Data mining: Traditional Spring Festival Associated With Hypercholesterolemia

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Research Article

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Abstract

Background
Serum lipid concentrations are affected by long-term high fat diets; thus, we hypothesise that lipid levels increase after Spring Festival in China. In total, 20,192 individuals (males, 10,108; females, 10,084) were enrolled in this retrospective cross-sectional study, based on clinical data from Laboratory Information System (LIS) and Hospital Information System (HIS) in Peking Union Medical College Hospital, from 2014 to 2018. Total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were analysed.

Results
Average age, BMI, SBP, and DBP of the participants were 39.4 years, 23.7 kg/m$^2$, 118 mmHg, and 73 mmHg, respectively. Serum TC, TG, and LDL levels were significantly higher in males than in females (P < 0.001); serum HDL-C was statistically lower in males (P < 0.001). In February, the TC, TG, and LDL-C levels were 8.4%, 16.3%, and 9.3% higher than the lowest levels recorded, respectively. Additionally, dyslipidaemia prevalence was statistically higher in the first week after Spring Festival than in May–January.

Conclusion
Higher TC, TG, LDL-C in winter could be associated with high fat diets during Spring Festival. Spring Festival was immediately followed by a higher lipid concentration. Thus, it is necessary accurately diagnose dyslipidaemia after Spring Festival.

1. Background
Lipid profiles including TC, TG, HDL-C, and LDL-C are primary analytes for the diagnosis of dyslipidaemia in clinical settings. Seasonal variation in lipid profiles has been reported by several studies in various countries [1-7], with higher serum lipid levels during the winter months than in the summer [1-4, 7]. A longitudinal study enrolled 517 healthy volunteers with a baseline TC of 5.75 mmol/L in men and 5.52 mmol/L in women [8] and found that the amplitude of seasonal variation in TC was 0.10 mmol/L (peaked in December) in men and 0.14 mmol/L (peaked in January) in women [8]. Moreover, a cross-sectional study enrolled 245 healthy young students (110 men and 135 women) using consignor analysis and found that TC, TG, HDL, and LDL levels exhibited statistically significant seasonal patterns [9].

Similarly, our previous study reported seasonal variation in lipid profiles, with peak values observed during the winter, which decreased in summer [4]. Although, the mechanism for this seasonal variation is unclear, we suspect that in China, specifically, the increased lipid levels are associated with high fat diets during Spring Festival, which is a traditional festival in China. During this time family members gather to celebrate often including high fat meals including pork, beef, lamb, chicken, etc. which may contribute to increased serum lipid levels. A meta-analysis study revealed that long-term high fat diets are associated with increased blood lipid levels [10]. Fatty diets also have a significant influence on blood lipid concentrations in overweight or obese individuals [11]. Alternatively, carbohydrate-restricted diets have been reported as associated with decreased LCL-C in overweight and obese adults [12]. Similarly, a randomised general community trial reported that replacement of saturated fats with carbohydrates from grains, vegetables, legumes, and fruits reduces TC and LCL-C levels.

An increasing number of studies are currently focusing on clinical laboratory big data to explore trends for a variety of common analytes by months or years. According to the Clinical and Laboratory Standard Institute, using clinical big data to establish reference intervals is not only cost-effective but also highly efficient.

Accordingly, in this study, we hypothesise that TC, TG, and LDL-C levels are increased along with dyslipidaemia, while HDL-C is decreased during the first week after Spring Festival, based on clinical laboratory big data.

2. Materials And Methods

2.1 Data collection
Data were derived from Laboratory Information System (LIS) and Hospital Information System (HIS) in Peking Union Medical College Hospital from 2014 to 2018. A total of 280,206 records from apparently healthy individuals were obtained. The inclusion and exclusion criterion schematic are described in our previous study [4]. Ultimately, a total of 20,192 individuals were enrolled for further analyses.

2.2 Laboratory measurements
Serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol, total protein (TP), albumin (Alb), total bilirubin (TBil), direct bilirubin (DBil), alanine aminotransferase (ALT), alanine aminotransferase (AST), creatinine (Cr), uric acid (UA), and glucose (Glu) were measured with a Roche C8000 automatic analyser (Roche, Basel, Switzerland).

2.3 Definition of Spring Festival and dyslipidaemia
According to the traditional festival in China, the first day of the lunar calendar marks the beginning of the Spring Festival. In China, seven days are allocated to the celebration of this festival from the last day of December to January 6th according to the lunar calendar. Thus, the timing of Spring Festival differs from year to year. The dates of Spring Festival during the study period are shown in Table 1.
Dyslipidaemia was defined as TC $\geq$ 5.2 mmol/L or TG $\geq$ 1.7 mmol/L or HDL-C $<$ 1.0 mmol/L or LDL-C $\geq$ 3.4 mmol/L [13].

2.4 Statistical analysis

Data were analysed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA), Excel 2010 (Microsoft Inc., USA) and GraphPad prism for Windows (GraphPad Software, San Diego, CA). Kolomogorov-Smirnov analysis was used to evaluate the distribution of data. The normal distribution data was presented as mean±standard deviation, while non-normally distributed data was expressed as median and quartiles. Kruskal-Wallis or Mann-Whitney U test were used to compare the differences. Chi-square test was used to analyse the differences in prevalence of dyslipidaemia by month. P values $<$ 0.05 were considered statistically significant.

3. Results

3.1 Basic characteristics of enrolled population

In total, 20,192 individuals, including 10,108 males and 10,084 females, were enrolled in this study. The average age, BMI, SBR and DBP were 39.4 years, 23.7 kg/m$^2$, 118 mmHg, and 73 mmHg, respectively. Basic characteristics of the enrolled participants by season are shown in Table 2. Differences were observed in serum TP, Alb, TBil, DBil, ALT, ALP, Glu, UA, and Cr levels by season (all $P > 0.05$). Lipid concentrations by sex are shown in Figure 1. Serum TC, TG, and LDL-C levels were significantly higher in males than in females (all $P < 0.001$), whereas the serum HDL-C levels in males was statistically lower than that in females ($P < 0.001$).

3.2 Distribution of lipid profiles by months

Serum TC, TG, HDL-C, and LDL-C distribution by months are shown in Figure 2. The highest levels of TC, TG, and LDL-C were observed in February, while HDL-C was highest in November. Importantly, the first week after Spring Festival took place in February. The deviation between lowest and highest TC, TG, HDL-C, and LDL-C were 8.4%, 16.3%, 6.3%, and 9.3%, respectively. Seasonal variations in lipid profiles by sex are shown in Supplemental Figure 1.

3.3 Distribution of lipid profiles between the first week after Spring Festival and other days

Distribution of lipid profiles between the first week after Spring Festival and other days in the year are shown in Figure 3. Kolomogorov-Smirnov analysis was used to compare the differences in lipid profiles between the first day after Spring Festival and other days. The serum TC, TG and LDL concentration in the first week after Spring Festival were significantly higher than that in other days (all $P < 0.05$), while the level of HDL-C in the first week after Spring Festival was statistically lower ($P = 0.04$).

3.4 Prevalence of dyslipidaemia

The overall prevalence of dyslipidaemia was 44.7%, with 59.4% in males and 30.0% in females. Hence, the prevalence was higher in males than females ($P < 0.001$). Moreover, the prevalence of dyslipidaemia in spring, summer, autumn, and winter were 48.3%, 42.5%, 42.3% and 47.7%, respectively. After stratifying by sex, the prevalence of dyslipidaemia in spring, summer, autumn, and winter were 61.5% and 32.8%, 56.3%, and 28.1%, 59.7% and 28.7%, 61.6%, and 32.2% for males and females, respectively. The prevalence of dyslipidaemia by month is shown in Figure 4, demonstrating that the prevalence was higher in the first week after Spring Festival than in the other months. Compared with first week after Spring Festival, the prevalence in January ($P = 0.037$), May ($P = 0.004$), June ($P = 0.005$), July ($P < 0.001$), August ($P < 0.001$), September ($P < 0.001$), October ($P < 0.001$), November ($P = 0.001$), and December ($P = 0.012$) were statistically lower. After stratifying by sex, the prevalence of dyslipidaemia between months and first week after Spring Festival are shown in Supplemental Figure 2.

4. Discussion

Seasonal variations in lipid levels have been confirmed by many studies [1-4, 9], some of which have indicated that attention must be paid to the increased risk of cardiovascular diseases in winter due to higher lipid levels [1, 4]. In this study, we found that serum lipid concentrations were higher (lower in HDL-C) in males than in females, which may be associated with different lifestyles and eating habits. Thus, to verify the interaction of sex of seasonal variation in lipid levels, we stratified analyses for seasonal variation in lipid levels based on males and females. We found that seasonal variation in lipid appeared to differ between males and females, suggesting that the differences in lifestyles and dietary intake affect lipid metabolism [14].

Increased LDL-C levels have been described to be associated with cardiovascular disease. In fact, reduced LDL-C levels are often prescribed as an effective method to prevent cardiovascular diseases [15]. Furthermore, increased TG concentration may also be associated with cardiovascular diseases [16]. Thus, lipid therapy and management could help to prevent cardiovascular diseases [17]. National Health and Nutrition Examination Survey data from 2003-2006 in the United States reported 53% of adults to have lipid abnormalities, 21% of whom have dyslipidaemia [15], which is an important risk factor for cardiovascular diseases [18, 19]. The prevalence of dyslipidaemia was 34% (35.1% in urban and 26.3% in rural area) based on a multi-stage, stratified sampling method in China [20]. However, the China National Stroke Screening and Prevention Projects reported the prevalence of dyslipidaemia as similar between rural and urban populations (43.2% vs 43.3%), which agreed with our study [21]. After stratifying by sex, we also found the prevalence of dyslipidaemia in the first week after Spring Festival was higher than other months.
In this study, we confirmed the association between increased lipid levels and high fat diet intake during Spring Festival, which was consistent with a Denmark study [1], which enrolled a total of 25,764 participants from the general population. They reported 15% higher TC and 20% higher LDL-C levels in the winter than in the summer, which was associated with high fat diets during Christmas holidays based on an observational study [1]. The same trend was also observed in a French study with 6.4% higher TC and 8.7% higher LDL-C in winter months than in the summer [2]. Further, the deviation in the current study between lowest and highest TC and LDL-C were 8.4% and 9.3%, which was similar to the French study [2]. Specifically, we found the prevalence of dyslipidaemia to be significantly higher the first week after Spring Festival than in the other months in both male and females, which was consistancy with a previous study [1]. A cross-sectional study that analysed data from normal-lipidemic individuals and dyslipidaemia individuals found strong positive cross-correlations between TC, TG, LDL-C, and HDL-C levels, suggesting a similar behaviour in normal- and dyslipidaemia populations [22].

There are several strengths to emphasise in this study. Firstly, we used clinical laboratory data downloaded from LIS and HIS to conduct this study, which is not only cost-effective but also efficient. Second, we only included information from the initial reports generated for individuals who visited the department of Health Medicine to ensure the consistency of all data. Additionally, to avoid having sex as a confounding variable when examining the seasonal variation and prevalence of dyslipidaemia, we performed individual analyses for variation and prevalence by sex. Lastly, this study was the first to report an association between increased lipid levels and Spring Festival in China.

However, certain limitations were also noted in this study. Although we used the clinical data to analyse the association between increased lipid levels and Spring Festival, we did not collect dietary intake information. However, it is well known that, during Spring Festival, a large proportion of the population gathers to celebrate the holiday with large meals with reduced levels of exercise. Moreover, information on whether participants were taking lipid-lowering therapy was unknown. Thus, to verify the association between high fat diet intake during Spring Festival and lipid levels, additional randomised studies are required.

5. Conclusion

In conclusion, we confirmed that higher lipid levels are associated with high fat diet during Spring Festival, with notable differences observed between males and females. However, the prevalence of dyslipidaemia during the first week after Spring was higher than that in any other month in both males and females. Thus, to accurately diagnose dyslipidaemia immediately after Spring Festival, it is necessary to consider the seasonal variations in lipid profiles.

Abbreviations

Alb, albumin; ALT, alanine aminotransferase; AST, alanine aminotransferase; Cr, creatinine; DBil, direct bilirubin; HDL-C, high density lipoprotein cholesterol; HIS, Hospital Information System; LDL-C, low-density lipoprotein cholesterol; LIS, Laboratory Information System; TBil, total bilirubin; TC, total cholesterol; TG, triglyceride; TP, total protein; UA, uric acid

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of Peking Union Medical College Hospital of the Chinese Academy of Medical Sciences (protocol number: S-K1158). All the data obtained was anonymized. The need for consent was waived by the Ethics Committee of Peking Union Medical College Hospital of the Chinese Academy of Medical Sciences. A statement to confirm that all methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and material

The datasets generated and analysed during the current study are available from the corresponding author Ling Qiu on reasonable request.

Competing interests

None.

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Authors' contributions

Danchen wang, Yutong Zou and Ling Qiu designed this study. Danchen Wang, Yutong Zou, and Songlin Yu wrote this manuscript. Danchen Wang, Ling Qiu, Honglei Li, Xinqi Cheng, and Liangyu Xia analysed the data. All of the authors reviewed this manuscript and approval to publish.

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References

1. Vedel-Krogh, S., et al., The Christmas holidays are immediately followed by a period of hypercholesterolemia. Atherosclerosis, 2019. 281: p. 121-127.

2. Nadif, R., et al., Seasonal variations of lipid profiles in a French cohort. Atherosclerosis, 2019. 286: p. 181-183.

3. Woodhouse, PR., K.T. Khaw, and M. Plummer, Seasonal variation of serum lipids in an elderly population. Age Ageing, 1993. 22(4): p. 273-8.

4. Wang, D., et al., Data mining: Seasonal fluctuations and associations between thyroid stimulating hormone and lipid profiles. Clin Chim Acta, 2020. 506: p. 122-128.

5. Cheng, T.O., Seasonal variation in serum cholesterol levels may be another explanation for seasonal variation in acute myocardial infarction. Int J Cardiol, 2005. 104(1): p. 101.

6. Mänttäri, M., et al., Seasonal variation in high density lipoprotein cholesterol. Atherosclerosis, 1993. 100(2): p. 257-65.

7. Kamezaki, F., et al., Seasonal variation in serum lipid levels in Japanese workers. J Atheroscler Thromb, 2010. 17(6): p. 638-43.

8. Ockene, I.S., et al., Seasonal variation in serum cholesterol levels: treatment implications and possible mechanisms. Arch Intern Med, 2004. 164(8): p. 863-70.

9. Cambras, T., et al., Seasonal variation in plasma lipids and lipases in young healthy humans. 2017. 34(9): p. 1248-1258.

10. Schwingshackl, L. and G. Hoffmann, Comparison of effects of long-term low-fat vs high-fat diets on blood lipid levels in overweight or obese patients: a systematic review and meta-analysis. J Acad Nutr Diet, 2013. 113(12): p. 1640-61.

11. Lu, M., et al., Effects of low-fat compared with high-fat diet on cardiometabolic indicators in people with overweight and obesity without overt metabolic disturbance: a systematic review and meta-analysis of randomised controlled trials. Br J Nutr, 2018. 119(1): p. 96-108.

12. Gjuladin-Hellon, T., et al., Effects of carbohydrate-restricted diets on low-density lipoprotein cholesterol levels in overweight and obese adults: a systematic review and meta-analysis. Nutr Rev, 2019. 77(3): p. 161-180.

13. Li, D.D., et al., Serum Gamma-Glutamyltransferase Levels are Associated with Cardiovascular Risk Factors in China: A Nationwide Population-Based Study. Sci Rep, 2018. 8(1): p. 16533.

14. Levy, S.B., et al., Lifestyle mediates seasonal changes in metabolic health among the yakut (sakha) of northeastern siberia. Am J Hum Biol, 2016. 28(6): p. 868-878.

15. Tóth, PP., D. Potter, and E.E. Ming, Prevalence of lipid abnormalities in the United States: the National Health and Nutrition Examination Survey 2003-2006. J Clin Lipidol, 2012. 6(4): p. 325-30.

16. Nordestgaard, B.G. and A. Varbo, Triglycerides and cardiovascular disease. Lancet, 2014. 384(9943): p. 626-635.

17. Michos, E.D., J.W. McEvoy, and R.S. Blumenthal, Lipid Management for the Prevention of Atherosclerotic Cardiovascular Disease. N Engl J Med, 2019. 381(16): p. 1557-1567.

18. Carroll, M.D., et al., Trends in lipids and lipoproteins in US adults, 1988-2010. Jama, 2012. 308(15): p. 1545-54.

19. Kopin, L. and C. Lowenstein, Dyslipidemia. Ann Intern Med, 2017. 167(11): p. Itc81-itc96.

20. Pan, L., et al., The prevalence, awareness, treatment and control of dyslipidemia among adults in China. Atherosclerosis, 2016. 248: p. 2-9.

21. Opoku, S., et al., Prevalence and risk factors for dyslipidemia among adults in rural and urban China: findings from the China National Stroke Screening and prevention project (CNSSPP). BMC Public Health, 2019. 19(1): p. 1500.

22. Moura, F.A., et al., Impact of seasonality on the prevalence of dyslipidemia: a large population study. Chronobiol Int, 2013. 30(8): p. 1011-5.

Tables

Table 1 Date of Spring Festival from 2014 to 2018

| Year | Spring Festival         |
|------|-------------------------|
| 2014 | 31, Jan-6, Feb          |
| 2015 | 18, Feb-24, Feb         |
| 2016 | 7, Feb-13, Feb          |
| 2017 | 27, Jan-2, Feb          |
| 2018 | 15, Feb-21, Feb         |

Table 2 Basic characteristics of enrolled population by season
| Analytes | Spring (n = 4819) | Summer (n = 6418) | Autumn (n = 5530) | Winter (n = 3425) | total (n = 20,192) | P value |
|----------|------------------|------------------|------------------|------------------|------------------|---------|
| age (years) | 40 31 49 37 30 47 36 29 46 37 30 46 37 47 30 | 23.8 21.3 26.3 23.2 21 25.9 23 20.6 25.6 23.5 21.1 26.3 23.4 26 21 | <0.00 |
| BMI (kg/m²) | 116 106 128 115 104.75 128 114 104 127 117 106 130 115 128 105 | 73 66 80 72 66 79 72 66 79 74 67 81 73 80 66 | <0.00 |
| SBP (mmHg) | 23.8 21.3 26.3 23.2 21 25.9 23 20.6 25.6 23.5 21.1 26.3 23.4 26 21 | 72 70 75 72 70 75 73 71 76 73 70 75 73 75 70 | <0.00 |
| DBP (mmHg) | 116 106 128 115 104.75 128 114 104 127 117 106 130 115 128 105 | 73 66 80 72 66 79 72 66 79 74 67 81 73 80 66 | <0.00 |
| TP (g/L) | 10.5 8.1 13.9 10.9 8.2 14.7 10.6 8.1 13.925 10.3 7.8 13.5 10.6 14.1 8.1 | <0.00 |
| Albin (g/L) | 4.1 3.3 5.1 4.1 3.3 5.3 4 3.2 5.1 3.9 3.2 4.9 4.1 5.1 3.3 | <0.00 |
| ALP (U/L) | 17 12 26 17 12 25 17 12 26 18 13 27 17 26 12 | <0.00 |
| AST (U/L) | 60 50 72 60 50 71 59 49 71 60 50 71 60 72 50 | 0.009 |
| ALT (U/L) | 5 4.7 5.4 5 4.7 5.3 4.9 4.7 5.3 | 5 4.7 5.4 5 5.3 4.7 | <0.00 |
| Glu (mmol/L) | 307 250 373 317.5 260 384 299 246 367 297 244 364 306 374 251 | <0.00 |
| UA (mmol/L) | 72 61 84 72 61 84 67 58 80 71 60 82 70 82 60 | <0.00 |

Data were expressed as median and quartiles. P value present the differences by season.

Figures

Figure 1

Basic lipid concentration of enrolled population by sex A to D represent the TC, TG, HDL-C, LDL-C distribution by sex. The x axis represents the subgroup by sex; the y axis represents the average concentrations of lipid profiles.
Figure 2
Distribution of lipid profiles by month

Figure 3
Distribution of lipid concentration by festival Group A represents the first week after Spring Festival. Group B represents other times of the year.

Figure 4
Prevalence of dyslipidemia between the first week after Spring Festival and other days. The red area represents the prevalence of dyslipidemia, whereas the blue area represents the prevalence of normal lipid concentrations.

**Supplementary Files**

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- SupplementaryMaterials.docx