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Systematic Review (Pages: 7575-7588)

Effect of Active and Passive Exposure to Cigarette Smoke on Lipid Profile of Children and Adolescents; A Systematic Review and Meta-Analysis

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Abstract

Background: The present systematic review and meta-analysis is designed in order to assess the association between passive and active smoking and lipid profile of children and adolescents.

Materials and Methods: An extensive search was done in databases of Medline, EMBASE, Web of Science, Scopus and CINAHL until October 2017. Two independent researchers screened articles and in the next step, full texts of probably relevant articles were read and summarized. At the end, results of mentioned studies were pooled and a standardized mean difference (SMD) with 95% confidence interval (95% CI) was reported.

***Results*:** Data from 17 studies (containing 41619 children and adolescents; age group between 4 and 18 years old; 51.72% boys) were entered. Comparing serum level of high density lipoprotein (HDL) in two groups of exposed and non-exposed to cigarette smoking showed that active exposure (SMD= -0.40, 95% CI: -0.59 to -0.21) and passive exposure to cigarette smoke (SMD= -0.18, 95% CI: -0.30 to -0.06) decreases the serum level of mentioned lipoprotein. Additionally, active exposure to cigarette smoke (SMD=0.16, 95% CI: 0.06 to 0.27) causes a modest increase in serum level of triglyceride. However, cigarette smoke exposure does not have any effect on the level of total cholesterol and low density lipoprotein (LDL).

***Conclusion*:** The present meta-analysis showed that exposure to cigarette smoke leads to a significant decrease in the level of HDL and triglyceride but, it does not have any effect of the level of total cholesterol and LDL in children and adolescents.

Key Words: Children**,** Lipid Profile, Meta-analysis, Smoking.

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1- INTRODUCTION

Effect of cigarette smoking on cardiovascular diseases is well recognized (1) but, its effect on platelet reactivity, endothelial dysfunction, atherosclerosis, inflammation and oxidative stress is still on debate (2-4). Moreover, effect of cigarette smoking either actively or passively on lipid profile is less recognized and a consensus based on available data has not been reached yet (5-7). Multiple studies have been conducted in the field of pediatrics in recent years regarding the relationship between active or passive cigarette smoking and lipid profiles such as total cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) (8-12). An agreement has not been reached yet about the association between exposure to cigarette smoke and lipid profile of children due to significant controversies among mentioned studies. Importance of this issue becomes evident when we realize that cigarette smoking is one of the most important risk factors of non-communicable diseases. Increased levels of LDL, total cholesterol and decreased level of HDL are considered markers for metabolic syndrome and other chronic metabolic diseases (13, 14). Therefore, simultaneous presence of two factors of active or passive exposure to cigarette smoke and abnormalities of lipid profile may lead to an increase in the risk of non-communicable diseases. The mentioned problem is more important in children as many diseases in adulthood are consequences of childhood events. Hence, the present systematic review and meta-analysis was designed in order to assess the association between passive and active smoking and lipid profile of children and adolescents.

2- MATERIALS AND METHODS

2-1. Study design

In the present meta-analysis, data from studies were entered which assessed the relation between lipid profile in children and adolescents between the ages of 1-18 years old and exposure to cigarette smoke. Instructions from Meta-analysis of observational studies in epidemiology (MOOSE) statement were used in the present study (14).

2-2. Search strategy

After choosing appropriate keywords and their combinations, an extensive search was done in databases of Medline, EMBASE, Web of Science, Scopus and CINAHL until October 2017. Search strategy was based on relevant keywords about active and passive exposure to cigarette smoke and lipid profile. Search strategy in Medline (via PubMed) is shown in **Table.1** *(Please see the table in the end of paper)*. A manual search was performed through three steps: 1) assessing bibliography of relevant studies 2) contacting authors in order to get access to unpublished data and 3) search for relevant theses in proQuest database.

2-3. Selection criteria

In the present study, observational studies (cohort, case-control and cross-sectional) about the effect of passive or active exposure to cigarette smoke on changes in lipid profile of children were entered. PICO included the following in the present study: P: children and adolescents between the ages of 1 and 18 years old without a history of hyperlipidemia I: indicating active or passive exposure to cigarette smoke C: comparison was done between the case (active or passive exposure to cigarette smoke) and control group (those without either active or passive exposure to cigarette smoke) O: indicating serum level of lipid profiles.

2-4. Quality assessment and Data Extraction

Methods of data gathering and assessment have been precisely explained in previous meta-analyses of authors of the present

study (15-33). In summary, after excluding same records, two independent researchers screened titles and abstracts and then full texts of probably relevant articles were read. Extracted data included information regarding study design, patient characteristics (age, sex), sample size, lipid profile status and probable biases. In cases with similar results, the study with larger sample size was entered in the study. In cases with multiple results in different stages, the last follow up was entered. Additionally, some studies had reported their results based on sex so they were entered in the present study in the same way. Quality of studies was assessed using suggested instructions of Newcastle-Otawa (34).

2-5. Statistical Analyses

All studies were summarized as mean value and standard deviation. Heterogeneity among studies was assessed using I^2 test and a p- value of less than 0.1 was considered significant (indicating presence of heterogeneity). Random effect model was used as there was a significant heterogeneity among studies. Additionally, publication bias was assessed by a Funnel plot and Egger's and Begg's tests (35). At the end, results of mentioned studies were pooled and a standardized mean difference (SMD) with 95% confidence interval (95% CI) was reported.

3- RESULTS

3-1. Demographic data

Overall 8,439 different studies were found in a systematic and manual search which after screening only 17 studies was entered in the present meta-analysis (36-52) (**Figure.1**); 14 studies were written in English (36, 38, 39, 41-48, 50-52), and 3 studies were written in Korean, Portuguese and Japanese (37, 40, 49). In these studies, data from 41,619 children and adolescents were assessed. The age group of study population ranged from 4 to 18 years old and 51.72% of children were boys. Daily smoking was considered as smoking in most studies (37, 39-41, 46, 47, 49-52). However, only one study hadn't reported a definition for smoking (44). Nine studies assessed the association between passive cigarette smoking and lipid profile (36, 39, 43-45, 48, 49, 51, 52), 6 studies assessed active exposure (37, 38, 40-42, 50), and one study assessed both types of exposures (46). **Table. 2** shows a summary of entered studies *(Please see the table in the end of paper).*

3-2. Publication bias and Risk of bias

Publication bias was stratified based on passive or active exposure. No bias was observed in both types of exposures. Quality control of articles showed that risk of bias is at a low risk in most studies for items such as "is the case definition adequate, Representativeness of the cases, Definition of controls, and comparability item". However, all studies had a high risk of bias for Ascertainment of exposure (**Figure.2**). In almost all analyses a significant heterogeneity was observed among studies (**Figure.3**). Hence, random effect model was used for analyses in the present study.

3-3. Meta-analysis

3-3-1. Association between exposure to cigarette smoke and serum total cholesterol level

Figure.3 depicts the forest plot comparing serum total cholesterol level in two groups of exposed and non-exposed to cigarette smoking. As shown, active exposure (standardized mean difference [SMD]=0.08, 95% CI: -0.09 to 0.25, $P_{for\ SMD}$= 0.34; I2=85.2, $P_{for\ I\text{-}squared}$<0.0001), and passive exposure to cigarette smoke (SMD=0.07, 95% CI: -0.05 to 0.20, $P_{for\ SMD}$=0.26; I2=85.2, $P_{for\ I\text{-}squared}$=0.001) did

not have any effect on total cholesterol level.

3-3-2. Association between exposure to cigarette smoke and serum triglyceride level

Comparison of serum triglyceride level in two groups of exposed and non-exposed to cigarette smoking showed that active exposure to cigarette smoke (SMD=0.16, 95% CI: 0.06 to 0.27, $P_{for\ SMD}$= 0.002; I2=57.4, $P_{for\ I\text{-}squared}$=0.016) leads to a modest increase in serum triglyceride level. However, passive exposure to cigarette smoke (SMD=0.16, 95% CI: -0.01 to 0.32, $P_{for\ SMD}$=0.062; I2=74.9, $P_{for\ I\text{-}squared}$<0.0001) did not have any effect on serum triglyceride level (**Figure.3**) but, the mentioned association was borderline.

3-3-3. Association between exposure to cigarette smoke and serum LDL level

Comparison of serum LDL level in two groups of exposed and non-exposed to cigarette smoking showed that active (SMD=0.10, 95% CI: -0.06 to 0.27, $P_{for\ SMD}$= 0.22; I2=85.0, $P_{for\ I\text{-}squared}$<0.0001), and passive exposure to cigarette smoke (SMD=0.10, 95% CI: -0.001 to 0.20, $P_{for\ SMD}$=0.06; I2=49.9, $P_{for\ I\text{-}squared}$=0.03) did not have any effect on serum LDL level. However, the association between passive exposure to cigarette smoke and serum LDL level was borderline (**Figure.3**).

3-3-4. Association between exposure to cigarette smoke and serum HDL level

Comparison of serum HDL level in two groups of exposed and non-exposed to cigarette smoking showed that active exposure to cigarette smoke (SMD= -0.40, 95% CI: -0.59 to -0.21, $P_{for\ SMD}$= 0.002; I2=88.2, $P_{for\ I\text{-}squared}$<0.0001) leads to a significant decrease in serum HDL level. Additionally, passive exposure to cigarette smoke (SMD= -0.18, 95% CI: -0.30 to -0.06, $P_{for\ SMD}$=0.062; I2=65.7, $P_{for\ I\text{-}squared}$=0.0001) also decreased serum HDL level (**Figure.3**).

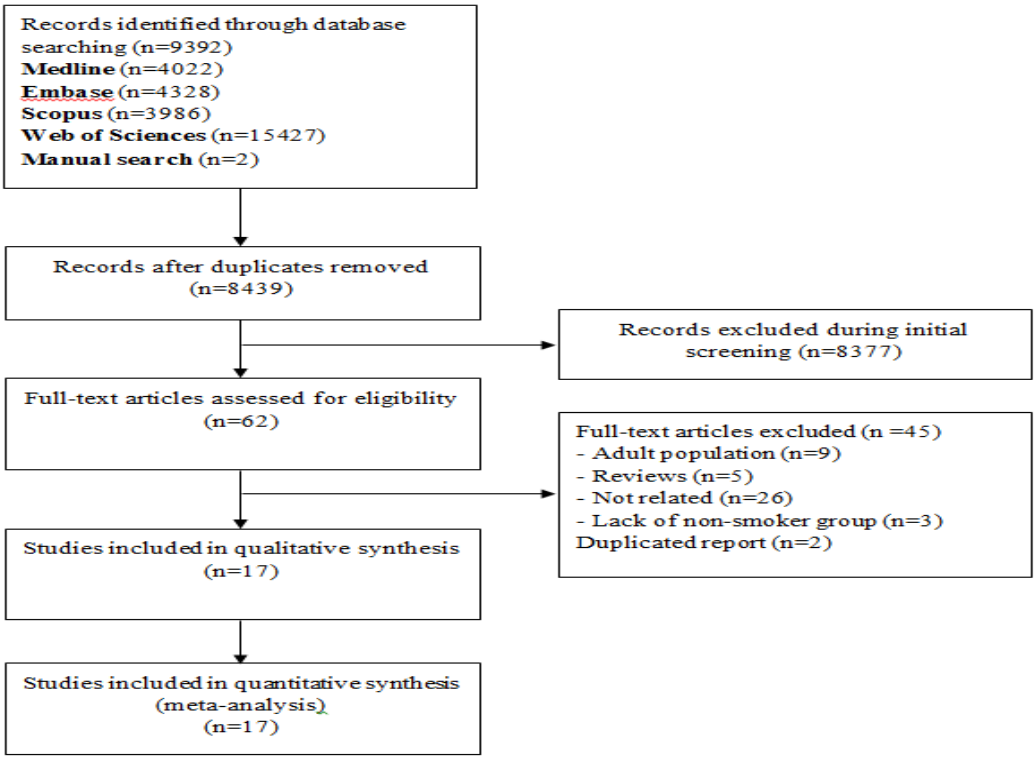


Fig.1: Flowchart of included studies**.**

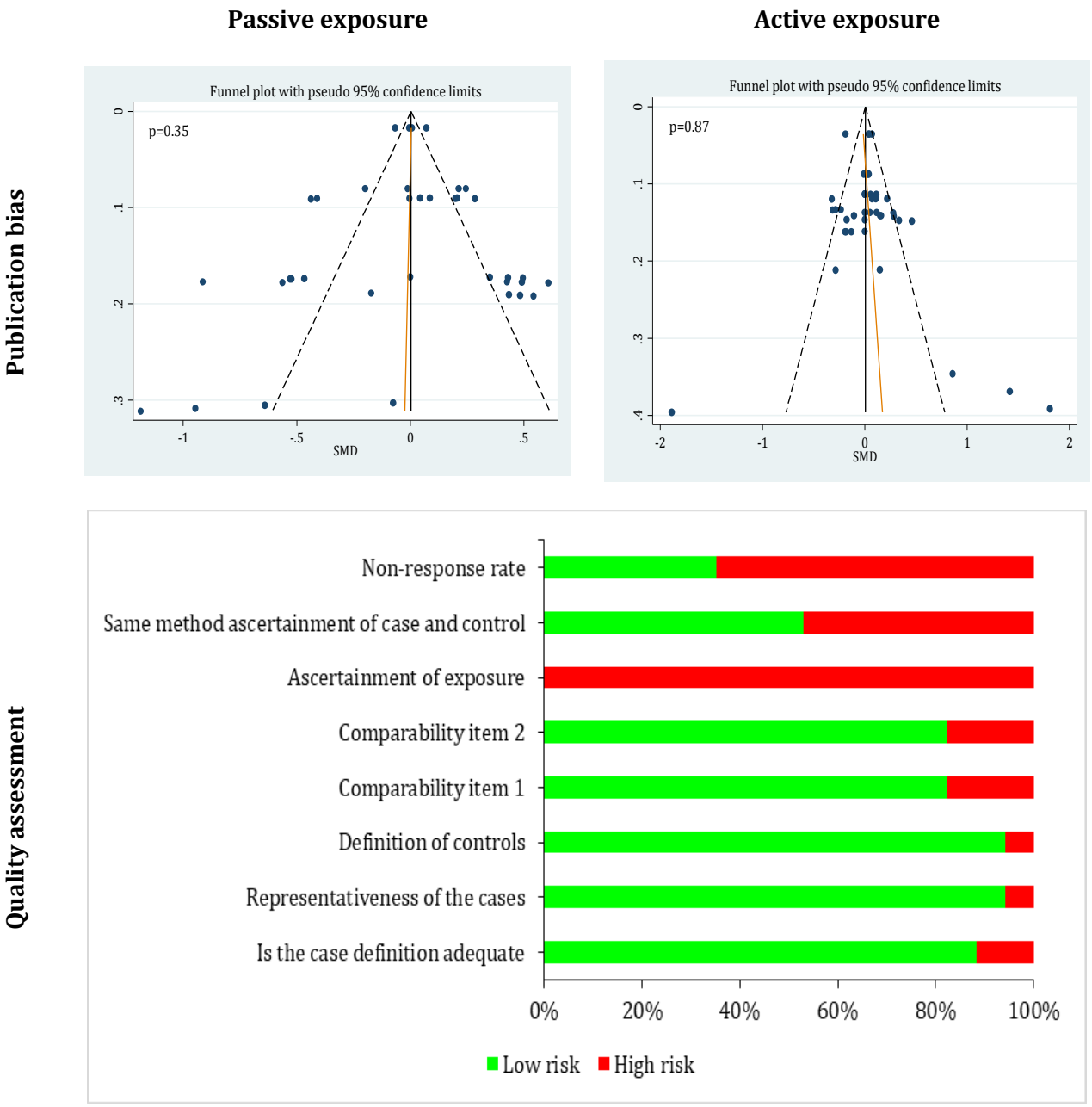
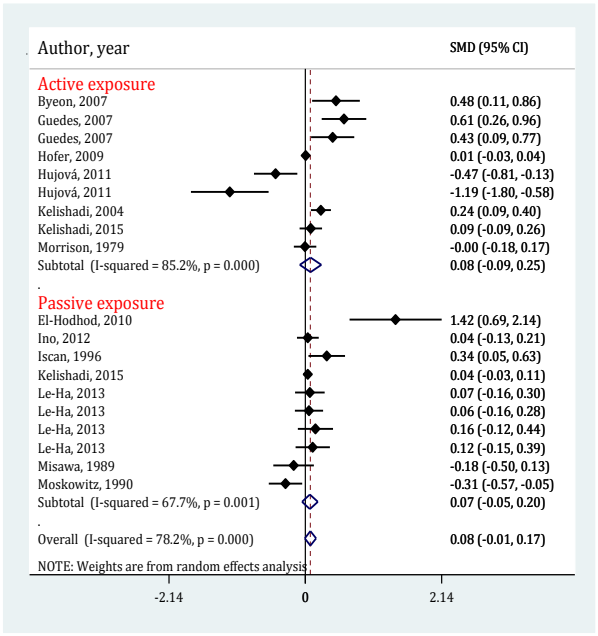
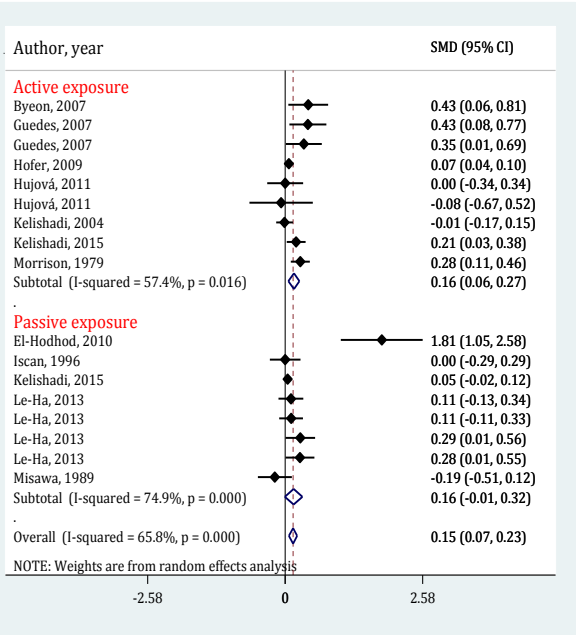
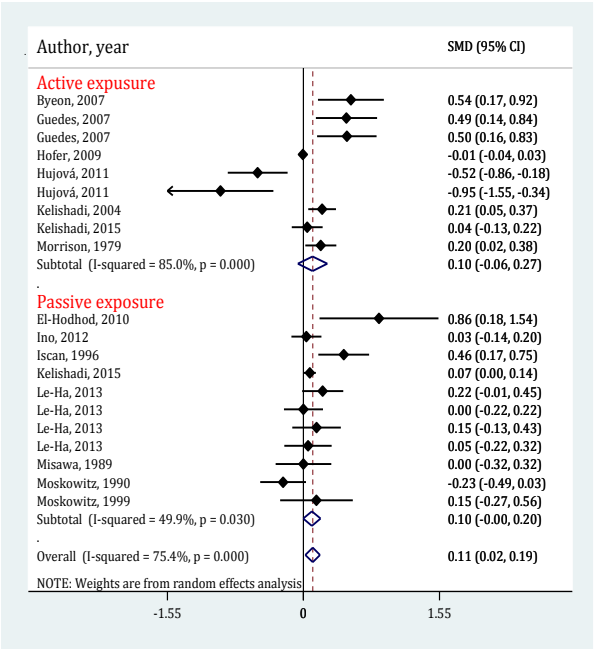


Fig.2: Risk of Bias in the present meta-analysis.





LD **HDL**



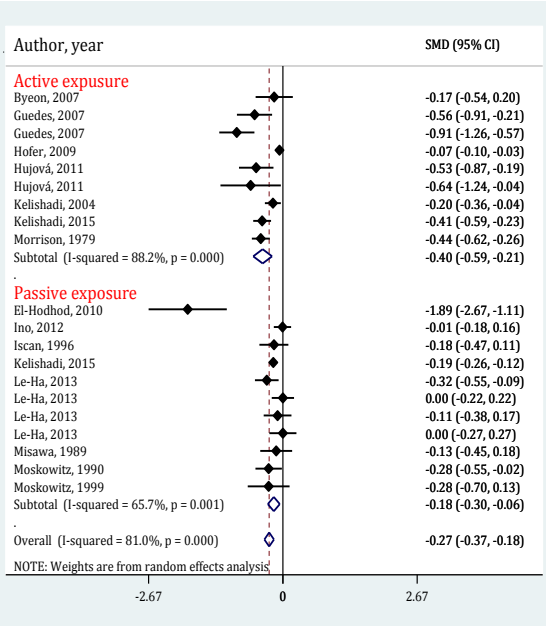


Fig.3: Forest plots for comparison of serum level of total cholesterol, triglyceride, low density lipoprotein (LDL), and high density lipoprotein (HDL) in smoking exposed group and non-exposed group. The analyses were stratify by active or passive exposure. CI: Confidence interval; SMD: Standardized mean differences.

4- DISCUSSION

The present meta-analysis showed that active and passive exposure to cigarette smoke significantly decreases serum HDL level. In addition, active smoking increases serum triglyceride level. However, active or passive exposure to cigarette smoke did not have any effect on serum level of total cholesterol and LDL. Due to our knowledge there is no meta-analysis with

the goal of assessing the association between passive and active smoking and lipid profile of children and adolescents. However, few meta-analyses have assessed the association between cigarette smoking and other chronic diseases and their risk factors in adults. Kar et al. conducted a study in order to assess the association between cardiometabolic parameters in diabetic patients who smoke and non-smokers and showed that hemoglobin A1C level is significantly lower in non-smokers compared to diabetics who smoke cigarette. Serum level of LDL had a similar pattern. However, serum HDL level was higher in non-smoker group (53). Pan et al. showed in their meta-analysis that active or passive exposure to cigarette smoke significantly increases relative risk of diabetes type 2 (54). However, Holmes et al reported that cigarette smoking status does not have any effect on genotypic difference in apolipoprotein E and its consequent heart diseases (55). The association between cigarette smoking and incidence of different diseases and effect of cigarette quitting strategies on lowering the burden of diseases has been proven in previous studies (56-59).

However, for the first time and in a meta-analytic approach, the present meta-analysis showed that in addition to direct and proved effect of cigarette smoking on the increased risk of chronic diseases such as ischemic heart disease, it indirectly increases the mentioned risk by worsening lipid profile status. Accompaniment of cigarette smoking and other risk factors of non-communicable diseases are reported in other studies. For example, smokers have unhealthy diets in addition to lower amount of physical activity per day (60, 61). More attention is needed regarding educations about avoiding cigarette smoking and behavior changes in consumers in order to solve mentioned issues (62). Multiple mechanisms are proposed for the effect of cigarette smoking on lipid profile. The best proposed mechanism is the role of cigarette smoking in increasing serum catecholamine level. With increased level of catecholamines, free fatty acids are increased in the circulation, and this accompanies increasing serum VLDL and LDL levels and decreasing serum HDL levels (63). However, the inhibitory effect of cigarette smoking on the function of enzymes responsible for HDL formation should not be ignored (64). In the present meta-analysis an extensive search was performed in electronic databases. This extensive search led to inclusion of 14 English studies in addition to 3 studies in Korean, Japanese and Portuguese.

Hence, no publication bias was observed in analyses. However, selection bias might be present which is a part of the nature of observation studies and cannot be completely omitted. Another limitation to the present study was differences in the definition of cigarette smoking among included studies which might have led to appearance of heterogeneity. Moreover, cumulative use is important in studies about cigarette smoking and this has led to emergence of the phrase "pack-year" which includes duration in addition to amount of cigarette smoking. However, none of entered studies have assessed the amount of cigarette smoking so a statement cannot be made about the effects exerted on lipid profile by the amount of cigarettes smoked.

5- CONCLUSIONS

The present systematic review and meta-analysis was designed in order to assess the association between passive and active smoking and lipid profile of children and adolescents. The results showed that active or passive exposure to cigarette smoke leads to a significant decrease in the serum level of HDL. Additionally, active smoking increases

serum triglyceride level. However, exposure to cigarette smoke does not have any effect of the level of total cholesterol and LDL.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENTS

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Table-1: Search strategy in Medline database (via PubMed)

1- "Lipids"[Mesh] OR "Cholesterol"[Mesh] OR "Cholesterol, VLDL"[Mesh] OR "Cholesterol, LDL"[Mesh] OR "Cholesterol, HDL"[Mesh] OR "Triglycerides"[Mesh] OR "Lipoproteins"[Mesh] OR "Lipoproteins, HDL3"[Mesh] OR "Lipoproteins, HDL2"[Mesh] OR "Lipoproteins, IDL"[Mesh] OR "Lipoproteins, VLDL"[Mesh] OR "Lipoproteins, LDL"[Mesh] OR "Lipoproteins, HDL"[Mesh] OR "Hypercholesterolemia"[Mesh] OR "Dyslipidemias"[Mesh] OR "Hyperlipidemias"[Mesh] OR "Lipid Metabolism Disorders"[Mesh] OR "Hypertriglyceridemia"[Mesh] OR "Hyperlipoproteinemias"[Mesh] OR "Lipids"[tiab] OR "Lipid"[tiab] OR "Lipid Profile"[tiab] OR "Cholesterol"[tiab] OR "Very Low Density Lipoprotein"[tiab] OR "Low Density Lipoprotein"[tiab] OR "High Density Lipoprotein"[tiab] OR "VLDL"[tiab] OR "LDL"[tiab] OR "HDL"[tiab] OR "Cholesterol, VLDL"[tiab] OR "Cholesterol, LDL"[tiab] OR "Cholesterol, HDL"[tiab] OR "Triglycerides"[tiab] OR "Lipoprotein"[tiab] OR "Lipoproteins"[tiab] OR "Lipoproteins, HDL3"[tiab] OR "Lipoproteins, HDL2"[tiab] OR "Lipoproteins, IDL"[tiab] OR "Lipoproteins, VLDL"[tiab] OR "Lipoproteins, LDL"[tiab] OR "Lipoproteins, HDL"[tiab] OR "Circulating Lipoproteins"[tiab] OR "Lipoproteins, Circulating"[tiab] OR "HDL3 Lipoproteins"[tiab] OR "Lipoprotein HDL3"[tiab] OR "High Density Lipoprotein HDL3"[tiab] OR "High Density Lipoprotein-3"[tiab] OR "High Density Lipoprotein 3"[tiab] OR "HDL-3"[tiab] OR "HDL3 Lipoprotein"[tiab] OR "Lipoprotein, HDL3"[tiab] OR "HDL2 Lipoproteins"[tiab] OR "HDL2 Lipoprotein"[tiab] OR "Lipoprotein, HDL2"[tiab] OR "High Density Lipoprotein-2"[tiab] OR "High Density Lipoprotein 2"[tiab] OR "Lipoprotein HDL2"[tiab] OR "HDL2, Lipoprotein"[tiab] OR "HDL-2"[tiab] OR "HDL 2"[tiab] OR "High Density Lipoprotein HDL2"[tiab] OR "IDL Lipoproteins"[tiab] OR "Lipoproteins, Intermediate Density"[tiab] OR "Lipoprotein, IDL"[tiab] OR "IDL Lipoprotein"[tiab] OR "Intermediate Density Lipoproteins"[tiab] OR "Intermediate-Density Lipoproteins"[tiab] OR "Lipoproteins, Intermediate-Density"[tiab] OR "alpha2-Very-Low-Density Lipoproteins"[tiab] OR "Lipoproteins, alpha2-Very-Low-Density"[tiab] OR "alpha2 Very Low Density Lipoproteins"[tiab] OR "alpha2-VLDL Lipoprotein"[tiab] OR "Lipoprotein, alpha2-VLDL"[tiab] OR "alpha2 VLDL Lipoprotein"[tiab] OR "alpha2-VLDL"[tiab] OR "alpha2 VLDL"[tiab] OR "beta-Very-Low-Density Lipoproteins"[tiab] OR "Floating beta-Lipoproteins"[tiab] OR "Broad-beta Lipoproteins"[tiab] OR "beta-VLDL"[tiab] OR "beta-VLDL Lipoproteins"[tiab] OR "VLDL Lipoproteins"[tiab] OR "Prebeta-Lipoproteins"[tiab] OR "Prebeta Lipoproteins"[tiab] OR "Very-Low-Density Lipoproteins"[tiab] OR "Lipoproteins, Very-Low-Density"[tiab] OR "Very Low Density Lipoproteins"[tiab] OR "Pre-beta-Lipoproteins"[tiab] OR "Pre beta Lipoproteins"[tiab] OR "Lipoproteins, VLDL2"[tiab] OR "VLDL2 Lipoproteins"[tiab] OR "Lipoprotein VLDL II"[tiab] OR "Lipoproteins, VLDL1"[tiab] OR "VLDL1 Lipoproteins"[tiab] OR "Lipoproteins, VLDL I"[tiab] OR "Lipoproteins, VLDL3"[tiab] OR "VLDL3 Lipoproteins"[tiab] OR "Lipoproteins, VLDL III"[tiab] OR "LDL Lipoproteins"[tiab] OR "Low-Density Lipoproteins"[tiab] OR "Lipoproteins, Low-Density"[tiab] OR "Low Density Lipoproteins"[tiab] OR "beta-Lipoproteins"[tiab] OR "beta Lipoproteins"[tiab] OR "LDL-1"[tiab] OR "LDL1"[tiab] OR "Low-Density Lipoprotein 1"[tiab] OR "Low Density Lipoprotein 1"[tiab] OR "LDL(1)"[tiab] OR "LDL-2"[tiab] OR "LDL2"[tiab] OR "Low-Density Lipoprotein 2"[tiab] OR "Low

Lipoproteins"[tiab] OR "alpha-1 Lipoprotein"[tiab] OR "Hypercholesterolemia"[tiab] OR "Dyslipidemias"[tiab] OR "Hyperlipidemias"[tiab] OR "Lipid Metabolism Disorders"[tiab] OR "Hypertriglyceridemia"[tiab] OR "Hyperlipoproteinemias"[tiab] OR "Epicholesterol"[tiab] OR "VLDL Cholesterol"[tiab] OR "Pre-beta-Lipoprotein Cholesterol"[tiab] OR "Cholesterol, Pre-beta-Lipoprotein"[tiab] OR "Pre beta Lipoprotein Cholesterol"[tiab] OR "Very Low Density Lipoprotein Cholesterol"[tiab] OR "Prebetalipoprotein Cholesterol"[tiab] OR "Cholesterol, Prebetalipoprotein"[tiab] OR "Low Density Lipoprotein Cholesterol"[tiab] OR "beta-Lipoprotein Cholesterol"[tiab] OR "Cholesterol, beta-Lipoprotein"[tiab] OR "beta Lipoprotein Cholesterol"[tiab] OR "LDL Cholesterol"[tiab] OR "Cholesteryl Linoleate, LDL"[tiab] OR "LDL Cholesteryl Linoleate"[tiab] OR "alpha-Lipoprotein Cholesterol"[tiab] OR "Cholesterol, alpha-Lipoprotein"[tiab] OR "alpha Lipoprotein Cholesterol"[tiab] OR "HDL Cholesterol"[tiab] OR "High Density Lipoprotein Cholesterol"[tiab] OR "Cholesterol, HDL2"[tiab] OR "HDL2 Cholesterol"[tiab] OR "HDL(2) Cholesterol"[tiab] OR "Cholesterol, HDL3"[tiab] OR "HDL3 Cholesterol"[tiab] OR "HDL(3) Cholesterol"[tiab] OR "HDL-C"[tiab] OR "Hypercholesterolemias"[tiab] OR "High Cholesterol Levels"[tiab] OR "Cholesterol Level, High"[tiab] OR "Cholesterol Levels, High"[tiab] OR "High Cholesterol Level"[tiab] OR "Level, High Cholesterol"[tiab] OR "Levels, High Cholesterol"[tiab] OR "Elevated Cholesterol"[tiab] OR "Cholesterol, Elevated"[tiab] OR "Cholesterols, Elevated"[tiab] OR "Elevated Cholesterols"[tiab] OR "Hypercholesteremia"[tiab] OR "Hypercholesteremias"[tiab] OR "Dyslipidemia"[tiab] OR "Dyslipoproteinemias"[tiab] OR "Dyslipoproteinemia"[tiab] OR "Hyperlipemia"[tiab] OR "Hyperlipemias"[tiab] OR "Hyperlipidemia"[tiab] OR "Lipidemia"[tiab] OR "Lipidemias"[tiab] OR "Lipemia"[tiab] OR "Lipemias"[tiab] OR "Lipid Metabolism Disorder"[tiab] OR "Metabolism Disorder, Lipid"[tiab] OR "Metabolism Disorders, Lipid"[tiab] OR "Triacylglycerol"[tiab] OR "Triacylglycerols"[tiab] OR "Triglyceride"[tiab] OR "Hypertriglyceridemias"[tiab] OR "Hyperlipoproteinemia"[tiab]

2- "Smoking"[Mesh] OR "Tobacco"[Mesh] OR "Tobacco Use"[Mesh] OR "Smoking"[tiab] OR "Tobacco"[tiab] OR "Tobacco Use"[tiab] OR "Cigar Smoking"[tiab] OR "Smoking, Cigar"[tiab] OR "Tobacco Smoking"[tiab] OR "Smoking, Tobacco"[tiab] OR "Hookah Smoking"[tiab] OR "Smoking, Hookah"[tiab] OR "Waterpipe Smoking"[tiab] OR "Smoking, Waterpipe"[tiab] OR "Pipe Smoking"[tiab] OR "Smoking, Pipe"[tiab] OR "Cigarette Smoking"[tiab] OR "Smoking, Cigarette"[tiab] OR "Tobaccos"[tiab] OR "Tobacco Uses"[tiab] OR "Tobacco Consumption"[tiab] OR "Consumption, Tobacco"[tiab] OR "Cigars"[tiab] OR "Cigar"[tiab] OR "Cigarettes"[tiab] OR "Cigarette"[tiab] OR "second hand smoke"[tiab] OR "secondhand smoke"[tiab] OR "second-hand smoke"[tiab] OR "passive smoking"[tiab] OR "tobacco consumption"[tiab] OR "cigarette smoke"[tiab] OR "tobacco consumption"[tiab]

3- #1 AND #2

Table-2: Characteristics of included studies

Author, year; country	Study type	Sample size	Male[1]	Age[2]	Smoking definition	Period of exposure	Type of exposure	Type assessed lipid
Ayer, 2011; Australia (36)	Cohort	405	201	8	Any smoking use	Pregnancy; domestic	Passive	HDL
Byeon, 2007; South Korea (37)	Cross-sectional	127	87	12 to 15	Daily smoking	NA	Active	TC, TG, LDL, HDL
Dwyer, 1988; Germany (38)	Cohort	691	300	12 to 14	More than 1 cigarette per week	Domestic	Active	HDL
El-Hodhod, 2010; Egypt (39)	Cross-sectional	40	14	5 to 12	Daily smoking	Domestic	Passive	TC, TG, LDL, HDL
Guedes, 2007; Brazil (40)	Cross-sectional	452	206	15 to 18	Daily smoking	NA	Active	TC, TG, LDL, HDL
Hofer, 2009; Austria and Germany (41)	Cross-sectional	27,561	14481	13.6	Daily smoking	NA	Active	TC, TG, LDL, HDL
Hujová, 2011; Slovakia (42)	Cross-sectional	305	155	7 to 18	Current smoking	NA	Active	TC, TG, LDL, HDL
Ino, 2012; Japan (43)	Cross-sectional	1,366	731	9 to 10	Any smoking	Pregnancy	Passive	TC, TG, LDL, HDL
Iscan, 1996; Turkey (44)	Cross-sectional	194	106	4 to 14	NR	Domestic	Passive	TC, TG, LDL, HDL
Jaddoe, 2008; Netherlands (45)	Cohort	350	192	5 to 19	Smoking during pregnancy	Pregnancy	Passive	HDL
Kelishadi, 2004; Iran (47)	Cross-sectional	1,950	946	7 to 18	Daily smoking	NA	Active	TC, TG, LDL, HDL
Kelishadi, 2015; Iran (46)	Cross-sectional	5625	2801	10 to 18	Daily smoking	Domestic	Passive; active	TC, TG, LDL, HDL
Le-Ha, 2013; Australia (48)	Cohort	1,057	546	17	Passive smoking exposure across 17 years	Pregnancy; domestic	Passive	TC, TG, LDL, HDL
Misawa, 1989; Japan (49)	Cross-sectional	202	NR	7 to 18	Daily smoking	Domestic	Passive	TC, TG, LDL, HDL
Morrison, 1979; USA (50)	Cross-sectional	965	NR	12 to 19	Daily smoking	NA	Active	TC, TG, LDL, HDL
Moskowitz, 1990; USA (51)	Cohort	216	106	11	Daily smoking	Domestic	Passive	TC, LDL, HDL
Moskowitz, 1999; USA (52)	Cohort	113	49	15	Daily smoking	Domestic	Passive	LDL, HDL

[1], data are present as number of male gender; [2], data are present as mean or age range (year); HDL: High-density lipoprotein; LDL: Low-density lipoprotein; NA: Not applicable; NR: Not reported; TC: Total cholesterol; TG: Triglyceride.