Association between smoking habits and acne. A case-control study and a systematic review and meta-analysis

Alice Mannocci[(1)], Leda Semyonov[(1)], Rosella Saulle[(1)], Nevena Skroza[(2)], Concetta Potenza[(2)], Ersilia Tolino[(2)], Antonio Boccia[(1)], Giuseppe La Torre[(1)]

ABSTRACT

BACKGROUND: Smoke increases the development of many diseases. Previous studies about its role in the pathogenesis of acne show contradictory results.

The objective of this paper is to conduct a case control study on the relationship between smoke and acne and a systematic review of case-control studies on this association.

METHODS: For the case-control study, a questionnaire was administrated to each participant, to assess the association acne – tobacco smoking. For the systematic review, a bibliographic search on electronic databases was performed (Pubmed, Scopus and Google Scholar). Only case-control studies in English-language from 1966 to 2010 were included. All publications were analyzed by two researchers. Quality assessment was performed using a score for observational study.

RESULTS: Of 93 cases of the case-control study, 6 patients had severe acne, 19 moderate acne and 68 had a mild acne, according to classification of Global Alliance to improve outcomes in acne. No one of the smokers had severe acne, only one smoker had moderate acne and 11 had mild acne. Smoking was associated with acne (crude OR = 7.26; 95%CI: 2.27-23.18; Adjusted OR = 5.47; 95%CI: 1.67-17.97).

The systematic review considered five population studies. First meta-analysis, with all investigations, showed a OR=2.03 (95% CI: 0.63–6.58). The sensitivity analyses include meta-analyses stratified by gender, and quality (score>6). Results for males were: OR=1.89 (95%CI:1.25-2.87); for female OR=1.84 (95%CI:0.36-9.51). The analysis using quality score reported OR=3.48, (95%CI: 1.58-7.68).

CONCLUSIONS: In conclusions, smokers have higher risk to develop acne, especially males. Conclusions are not robust, because of heterogeneity definitions of smokers and acne grading.

(1) Clinical Medicine and Public Health, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy

(2) Dermatology Unit "D. Innocenzi", Polo Pontino, Sapienza University of Rome, Italy

CORRESPONDING AUTHOR: Leda Semyonov, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Piazzale Aldo Moro 5 – 00185 Rome (Italy), phone +390649970388, fax +390649972473. e-mail: leda.semyonov@uniroma1.it

INTRODUCTION

Previous studies have reported conflicting results about the association between smoking habit and acne.

It's well known that cigarette smoking contributes to an increased risk of coronary artery disease, stroke, atherosclerotic peripheral vascular disease, many types of cancer, chronic pulmonary disease [1]. While ample clinical evidence suggests that smoking is associated with several dermatologic diseases and with several adverse effects on the skin like psoriasis, pustulosis palmoplantaris, *hydrosadenitis suppurativa, systemic and discoid lupus erythematosus, labial squamous* cell carcinoma, premature skin aging, melanoma, squamous and basal cell carcinoma of the skin [2-4].

The role of smoking habit regarding acne is more discussed.

Acne is a common skin disease with a multifactorial pathogenesis, that usually starts in adolescent and resolves slowly by mid-20s but it may persist up to the age of 40 or more [5,6].

Post-pubertal acne is described as an inflammatory mild-moderate form, with increasing incidence [7].

Recent investigation studies revealed smoking to be a clinically important contributor to acne prevalence and severity [4,7-10], although some studies did not confirm this association: in fact, even data exists on possible smoking protective effects due to the anti-inflammatory properties of nicotine, or possibly some other components of cigarettes [6,11-14].

The aim of this study was to conduct a case-control study and a systematic review and a meta-analysis to investigate the possible relationship between smoking habit and acne appeared.

METHODS

Case-control study

A case-control study was carried out. Cases were outpatients of the Ambulatory of acne, Dermatology Unit "D. Innocenzi", Sapienza University of Rome (Lazio, Italy), and controls were chosen among healthy population, age and gender-matched to the cases, among the same community where the cases arose (community-based case-control study).

The ratio cases-controls was 1:2 and we used the following parameters to make the sample size calculations: sensibility = 0.95, power = 0.80, estimation of smoking prevalence among general population = 25%, OR estimating the relationship between tobacco smoking and acne vulgaris = 2.5.

According to the above parameters, using the Statcalc EpiInfo Calculator, we estimated to enroll in the study 69 cases and 138 controls.

A questionnaire was administrated to each participant in order to assess the correlation between acne and smoke. The questionnaire comprised essentially socio-demographic data and a question on tobacco smoking. The smoking habits were classified as current and no smoking. The questionnaire was administered during the clinical examination for the cases and at high school and university classes for controls.

We composed absolute and relative frequency distribution and contingency tables.

Differences between cases and controls were analyzed using parametric and non-parametric tests. Differences for categorical variables were tested using chi-square test, while those pertaining continuous ones were analyzed using the Student t-test.

A univariate logistic regression analysis was conducted for estimating the variables who predicted the odds of being case (being a patient with acne). This risk was estimated through the calculation of the Odds Ratio (OR) and the relative 95% confidence interval (95%CI).

Finally, a multiple logistic regression analysis was conducted for assessing the influence on the outcome (being a patient with acne) of the variables that at the univariate analysis yielded a p-value < 0.25, using the procedure described by Hosmer and Lemeshow. The stepwise approach with "backward elimination" procedure was followed. The goodness of fit of the model was estimated using the Hosmer-Lemeshow test [15].

The statistical analysis was conducted using the statistical package SPSS for Windows (release 12.0). the statistical significance was set at p < 0.05.

Systematic review

Literature review was based on Electronic medical databases. The search was applied to Medline, Scopus and Google Scholar. For each

database, we used the keyword: "smoking AND acne", "tobacco AND acne", "nicotine AND acne", "cigarettes smoking AND acne".

We only selected articles from medical area (Pubmed) and articles from *medicine, pharmacology and veterinary science* area (Google Scholar). Only published papers were reviewed.

Study Selection

The identification of relevant studies was carried out until May 20th 2010 and it was restricted to English-language articles.

The selection of articles is shown in the flow-chart (Figure 1) that was performed according to the PRISMA statement è [16].

Studies without a thorough correlation of smoking and acne relationship outcome were excluded and all duplicate records in medical databases too. Subsequently, for our search, only case-control studies with available full text and with data about cases of acne in current smokers and no smokers (never smokers and ex- smokers) were included in the meta-analysis.

All publications were analyzed by two different researchers. Both independently reviewed the full texts to identify relevant information: number of cases, study design, classification of acne, kind of smokers.

Moreover, the quality assessment for all included studies was performed using a quality scoring for observational studies assessment [17].

Any disagreements between the two researches was solved with a discussion and a second examination.

FIGURE 1

SELECTION OF THE STUDIES
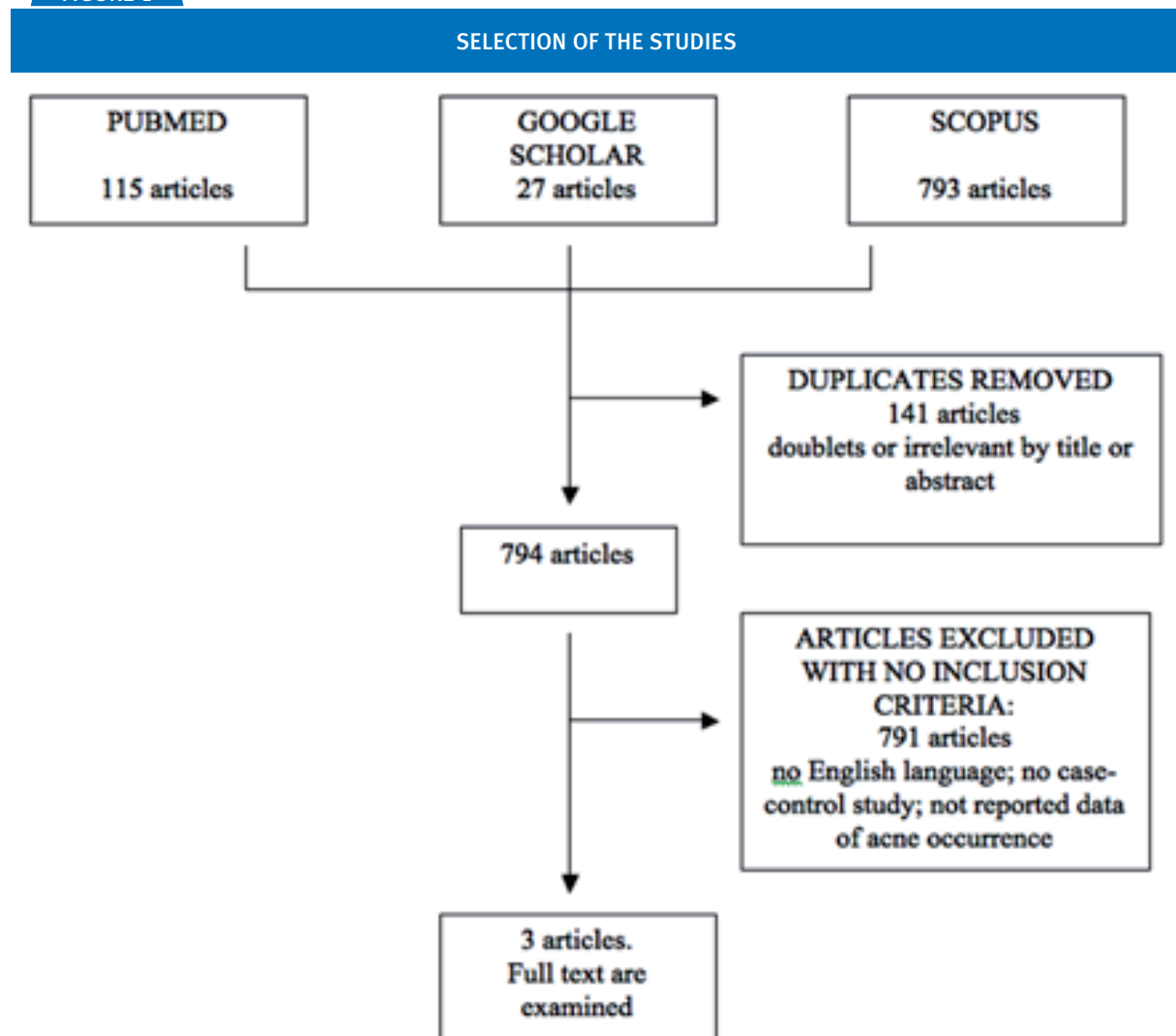
A total 934 studies were found through Pubmed, Google Scholar and Scopus. 115 articles were found in Medline (Figure 1). The same process was performed for Scopus and Google Scholar searches: 793 and 27 articles obtained respectively. From these last ones, no studies were selected cause exclusion criteria and overlapping on Medline outcomes.

For our analysis 3 case control studies were finally selected (Table 2), each one from Medline outcomes [6,8,9], in addition to our own case-control study.

Three different analysis were carried out: the first one, including all selected case control records, that evaluated the association between smoking habit and acne; the second group of analysis included only case control studies that stratified the data by gender, and we conducted analyses separately for male and female; the third one included only studies with a quality score > 6.

In order to assess association between smoking habit and acne, we used the Odds Ratio (OR) measure with relative 95% confidence interval (95%CI). The Chi-square test was computed to evaluate studies heterogeneity, thus using the random effect model when the test highlighted differences between studies and the fixed effect model when no significant differences were shown [18].

The level of significance was set $p<0.05$.

Meta-analysis was performed using RevMan software version 5 for Windows [19].

RESULTS

Case-control study

As is showed in Table 1, total of 293 patient records of 93 patients with acne and 200 controls were reviewed.

Of the 93 patients with acne, 34 were male and 59 were female, 68 cases were patients affected by mild, 19 moderate e 6 severe acne.

Median age of female smokers were 25 years (range of median age of female with acne was 11-37 years); median age of male smokers were 18 years (range of median age of male with acne was 12-22 years). Median age of no-smoker people were 16 for female and 16 for male.

Smoking male were totally 4 and, of those, just 1 guy was affected by acne; smoking female, instead, were 12 and 11 of them had acne. Non smokers male were 94: 33 cases and

61 controls; non smokers female were 183: 48 cases and 135 controls.

Crude OR for the association between acne and smoke was 7.26 (IC=2.27-23.18), while the adjusted OR for sex and age was 5.47 (IC=1.67-17.97)

Of 93 cases of the case-control study, 6 patients had a severe acne (6.5%), 19 moderate acne (20.4%) and 68 had a mild acne (73.1%), according to classification of Global Alliance to improve outcomes in acne [20]. No one of the smokers had a severe grade of acne, only one smoker had an intermediate grade of acne and 11 smokers had mild acne; anyway these differences are not statistically significant.

Systematic review

The result about first meta-analysis, including all the studies selected, was not significant risk: OR=2.54 (95% CI: 0.91–7.08) using effect random estimate as suggested by the heterogeneity test's level of significance (p<0.00001) (Figure 2).

The second group, concerning the articles with data stratified by gender, showed a significant higher risk for male smokers versus male no-smokers [OR=1.82 (95%CI: 1.21–2.73)] estimated with fixed effect approach (heterogeneity test p=0.09), while for females it was not significant increase of the risk [OR=3.01 (95%CI: 0.72–12.62)] with random effect estimate (heterogeneity test p=0.0002) (Figure 3).

The last one (Figure 4), made with studies with a quality score > 6, reported a significant OR=3.48 (95%CI: 1.58–7.68) estimated with random effect (heterogeneity test p=0.002): in this case the risk of having acne was more than three times as much among smokers than in no-smokers.

Concerning publication bias, the results of the funnel plot (Figure 5) show that there is no evidence of this kind of potential error.

DISCUSSION

Tobacco is the most preventable cause of morbidity and death [6]. In addition, it is involved in many skin disorders. Previous studies, concerning the association between acne and smoke, showed contradictory results.

Recent investigation studies revealed smoking to be a clinically important contributor

ORIGINAL ARTICLES

TABLE 1

DESCRIPTION OF THE CASE-CONTROL STUDY CHARACTERISTICS				
VARIABLES	**CASES (%)**	**CONTROLS (%)**	**OR (IC 95%)**	**OR ADJ* (IC 95%)**
CURRENT SMOKERS	12 (12.9)	4 (2)	7.26 (2.27-23.18)	5.47 (1.67-17.97)
NO SMOKERS †	81 (87.1)	196 (98)		
FEMALE	59 (63.4)	136 (68)	0.82 (0.49-1.37)	0.72 (0.42-1.24)
MALE †	34 (36.6)	64 (32)		
≥ 18 YEARS	50 (53.8)	67 (33.5)	2.31 (1.40-3.81)	2.01 (1.19-3.40)
‹ 18 YAERS †	43 (46.2)	133 (66.5)		

*Adjusted considering the model with the following variables: current smokers, gender, age
† Reference group

TABLE 2

DESCRIPTION OF THE META-ANALYSIS CHARACTERISTICS									
AUTHOR	**YEAR**	**GENDER/AGE**		**ACNE CLASSIFI-CATION**	**COMPARED GROUPS**	**SMOKERS WITH ACNE**	**TOT SMOKERS**	**NO SMOKERS WITH ACNE**	**TOT NO SMOKERS**	**QUALITY ASSESMENT**
B. Capitanio	2009	Female 20-50 ys		Inflammatory Acne	Current Smokers	10		37		8
				Non Inflammatory Acne		105		33		
				Tot		115	277	70	723	
A. Firooz	2005	Male 15-40 ys		n.r.	Current Smokers	9	29	55	96	6
		Female 15-40 ys				3	10	226	178	
		Tot 15-40 ys				12	39	281	274	
A.A.T. Chuh	2004	Hong Kong	Male (mean age 32.8)	n.r.	Smokers vs*	9	29	55	96	10
			Female (mean age 31.3)			3	10	226	178	
			Tot			12	39	281	274	
		India	Male (mean age 26)			40	59	235	529	
			Female (mean age 36)			2	3	123	247	
			Tot			42	62	358	776	

* = ex smokers and never smokers
n.r.= not reported
vs= versus
ys= years

to acne prevalence and severity (with OR between 1.45 and 6.62) [4,7-10], although some studies did not confirm this association: in fact, even data exists on possible smoking protective effects due to the anti-inflammatory properties of nicotine, or possibly some other components of cigarettes (was found OR included between 0.43 and 0.71) [6,11-14].

As is shown in our case-control study, acne remains a rare disease in non-Westernized

FIGURE 2

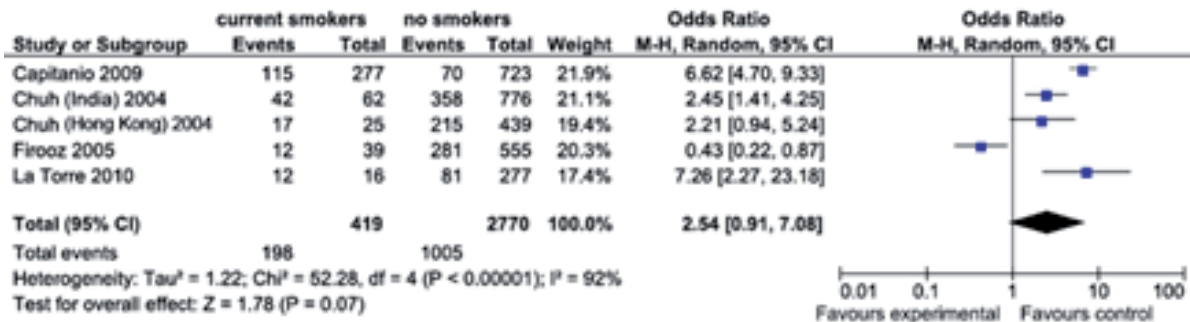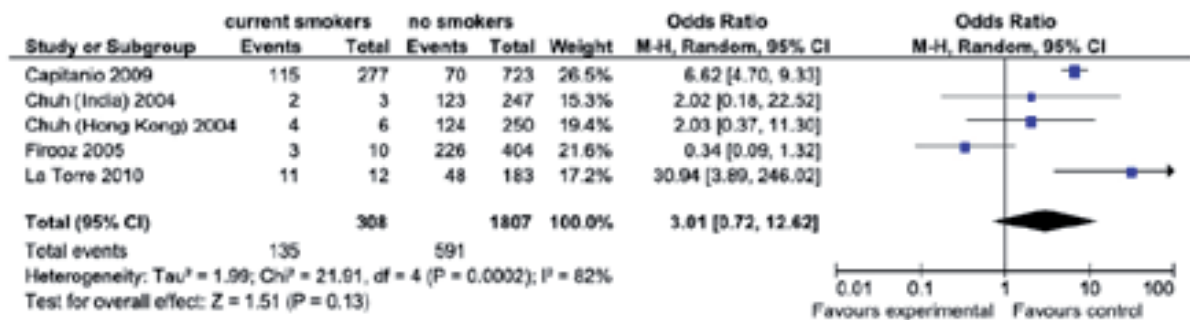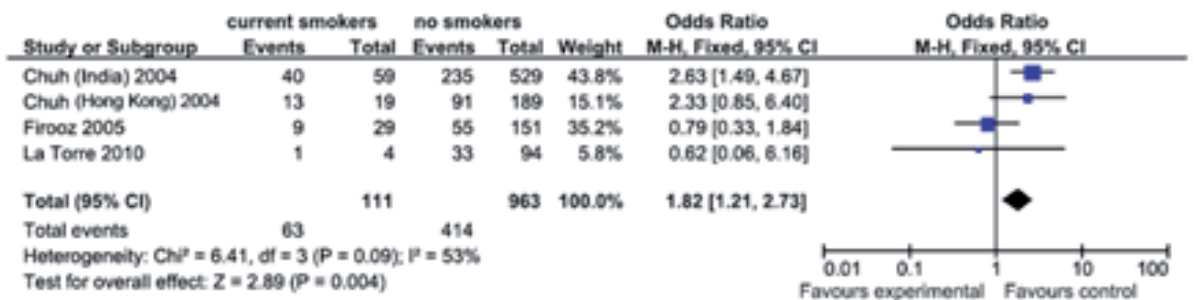**FOREST-PLOT OF ACNE RISK IN CURRENT SMOKERS VERSUS NO SMOKERS, CONSIDERING ALL STUDIES SELECTED**

FIGURE 3

FOREST-PLOTS USING ONLY STUDIES THAT STRATIFIED BY GENDER ACNE RISK IN SMOKERS VERSUS NO SMOKERS

Female

Male

societies, but incidence rates of acne have increased with the adoption of Western lifestyle, such as smoking habit.

According to some authors, smoking seems to exert an anti-inflammatory role in the pathogenesis of acne11 and tobacco appears to be protective in the development of this disease [14].

Other authors, instead, did not found any association between acne and smoking [6,7,10].

In our case-control study, the association between acne and smoke shows an increased risk with a statistically significant Confidence Interval.

A recent meta-analysis [21], examining only cross-sectional studies, underlines that there is not a significant evidence of the association between smoke and acne, neither as a risk factor, nor as protective factor. In the same study a not significant association by gender was observed.

Our meta-analysis made with case-control studies concerning the articles with data stratified by gender, instead, showed a
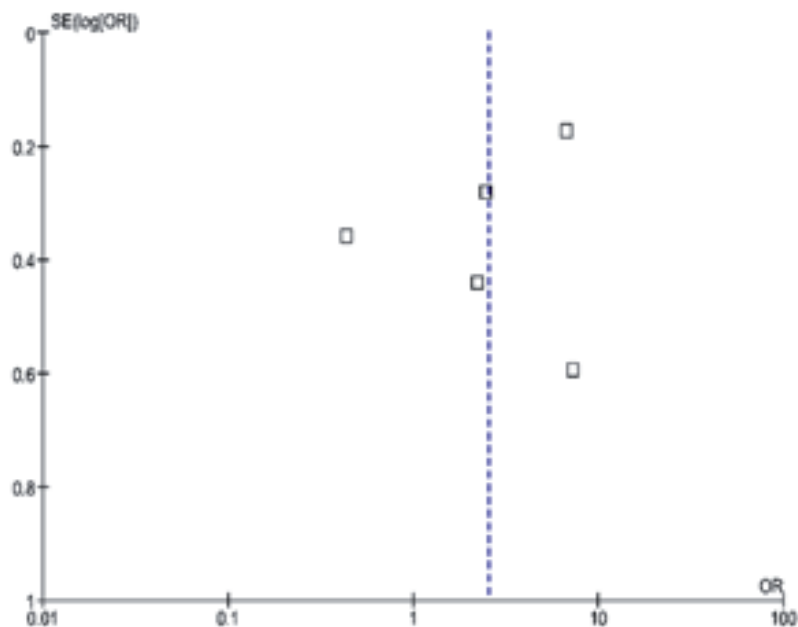
FIGURE 4

FOREST-PLOT CONSIDERING STUDIES WITH QUALITY SCORE › 6

FIGURE 5

OVERALL FUNNEL PLOT

significant pooled risk for males while for females IC it was not significant even if it showed an amplified risk for smokers to develop acne (Figure 3).

In the analysis made with case-control studies with a quality score > 6, the association between smoke and acne reported a significant increase of the risk. A contradictory result was obtained in the analysis prepared with cross-sectional studies with a quality score > 6: it reported OR=0.69 and 95%CI=(0.55–0.85) that means that in this case the association shows a significant reduction of the risk of having acne for the smokers.

Limitations of this study was that, in several studies, the distinction of ex-smokers and never smokers was not clearly explained or even not reported: in this way, it's difficult to comprehend if the cumulative dose of nicotine got in the past years could still play a role in pathogenesis of acne. Another bias was represented by the age of the samples: the selected studies take into consideration patients of different ages and that makes complicate to differentiate the task of age from the role of smoking itself in the acne development. One more limit of this study is due to acne classification: in the studies acne is classified as mild, moderate, severe or simply as presence/absence and this makes hard to make a comparison of the data. Moreover, as were selected the only 3 case-control studies available for this meta-analysis, our estimate is far to being absolutely accurate.

CONCLUSIONS

In conclusion, the results of our meta-analysis underlines that there is a manifest evidence of the association between smoke and acne as a risk factor, especially considering studies with a quality score >6. In addition, the dissimilarity of the outcomes get by the two meta-analysis (made respectively with case-control and cross sectional studies), shows that different results could be obtained using different study design. The analysis with the case-control studies is more trustworthy, as it correlates the incident cases with the smoke exposure, that certainly come before the disease (acne). The role of smoking in the developing of acne could be due to its inflammatory role, however the heterogeneity of results is an issue and further research on this relationship will enlight this topic.

References

[1] Smith JB, Fenske NA. Cutaneous manifestations and consequences of smoking. J Am Acad Dermatol. 1996;34:717–32.

[2] Misery L. Nicotine effects on the skin: are they positive or negative? Exp Dermatol. 2004;13:665–70.

[3] Koh JS, Kang H, Choi SW, Kim HO. Cigarette smoking associated with premature facial wrinkling: image analysis of facial skin replicas. Int J Derm. 2002;41:21–7.

[4] Ghodsi SZ, Orawa H, Zouboulis CC. Prevalence, severity and severity risk factors of acne in high school pupils: A community-based study. J Invest Dermatol. 2009;129(9):2136-41.

[5] Williams C, Layton AM. Persistent acne in women: implications for the patient and for therapy. Am J Clin Dermatol. 2006;7:281–90.

[6] Firooz A, Sarhangnejad R, Davoudi SM, Nassiri-Kashani M. Acne and smoking:is there a relationship? BMC Dermatol. 2005 Mar 24;5:2.

[7] Schäfer T, Nienhaus A, Vieluf D, Berger J, Ring J. Epidemiology of acne in general population: the risk of smoking. Br J Dermatol. 2001;145:100–4.

[8] Chuh AA, Zawar V, Wong WC, Lee A. The association of smoking and acne in men in Hong Kong and in India: a retrospective case-control study in primary care settings. Clin Exp Dermatol. 2004;29:597–9.

[9] Capitanio B, Sinagra JL, Ottaviani M, Bordignon V, Amantea A, Picardo M. Acne and smoking. Dermatoendocrinol. 2009;1(3):129-35.

[10] Petrou I. Smoke and mirrors: Study shows relationship between cigarette use and acne intensity. ModernMedicine2009.(www.modernmedicine.com/modernmedicine/article/articleDetail.jsp?id=599853. Last access 1st July 2010).

[11] Jemec GB, Linneberg A, Nielsen NH, Frølund L, Madsen F, Jørgensen T. Have oral contraceptives reduced the prevalence of acne? A population-based study of acne vulgaris, tobacco smoking and oral contraceptives. Dermatology. 2002;204:179–84.

[12] Mills CM, Peters TJ, Finlay AY. Does smoking influence acne? Clin Exp Dermatol. 1993;18:100–1.

[13] Klaz I, Kochba I, Shohat T, Zarka S, Brenner S. Severe acne vulgaris and tobacco smoking in young men. J Invest Dermatol. 2006;126:1749–52.

[14] Rombouts S, Nijsten T, Lambert J. Cigarette smoking and acne in adolescents: results from a cross-sectional study. J Eur Acad Dermatol Venereol. 2007;21(3):326-33.

[15] Lemeshow, S, Hosmer DW. A review of goodness of fit statistics for use in the development of logistic regression models. American Journal of Epidemiology, 1982;115(1), 92-106.

[16] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ital J Public Health 2009; 6(4): 354-91.

[17] La Torre G, Chiaradia G, Gianfagna F, De Laurentis A, Boccia S, Ricciardi W. Quality assessment in meta-analysis. Ital J Public Health 2006; 3(2): 44-50.

[18] DerSimonian R, Laird N. Meta-analysis in Clinical Trials. Control Clin Trials 1986;7:177-88.

[19] http://www.cc-ims.net/revman (last accessed 8 September 2010).

[20] Gollnick H, Cunliffe W, Berson D, et al. Management of acne: a report from a Global Alliance to Improve Outcomes in Acne. J Am Acad Dermatol. 2003;49(1 Suppl):S1.

[21] Mannocci A, Semyonov L, Saulle R, Boccia A. Evaluation of the association between acne and smoking attitude: systematic review and meta-analysis of cross-sectional studies. Ital J Public Health 2010;7(3):256-61.