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Cigarette smoking triggers inflammatory response by enhancing secretion of HS-CRP

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Smoking is a major potential risk that could affect variety of organs. In smokers, the pattern of inflammatory process as evaluated by circulating levels of C-reactive protein is associated with a higher risk of CVD and cancer. There are limited local data about the effect of cigarette smoking on the serum levels of HS-CRP. Therefore, the study aimed to estimate of level of serum HS-CRP in Sudanese healthy Cigarette smoker.Blood samples collected from75 Sudanese healthy cigarette smokers and 75 apparently healthy individual nonsmokers as control group recruited in period from January to August 2019. Serum HS-CRP was estimated by Fine care™ data were analyzed using SPSS version 20.The mean of Serum HS-CRP in case and control group was (2.7mg/L±1.3, and 0.16mg/L±0.4) respectively, P value (0.002).The mean of serum HS-CRP among case group according to age from 18-27 was (2.0mg/L± 0.8), while the of age from 28-45 was (3.9 mg/L±1.1). serum level of HS-CRP protein was statistically significant twice high in smokers who smoked for more than 8 and less than 24 years P value (0.00).The mean level of Serum HS-CRP is statistically significant elevated in healthy cigarette smokers in compared to non-smokers. There is significant positive correlation between serum HS-CRP with the duration of cigarette smokers as well as advance age; this is because the dangerous chemicals in cigarettes negatively affect the immune, respiratory, and circulatory systems.

Keywords: C-reactive Protein, Cigarette Smoking, Inflammation, Inflammatory Mediator.

INTRODUCTION

Inflammation is linked to a variety of chronic health conditions, including cardiovascular disease and cancer, and inflammation reduction may help in the prevention or therapeutic interventions of such circumstances (Aldaham et al. 2015). Smoking is the most common method of consuming tobacco, which may increase inflammatory mediators in the human body and thus may lead to a massive risk factor for lung cancer (the most widely known cancer in the world) as well as cardiovascular diseases, and it is the main risk factor of morbidity and mortality around the world (Gately et al. 2001).

Cigarette smoke contains multitude of chemical components, including many well-known toxins and carcinogens, hence it is consumption has been linked to elevated CRP levels, and past

studies has shown that greater CRP levels are a consequence of cigarette smoking and indicate tissue damage. Number of researches indicated that smoking has numerous immediate health effects on the liver, respiratory, cardiovascular, gastrointestinal, immune and metabolic system. Lung cancer, other cancer, heart disease, and stroke typically do not occur until years after person's first cigarette (Alberg et al. 2002).

Regular tobacco uses enhance an immune response to tissue damage that is characterized by excessive production of inflammatory cytokines and mediators such as C - reactive protein and white blood cell count. Numerous researches has conclude that these markers possibly can lead to coronary heart disease. Fortunately, there have been some gaps in our understanding of cardiovascular disease, smoking, and the forecasting use of these markers. Few studies, for example, have investigated the impact of cigarette smoking on inflammatory marker amounts or cardiovascular disease prevention; the level and frequency where the inflammatory response diminished after quitting smoking is also unknown. Besides that, it is ambiguous if either habitual risk factors can justify the decrease in heart disease risk associated with smoking discontinuation (Casas et al. 2008).

C-reactive protein is an acute phase plasma protein that is produced in due to broad sense inflammatory process in the body (Black S et al. Pepys MB et al. 2003), it is primarily produced by hepatocytes, but it can also be represented by adipocytes (Ouchi et al. 2003) and incubated coronary artery smooth muscle cells (Calabro et al. 2005), implying that regionalized inflammation can stimulate CRP expression.

Several studies have shown a correlation between excessive concentrations of CRP as well as other markers of inflammation and tobacco smoking. Due to the extreme dangerous substances in tobacco, the white blood cell count has elevated, primarily due to an increase in polymorph nuclear neutrophils, which are discharged from the bone marrow and enrolled to inflamed tissue (Van Eeden et al. 2000). IL-and IL-6, which have been elevated in responding to lung inflammation and have been linked to the activation of CRP gene expression, could activate bone marrow cell excitation. (Van Eeden et al. 2005). Large volume of studies some of which are conflicting, in which serum CRP concentrations have been measured in parallel to smoking status because of the possible link between smoking and the induction of inflammatory pathways (Yanbaeva et al. 2007). And also another study conducted by (Shamima et al. in 2015), the mean serum HS-CRP level was significantly higher in male smokers than that of non-smokers which was progressively increase with duration of smoking.

Pervious study conducted in 2005 by Wannamethee et al. and Hastie, et al. 2008) showed that never-smokers had statistically significantly lower CRP levels than regular smokers. In Sudan smoking is become a common condition with increasing rate in both sex's males and females and occurs in different age groups, it can cause many organ damages and dysfunctions. This study was conducted to verify the effect of cigarette smoking on C reactive protein using HS_CRP as a sensitive marker of inflammatory condition, among Sudanese Cigarette Smokers in Khartoum state.

MATERIALS AND METHODS

Study design:

Analytical cross sectional study was carried out in Khartoum state during period of January 2019 to August 2019. The study were approved by the Ethics Committee of National University-Sudan Faculty of Medical Laboratory sciences and performed in accordance with relevant guidelines and regulations. Prior to actually enrolling, all selected patients signed a consent form.

Study population:

The study population was Sudanese cigarette smokers as case group (CG), their age range between 18-45 years old and apparently healthy individual (non-smokers) as control group (CG). At start point, for every participant's age, gender, smoking status (participants who had quit smoking for at least one year), numbers of cigarettes consumption/day, age at starting smoking, age at stopping, and lung function were all recorded. Participants suffer from any diseases and treatments that cause HS-CRP imbalance, patients with chronic infection, coronary heart disease, neoplastic proliferation, SLE, congestive heart failure and marked hypertension were excluded from study.

Sampling technique and sample size:

A total of 150 blood samples were collected (75 CG and 75 as CG) using non-probability sampling technique (namely convnious sampling method). Blood samples withdrawn into sterile,

plastic syringes, blood samples (5ml) was collected in plain containers from each volunteer under a septic condition, then they were centrifuged at 4000 rpm to obtain the serum samples, and stored in -20° until the analyzed.

Methods:

The fine care ™(FS-1121706004316, made in china), CRP rapid quantitative test was used for determination of C reactive protein is based on fluorescence immunoassay technology. The fine care ™ CRP rapid quantitative test uses a sandwich immune detection method, when sample is added to the sample well of the Test Cartridge, the fluorescence-labeled detector CRP antibody binds to CRP antigen in blood specimen. As the sample mixture migrate on the nitrocellulose matrix of test strip by capillary action, the complexes of detector antibody and CRP are captured to CRP antibody that has been immobilized on test strip. Thus the more CRP antigen is in blood specimen, the more complexes are accumulated on test strip. Signal intensity of fluorescence of detector antibody reflects amount of CRP captured and finecare™ FIA Meter shows CRP concentrations in blood specimen. The default results unit of finecare™ CRP rapid quantitative test is displayed as mg/L from finecare ™ FIA Meter. The working range and the detection limit of the CRP Test system are 0.5~200 mg/l and 0.5mg/l. The precision and accuracy of all methods use in this study were checked at each batch using commercially prepared control sera.

Data collection:

Structural interviewing questionnaire was used as tool for data collection, it was intended to collect and maintain all demographic and clinical data concerning with case group.

Ethical Considerations:

A Study was approved from ethical committee of the National University (IRB reference NO NU/FM/EC.94, verbal informed consent was obtained and all patients were informed by aims of the study.

Statistical analysis:

The collected data were analyzed by the use of statistical package of social science (version 20, SPSS Inc.).The parameter was compared between smokers and non-smokers, by mean, SD and Regression.

RESULTS

Among one hundred and fifty subject participate in the study about 75 were smoker group and others were non-smoker control group; all participants were males their age range between 18-45 years old with mean age 39±4.4SD. Disparities in the levels of CRP as inflammatory biomarkers between case and control displayed in Table 1, where mean of HS-CRP level in smokers group 2.7 mg/l which was significantly higher than control (1.6 mg/l) (P. value 0.001).

Table 2 stated the comparison between the means of serum HS-CRP level in smokers with regard of age of study subjects. About 53 (70.6%) of participants in age group (18-27years) and 25 (29.4%) where in age group between (28-45years). The mean of HS-CRP was significantly twice increased in age group between 28-45 years old. The effect of duration of cigarette smoking on level of CRP in table 3, the first group were smoking for 1 to 7 years (52%) and second group smoking duration between 8-24 years old (48%), and the serum level of CRP protein was statistically significant twice as high in smokers who smoked for more than 8 and less than 24 years.

Table 1: Comparison between the means of serum HS-CRP level in smokers as case group and non-smoker as control group

Parameters	N=150 (%)	Mean (mg/l)	±SD	P. value
Cases	75 (50%)	2.7	1.3	
Controls	75 (50%)	1.6	0.4	0.001

Table 2: Comparison between the means of serum HS-CRP level in smokers with age(18-27years)and with (28-45years)

Age /years	N= 75 (%)	Mean (mg/l)	±SD	P. value
18-27 Years old	53 (70.6%)	2.0	0.8	0.000
28-45 Years old	23 (29.4%)	3.9	1.1	

Table 3: Comparison between the Means of Serum HS-CRP in smokers with duration (1-7 years) and in smokers with duration (8-24 years)

Duration	N=75 (%)	Mean (mg/l)	±SD	P. value
1-7 Year	39 (52%)	1.8	0.76	
8-24 Year	36 (48%)	3.7	1.0	0.002

DISCUSSION

There is a surge of attention in evaluating the such relation between inflammatory mediators and smoking in order to find justifications for smoking-regarding comorbidities and death. Hence the current study attempted to estimate the level of CRP among Sudanese cigarette smoking to determine such correlation. The study showed statically significant difference (P value 0.001) in the mean of HS-CRP between cases and control (2.7 mg/l and 1.6 mg/l respectively). This finding was agree with numerous studies who found cigarette smoking is lead to increase of HS-CRP levels in cigarettes smoker, where the mean CRP levels were significantly lower in never-smokers than in current smokers (Wannamethee et al. Ohsawa et al. 2005, Alyan et al. 2008), however conflict with (Yanbaeva G et al. 2007), so in even the most healthy smokers, smoking disturbs sympathovagal harmony and rises HS-CRP activity, both of which may perhaps participate to a higher rate of cardiovascular events. The discrepancies in findings could be attributed to different factors such as sample size, ethnic groups of participants, as well as lipid profile, immune status, and life style of subjects.

With regard the comparison between participant's age and the means level of serum High sensitive C-reactive protein there was significance deference between age of smokers group (18-27 years old) and in age group (28-45 years old), where mean level increased as doubled with advanced age. This may attributed to much damage and worsen of immune system by regular secretion of inflammatory mediator due to direct effect of toxic substance found in cigarette.

There was also statistically significance difference between the serum High sensitive C-reactive protein with duration of smoking (P value 0.002), 48% of smoker who smoke more than 8 years till 24 years their mean serum HS-CRP level was much higher than that those smokers for less than 8 years. So the CRP was progressively increase with duration of smoking, a study conducted by (Aldaham et al. 2015) no significant variation in CRP levels were revealed between smokers and former smokers in subjects under study with more than 30 years of smoking consumption. Conversely, serum IL-6 scores were significantly increased in current smokers than in former smokers. An even more study, published in 2007, by Diettrich et al. noticed that smoking is associated with dosages and moment rises in CRP concentration. In the case group, there was a strong positive association between serum HS-CRP and maturity level. Compared with a non-smokers smoking is estimated to increase the risk of coronary heart disease and stroke by 2 to 4 times, and men developing lung cancer by 23 times, and death rate from chronic obstructive lung disease (such as chronic bronchitis and emphysema) by 12 to 13 times (Ramage et al. 2009), due to the extreme potential association between smoking and the activation of inflammatory pathways (Sunyer et al. 2009). Hence an exposure to cigarette smoke induces oxidative stress that might give rise to inflammatory processes than may lead to other comorbidities like coronary heart disease, pulmonary distress and lung cancer.

CONCLUSION

The mean level of Serum HS-CRP is statistically significant elevated in healthy cigarette smokers in compared to non-smokers. A positively significant correlation revealed between serum HS-CRP with the duration of cigarette smokers as well as advance age, this is because the dangerous chemicals in cigarettes negatively affect the immune, respiratory, and circulatory systems.

Limitation of the study and prospective:

The present study enrolled only a total of 150 male participants in across sectional study, and this is small sample size with regard large number of smokers, so another well-constructed study design with probability sampling technique include both gender is contraindicated, as well as much more variables such as lipid profile and inflammatory mediators such as pro inflammatory cytokines must be investigated, also the variables investigated depended on patients' records.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

MMA (Sample collection, Laboratory work, and purchasing reagents)

MA (Preparation of questionnaire, Supervision, Proof reading scientific writing)

SA (Laboratory works, and Calibration of machines)

LB (Statistics, Scientific writing, publication)

REFERENCES

Alberg AJ. The influence of cigarette smoking on circulating concentrations of antioxidant micronutrients. Toxicology. 2002;180(2):121–37.

Aldaham S, Foote JA, Chow HH, Hakim IA. Smoking Status. Effect on Inflammatory Markers in a Randomized Trial of Current and Former Heavy Smokers. Int J Inflam. 2015;2015:439396.

Alyan O, Kaçmaz F, Ozdemir O, Karahan Z, Taşkesen T, Iyem H, Alan S, Karadede A, Ilkay E. Sigara içenlerde artmiş yüksek duyarlikli C-reaktif protein düzeyleri ve bozulmuş otonomik aktivite [High levels of high-sensitivity C-reactive protein and impaired autonomic activity in smokers]. Turk Kardiyol Dern Ars. 2008;36(6):368-75. Turkish. PMID: 19155639.

Black S, Kushner I, Samols D. C-reactive protein. *J Biol Chem.* 2004;279:48487 90.

Calabro P, Chang DW, Willerson JT, Yeh ET. Release of C-reactive protein in response to inflammatory cytokines by human adipocytes: linking obesity to vascular inflammation. J Am Coll Cardiol. 2005 20;46(6):1112-3.

Casas JP, Shah T, Hingorani AD, Danesh J, Pepys MB. C-reactive protein and coronary heart disease: a critical review. J Intern Med. 2008 Oct;264(4):295-314.

Dietrich T, Garcia RI, de Pablo P, Schulze PC, Hoffmann K.The effects of cigarette smoking on C-reactive protein concentrations in men and women and its modification by exogenous oral hormones in women. Eur J Cardiovasc Prev Rehabil. 2007;14(5):694-700.

Gately, lain, (2001), Tobacco: a cultural history of how and exotoxic plant seduced Civilization. London: Simon& Schuster.p.3-7.

Jahan S, Qazi A. serum high sensitive c reactive protein in male smokers of Bangladesh. J Bangladesh Soc physiol. 2015;10(1):36-40.

Ohsawa M, Okayama A, Nakamura M, Onoda T, Kato K, Itai K, Yoshida Y, Ogawa A, Kawamura K, Hiramori K. CRP levels are elevated in smokers but unrelated to the number of cigarettes and are decreased by long-term smoking cessation in male smokers. Prev Med. 2005 Aug;41(2):651-6. doi: 10.1016/j.ypmed.2005.02.002. PMID: 15917065.

Ouchi N, Kihara S, Funahashi T, Nakamura T, Nishida M, Kumada M, Okamoto Y, Ohashi K, Nagaretani H, Kishida K, Nishizawa H, Maeda N, Kobayashi H, Hiraoka H, Matsuzawa Y. Reciprocal association of C-reactive protein with adiponectin in blood stream and adipose tissue. Circulation. 2003;107(5):671-4.

Pepys MB, Hirschfield GM. C-reactive protein: a critical update. *J Clin Invest.* 2003;111:1805–12.

Ramage L, Guy K. Expression of C-reactive protein and heat shock protein -70 in the lung epithelial cell line A549, in response to PM10 exposure. Inhal.Toxicol. 2009;16(6–7), 447–452.

Sunyer J, Forastiere F, Pekkanen J, Plana E, Kolz M, Pistelli R, Jacquemin B, Brüske-Hohlfeld I, Pitsavos Ch, Bellander T, Koenig W, Peters A; AIRGENE Study Group. Interaction between smoking and the interleukin-6 gene affects systemic levels of inflammatory biomarkers. Nicotine Tob Res. 2009 ;11(11):1347-53.

Van Eeden SF, Hogg JC. The response of human bone marrow to chronic cigarette smoking. EurRespir J. 2000, 15:915–21.

Van Eeden SF, Yeung A, Quinlam K. Systemic response to ambient particulate matter: relevance to chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2005;2:61–7.

Wannamethee G, Lowe D, Shaper G. Associations between cigarette smoking, pipe/cigar smoking, and smoking cessation, and haemostatic and inflammatory markers for cardiovascular disease.Eur Heart J. 2015;26:1765–73.

Yanbaeva DG, Dentener MA, Creutzberg EC, Wesseling G, Wouters EF. Systemic effects of smoking. Chest. 2007;131(5):1557-66.

Yanbaeva G, Dentener A, Creutzberg E, Wesseling G, and Wouters M, “Systemic effects of smoking,” *Chest*, vol. 131, no. 5, pp. 1557–1566, 2007.