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Research Article

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Relationship between shift work and liver enzymes: a cross-sectional study based on the Korea National Health and Examination Survey (2007–2015)

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ABSTRACT

Background: Shift work has well-known adverse effects on health. However, few studies have investigated the relationship between shift work and hepatic disorders. This study aimed to evaluate the association between shift work and abnormal level of liver enzymes.
Methods: The aggregated data from the 2007–2009, 2010–2012, and 2013–2015 cycles of the Korea National Health and Nutrition Examination Survey was used for this study. The χ^2 test and multiple logistic regression analysis were used to assess relationship between shift work and abnormal level of liver enzymes stratified by gender.
Results: The odds ratio (OR) of abnormal serum level of alanine aminotransferase (abnormal ALT) in female shift workers was higher with 1.31 (95% confidence interval: 1.00–1.71) compared with day workers after adjusting for covariates. After dividing into subgroups of the shift work pattern, the ORs of abnormal liver enzymes for each pattern compared with day work were not significantly higher.
Conclusions: This study provides limited support for the hypothesis that shift work is related to liver enzyme abnormalities, but offers some evidence in favor of the idea that shift work affects female workers more than males on abnormal ALT. Further studies are needed to define the relationship between shift work and abnormal liver enzymes to be carried out as well as the gender difference in the association.

Keywords: Shift work; Abnormal level of liver enzymes; Aspartate aminotransferase; Alanine aminotransferase; KNHANES

BACKGROUND

Hepatic disorder is a major concern in Korea and many other countries. Since the liver is a primary organ involved in biotransformation of food and drugs, hepatic disorders are very often. The determination of various liver enzymes in serum is used to evaluate the functional status of the liver. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities in serum are the most frequently used indicators for evaluation of liver dysfunction [1,2]. The increase in these liver enzymes can be caused by viruses, bacterial infections, alcohol or toxic substances, excessive accumulation of fat or heavy metals, and abnormal immune responses [3].

Abbreviations

KNHANES: Korea National Health and Nutrition Examination Survey; AST: aspartate aminotransferase; ALT: alanine aminotransferase; abnormal AST: abnormal serum level of aspartate aminotransferase; abnormal ALT: abnormal serum level of alanine aminotransferase; BMI: body mass index; OR: odds ratio; CI: confidence interval; DM: diabetes mellitus.

Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

KNHANES data is open to all researchers. And KNHANES data are available on the KNHANES website (https://knhanes.cdc.go.kr).

Authors contributions

Conceptualization: Choi H; Data curation: Oh HJ, Shin JS, Lim M; Formal analysis: Choi H; Supervision: Kim SK, Kang HT, Oh SS, Koh SB; Writing - original draft: Choi H; Writing - review & editing: Koh SB.

In addition, recent studies suggest that there is a relationship between liver health and specific occupations, especially shift work. Shift work has become universal throughout the world. At least 15% of workers are engaged in shift work in the European Union [4] and United States [5] and estimated 10.2–14.5% of wage earners in Korea (1.27–1.97 million people) perform night shift work [6,7]. Shift work is an important and well-known health hazard in the modern workplace. Unlike day workers, shift workers are exposed to light at night and can interfere with sleep and circadian rhythms [8]. And it can cause various health problems. Shift work is known to be related with chronic diseases such as cardiovascular diseases, diabetes mellitus (DM), metabolic syndrome, and breast cancer [9]. Interestingly, abnormal liver function is widespread among many occupations including shift work. Although inconclusive, several studies have shown that shift work is associated with abnormal level of liver enzymes [10-13].

The aim of the present study was to investigate the relationship between shift work and abnormal level of liver enzymes, utilizing data from the Korea National Health and Nutrition Examination Survey (KNHANES).

METHODS

Participants

This study used aggregated data from the 2007–2009, 2010–2012, and 2013–2015 cycles of the KNHANES. The KNHANES is a national cross-sectional survey gathered annually by the Korea Centers for Disease Control and Prevention, and is designed according to multistage stratified and cluster sampling. The data includes health questionnaire and blood test results. Participants who were at least 18 years old, and who had occupational information were included in this study. Individuals who had Hepatitis B and Hepatitis C were excluded from the analysis. In addition, individuals with missing values for major variables and covariates were also excluded. Finally, 51,402 were excluded from the analysis and a total of 21,951 participants were included in the analysis (**Fig. 1**).

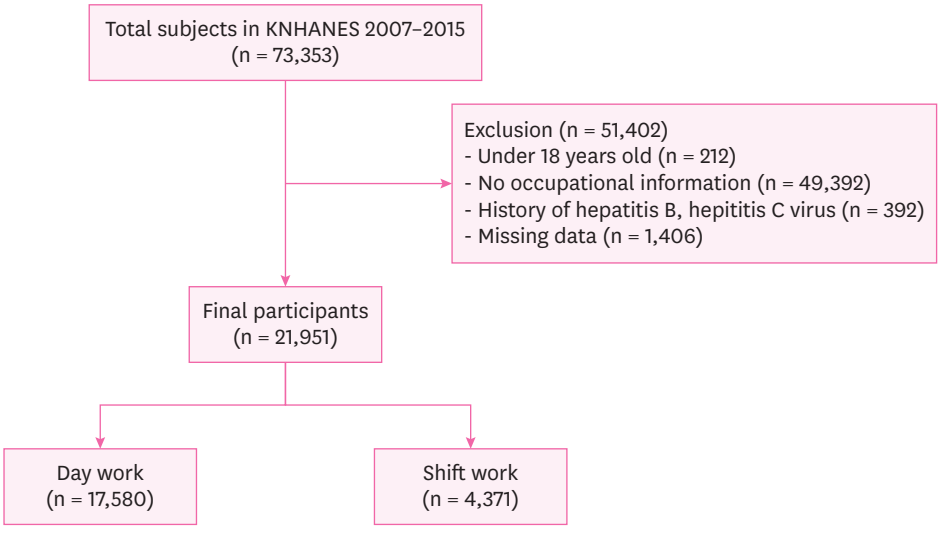

Fig. 1. A flow of the study design.
KNHANES: Korea National Health and Nutrition Examination Survey.

Shift work and day work

In KNHANES, work groups were divided as follows. "Do you usually work during the day time (between 6 a.m. and 6 p.m.)? Or are you working in another time?" Participants who answered "Usually work during the day time (between 6 a.m. and 6 p.m.)" were classified as day workers, and other participants who answered "fixed-evening shift (between 2 p.m. and 24:00), fixed-night shift (between 9 p.m. and 8 a.m. next day), regular day and night rotating shift, 24-hours rotating shift, split shift (working 2 shifts in 1 day), irregular rotating shift, and others" were classified as shift workers.

Definition of abnormal level of liver enzymes

According to the standard reference limit, abnormal serum level of AST (abnormal AST) was defined as AST > 40 IU/L, and abnormal serum level of ALT (abnormal ALT) was defined as ALT > 35 IU/L [14].

Covariates

Age, sex, smoking status, drinking status, hours of sleep, body mass index (BMI), physical activity and history of disease (hypertension, DM, and dyslipidemia) were included as potential confounding variables. Information regarding demographic and social factors was obtained using a standardized questionnaire in health interviews. Age was divided into 6 groups: 18–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years and above 70 years. Smoking status was divided into non-smokers, ex-smokers, and current smokers. Drinking status was divided into non-drinkers, social-drinkers, and binge-drinkers. Social drinkers are categorized as drinking less than 5 units of alcohol per time, and binge drinkers are categorized as drinking 5 or more units of alcohol per time [15]. Hours of sleep were categorized into 3 groups (< 7 hours, 7–9 hours and > 9 hours per night) according to appropriate sleep durations recommended by the National Sleep Foundation [16]. BMI was calculated by dividing body weight by height squared (kg/m^2). As for physical activity, the subjects were grouped according to whether they performed exercise over 10 minutes that are more strenuous than usual activities or not.

Statistical analysis

The t-test and the χ^2 test were used to examine the general characteristics of the study population with regarding to the abnormal level of liver enzymes. Relationship between the shift work and abnormal level of liver enzymes was examined using multiple logistic regression after stratification for gender. To reflect the impact of each variable, age, smoking status, drinking status, and physical activity were adjusted in model 1, and hours of sleep, BMI, and history of disease were additionally adjusted in model 2. The statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA) to take into account sample weights and complex sample design effects.

Ethics statement

All participants of the KNHANES used in the current study provided written informed consent. This national survey was approved by the Institutional Review Board (IRB) of the KCDC (IRB No. 2007-02CON-04-P, 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, 2011-02CON-06-C, 2012-01EXP-01-2C, 2013-07CON-03-4C, 2013-12EXP-03-5C, 2015-01-02-6C).

RESULTS

General characteristics

The general characteristics of participants are shown in **Table 1**. From a total of 21,951 participants included in the final analysis, 11,288 (51.4%) were male and 10,663 (48.6%) were female. In the mean age, shift workers were younger than day workers in both male and female. The proportion of day workers was higher in both male and female workers. In patterns of shift work schedule, the proportion of fixed-evening shift was the highest in both male and female shift workers. Among lifestyle factors, the smoking rate and the proportion of sleeping less than 7 hours were higher in shift workers and the proportion of binge drinker in female shift workers was higher compared with female day workers.

Odds ratios (ORs) of abnormal AST and abnormal ALT according to shift work

Association between shift work and abnormal AST, and between shift work and abnormal ALT by multiple logistic regression analysis are shown in **Table 2**. For male, the ORs of abnormal AST and abnormal ALT in shift workers were found to be low, but the difference was not significant. For female, the OR of abnormal ALT in shift workers was 1.19 (95% confidence interval [CI]: 0.92–1.54) compared with day workers. After adjusting for age, smoking status, drinking status, and physical activity, the OR of abnormal ALT was significantly higher with OR 1.30 (95% CI: 1.00–1.69). After additionally adjusting for hours of sleep, BMI, and history of disease, the same results were obtained 1.31 (95% CI: 1.00–1.71).

ORs of abnormal AST and abnormal ALT according to work patterns

The work patterns were divided into 7 groups of day work, fixed-evening shift, fixed-night shift, regular day and night rotating shift, 24-hours rotating shift, split shift (working 2 shifts in 1 day), and irregular rotating shift (**Table 3**). The ORs of abnormal AST and abnormal ALT for all patterns of shift work compared with day work were not significantly higher in analysis stratified by sex.

DISCUSSION

This study analyzed relationship between shift work and abnormal level of liver enzymes in Koreans, using large-scale survey data. Gender difference on the association between shift work and abnormal liver enzymes was shown in this study. The results of the current study showed that shift work was associated with abnormal ALT in female workers (adjusted OR: 1.31, 95% CI: 1.00–1.71). The association between shift work and abnormal AST in female was shown as the OR: 1.30 (95% CI: 0.90–1.87), but not statistically significant. However, there was no significant association between shift work and abnormal liver enzymes among male workers. When patterns of shift work were divided into subgroups, there were no significant differences between all patterns of shift work and risk of abnormal liver enzymes stratified by gender.

Abnormal liver function, usually indicated by liver enzyme abnormalities is common among workers in many occupations, which involve shift work [10,11,13]. The circadian clock system is the main factor in the association between shift work and the abnormal level of liver enzymes. Circadian clock system consists of a central clock located in the suprachiasmatic nucleus in the hypothalamus and peripheral clocks in peripheral tissues. Peripheral clocks in the liver play a fundamental role in maintaining liver homeostasis, including the regulation of energy metabolism and the expression of enzymes regulating the absorption and metabolism

Table 1. General characteristics of the subjects

Variable	Male			Female		
	Day work	Shift work	*p*-value	Day work	Shift work	*p*-value
Total (No.‡)	8,954	2,334	-	8,626	2,037	-
Shift work patterns			-			-
Fixed-evening shift	-	795 (34.06)		-	1,318 (64.70)	
Fixed-night shift	-	427 (18.29)		-	232 (11.39)	
Regular day and night rotating shift	-	450 (19.28)		-	181 (8.89)	
24-hours rotating shift	-	312 (13.37)		-	65 (3.19)	
Split shift	-	135 (5.78)		-	113 (5.55)	
Irregular rotating shift	-	215 (9.21)		-	128 (6.28)	
Age (years)	48.04 ± 14.43	44.24 ± 15.74	< 0.01*	46.82 ± 14.87	41.65 ± 14.35	< 0.01*
Age group			< 0.01†			< 0.01†
18–29	965 (10.78)	503 (21.55)		1,314 (15.23)	519 (25.48)	
30–39	1,850 (20.66)	483 (20.69)		1,591 (18.44)	370 (18.16)	
40–49	2,002 (22.36)	458 (19.62)		1,932 (22.40)	481 (23.61)	
50–59	2,010 (17.81)	394 (16.88)		1,938 (22.47)	448 (21.99)	
60–69	1,420 (15.86)	373 (15.98)		1,177 (13.64)	167 (8.20)	
≥ 70	707 (7.90)	123 (5.27)		674 (7.81)	52 (2.55)	
Smoking status			< 0.01†			< 0.01†
Non-smoker	1,747 (19.51)	515 (22.07)		7,721 (89.51)	1,694 (83.16)	
Ex-smoker	3,347 (37.38)	604 (25.88)		406 (4.71)	87 (4.27)	
Current smoker	3,860 (43.11)	1,215 (52.06)		499 (5.78)	256 (12.57)	
Drinking status§			0.26†			< 0.01†
Non-drinker	1,177 (13.14)	286 (12.25)		2,568 (29.77)	481 (23.61)	
Social-drinker	2,958 (33.04)	750 (32.13)		4,667 (54.10)	1,059 (51.99)	
Binge-drinker	4,819 (53.82)	1,298 (56.61)		1,391 (16.13)	497 (24.40)	
Hours of sleep (hours/day)			< 0.01†			< 0.01†
< 7	3,804 (33.70)	1,017 (43.57)		3,632 (42.11)	887 (43.54)	
7–9	4,649 (51.92)	1,152 (49.36)		4,424 (51.29)	945 (46.39)	
> 9	501 (5.60)	165 (7.07)		570 (6.61)	205 (10.06)	
BMI (kg/m^2)			0.92†			< 0.01†
< 23	205 (2.29)	54 (2.31)		521 (6.04)	156 (7.66)	
23–25	5,345 (59.69)	1,403 (60.11)		5,747 (66.62)	1,376 (67.55)	
≥ 25	3,404 (38.02)	877 (37.57)		2,358 (27.34)	505 (24.79)	
Physical activity‖			< 0.01†			< 0.01†
No	1,597 (17.84)	293 (12.55)		1,908 (22.12)	383 (18.80)	
Yes	7,357 (82.16)	2,041 (87.45)		6,718 (77.88)	1,654 (81.20)	
Hypertension			< 0.01†			< 0.01†
No	7,258 (81.06)	1,956 (83.80)		7,235 (83.87)	1,817 (89.20)	
Yes	1,696 (18.94)	378 (16.20)		1,391 (16.13)	220 (10.80)	
DM			0.03†			< 0.01†
No	8,272 (92.38)	2,186 (93.66)		8,216 (95.25)	1,974 (96.91)	
Yes	682 (7.62)	148 (6.34)		410 (4.75)	63 (3.09)	
Dyslipidemia			0.01†			0.01†
No	8,090 (90.35)	2,146 (91.95)		7,766 (90.03)	1,869 (91.75)	
Yes	864 (9.65)	188 (8.05)		860 (9.97)	168 (8.25)	
AST (IU/L)	24.77 ± 14.65	23.85 ± 11.88	< 0.01*	20.03 ± 8.51	19.81 ± 8.51	0.29*
AST status¶			0.05†			0.35†
Normal	8,350 (93.25)	2,203 (94.39)		8,439 (97.83)	1,986 (97.50)	
Abnormal	604 (6.75)	131 (5.61)		187 (2.17)	51 (2.50)	
ALT (IU/L)	26.64 ± 21.94	25.87 ± 18.01	0.12*	17.25 ± 12.86	17.01 ± 12.51	0.44*
ALT status#			0.67†			0.19†
Normal	7,304 (81.57)	1,895 (81.19)		8,195 (95.00)	1,921 (94.31)	
Abnormal	1,650 (18.43)	439 (18.81)		431 (5.00)	116 (5.69)	

Data are shown as No.‡ (estimated percentage) for categorical variables and as mean ± standard error for continuous variables.
BMI: body mass index; DM: diabetes mellitus; AST: aspartate aminotransferase; ALT: alanine aminotransferase.
*The *p*-value by independent 2 sample t-test; †The *p*-value by χ^2 test; ‡Unweighted count; §Categorized as drinking units of alcohol per time (social drinkers < 5 units, binge drinkers ≥ 5 units); ‖Grouped according to whether performed exercise over 10 minutes that are more strenuous than usual activities or not; ¶Abnormal AST > 40 IU/L; #Abnormal ALT > 35 IU/L.

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Table 2. Crude and adjusted OR for abnormal AST and abnormal ALT by shift work in male and female subjects

Variable	Abnormal AST		Abnormal ALT	
	Male	Female	Male	Female
Crude OR (95% CI)				
Day work	Reference	Reference	Reference	Reference
Shift work	0.81 (0.65–1.02)	1.20 (0.83–1.72)	0.99 (0.87–1.14)	1.19 (0.92–1.54)
Model 1*				
Day work	Reference	Reference	Reference	Reference
Shift work	0.85 (0.68–1.06)	1.30 (0.90–1.87)	0.95 (0.83–1.09)	1.30 (1.00–1.69)
Model 2†				
Day work	Reference	Reference	Reference	Reference
Shift work	0.85 (0.68–1.07)	1.30 (0.90–1.87)	0.96 (0.84–1.11)	1.31 (1.00–1.71)

OR: odds ratio; CI: confidence interval; Abnormal AST: abnormal serum level of aspartate aminotransferase; Abnormal ALT: abnormal serum level of alanine aminotransferase.
*Model 1: adjusted by age, smoking status, drinking status, physical activity; †Model 2: model 1+ hours of sleep, body mass index, hypertension, diabetes mellitus, dyslipidemia.

Table 3. Crude and adjusted OR for abnormal AST and abnormal ALT by shift work patterns male and female subjects

Variable	Abnormal AST		Abnormal ALT	
	Male	Female	Male	Female
Crude OR (95% CI)				
Day work	Reference	Reference	Reference	Reference
Fixed-evening shift	0.85 (0.63–1.15)	0.88 (0.54–1.42)	1.08 (0.90–1.30)	1.20 (0.85–1.69)
Fixed-night shift	1.13 (0.67–1.89)	1.68 (0.71–3.98)	1.02 (0.73–1.43)	1.35 (0.76–2.39)
Regular day and night rotating shift	0.89 (0.52–1.53)	1.31 (0.53–3.27)	1.07 (0.77–1.50)	0.74 (0.36–1.54)
24-hours rotating shift	0.91 (0.45–1.86)	0.17 (0.02–1.23)	1.01 (0.64–1.58)	0.49 (0.22–1.11)
Split shift	1.78 (0.88–3.58)	1.22 (0.27–5.44)	1.48 (0.92–2.38)	0.96 (0.36–2.58)
Irregular rotating shift	0.69 (0.36–1.35)	1.46 (0.46–4.67)	1.12 (0.73–1.71)	1.59 (0.79–3.19)
Model 1*				
Day work	Reference	Reference	Reference	Reference
Fixed-evening shift	0.86 (0.63–1.16)	0.91 (0.56–1.47)	1.06 (0.88–1.28)	1.24 (0.88–1.74)
Fixed-night shift	1.11 (0.66–1.87)	1.74 (0.73–4.17)	0.98 (0.70–1.37)	1.39 (0.78–2.47)
Regular day and night rotating shift	0.92 (0.53–1.59)	1.29 (0.52–3.21)	1.04 (0.75–1.46)	0.75 (0.36–1.54)
24-hours rotating shift	0.89 (0.43–1.81)	0.18 (0.03–1.30)	1.00 (0.64–1.57)	0.50 (0.22–1.15)
Split shift	1.74 (0.85–3.54)	1.41 (0.32–6.31)	1.46 (0.90–2.37)	1.06 (0.40–2.84)
Irregular rotating shift	0.75 (0.38–1.47)	1.67 (0.52–5.39)	1.10 (0.72–1.69)	1.76 (0.88–.3.56)
Model 2†				
Day work	Reference	Reference	Reference	Reference
Fixed-evening shift	0.86 (0.63–1.17)	0.92 (0.56–1.49)	1.06 (0.87–1.30)	1.27 (0.91–1.78)
Fixed-night shift	1.11 (0.66–1.87)	1.75 (0.74–4.15)	1.00 (0.72–1.38)	1.40 (0.80–2.46)
Regular day and night rotating shift	0.92 (0.53–1.60)	1.33 (0.53–3.34)	1.07 (0.76–1.51)	0.77 (0.36–1.61)
24-hours rotating shift	0.91 (0.44–1.86)	0.18 (0.03–1.35)	1.07 (0.69–1.67)	0.53 (0.23–1.22)
Split shift	1.74 (0.86–3.55)	1.39 (0.31–6.21)	1.47 (0.89–2.43)	1.03 (0.38–2.77)
Irregular rotating shift	0.69 (0.35–1.36)	1.67 (0.53–5.24)	0.97 (0.61–1.54)	1.77 (0.85–3.68)

OR: odds ratio; CI: confidence interval; abnormal AST: abnormal serum level of aspartate aminotransferase; abnormal ALT: abnormal serum level of alanine aminotransferase.
*Model 1: adjusted by age, smoking status, drinking status, physical activity; †Model 2: model 1+ hours of sleep, body mass index, hypertension, diabetes mellitus, dyslipidemia.

of xenobiotics [17]. Many experimental animal studies and clinical trials revealed that significant genes, proteins and enzymes levels in livers are controlled by circadian rhythms to a great extent [18-20]. Also, there is still more evidence to support that the disruption of circadian rhythm is a crucial molecular mechanism in the pathogenesis from organic injury to fibrosis [21-24]. Shift work causes circadian disorganization between workers' activity and the normal rhythm of the liver. Such disorganization might exacerbate liver diseases, including fatty liver, cholestasis, hepatitis, cirrhosis and liver cancer, and these diseases can in turn disrupt the circadian clock system [17].

Several previous studies have shown that shift work affects the risk of liver disorder. A 5-year retrospective cohort study by Lin et al. [12] evaluated the impact of shift work on liver health and concluded that night shift work hindered the normalization of ALT. In another study, it was found that persistent rotating shift work exposure significantly aggravates the development of abnormal ALT among employees with preexisting sonographic fatty liver [11]. A prospective cohort study by Wang et al. [13] examined the relationship between night shift work and abnormal ALT showed that compared with day workers, current night shift workers had a higher risk of abnormal ALT (OR: 1.19, 95% CI: 1.00–1.42) after adjusting confounding factors. And an increasing trend ($p = 0.031$) of abnormal ALT risk was observed in night shift workers without non-alcoholic fatty liver, the prevalence of abnormal ALT increased from 9.7% to 13.3% as the number of night shift work years increased [13].

In our study, we expected that shift work, which interferes circadian rhythms, would be related to abnormal level of liver enzymes, and the results showed a significant association between shift work and abnormal ALT among female workers. This result partially supported previous studies which reported the positive association of abnormal ALT [10,11,13]. There was no significant association between shift work and abnormal AST. It may have occurred as a characteristic difference between ALT and AST. ALT is a highly specific marker of liver pathology, restricted to the cytosolic component of the hepatocytes. However, AST is less liver specific, as it is released by damage to the liver, and also to the heart, skeletal muscle, kidney, brain, pancreas, and erythrocytes [25,26].

In addition, there was no significant association between shift work and abnormal level of liver enzymes among male workers. The reasons for this finding are not clear. The published data on the liver function of shift workers are limited, and no research of gender specific differences between liver functions and shift work was found. However, there are several possible factors for this gender difference. While disturbance of circadian rhythm is the most important factor of abnormal liver enzymes in shift workers, shift work related factors such as insulin resistance [27-31], sleep disorder [32,33], and poor eating habits [34] can also affect liver disorders indicated by abnormal liver enzymes. In the Swedish study, although insulin resistance was not possible to estimated, it was found that the prevalence of subjects with impaired glucose tolerance was higher among women than men, and the proportion with impaired glucose tolerance among shift working women was significantly higher than among corresponding day working women [35]. Marquie and Foret [36] examined the effects shift work experience on sleep, it was found that female shift workers report more sleep problems and more use of hypnotics to fall asleep than male shift workers. In addition, according to 2 studies of sleep and insulin resistance, it was reported that short sleep duration or sleep disturbance may lead to the development of insulin resistance in women only, supporting a possible gender difference [37,38]. Lastly, in a study of industrial workers who work day and night shifts in Korea, the eating habits and nutrient intake of the female night workers was the worst [39]. Therefore, another biological factor may play a role in the association between shift work and risk of abnormal liver enzymes in women. Further research is needed to reveal the potential gender difference underlying this association.

This study did not find significant differences between patterns of shift work and abnormal liver enzymes when shift work were divided into 6 groups. Previous studies have reported that the duration and pattern of the shift work appear to have different biological effects on humans [40-42]. However, the pattern of shift work cannot always be categorized clearly, and workers are not permanently engaged in the same pattern of shift work. We could not

get precise information on the duration of each pattern, extra work and other possible differences between the shift groups, which could have helped us better interpret the results. This is a limitation of our study and more studies should be conducted between the type of shift work and the risk of liver enzyme abnormalities.

This study has some limitations. First, as the KNHANES is a cross-sectional study, only relation between shift work and abnormal level of liver enzymes could be established, not causal relationships. Second, there was no information about the duration of the shift work, so we could not investigate the dose response relationship with shift work and liver enzymes. Lastly, we could not get detailed information on the possible differences between shift patterns.

Despite these limitations, the strengths of this study are the use of a nationally representative large scale survey, and data was analyzed after stratification for gender considering multiple variables such as age, smoking status, drinking status, hours of sleep, BMI, physical activity. Additionally, to our knowledge, this is the first study that shows gender differences between abnormal ALT and shift work, though there are previous studies reported that shift work is associated with abnormal level of liver enzymes [10-12].

CONCLUSIONS

There was a relationship between shift work and abnormal ALT in female workers. This study provides limited support for the hypothesis that shift work is related to liver enzyme abnormality, but offers some evidence in favor of the idea that shift work affects female workers more than males on abnormal ALT. Therefore, the results of this study are regarded as preliminary and further studies are needed to define the relationship between shift work and abnormal liver enzymes to be carried out as well as the gender difference in the association.

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