Prevalence and factors associated with dyslipidemia in otherwise healthy Asian Indian American adolescents.

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Abstract

Introduction: This study was designed to evaluate results of lipid screening of American Asian Indian adolescents in a primary care setting to define prevalence and factors associated with development of dyslipidemias. Methods: An administrative database was used to select American Asian Indian adolescents (10-20 years) whose lipid profiles were measured during 2013. Demographics, obesity/overweight, and summary of lipid measures defined as acceptable, borderline, and high were analyzed. Dyslipidemia was defined as combined if triglyceride to the high-density lipoprotein cholesterol ratio was more than 3 and multifactorial if total cholesterol was 200 mg/dL or more and/or low-density lipoprotein cholesterol was 130 mg/dL or more. Statistical analysis included analysis of variance, chi-square, and multivariate regression. Data presented as proportion, mean and odd ratios (OR) with a 95% confidence interval (95% CI). Results: Of 244 American Asian Indian adolescents studied (55.7% males), dyslipidemia borderline and high was classified in 151 (61.9%), and between 75 adolescents with high dyslipidemia, 32 (42.7%) had combined and 20 (26.7%) multifactorial dyslipidemia. The increased risk for overweight and obesity was associated with high dyslipidemia (OR 1.48, 95% CI 1.03, 2.11) and (OR 1.78, 95% CI 1.10, 2.87), respectively. Moreover, 65.5% of patients with combined and 55% with multifactorial were overweight or obese. Conclusions: Lipid profiles were abnormal in most American Asian Indian adolescents, including one-third with high dyslipidemia, defined as combined and/or multifactorial, and significantly associated with overweight/obesity. Study findings allow for better understanding of the prevalence of dyslipidemia in this population, and therefore, increase parental and pediatricians' responsiveness to reduce the risk for further progression to cardio-vascular diseases in Asian Indian adults.

Keywords: Adolescents, Dyslipidemia, Asian Indian American, Prevalence, Risk factors.

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Introduction

Dyslipidemia is a generally accepted risk factor for cardiovascular morbidity that could be initiating and progressing early in life [1,2]. Longitudinal data has shown direct association of low-density lipoprotein cholesterol (LDL-C) levels above the 80th percentile in adolescents and subclinical atherosclerosis in adulthood [3]. Dyslipidemia in younger ages is one of the modifiable risk factors for development of cardio-vascular diseases (CVD) in adulthood [4]. As such, in 2011, the National Heart Blood and Lung Institute (NHBLI) and American Academy of Pediatrics (AAP) endorsed universal lipid screening for the general children and adolescent population [5]. However, US Preventive Services Task Force implied insufficiency of evidence regarding balance between benefit and harms for screening of lipid abnormality in the pediatric population [6]. Moreover, most AAP members do not identify universal lipid screening as a high practicing priority [7]. Selective approach in assessment of lipid profile in children used previously influenced research focused on dyslipidemia in overweight/obese children and adolescents. Only a few studies have presented epidemiology of lipid abnormalities in the general pediatric population using data from the National Health and Nutrition Examination Survey (NHANES) or the Centers for Disease Control and Prevention (CDC). NHANES reported total cholesterol (TC) of ≥ 200 mg/dL in 10% youths aged 6 to 19 years [8] and CDC in 43% of overweight/obese American adolescents [9]. Furthermore, NHANES identified TC ≥ 200 mg/dL, high-density lipoprotein cholesterol (HDL-C) of <40 mg/dL and non-HDL-C of ≥145 mg/dL in 20% of children aged 8 to 17 years-old [10]. A US-based large study performed prior to 2011 reported a comparable prevalence of TC ≥ 200 mg/dL, a higher prevalence of TG ≥ 130 mg/dL in white and Asian/Pacific Islanders than black adolescents and a lower prevalence of HDL-C (<40 mg/dL) in Asian/Pacific Islander and black adolescents than in whites [11]. Although prevalence of dyslipidemia in culturally diverse populations of US children and adolescents has been explored in a few epidemiological reports [8-11], the Asian Indian American ethnicity of studied youth has not been specified. Americans of Asian Indian descents show a disproportionately higher prevalence of CVD [12] as well as CVD- related risk factors, including dyslipidemia, diabetes, obesity, and unhealthy diet [13]. In addition, a higher prevalence of low HDL-C and preponderance of dysfunctional HDL particles has been identified in Asian Indian American men compared to their white counterparts [14]. This study

was designed to identify the prevalence and factors associated with dyslipidemia in Asian Indian American adolescents who underwent the universal cholesterol screening in the primary care pediatric setting. We believe that study findings allow for better understanding of risk for dyslipidemia at an early-life stage and help to develop strategies to prevent further progression to CVD in adulthood in American adolescents from Asian Indian families.

Materials and Methods

This retrospective study from a single primary care pediatric setting was approved by the Institutional Review Board of Saint Peter's University Hospital in New Jersey. Study participants were Asian Indian American adolescents at the primary care pediatric setting where universal blood cholesterol screening [5] had been implemented.

Data collection

The administrative database was utilized to identify all adolescents aged 10 to 20 years who visited the primary care pediatric office for a preventive well visit during 2013. The Current Procedural Terminology codes 99393, 99394, 99395, 99383, 99384, and 99385 were used as filter criteria to extract the report of the total number of adolescent patients (10-20 years) seen during the specified time frame. The primary care physician verified the Electronic Health Record (EHR) of selected adolescents to identify those whose last names were reflective of their Asian Indian origin. The data extraction included patient's age, gender, insurance status, weight, height, BMI, summary of standard blood lipid measurements (TC, LDL-C, triglyceride [TG], and HDL-C) and result of simultaneously measured blood sugar. Collected data were entered in Excel without any personal identifiers. Stages of adolescence life [15] were used to classify age of studied patients as follows: early (10 to 13 years), middle (14 to 17 years), and late (18-21 years) stages. Sex-age based percentile for BMI from 85th to below 95th and 95th and above percentile was used to categorize overweight and obese adolescents [16].

Study outcome

We identified adolescents with borderline and high dyslipidemia, as well as those with combined and multifactorial dyslipidemia using results of the lipid profile. The results of lipid levels were stratified using existing classification [17] as acceptable, borderline, and high levels. Borderline dyslipidemia was classified as blood lipid and lipoprotein concentrations (mg/dL) of single or combination of TC (170-199), or LDL-C (110-129), or TG (90-129). High dyslipidemia was classified if a single or combination of TC ≥ 200 mg/dL, or LDL-C ≥ 130 mg/dL, or TG ≥ 130 mg/dL or HDL-C <40mg/dL were detected. We classified TG/HDL-C ratio to identify adolescents with combined dyslipidemia (CD) using a cut-off point of 3 suggested for definition of CD in whites, which is 0.5 point higher than in black children and adolescents [18] as lower triglycerides and higher HDL-C concentrations have been reported in African-Americans adolescents [19]. In addition, patients with multifactorial dyslipidemia were identified if TC level was ≥ 200 mg/dL and/or LDL-C level was ≥ 130 mg/dL [20].

Data presentation and statistical analysis

We describe the adolescents' demographics and weight characteristics as well as distribution of levels of measurements included in the lipid profile. The level of each lipid test was assessed with respect to the magnitude of elevation from acceptable levels to classify patients with borderline, high, combined, and multifactorial dyslipidemia. Descriptive analyses of all types of dyslipidemia are presented. Univariate analysis was conducted to identify the difference in characteristics of adolescents classified with borderline and high dyslipidemia using analysis of variance (ANOVA) for continuous and Chi-square statistics for categorical variables. We also performed multivariate regression analysis to define factors associated with development of borderline and high dyslipidemia, including age (continuous variable), gender (male vs. female), overweight (yes vs. no), and obesity (Yes vs. No). Categorical data are presented as a proportion (in percent) and continuous as mean with a 95% confidence interval (95% CI). Identified associations are expressed as odds ratios (OR) with 95% CI. Data were analyzed statistically using STATISTICA 13.3 (StatSoft Inc., Tulsa, OK, USA). All statistical tests were 2-sided with the significance level set at a p value of <0.05.

Results

Of the 567 adolescents who underwent lipid screening during the study period, 244 recognized as Asian Indian were included in this study. Private insurance covered health care for all adolescents in this study. Participant ages ranged from 10 to 20 years (Mean=13.2, 95% CI 13.2, 13.8). Majority were in early-middle stages, and only 9% were in the late stage of adolescent life (Table 1). Half of the adolescents were overweight or obese. As shown in Table 1, the lipid profile measurements were widely ranged. There were correlations between lipid levels, for instance, between TC and HDL-C (r=0.24, p<0.001) and TC and TG (r=0.35, p<0.001) as well as TG and HDL-C (r=-0.44, p<0.0001).

Borderline and high dyslipidemia

Overall, 151 (61.9%) patients were classified with dyslipidemia, including 76 (50.3%) with borderline and 75 (49.7%) with high dyslipidemia. We found that single measurement in the borderline

Table 1. *Characteristics of study participants (%, range mean, 95% CI).*

Characteristics	Distribution (n=244)
Early adolescence age 10 -13 years	54.9% (95% CI 48.7%, 61.0%)
Middle adolescence 14-17 years	36.1% (95% CI 30.3%, 42.3%)
Late adolescence 18-20 years	9.0% (95% CI 6.0%, 13.3%)
Male gender	55.7% (95% CI 49.5%, 61.8%)
Overweight	27.5% (95% CI 22.2%, 33.4%)
Obese	11.9% (95% CI 8.4%, 16.6%)
Glucose (mg/dL)	57.0-128.0 (88.8, 95% CI 87.8, 89.8)
TC (mg/dL)	96-292 (160.0, 95% CI 156.3, 163.6)
LDL-L (mg/dL)	16-221 (88.8, 95% CI 85.6, 92.0)
HDL-L (mg/dL)	27-93 (52.7, 95% CI 51.1, 54.2)
TG (mg/dL)	13-288 (90.7, 95% CI 85.3, 96.2)

or high category predominantly contributed to the diagnosis of borderline and high dyslipidemia (Figure 1). Among patients with borderline dyslipidemia, the TG, LDL-C, and TC were in borderline levels in 59.2% 25.0% and 64.7% of cases. Low HDL-C and levels of TG, LDL-C, TC in the high lipid category contributed to classification of high dyslipidemia in 40%, 62.7%, 16.0%, and 25.3% of cases, respectively. In addition, 16.0%, 22.7%, and 20.0% of patients with high dyslipidemia had TG, LDL-L, and TC in borderline-high levels. Patients with acceptable lipid levels and dyslipidemia (borderline and high) were comparable for age, gender, and blood glucose levels but an increased number of obese adolescents among those with high dyslipidemia were recorded (Table 2).

Overall, the prevalence of adolescents in the overweight and obese range was significant with high but not borderline levels as compared to adolescents with acceptable lipid levels. Overweight/obesity was recorded in 57.9% of patients with TC ≥ 200 mg/dL, 50% of patients with LDL-C ≥ 130 mg/dL, 48.9% of patients with TG ≥ 130 mg/dL, and in 68.0% of those with HDL-C <40 mg/dL. Data from multivariate controlled models confirmed increased risk for development of high dyslipidemia in overweight (OR 1.48, 95% CI 1.03, 2.11) and obese (OR 1.78, 95% CI 1.10, 2.87) adolescents, independent of age and gender.

Combined and multifactorial dyslipidemia

A TG/HDL-C ratio of 3 or more used to classify combined dyslipidemia was recorded in 32 adolescents from adolescents classified with high dyslipidemia (42.7%). Among 32 adolescents with combined dyslipidemia, 21 (65.5%) were overweight or obese compared to 70 of 211 (33.2%) with TG/HDL-C ratio less than 3 (p<0.001). The magnitude of association between combined dyslipidemia and overweight/obesity reduced after controlling for adolescents' gender and age (OR crude 3.9, 95% CI 1.8, 8.4 vs. OR adjusted 2.0, 95% CI 1.3, 2.9).

Multifactorial dyslipidemia classified as TC ≥ 200 mg/dL and/or LDL-L ≥130 mg/dL was recorded in 20 among 75 patients with high dyslipidemia (26.7%). Among 20 adolescents with multifactorial dyslipidemia, 11 (55%) were overweight or obese compared to 35.9% of patients without multifactorial dyslipidemia (p=0.09). We identified that 6 (18.8%) adolescents among 32 with combined dyslipidemia also had multifactorial dyslipidemia.

Discussion

In the present study, screening of blood lipid profile revealed at least one or more abnormal measures displaying equal proportion of borderline and high dyslipidemia in more than 60% of the otherwise healthy American Asian Indian adolescents. Dyslipidemia defined as combined or multifactorial have been identified in one-fourth and one-fifth of adolescents with high dyslipidemia, respectively. The risk for development of high and combined dyslipidemia significantly increased in overweight/obese adolescents independently of age and gender, which correlates with studies showing predominance of obesity in adolescents with hypertriglyceridemia combined with low HDL-C [18,21] or alone [22]. It has been shown that

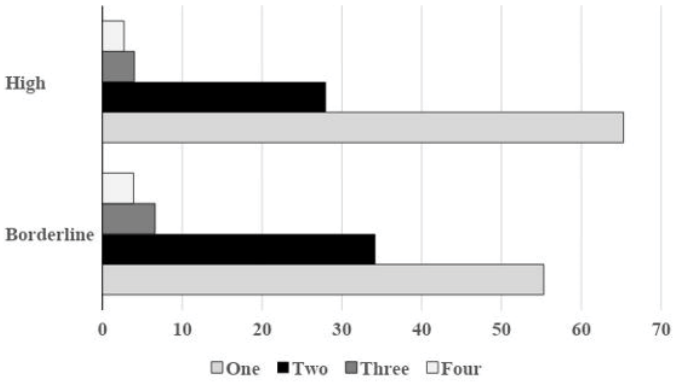

Figure 1. *Number of pathological measurements in adolescents classified with borderline and high dyslipidemia (p=0.23).*

Table 2. *Comparison of children with and without dyslipidemia.*

Characteristics	Dyslipidemia			p-value
	Acceptable (n=93)	Borderline (n=76)	High (n=75)	
Male, n (%)	55 (59.1)	37 (48.7)	44 (58.7)	0.32
Age, years, mean (95% CI)	13.3 (12.8, 13.8)	13.3 (12.7, 13.9)	14 (13.4, 14.6)	0.1
Age stages, n (%) Early Middle Late adolescence	 54 (58.1) 34 (36.6) 5 (5.3)	 47 (61.8) 22 (29.0) 7 (9.2)	 33 (44.0) 32 (42.7) 10 (13.3)	0.13
Overweight, n (%)	18 (19.4)	23 (33.8)	21 (38.1)	0.1
Obesity, n (%)	7 (7.5)	7 (9.3)	15 (20.0)	<0.04
Overweight/obesity, n (%)	25 (26.9)	30 (40.0)	36 (48.0)	<0.02
Glucose, mg/dL, mean (95% CI)	n=90 n=9089.6 (88.0, 91.2)	n=75 87.6 (85.6, 89.5)	n=71 89.2 (87.5, 90.9)	0.21

inter-relationship of hypertriglyceridemia with low HDL-C is responsible for development of atherosclerotic vascular change and subsequent premature cardiovascular conditions [23]. Moreover, high TG/HDL-C ratio used to classify combined dyslipidemia is an independent determinant of arterial stiffness, especially in obese youth [24]. To the best of our knowledge, features of dyslipidemia in American adolescents of Asian Indian descent have not been investigated. Few reports from different parts of India have provided information regarding lipid profiles in adolescents with a prevalence of hypertriglyceridemia in 28% [25] and 20.4% [26] and low HDL-C in 60% [25] and 28% [26] of adolescents. Contrary to our data, only 6% of adolescents in the Indian studies were overweight and no one was obese [25,26]. Evaluation of lipid measures with cut offs proposed by the National Cholesterol Education Program (NCEP) [27] have identified 30% of Brazilian adolescents with high dyslipidemia [28], which is similar to findings in our study. A school-based national study from Brazil which defined lipid abnormality if LDL-C ≥ 100 mg/dL, HDL-C <45 mg/dL, and triglycerides (TG) ≥ 100 mg/dL [21] reported at least one measure in 64.7% and all three in 3.7% of adolescents. We also recorded the predominance of contribution of a single lipid measure in definition of borderline and high dyslipidemias. A population-based cohort of white children and adolescents

from Denmark showed the increased risk for dyslipidemia in 28% of overweight/obese compared to 6% of participants with normal weight [29]. The result of this study is comparable to our findings, although the prevalence of overweight/obesity was substantially higher in Asian Indian American adolescents.

Limitations

The potential limitations of this study include a single study site that represents a socio-economically homogenous population of Asian Indian American adolescents. Furthermore, a retrospective design limited the evaluation role of a variety of known dyslipidemia-related factors, including nutritional habits, level of physical activity, family history of premature CVD [30], maternal lipid levels [31], and early breastfeeding [32]. We recognize the risk of misclassification of adolescents' ethnicity because only their last name had been used as an indicator for selection of study participants. Moreover, such selection strategies did not ensure the homogeneity of parental ethnicity, which could impact nutritional habits of studied adolescents [33] and therefore, modify the risk for both dyslipidemia and obesity. Additionally, inconsistency in reference values used for the definition of dyslipidemia [28] reduces the ability for comparison of our findings with other reports. We conclude that acceptable normal levels of lipid profile measures were identified in less than 40% of otherwise healthy Asian Indian American adolescents [33].

Conclusion

Although development of the high type of dyslipidemia was more likely associated with overweight/obesity, nearly one-third of adolescents with high or combined dyslipidemia were without adiposity, which support the need for universal screening. Further studies using a prospective design and parental surveys will be needed to assess the role of different factors in alteration of lipid levels in socio-economic diverse American adolescents of Asian Indian origin.

Ethical Compliance

This research study maintained the rules for ethical compliance. There was no external source of funding used to conduct the research. The authors declare that they have no conflict of interest. Informed consent was not needed for data collection. This study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments and was approved by the IRB at Saint Peter's University Hospital in New Jersey, USA.

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References

1. Lozano P, Henrikson NB, Morrison CC, et al. Lipid screening in childhood for detection of multifactorial dyslipidemia. A Systematic Evidence Review for the U.S. Preventive Services Task Force [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US).
2. Newman III WP, Freedman DS, Voors AW, et al. Relation of serum lipoprotein levels and systolic blood pressure to early atherosclerosis. N Engl J Med. 1986;314:138-44.
3. Raitakari OT, Juonala M, Rönnemaa T, et al. Cohort profile: The cardiovascular risk in Young Finns Study. Int J Epidemiol. 2008;37:1220-6.
4. Magnussen CG, Smith KJ, Juonala M. When to prevent cardiovascular disease? As early as possible: lessons from prospective cohorts beginning in childhood. Curr Opin Cardiol. 2013;28:561-8.
5. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics. 2011;128:S213.
6. Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for lipid disorders in children and adolescents: US Preventive Services Task Force recommendation statement. JAMA. 2016;316:625-33.
7. Rodday AM, Leslie L, O'Connor K, et al. Pediatric cholesterol screening and treatment. Presented at the 2015 Pediatric Academic Societies Annual Meeting. https://www.aap.org/en-us/professional-resources/Research/research-findings/Pages/Pediatric-Cholesterol-Screening-and-Treatment.aspx
8. Kit BK, Carroll MD, Lacher DA, et al. Trends in serum lipids among US youths aged 6 to 19 years, 1988-2010. JAMA. 2012;308:591-600.
9. May AL, Kuklina EV, Yoon PW. Prevalence of abnormal lipid levels among youths-United States, 1999-2006. Morbidity and Mortality Weekly Report. 2010;59:29-33.
10. Kit BK, Kuklina E, Carroll MD, et al. Prevalence of and trends in dyslipidemia and blood pressure among US children and adolescents, 1999-2012. JAMA Pediatr. 2015;169:272-9.
11. Margolis KL, Greenspan LC, Trower NK, et al. Lipid screening in children and adolescents in community practice: 2007 to 2010. Circ Cardiovasc Qual Outcomes. 2014;7:718-26.
12. Singh V, Deedwania P. Dyslipidemia in special populations: Asian Indians, African Americans, and Hispanics. Curr Atheroscler Rep. 2006;8:32-40.
13. Misra A, Khurana L. Obesity-related non-communicable diseases: South Asians vs White Caucasians. Int J Obes. 2011;35:167-87.
14. Vikenes K, Andersen KS, Melberg T, et al. Long-term prognostic value of cardiac troponin I and T versus creatine kinase-MB mass after cardiac surgery in low-risk patients with stable symptoms. Am J Cardiol. 2010;106:780-6.
15. American Academy of Pediatrics. Ages & Stages. Healthy Children. https://www.healthychildren.org/English/ages-stages/Pages/default.aspx. Accessed August 11, 2020.
16. Centers for Disease Control and Prevention. Defining Childhood Obesity. https://www.cdc.gov/obesity/childhood/defining.html. Published July 3, 2018. Accessed August 11, 2020.
17. Expert panel on integrated guidelines for cardiovascular health

and risk reduction in children and adolescents: summary report. Pediatrics. 2011 Dec;128:S213-56.

18. Kavey RE. Combined dyslipidemia in childhood. J Clin Lipidol. 2015;9:S41-56.
19. D'Adamo E, Northrup V, Weiss R, et al. Ethnic differences in lipoprotein subclasses in obese adolescents: importance of liver and intraabdominal fat accretion. Am J Clin Nutr. 2010;92:500-8.
20. Lozano P, Henrikson NB, Morrison CC, et al. Lipid Screening in Childhood and Adolescence for Detection of Multifactorial Dyslipidemia: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016;316:634-44.
21. Kaestner TL, Santos JA, Pazin DC, et al. Prevalence of combined lipid abnormalities in brazilian adolescents and its association with nutritional status: Data from the Erica Study. Glob Heart. 2020;15:23.
22. Elmaoğulları S, Tepe D, Uçaktürk SA, et al. Prevalence of dyslipidemia and associated factors in obese children and adolescents. J Clin Res Pediatr Endocrinol. 2015;7:228.
23. Grundy SM. Atherogenic dyslipidemia: Lipoprotein abnormalities and implications for therapy. Am J Cardiol. 1995;75:45B-52B.
24. Urbina EM, Khoury PR, McCoy CE, et al. Triglyceride to HDL-C ratio and increased arterial stiffness in children, adolescents, and young adults. Pediatrics. 2013;131(4):e1082-90.
25. Bhalavi V, Deshmukh PR, Goswami K, et al. Prevalence and correlates of metabolic syndrome in the adolescents of rural Wardha. Indian J Community Med. 2015;40:43.
26. Singh N, Parihar RK, Saini G, et al. Prevalence of metabolic syndrome in adolescents aged 10-18 years in Jammu, J and K. Indian J Endocrinol Metab. 2013;17:133.
27. Cleeman JI, Grundy SM, Becker D, et al. Expert panel on detection, evaluation and treatment of high blood cholesterol in adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP III). JAMA. 2001;285:2486-97.
28. Tomeleri CM, Ronque ER, Silva DR, et al. Prevalence of dyslipidemia in adolescents: Comparison between definitions. Rev Port Cardiol. 2015;34:103-9.
29. Kuziga F, Adoke Y, Wanyenze RK. Prevalence and factors associated with anaemia among children aged 6 to 59 months in Namutumba district, Uganda: A cross-sectional study. BMC Pediatr. 2017;17:25.
30. Khoury M, Manlhiot C, Gibson D, et al. Universal screening for cardiovascular disease risk factors in adolescents to identify high-risk families: A population-based cross-sectional study. BMC Pediatr. 2016;16:11.
31. Nam JH, Shin J, Jang SI, et al. Associations between lipid profiles of adolescents and their mothers based on a nationwide health and nutrition survey in South Korea. BMJ Open. 2019;9:e024731.
32. Hui LL, Kwok MK, Nelson EA, et al. Breastfeeding in infancy and lipid profile in adolescence. Pediatrics. 2019;143: e20183075.
33. De Hoog ML, Kleinman KP, Gillman MW, et al. Racial/ethnic and immigrant differences in early childhood diet quality. Public Health Nutr. 2014;17:1308-17.

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