

Research Article

Vaping related heavy metal exposure and its impact on Rheumatoid Arthritis

Tuqa A. Abdulkareem^{1, *}, Nada Abdul Rahman Fleeheh^{1,}¹ Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq.

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ABSTRACT

As vaping become more commonly practiced, it considered safer and better than traditional cigarette, their safety is still debated, highlighting the need for more rigorous research and clear regulatory oversight. This study Estimate heavy metal concentrations in blood serum. And evaluate the inflammatory effect, immune response alteration of inhaling vape smoke in regular smoker and arthritis patients, whether vaping worsens the progression of Rheumatoid Arthritis (RA).

level of heavy metal were analyzed in both vape liquid sample and serum of all participants using Graphite Furnace Atomic Absorption Spectroscopy, statistical comparison were conducted between vape-smoker healthy individuals, rheumatoid patients (RP), vape-smoker RP, and control group. Heavy metal are chemical elements it is toxic even in low concentration, nickel(Ni), cadmium(Cd) and lead(Pb) are the most concerning heavy metal in vape liquid. the concentration of three elements in vape smoker group are (27.3±3.78, 2.33±0.58, and 1.0±0.0)ppb respectively. biomarker used in this study include Erythrocyte sedimentation rate(ESR) and C-reactive protein (CRP).

The result of suggest that inhaled heavy metal in many age groups may contribute to inflammatory response, RA biomarker. The findings of ESR revealed that statistically significant difference ($p < 0.0001$) between healthy E-smoker individuals with RP and E-smoker RP in addition to significant difference in CRP was observed in middle age groups (36-50) between control and RP group, RP vape smoker group ($p < 0.0001$). In RP group and RPs vaping group there was a significant difference between young (20-35) and middle-aged (36-50) patients at p -value < 0.0001 . It indicates the possible connection between vaping related heavy metal exposure and joint problems. Additional studies are required to clarify the causing mechanism and potential long-term exposure.

1. INTRODUCTION

The trend of e-cigarette use among teens continues to rise, information on the effects of e-cigarette smoke overall health is still scarce, e-cigarette, or Vape, are modern devices introduced in 2003, classified under electronic nicotine delivery systems [1]. Heavy metal have been found to be released from vape and structural element at levels that may exceed regulatory limits raising concern about potential health risk which could effect multiple organ [2]. There are a growing environmental concern is vape waste, which includes disposable devices, e-liquid containers, packaging, and batteries combining three different types of waste in a single stream [3].

In spite of years of efforts to reduce tobacco consumption, the World Health Organization has estimated that tobacco use and exposure is Currently attributed with causing the deaths of around six million people across the world each year in addition to social, economic, and environmental consequences [4]. Even individual who do not smoke can be effected by harmful substances present in tobacco smoke leaving them indirectly exposed to its adverse health impacts through surrounding environment [5]. Smoke-free rules and the continuously rising prices of tobacco products have provoked consumers to seek alternatives to traditional smoking. Among these alternatives, electronic nicotine delivery systems [6]. These devices mimic smoking by heating a liquid-typically containing propylene glycol, glycerin, or both-to produce an aerosol. This liquid usually contains nicotine, flavorings, and various other additives [7].

Rheumatoid arthritis (RA) is a systemic inflammatory disease that usually affects the synovium, with local symptoms of joint swelling, morning stiffness and pain as well as inflammation and subsequent cartilage damage with destruction [8]. The exact cause of rheumatoid arthritis is still not completely known. Its development involves persistent inflammation of the synovial membrane, which eventually results in the deterioration of cartilage and bone [9].

*Corresponding author email: Tuqa.abd2402p@sc.uobaghdad.edu.iqDOI: <https://doi.org/10.70470/SHIFAA/2026/004>

The exact pathogenic mechanisms of which are not fully understood, although both genetic predisposition and environmental factors are known to contribute [10]

Established rheumatoid arthritis is characterized by ongoing inflammatory involvement of the synovial tissue, predominantly affecting peripheral joints in a symmetrical manner [11].

Since there are currently some comprehensive studies investigating metal biomarkers associated with e-cigarette use, the present study was designed to explore the internal metal exposure levels among e-cigarette users.

2. METHODOLOGY

2.1 Materials and methods

Graphite Furnace Atomic Absorption Spectroscopy (GFAAS), GC2010 plus, centrifuge, vortex, collection tubes, micropipettes, pipette tips, deep freeze, , automated clinical chemistry analyzer (GenoLabTEK Inc), westergren tube.

2.2 Experimental Design and Procedures

The sample of vape liquid were analysed by (GFAAS), to detect the concentration of following heavy metal nickel (Ni) , cadmium(Cd) and lead(Pb).

A total 140 blood samples were collected from men including 40 vape smoker RA patients, 40 non-smoker RA patients (those receiving remicade & DMARDs) attended the attending Biological Therapy Unit – Al-Yarmouk Teaching Hospital in Baghdad governorate during the period between November and April and additional two groups include 30 young vape smoker and 30 healthy nonsmoker control group were included in this study , they had no history of clinical evidence of RA or any other chronic disease , all samples ages range from 18 to more than 50 years old. Specific exclusion criteria were applied to minimize potential factors that could interfere with the study outcomes.

2.3 Samples collection

Five millilitres of blood were collected and divided in to two portions: First portion collected in to EDTA containing tube to use for ESR test, second portion collected in to gel tube allow the blood to clot and then centrifuge to separate serum from blood cells. Serum was collected and stored freeze until used for assessment of various tests which include heavy metal concentration assessment, CRP and ESR.

2.4 Statistical analysis

The statistical analysis was performed using GraphPad Prism version 9.2 (GraphPad Software Inc., LaJolla, CA). One Way and 2-Way Analysis of Variance (ANOVA) (Tukey's Test) were used to determine whether group variance was significant or not. Pearson coefficient r value was employed to assess correlation for all possible combinations. Receiver operating characteristic (ROC) curve analysis was performed to determine area under curve and the optimum cut-off value of serum markers best prediction. Quantitative parametric data were subjected to Shapiro-Wilk test to confirm the normal distribution and were expressed as mean $\pm$ SD and statistical differences were defined as * $p < 0.05$ and ** $p < 0.01$.

3. RESULTS AND DISCUSSION

3.1 The influence of vaping on serum heavy metal accumulation

The main ingredients found in e-liquids are the base substances propylene glycol and glycerol. In contrast, flavouring additives remain the least investigated group. Nicotine is considered separately because of its role in creating physical dependence. In addition, vaporisation can generate a wide variety of chemical by-products, adding another diverse category of compounds present in these products [12].

In present study vape liquid was examined first by Graphite Furnace Atomic Absorption Spectroscopy (GFAAS) to analyze the concentration of elements in samples which include: Nickel, cadmium, lead (61, 15, 1637) ppb respectively. And second by the GC-2010 Plus for analyzing volatile and semi-volatile organic compounds which include glycerine and propylene glycol figure (1).

The chief recognized environmental risk factor for rheumatoid arthritis is smoking [12]. The increasing s, constantly changing designs, and wide range of e-liquids present major obstacles to effective safety evaluation of these products (Zhu et al., 2014).while numerous studies focus on identifying the substance present in electronic cigarette liquid and aerosols , fewer has examined health effect on human [14].

the results of this study revealed statistically significant differences in cadmium concentration among several serum samples in different study groups. A significant increase was observed between the control group and healthy vape smokers ($p = 0.0296$), indicating that even in the absence of clinical rheumatoid arthritis, vaping exposure may result in heavy metal accumulation.

Moreover, RP vape smokers exhibited significantly higher Cd compared to both controls ($p = 0.0004$) and healthy vape smokers ($p = 0.0408$). Additionally, the comparison between RA patients with and without vaping exposure also showed

a significant difference ($p = 0.0220$), reinforcing that cadmium, nickel, lead and free radicals were recognized in vaping Solution formulated for use in electronic cigarettes and were present in all vapors generated from e-cigarettes [15]. On another hand serum nickel concentration results of statistically significant differences among most of the studied groups. A highly significant difference was observed between the control group and the healthy vape smokers ($p = 0.0002$), as well as between the control group and rheumatoid arthritis (RA) patients ($p = 0.0036$), and between the control group and RA patients who vape ($p < 0.0001$). A published study identified the presence of around sixty different chemicals found in e-liquid and aerosols including measurable amount of lead and nickel in addition to others many chemicals [16]. In present study highly significant increase in lead serum concentration was observed when comparing the control group with the healthy vape smokers ($p = 0.0005$), as well as between the control group and rheumatoid arthritis (RA) patients ($p < 0.0001$), and between the control group and vape smoker RA patients ($p = 0.0005$). The findings suggest that metals can leach from e-cigarette coils into the aerosol, making e-cigarette use a potential source of metal exposure, including chromium, copper, nickel, and lead [17]. With regard to Nickel the result indicating that comparing healthy vape smokers with RP group, no significant difference was found ($p = 0.2656$), suggesting that the effect of vaping alone may share some biological similarities with the alterations seen in RA. However, a significant difference between healthy vape smokers and RA patients who vape ($p = 0.0357$) implies that the combination of vaping and rheumatoid arthritis could exacerbate these changes. Additionally, the comparison between RP and RP vape smoker ($p = 0.0013$) showed a significant difference, further supporting the potential aggravating role of vaping in individuals already affected by rheumatoid arthritis.

TABLE I. COMPARISON OF SERUM CADMIUM, NICKEL, LEAD LEVELS (MEAN $\pm$ SD) AMONG STUDY GROUPS

Metals	Mean $\pm$ SD				Sig.	p Value
	Control	Healthy vape S.	Rheumatoid p.	Vape S. rheumatoid p.		
Cadmium	1.0 $\pm$ 0.0a	2.33 $\pm$ 0.58b	2.00 $\pm$ 0.0ab	3.50 $\pm$ 0.58c	**	0.0007
Nickel	9.0 $\pm$ 3.46a	27.3 $\pm$ 3.78b	21.8 $\pm$ 2.1c	36.3 $\pm$ 5.85b	**	<0.0001
Lead	0.0 $\pm$ 0.0a	1.0 $\pm$ 0.0b	1.25 $\pm$ 0.5b	1.0 $\pm$ 0.0b	**	<0.0001

Different letters (a, b,c) considered significant at $p < 0.0$.

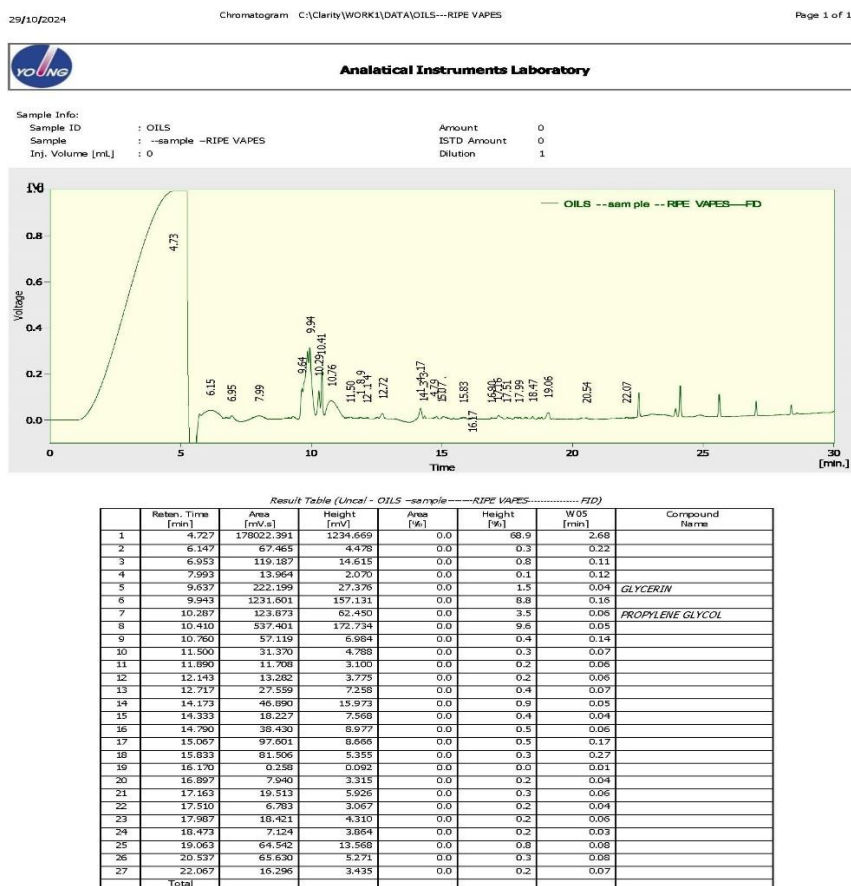


Fig. 1. Gas Chromatographic (GC) Chromatogram of the E-Liquid Sample Showing the Identified Chemical Constituents.

3.2 impact of vaping on inflammatory markers ESR & CRP

The erythrocyte sedimentation rate (ESR), is a commonly used hematological test for identifying and monitoring elevated inflammatory activity associated with conditions such as autoimmune diseases, infections, and malignancies. While ESR is not specific to any single disorder, it provides supportive information on inflammatory status when interpreted in conjunction with other clinical and laboratory findings [18].

Regarding erythrocyte sedimentation rate (ESR) figure (2), the findings of present study indicate that ESR tends to rise progressively with age, particularly after the age of 51. A statistically significant difference was observed in middle age groups between control and RP Group, healthy vape smoker group and RP group ($p=0.0014$), ($p < 0.0001$) respectively. In middle age group a statistical comparison was performed a marked and statistically significant difference ($p < 0.0001$) between healthy vape smoker individuals with RP and RP vape smoker. Therefore, among participants aged over 51 years, a statistically significant difference was observed when comparing the control group and healthy vape smoker with the two other groups RP, vaping RP ($p < 0.0001$). In addition, significant difference record $p=0.9103$ when comparing between RP and vaping RP. Collectively, these findings support the notion that vaping may not only influence the onset of autoantibody formation but also enhance disease activity in predisposed or affected individuals.

however, another study showing that ESR increased after age of 40 with a more marked increase observed beyond 60 years [19]. Age and sex were found to independently influence the levels of both acute-phase reactants in early rheumatoid arthritis, highlighting the importance of considering these factors when assessing disease activity. In addition, body mass index seems to play a more significant role during the later stages of the disease [20]. Research suggests that smoking and vaping may lead to alterations in hematological parameters, including the (ESR) and components of the complete blood count [21].

Persistently elevated CRP and ESR levels were significantly associated with greater radiographic joint damage, regardless of rheumatoid factor status. Measuring both markers together was more informative than using either alone, though CRP appeared to be the stronger indicator. Additionally Regular monitoring effectively distinguishes between treatments that offer only symptomatic relief and those with deeper therapeutic impact [22]. As for second parameter a notable change was observed in middle age and age more than 51years group, there was a significant difference between control and RP , RP vape smoker in addition to the same difference when comparing healthy vape smoker with RP , RP vape smoker ($p < 0.0001$) in the two age groups .there are no significant between RP and vaping RP in middle age $p=0.0707$ however it is significant in more than 51years group $p=0.0070$, Figure (3) illustrates the distribution of CRP levels among the study groups according to age categories.

There was a link between e-cigarette use and inflammatory arthritis disorders, the association remained consistent among individuals besides, these findings suggest that e-cigarette consumption could play a role as a potential risk factor for arthritis, highlighting the need for consideration in future public health and regulatory policies regarding e-cigarette use [23].

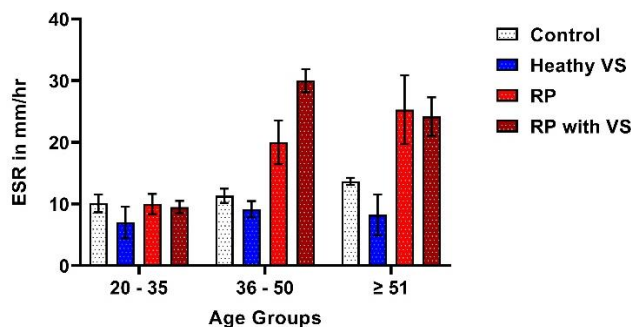


Fig. 2. distribution of ESR levels among study groups according to age categories.

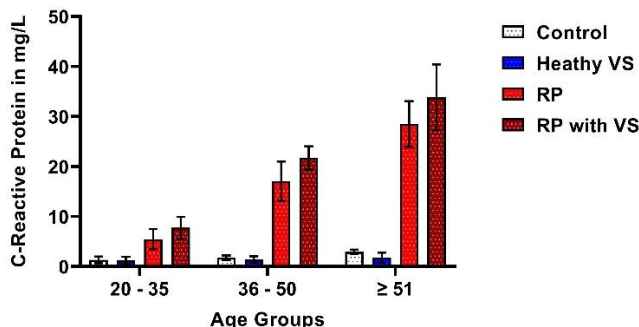


Fig. 3. distribution of CRP levels among study groups according to age categories

TABLE II. MEAN AND STANDARD DEVIATION OF CRP AND ESR LEVELS AMONG STUDY GROUPS BASED ON AGE CATEGORIES.

Age groups	CRP			
	Control	Healthy vape s.	Rheumatoid p.	Vape s. rheumatoid p.
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
20 - 35	1.33 $\pm$ 0.66	1.23 $\pm$ 0.75	5.48 $\pm$ 2.03	7.75 $\pm$ 2.17
36 - 50	1.74 $\pm$ 0.45	1.38 $\pm$ 0.65	17.08 $\pm$ 3.90	21.72 $\pm$ 2.33
≥ 51	2.93 $\pm$ 0.45	1.80 $\pm$ 0.98	28.49 $\pm$ 4.58	33.83 $\pm$ 6.59
	ESR			
	Control	Healthy vape s.	Rheumatoid p.	Vape s. rheumatoid p.
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
20 - 35	10.11 $\pm$ 1.45	7.00 $\pm$ 2.56	10.00 $\pm$ 1.63	9.50 $\pm$ 1.00
36 - 50	10.20 $\pm$ 1.79	9.17 $\pm$ 1.33	20.00 $\pm$ 3.54	30.00 $\pm$ 1.90
≥ 51	13.67 $\pm$ 0.58	8.25 $\pm$ 3.30	25.30 $\pm$ 5.56	24.20 $\pm$ 3.11

4. CONCLUSION

vape products can act as a cause of exposure to heavy metals such as lead, nickel, and cadmium. These metals may be released during the vaping process and inhaled into the body, where they can circulate systemically and accumulate over time. Based on these mechanisms, exposure to heavy metals from vaping may contribute to decline inflammatory responses or increased disease activity in RA patients.

Vape smoking directly contributes to the development of numerous diseases. the current outcome underlines the criticality of smoking prevention and eradication not only in respiratory disorders but also in autoimmune situation as well.

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6. ETHICAL APPROVAL

The study protocol was reviewed and approved by the Ethics Committee of the College of Science, University of Baghdad (Ref.: CSEC/0825/0092, dated August 14 ,2025).

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Conflicts of Interest:

The authors declare that there are no conflicts of interest regarding this publication.

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