original article

Influence of baseline weight on relationship between shift work and longitudinal changes of cholesterol

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ABSTRACT

Aims: The aim of this study was to investigate the relationship between longitudinal change in total cholesterol as a main cardiovascular disease risk factor and shift work, controlling for the effect of the weight at baseline of recruitment.

Materials and Methods: This retrospective cohort study consists of 674 employees of Iranian Corporation Polyacril from 1992 to 2009. Stratified analysis of the relationship between shift work and cholesterol based on weight status at baseline of recruitment controlled for the effect of confounders including age, body mass index, pre-employment cholesterol, glucose, triglyceride, urea, work types, education, and marital status. A linear mixed model used for analyzing the data. Estimation of parameters has done by Bayesian approaches using Winbugs statistical software. Bayesian confidence interval (CI) was used for testing regression coefficients.

Results: Average age mean at employment was 25 years (standard deviation [SD] =3.3); the average number of measurement for each individual was 3.7 times (SD = 0.6). In this model, relationship between shift work and cholesterol changes controlled for confounding factors was significant in whom overweight was at baseline (beta = 2.25, $P < 0.001$, 95% CI: 0.67-3.88) but was not significant for whom overweight was at baseline of employment.

Conclusions: The rate of cholesterol changes was higher for normal weight shift workers compared with workers who were overweight at baseline of recruitment.

Key words: Cholesterol, linear mixed model, occupational diseases, shift work

INTRODUCTION

Relationship between shift work and chronic diseases such as cardiovascular diseases (CVDs) has been investigated in several studies.[1] Knutsson *et al*.[2] estimated that CVD risk is higher in day workers by 40%. Different studies have suggested various potential mechanisms for justifying relationship between shift work and CVDs including metabolic disorders, lifestyle changes, stress, and disruption in body circadian rhythm.[3] Some studies have pointed the relationship between work shift and increasing weight[4] and also there is evidence on relationship between shift work and metabolic syndrome.[5] Some others have reported significant relationship between shift work and blood fats like cholesterol.[6-8] However, some do not support this finding.[9,10] On the other hand, recent works have reported blood lipid change in shift workers associated with the weight

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at baseline of recruitment so that in workers who were not overweight at the time of entry into the study, "shift work is a risk factor for increased total cholesterol."[11] Since lipid disorder is one of the main risk factors for CVD, investigating its relationship with shift work may be useful in explaining relationship between shift work and CVDs. Considering the lack of longitudinal studies related to this issue in Iran, this retrospective cohort study aims at investigating relationship between cholesterol longitudinal changes and shift work in terms of weight at baseline of recruitment in employees of Iranian Corporation Polyacril (ICP).

MATERIALS AND METHODS

This retrospective cohort study consists of 674 employees of ICP. Inclusion criteria were formal or informal employment during 1992-2009 and lack of incidence of CVDs in medical records and having pre-recruitment information including cholesterol and body mass index (BMI). If the subject's file lacked pre-recruitment information or suffered from any CVD, then he would be excluded from the study. Data collection was based on information recorded in Health System and Industrial Medicine Unit of Isfahan Poly Acryl located in Isfahan Poly Acryl Plant which included annual measurements of cholesterol, BMI, glucose, triglyceride, urea, work types (administrative and non-administrative), education, and age. All measurements were carried out in morning shift work before initiating work when subjects were fast. Working shift is divided into three times: Day worker, two-rotation shift workers (2 days in morning, 2 days in evening, and 2 days in rests), and three-rotation shifts workers (2 days in morning, 2 days in evening, and 1 day in rests, 2 nights, and 1 day in rest).

First, data were described in terms of pre-recruitment BMI as higher and lower than 25 (overweight and non-overweight workers, respectively) which is given in Table 1. Quantitative variables were described as average ± standard deviation and qualitative variables were described as frequency percent (number). Potential correlation between measured observations over the time is required by the nature of longitudinal data. Thus, in order to manage correlation between recorded observations of individuals and to deal with response missing which is one of the common problems in longitudinal studies, linear mixed model was used. Mixed models are capable of controlling individual and environmental effects which are sometimes non-observable.[12,13] Recently, efforts have been done for making linear mixed models more robust toward violation of the assumed normal errors and random effects.[14-16] Regarding the fact that lipids have non-normal distribution and are usually skewed to the right and, on the

Table 1: Baseline characteristic of 674 employees

Variables	Day workers	2-Rotation shift	3-Rotation shift
Without overweight (BMI<25)			
Number	153	28	248
Age (years)	25.86±3.25	24.24±2.35	24.40±2.86
Cholesterol (mg/dl)	150.15±29.14	146.14±30.77	144.84±29.00
Triglyceride (mg/dl)	96.04±46.81	87.53±40.72	94.77±49.03
Glucose (mg/dl)	82.94±8.07	83.67±9.06	82.57±8.34
Urea (mg/dl)	26.68±6.34	25.79±5.87	27.11±6.34
Education			
Diploma and lower	12.4 (19)	82.1 (23)	57.3 (142)
Higher diploma	87.6 (134)	17.9 (5)	42.7 (106)
Marital status			
Married	35.9 (55)	17.9 (5)	32.3 (80)
Single	64.1 (98)	82.1 (23)	67.7 (168)
Type of work			
Official	7.8 (12)	-	-
Non-official	92.2 (141)	100 (28)	100 (248)
With overweight (BMI≥25)			
Number	88	16	141
Age (years)	26.54±3.93	25.09±2.89	25.56±3.32
Cholesterol (mg/dl)	162.17±30.71	148.81±28.68	160.32±29.40
Triglyceride (mg/dl)	138.02±71.93	94.12±30.08	132.14±88.01
Glucose (mg/dl)	86.10±9.21	85.50±7.85	84.11±8.67
Urea (mg/dl)	26.93±6.31	24.31±4.82	25.66±6.13
Education			
Diploma and lower	17.0 (15)	62.5 (10)	50.4 (71)
Higher diploma	83.0 (73)	37.5 (6)	49.6 (70)
Marital status			
Married	48.9 (43)	68.8 (11)	48.2 (68)
Single	51.1 (45)	31.3 (5)	51.8 (73)
Type of work			
Official	19.3 (17)	-	0.7 (1)
Non-official	80.7 (71)	100 (16)	99.3 (140)

BMI: Body mass index

other hand, the variable under study here is total cholesterol, model errors distribution was changed in order to optimize estimations regarding violation of assumed normality. Normal distribution, *t*, and skew-normal distribution were used as special modes of skew-elliptical distribution[17] as model errors distribution and estimation of parameters were done using Bayesian approach. Used models were special forms of mixed models introduced by Valle *et al*. (2007) and Jara *et al*. (2008).[14,15] Model parameters were estimated using Bayesian approach and Gibbs sampling method. Iterations of 100,000 after discarding a 10,000 sample burn-in ere used for inferring parameters and convergence of chains generated by density graph of posterior distribution, time series, autocorrelation, and Gelman–Rubin chart was studied.[18] Deviance information criterion was used for comparing models.[19] The model with least deviance information will be the better one. Shapiro–Wilk test was used for testing normality of model errors. Model coefficients test was done using Bayesian confidence interval (CI) and models were fitted using Winbugs software.

RESULTS

Subjects' information at baseline of recruitment is given in Table 1 in terms of overweight status. In addition, Shapiro–Wilk test showed that errors of standard linear mixed model do not follow normal distribution (*P*-value < 0.001), thus regarding Table 2, skew-normal linear mixed model was used for interested inferences. Table 3 reports the results of linear mixed model with skew-normal error which was the best one among three models. Considering the fact that age effect was an important factor, its interaction with shift work was entered into the model. It should be noted that coefficients related to two-rotation shift work in absence of interaction of subjects with overweight and without overweight at baseline of recruitment were 5.93 (4.6) and 3.96 (3.36), respectively, both of which were not significant. However, coefficients related to three working shifts in absence of interaction of subjects with overweight and without overweight at baseline of recruitment were 0.22 (2.47) and 5.63 (1.81), respectively, which was significant for subjects without overweight. Following introducing interaction, by increasing age, the rate of cholesterol changes was significantly higher for normal weight shift workers compared to workers who were overweight at baseline of recruitment.

DISCUSSION

Investigating data resulting from 17-year follow-up of employees in Poly Acryl Plant indicated that shift work can be predictor of cholesterol changes in interaction with age in shift workers. In addition, this relationship can be influenced by overweight at baseline of recruitment. This finding is consistent with the study done in 2011.[11] That work indicated relationship between shift work and cholesterol with controlling confounding variables such as

Table 2: Deviance information criteria

	Normal	*t*	Skew-normal
Employees with baseline overweight	5450.35	5436.13	5021.37
Employees without baseline overweight	9955.65	9859.63	8683.25

*Lower DIC is better, DIC: Deviance information criteria

Table 3: Bayesian estimation of linear mixed model parameters with skew-normal error

Parameters	Employees with baseline over weight				Employees without baseline over weight			
	Beta	SD	Bayesian CI		Beta	SD	Bayesian CI	
			Low bound	Up bound			Low bound	Up bound
Baseline cholesterol	0.646*	0.034	0.578	0.712	0.594*	0.025	0.545	0.644
Triglyceride	0.077*	0.011	0.055	0.098	0.067*	0.011	0.046	0.088
Glucose	0.245*	0.0762	0.093	0.392	0.298*	0.066	0.169	0.430
Urea	0.208	0.110	−0.006	0.424	0.303*	0.077	0.152	0.456
BMI	1.511*	0.391	0.745	2.278	1.776*	0.301	1.185	2.357
Type of work								
Official	10.61*	4.289	2.092	18.94	2.801	4.482	−5.999	11.790
Non-official	-	-	-	-	-	-	-	-
Marital status								
Single	3.594	2.273	−0.8598	8.067	5.454*	1.658	2.21	8.683
Married	-	-	-	-	-	-	-	-
Education								
Higher diploma	−2.005	2.29	−6.522	2.519	0.5218	1.669	−2.737	3.843
Diploma and lower	-	-	-	-	-	-	-	-
Age	0.151	0.378	−0.586	0.892	0.9074*	0.3173	0.278	1.529
Shift work								
2-Rotation	−51.410	34.360	−118.400	16.490	−57.42*	23.48	−103.3	−12.41
3-Rotation	−22.83	15.35	−52.62	7.034	21.66	12.41	−2.864	45.36
Day	-	-	-	-	-	-	-	-
Age×2-rotation shift	2.004	1.205	−0.3809	4.346	2.252*	0.8255	0.6682	3.878
Age×3-rotation shift	0.818	0.5141	−0.178	1.817	−0.928	0.4295	−1.751	0.074
Age×day	-	-	-	-	-	-		-

*$P<0.05$; SD: Standard deviation, BMI: Body mass index, CI: Confidence interval

age and BMI and variables related to lifestyle in workers without overweight at baseline of recruitment were positive, while it was reported that this relationship in workers with overweight at baseline of recruitment was not significant. The authors explained that this relationship was due to difference in body metabolism of overweight workers compared to normal workers. In this study, the interaction of age and shift work was also considered. This effect was not significant in workers with overweight at baseline of recruitment; however, our findings showed that two-rotation shift workers who did not have overweight at baseline of recruitment experience increasing cholesterol changes by growing older. It should be mentioned that direction of relationship between two-rotation shift and cholesterol changes was maintained both in model with interaction with age and model without interaction with age and both in workers with overweight and in workers without overweight; however, it lost its significance in workers with overweight. On the other hand, regardless of interaction in normal workers, it was observed that cholesterol was significantly reduced in three-rotation shift workers. This finding is consistent with some studies,[20] but it is inconsistency with others.[21] These descending changes can be attributed to lower stress level in workers working in three-rotation shift workers who experience working overnight. They are less supervised in night shifts and have lighter works which is unlike workers working during daytime and two-rotation shift workers. Of course, the effect of altered relationship, say with effect of an unhealthy worker, cannot be ignored. In other words, it is likely that workers who are not able to work in three-rotation shift gradually experience change in their condition and three-rotation shift workers in our sample consist of those who have higher capacity in terms of matching to shift work and health condition. However, some studies have not found any relationship between shift work and cholesterol change.[9,22] In explaining relationship observed in this study and even similar works, it should be noted that there are different definitions for shift work in various studies, and work type may influence on the response and thus comparison of various works' results would be made impossible. This fact along with lack of some main confounding variables in most studies related to shift work makes the need for caution in interpreting the results more evident.[1,23] A statistical model was also used which have been considered in recent decade. Our results indicated that when there is a violation of mixed models' main assumption which is normality for errors and random effects, changing distribution in such a way that consider nature of the data will improve model fitting. This finding is consistent with previous works in this regard.[14,15,24] One of limitations in this work was lack of some confounding factors such as physical activity, variables related to lifestyle such as smoking and diet as well as socioeconomic situation. Of course, change in condition and type of shift work was not available for the authors. However, using a robust statistical model for longitudinal data management and thus using all available data as well as acceptable sample size and controlling some confounding variables can be mentioned as strengths of this work.

CONCLUSION

By increasing age, the rate of cholesterol changes was significantly higher in shift workers who had normal weight at baseline of recruitment compared with shift workers who were overweight at baseline of recruitment. In addition, linear mixed model with heavy tail and skewed errors showed better fitting compared to normal mixed model.

REFERENCES

1. Wang XS, Armstrong ME, Cairns BJ, Key TJ, Travis RC. Shift work and chronic disease: The epidemiological evidence. Occup Med (Lond) 2011;61:78-89.
2. Knutsson A, Akerstedt T, Jonsson BG, Orth-Gomer K. Increased risk of ischaemic heart disease in shift workers. Lancet 1986;2:89-92.
3. Knutsson A, Bøggild H. Shiftwork and cardiovascular disease: Review of disease mechanisms. Rev Environ Health 2000;15:359-72.
4. Suwazono Y, Dochi M, Sakata K, Okubo Y, Oishi M, Tanaka K, *et al*. A longitudinal study on the effect of shift work on weight gain in male Japanese workers. Obesity (Silver Spring) 2008;16:1887-93.
5. De Bacquer D, Van Risseghem M, Clays E, Kittel F, De Backer G, Braeckman L. Rotating shift work and the metabolic syndrome: A prospective study. Int J Epidemiol 2009;38:848-54.
6. Ha M, Park J. Shiftwork and metabolic risk factors of cardiovascular disease. J Occup Health 2005;47:89-95.
7. Dochi M, Sakata K, Oishi M, Tanaka K, Kobayashi E, Suwazono Y. Relationship between shift work and hypercholesterolemia in Japan. Scand J Work Environ Health 2008;34:33-9.
8. Theorell T, Akerstedt T. Day and night work: Changes in cholesterol, uric acid, glucose and potassium in serum and in circadian patterns of urinary catecholamine excretion. A longitudinal cross-over study of railway workers. Acta Med Scand 1976;200:47-53.
9. Morikawa Y, Nakagawa H, Miura K, Soyama Y, Ishizaki M, Kido T, *et al*. Effect of shift work on body mass index and metabolic parameters. Scand J Work Environ Health 2007;33:45-50.
10. Knutsson A, Akerstedt T, Jonsson BG. Prevalence of risk factors for coronary artery disease among day and shift workers. Scand J Work Environ Health 1988;14:317-21.
11. Uetani M, Sakata K, Oishi M, Tanaka K, Nakada S, Nogawa K, *et al*. The influence of being overweight on the relationship between shift work and increased total cholesterol level. Ann Epidemiol 2011;21:327-35.
12. Hox J. Multilevel Analysis: Techniques and Applications. USA: Lawrence Erlbaum Associates, Inc.; 2002.
13. Goldstein H. Multilevel Models in Educational and Social Research. New York: Oxford University Press; 1987.
14. Jara A, Quintana F, Martín ES. Linear mixed models with skew-elliptical distributions: A Bayesian approach. Comput Stat Data Anal 2008;52:5033-45.
15. Arellano-Valle RB, Bolfarine H, Lachos VH. Bayesian inference for skew-normal linear mixed models. J Appl Stat 2007;34:663-82.
16. Pinheiro J, Liu C, Wu Y. Efficient algorithms for robust estimation in linear mixed-effects models using the multivariate t distribution. J Comput Graph Stat 2001;10:249-76.
17. Liu J, Dey DK. Skew-elliptical distributions. In: Genton, M.G. editor. Skew-Elliptical Distributions and their Applications: A Journey Beyond Normality. Boca Raton, FL: Chapman and Hall; 2004. p. 43-64.
18. Ntzoufras I. Bayesian Modeling Using Winbugs. Hoboken, New Jersey: Wiley and Sons; 2009.

19. Spiegelhalter DJ, Best NG, Carlin BP, Van der Linde A. Bayesian measures of model complexity and fit (with discussion). J R Stat Soc Series B Stat Methodol 2002;64:583-639.
20. van Amelsvoort LG, Schouten EG, Kok FJ. Impact of one year of shift work on cardiovascular disease risk factors. J Occup Environ Med 2004;46:699-706.
21. Dochi M, Suwazono Y, Sakata K, Okubo Y, Oishi M, Tanaka K, *et al*. Shift work is a risk factor for increased total cholesterol level: A 14-year prospective cohort study in 6886 male workers. Occup Environ Med 2009;66:592-7.
22. Knutson A, Andersson H, Berglund U. Serum lipoproteins in day and shift workers: A prospective study. Br J Ind Med 1990;47:132-4.
23. Frost P, Kolstad HA, Bonde JP. Shift work and the risk of ischemic heart disease-a systematic review of the epidemiologic evidence. Scand J Work Environ Health 2009;35:163-79.
24. Arellano-Valle RB, Bolfarine H, Lachos VH. Skew-normal linear mixed models. J Data Sci 2005;3:415-38.

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