainment ^a			
Kindergarten or lower	30 (11.5)	227 (51.5)	257 (36.7)
Elementary school	128 (49.2)	152 (34.5)	280 (39.9)
Middle school or higher	102 (39.2)	62 (14.1)	164 (23.4)
Marital status ^a			
Married	242 (93.1)	329 (74.6)	571 (81.5)
Others	18 (6.9)	112 (25.4)	130 (18.5)
Type of health insurance			
National health insurance	154 (59.2)	258 (58.5)	412 (58.8)
Medicaid	106 (40.8)	183 (41.5)	289 (41.2)
Monthly household income (KRW) ^a			
< 500,000	144 (55.4)	293 (66.4)	437 (62.3)
500,000–999,999	35 (13.5)	67 (15.2)	102 (14.6)
1,000,000–1,999,999	49 (18.8)	51 (11.6)	100 (14.3)
≥ 2,000,000	32 (12.3)	30 (6.8)	62 (8.8)
Religion ^a			
Yes	120 (46.2)	257 (58.3)	377 (53.8)
No	140 (53.8)	184 (41.7)	324 (46.2)
Occupation ^a			
Farming and fishing	154 (59.2)	182 (41.3)	336 (47.9)
Others	106 (40.8)	259 (58.7)	365 (52.1)
Body mass index (kg/m ²)			
Underweight to normal (< 23.0)	77 (30.8)	119 (27.8)	196 (28.9)
Overweight (23.0–25.0)	61 (24.4)	101 (23.6)	162 (23.9)
Obese (> 25.0)	112 (44.8)	208 (48.6)	320 (47.2)
Chronic disease ^b			
Yes	112 (43.1)	190 (43.1)	302 (43.1)
No	148 (56.9)	251 (56.9)	399 (56.9)
Smoking ^a			
Non-smoker	140 (54.3)	428 (97.3)	568 (81.4)
Ex-smoker	61 (23.6)	4 (0.9)	65 (9.3)
Smoker	57 (22.1)	8 (1.8)	65 (9.3)
Drinking ^a			
Yes	139 (53.9)	54 (12.3)	193 (27.7)
No	119 (46.1)	386 (87.7)	505 (72.3)
Weekly exercise frequency			
None	181 (70.2)	313 (71.1)	494 (70.8)
1 or 2 times	13 (5.0)	37 (8.4)	50 (7.2)
3 or 4 times	24 (9.3)	36 (8.2)	60 (8.6)
5 or 6 times	40 (15.5)	54 (12.3)	94 (13.5)
Total	260 (100.0)	441 (100.0)	701 (100.0)

Values are presented as number (%).

Because study subjects didn't respond to some independent variables, sum of frequencies in this table are less than number of total subjects.

^a*p* < 0.05 by chi-square test.

^bChronic diseases: hypertension, diabetes mellitus, asthma, thyroid disease, anemia, chronic obstructive pulmonary disease, stroke and cerebrovascular disease, cardiac angina, and cardiovascular disease.

posttraumatic stress disorder.

Days of participating in the clean-up work during the acute phase of the Hebei Spirit Oil Spill accident were divided into 1–14,

15–19, and 20–24 days, from December 7 to 31, 2007. The total numbers of days of participation in the clean-up work up to the date of the first survey were divided into 3–60, 61–90, 91–120,

Table 2. Exposure characteristics of the subjects by sex

Variable	Male	Female	Total
Number of clean-up days in acute stage ^a			
1–14	10 (3.7)	32 (6.9)	42 (5.7)
15–19	14 (5.5)	37 (8.6)	51 (7.5)
20–24	232 (90.6)	359 (83.9)	591 (86.4)
Total number of clean-up days ^a			
3–60	26 (10.0)	76 (17.3)	102 (14.6)
61–90	30 (11.6)	83 (18.9)	113 (16.2)
91–120	41 (15.8)	70 (15.9)	111 (15.9)
121–150	84 (32.4)	125 (28.5)	209 (29.9)
151–325	78 (30.1)	85 (19.4)	163 (23.4)
Distance from the accident point (km)			
≤ 14.0	48 (18.7)	81 (18.5)	129 (18.6)
14.1–15.0	68 (26.5)	92 (21.1)	160 (23.1)
15.1–16.0	62 (24.1)	106 (24.3)	168 (24.2)
16.1–17.0	21 (8.2)	54 (12.4)	75 (10.8)
> 17.0	58 (22.6)	104 (23.8)	162 (23.3)
Distance from contaminated seashore (km)			
≤ 0.20	56 (22.3)	91 (21.5)	147 (21.8)
0.21–0.40	38 (15.1)	65 (15.3)	103 (15.3)
0.41–0.60	56 (22.3)	92 (21.7)	148 (21.9)
0.61–0.80	40 (15.9)	60 (14.2)	100 (14.8)
> 0.80	61 (24.3)	116 (27.4)	177 (26.2)
Respiratory symptoms			
Yes	122 (47.1)	203 (46.1)	325 (46.5)
No	137 (52.9)	237 (53.9)	374 (53.5)
Dermatologic symptoms			
Yes	53 (20.5)	108 (24.5)	161 (23.0)
No	206 (79.5)	332 (75.5)	538 (77.0)
PTSD risk			
Yes	87 (33.9)	173 (40.0)	260 (37.7)
No	170 (66.1)	260 (60.0)	430 (62.3)
Total	273 (100.0)	463 (100.0)	736 (100.0)

Values are presented as number (%).

Because study subjects didn't respond to some independent variables, sum of frequencies in this table are less than number of total subjects.

Acute stage: December 7–31, 2007; Respiratory symptoms: wheezing, sneezing, rhinorrhea, or allergic rhinitis during living or exercising in the recent 12 months; Dermatologic symptoms: eczema, urticaria, or atopy in the recent 12 months; PTSD risk: a score of ≥ 15 points in the posttraumatic diagnostic scale questionnaire.

PTSD: posttraumatic stress syndrome.

^a*p* < 0.05 by chi-square test.

121–150, and 151–325 days. The distance from the accident site to the residence area were divided into ≤ 14.0 , 14.1–15.0, 15.1–16.0, 16.1–17.0, > 17.0 km. The distances from the contaminated seashore to the residence area was measured using the geographic information system and divided into ≤ 0.20 , 0.21–0.40, 0.41–0.60, 0.61–0.80, > 0.80 km. The risk of posttraumatic stress disorder was defined as a total score of ≥ 15 in the 17 items of the posttraumatic diagnostic scale [21,22].

3. Outcome variables

Outcome variables included 14 items of blood tests, including complete blood count (CBC), liver function test, renal function test, diabetic mellitus test, and lipid test. The CBC test results were composed of white blood cell (WBC) count, hemoglobin (Hb) level, hematocrit (Hct) level, and platelet (PLT) count. The liver function test included the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma glutamyl transferase (γ -GT). Blood urea nitrogen (BUN) and creatinine (Cr) were tested to reflect kidney function. Fasting blood glucose (glucose) and glycosylated hemoglobin (HbA1c) levels were measured. We also tested for total cholesterol (T-chol), high-density lipoprotein (HDL), and triglyceride (TG) levels.

4. Statistical analysis

A paired *t*-test was conducted to examine differences in measurements in the 14 items of the blood test between years 2009 and 2012. Independent sample *t*-test, one-way analysis of variance, and linear regression analysis were used to determine any differences in the levels of the 14 blood test items according to demographic, health behavior, and exposure level to oil. Data were analyzed using IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA) based on a significance level of 0.05.

RESULTS

Table 1 shows the demographic characteristics of the study subjects according to sex. The independent variables of educational attainment, marital status, monthly household income, type of occupation, smoking, and drinking showed statically significant differences according to sex. Age, type of health insurance, BMI, presence of chronic disease, and weekly frequency of exercise showed no significant difference according to sex.

The levels of exposure to oil according to sex are displayed in

Table 3. Hematologic parameters of the subjects in 2009 and 2012

Hematologic tests	Subject (n)	2009	2012	<i>p</i> -value ^a
CBC				
WBC count (/ μ L)	698	6,176.5 \pm 1672.9	6,356.0 \pm 2034.1	0.011
Hb (mg/dL)	698	14.0 \pm 1.3	14.0 \pm 1.3	0.798
Hct (%)	698	39.3 \pm 3.5	39.5 \pm 3.5	0.027
PLT count (/ μ L)	692	25.1 \pm 5.3	25.2 \pm 6.1	0.532
Biochemistry				
AST (IU/L)	699	26.7 \pm 13.5	29.0 \pm 12.3	0.000
ALT (IU/L)	699	25.8 \pm 16.9	28.2 \pm 18.9	0.002
γ -GT (IU/L)	699	44.7 \pm 61.4	41.7 \pm 55.4	0.143
Glucose (mg/dL)	699	103.6 \pm 22.8	106.6 \pm 25.0	0.000
HbA1c (%)	698	5.9 \pm 0.7	6.1 \pm 0.8	0.000
BUN (mg/dL)	699	16.1 \pm 4.7	15.3 \pm 4.1	0.001
Cr (mg/dL)	699	0.9 \pm 0.2	0.8 \pm 0.2	0.000
T-chol (mg/dL)	699	207.9 \pm 39.8	206.2 \pm 38.3	0.250
HDL (mg/dL)	699	51.9 \pm 12.2	50.1 \pm 12.3	0.000
TG (mg/dL)	699	145.9 \pm 99.9	135.4 \pm 93.1	0.004

Values are presented as mean \pm standard deviation.

CBC, complete blood count; WBC, white blood cell; Hb, hemoglobin; Hct, hematocrit; PLT, platelet; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ -GT, gamma glutamyl transferase; HbA1c, glycosylated hemoglobin; BUN, blood urea nitrogen; Cr, creatinine; T-chol, total cholesterol; HDL, high-density lipoprotein; TG, triglyceride.

^aBy paired *t*-test.

Table 4. Multiple regression analysis of the changes in Hct, AST, ALT, glucose, HbA1c, BUN, HDL, TG, and Cr levels

Variable	Regression coefficients								
	Hct	AST	ALT	Glucose	HbA1c	BUN	HDL	TG	Cr
Women (ref. men)						1.089*			0.215*
Age (y) (ref. 26–49 y)									
50–59						–0.941			
60–69						–1.444			
70–81						–2.514*			
Education (ref. kindergarten or lower)									
Elementary school									0.000
Middle school or higher									–0.012
Marital status (ref. married)		–2.498							
Medicaid (ref. health insurance)			3.686*	2.621					
Monthly household income (KRW) (ref. < 500,000 KRW)									
500,000–999,999		5.372*	4.879*						0.016
1,000,000–1,999,999		3.653*	4.447*						–0.017
≥ 2,000,000		0.029	–0.480						–0.058
Not having a religion (ref. yes)								19.108*	–0.028
Occupation (ref. farming and fishing)								–15.888*	
Body mass index (kg/m ²) (ref. < 23.0 kg/m ²)									
23.0–25.0					–0.004	–1.330			–0.038
> 25.0					–0.120*	–1.726*			–0.063*
Presence of a chronic disease (ref. no)									–0.051*
Smoking (ref. nonsmoker)									
Ex-smoker							0.478	–36.379*	–0.036
Smoker							–3.093*	14.253	–0.044
Drinking (ref. none)								17.321*	0.026
Number of days of clean-up work during the acute stage (ref. 1–14)									
15–19								–10.584*	
20–24								–12.226*	
Number of days of total clean-up work (ref. 3–60)									
61–90						1.435			
91–120						–0.897			
121–150						0.035			
151–325						0.739			
Distance (km) from the accident site (ref. > 17.0)									
≤ 14.0				–6.384*			–3.225*		
14.1–15.0				0.120			0.373*		
15.1–16.0				2.012			–2.207*		
16.1–17.0				0.706			–3.550*		
Distance (km) from contaminated seashore (ref. > 0.80)									
≤ 0.20	–0.631			–6.412*		–1.629*			
0.21–0.40	0.121			0.498		–1.819			
0.41–0.60	–0.532*			2.040		–0.671			
0.61–0.80	–0.799*			–1.248		0.201			
Presence of respiratory symptoms					0.095*	0.704			
Risk of PTSD						0.740			
R ²	0.018	0.025	0.020	0.053	0.021	0.071	0.006	0.044	0.215
F statistics	3.028*	4.426*	3.549	4.077*	4.804*	2.984*	3.078*	6.372*	13.853*

Hct, hematocrit; AST, aspartate aminotransferase; ALT, alanine aminotransferase; HbA1c, glycosylated hemoglobin; BUN, blood urea nitrogen; HDL, high-density lipoprotein; TG, triglyceride; Cr, creatinine; ref., reference; PTSD: posttraumatic stress syndrome.

**p* < 0.05.

Table 2. The numbers of days of participating in clean-up work during the acute phase and total clean-up work were significantly higher for men than for women. The distance from the accident site and contaminated seashore, the presence of respiratory and dermatologic symptoms, and the risk of PTSD showed no significant differences by sex.

We compared blood test results between 2009 and 2012 (Table 3) and found statistically differences in WBC count and levels of Hct, AST, ALT, BUN, Cr, glucose, HbA1c, HDL, and TG. The test results for WBC count and levels of Hct, AST, ALT, glucose, and HbA1c in 2012 significantly increased from those in 2009, but the test results for BUN, Cr, HDL, and TG levels significantly decreased.

Linear regression analyses were conducted to find contributing factors to changes in blood test results for WBC count, and levels of Hct, AST, ALT, BUN, Cr, glucose, HbA1c, HDL, and TG between 2009 and 2012 (Table 4). None of the predictive factors affected the difference in WBC count. Long distance from the contaminated seashore to the residence areas significantly contributed to the negative change in Hct level ($R^2 = 0.018$, $F = 3.028$). High monthly household income was a significant predictor of positive change in AST level ($R^2 = 0.025$, $F = 4.426$). Residents with Medicaid and higher monthly household income showed a significant relationship to positive change in ALT level ($R^2 = 0.020$, $F = 3.549$). Long distances from the accident site and contaminated seashore to the residence area were related to negative change in glucose level ($R^2 = 0.053$, $F = 4.077$). Residents with obesity and without respiratory symptoms were related to negative change in HbA1c level ($R^2 = 0.021$, $F = 4.804$). BUN level negatively changed in the residents who were elderly men with obesity, participated in total clean-up work during a short period, and had no respiratory symptom and PTSD risk ($R^2 = 0.071$, $F = 2.984$). Negative changes in HDL level were found in the residents who had no religion, were farmers and fishermen, were ex-smokers, and had no drinking habit ($R^2 = 0.006$, $F = 3.078$). Residents who had no religion, were farmers and fishermen, were nonsmokers, and had no drinking habit showed positive changes in TG level ($R^2 = 0.044$, $F = 6.372$). Negative changes in Cr level were observed in the residents who were men and had obesity, and had no chronic disease ($R^2 = 0.215$, $F = 13.853$).

DISCUSSION

The characteristics of the exposure to oil from the Hebei Spirit Oil Spill contributed to the changes in the various blood test results between years 2009 and 2012. Living in the area close to the accident site and contaminated seashore was related to

the changes in the test results for Hct, glucose, BUN, and HDL levels. Residents who participated in clean-up work during 2 or more months showed positive changes in BUN level. These results are consistent with the findings of previous studies [15–17] that reported changes in blood, liver, respiratory, kidney, and nervous system functions after an oil exposure accident. Spilled oil that contains various components such as VOCs and PAHs may remain in the environment and negatively impact human health and ecosystems during several years. The higher the pollution level of the area, the higher the participation rate of the residents in the clean-up work, the longer the work period and time, and the higher the possibility of getting oil on clothes, and the face and limbs [19]. When VOCs and PAHs are mainly absorbed through the respiration or the skin [6], these substances are mainly metabolized in the liver. The metabolites are excreted in urine and produce reactive oxygen species that cause oxidative stress in the body, affecting biomaterials such as DNA, protein, and lipids [23].

Of the oil components that were released, only a few are known to have toxic and adverse health effects. Most toxic components are known to be toxic only when they act as a single substance, and their toxic mechanisms have not been studied in mixtures such as crude oil. In a study of the association of organic solvent and lead exposure to hepatic function tests results, Chang et al. [24] found that the group of workers exposed simultaneously to organic solvents and lead showed a greater increase in liver function index than those exposed to only a single substance. Accordingly, additive actions and interactions should be considered in mixed substance exposure, even if heavy metals such as organic solvents and lead are at or below the permissible exposure limit. If each substance is exposed to the same or lower than the permitted exposure standard, it may be harmful to the human body [25].

The limitations of this study are as follows: The blood test results used in this study were not the result of an acute period of several days or weeks after the accident but rather the result of a considerable period after the accident, so many confounding factors such as age, personal illness, eating habits, and environment can be interrelated. Therefore, interpretation of the results is limited. Unfortunately, in the case of the largest oil spill incident in the history of the Republic of Korea, both the government and the residents were ignorant about the necessity of a health impact investigation. The residents were forced to ignore the immediate effects of the oil spill on their livelihood, so the right time for the investigation was missed. If this situation is resumed in Korea or abroad, it is desirable to conduct a survey on the health effects of the acute period in addition to the control work. In 2010, the National Institute of Environmental Health Sciences (NIEHS) of the

National Institutes of Health conducted a health impact survey in residents during an acute period in a British oil spill accident [25].

Another limitation was that we conducted this survey only among residents who participated in the oil accident prevention work without a control group. Most previous studies on the health impact of oil spill accidents compared an exposed group with a control group of subjects who were not exposed to the oil accident. This is useful for the generalization of the results of the study because the effect of the oil exposure can be more clearly and easily confirmed by comparing the results of the exposed and unexposed groups when a control group is present. In 2010, the United States Gulf of Mexico British Petroleum oil spill incident was also subjected to a cross-sectional survey led by the NIEHS and a follow-up survey of residents and control workers [15,25]. In environmental health research, a control group with similar characteristics as the exposed group is not easy to obtain, and obtaining consent from the farmers and villagers who

are busy in agriculture and fisheries is practically impossible. In some cases, it is difficult to interpret the differences in results between exposure to oil toxins and other personal factors.

Our results suggest that exposure to spilled oil is a risk factor for worsening changes in some blood test results such as Hct, glucose, BUN, and HDL levels. Further studies should be conducted to demonstrate the causal relationship between oil spill exposure and the incidence or aggravation of diseases such as diabetes mellitus and renal failure, which are related to exposure to VOCs and PAHs in crude oil.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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