2-18-2023

Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV)

Aramandla Ramesh
Meharry Medical College

Leslie R. Halpern
Metropolitan Hospital Center

Janet H. Southerland
LSU Health Sciences Center - New Orleans, jsouther@lsuhsc.edu

Samuel E. Adunyah
Meharry Medical College

Pandu R. Gangula
Meharry Medical College

Available online at www.sciencedirect.com

ScienceDirect

Biomedical Journal

journal homepage: www.elsevier.com/locate/bj

Original Article

Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV)

Aramandla Ramesh [a,*], *Leslie R. Halpern* [b], *Janet H. Southerland* [c], *Samuel E. Adunyah* [a], *Pandu R. Gangula* [d]

[a] *Department of Biochemistry, Cancer Biology, Neuroscience & Pharmacology, School of Medicine, Meharry Medical College, Nashville, TN, USA*

[b] *Department of Dental Medicine, New York Medical College/ NYCHHC, Metropolitan Hospital, New York, USA*

[c] *Departments of Oral and Maxillofacial Surgery, Louisiana State University Health Sciences Center, New Orleans, LA, USA*

[d] *Department of Oral Diagnostic Sciences & Research, School of Dentistry, Meharry Medical College, Nashville, TN, USA*

ARTICLE INFO

Article history:
Received 7 December 2022
Accepted 14 February 2023
Available online xxx

Keywords:
Saliva
Biomonitoring
Oral health
benzo(a)pyrene
Polycyclic aromatic hydrocarbons
Intimate partner violence

ABSTRACT

Background: Social habits such as tobacco use, alcohol consumption, and chemically contaminated diet contribute to poor oral health. Intimate Partner Violence (IPV) is a global public health epidemic which can exacerbate the prevalence of health conditions affecting a victim's lifespan. This study investigates using saliva as a biomarker for detecting levels of benzo(a)pyrene [B(a)P]; a toxicant present in cigarette smoke and barbecued meat in a population of IPV + female patients.

Methods: A cross-sectional IRB-approved study utilized 63 female participants (37 African Americans [AA], and 26 non-African Americans [NAA]), who provided consent for the study. Participants submitted samples of saliva, as well as questionnaires about demographics, health history, and a well-validated (IPV) screen.

Results: The prevalence of IPV was greater in AA compared to NAA. While the concentrations of PAHs/B(a)P detected in saliva of IPV samples in NAA were generally within the range of B(a)P reported for saliva from elsewhere, the concentrations were high in some IPV positive samples. Among the B(a)P metabolites, the concentrations of B(a)P 7,8-diol, B(a)P 3,6- and 6,12-dione metabolites were greater than the other metabolite in both AA and non-AA groups who were positive.

Conclusion: Our study supports the use of saliva as a potential "diagnostic rheostat" to identify toxicants that may exacerbate/precipitate systemic disease in female victims of IPV. In addition, our study is the first to report that IPV may precipitate the accumulation of B(a)P in oral cavity that can alter inflammatory cascades and increase risk of poor health outcomes in this population of patients.

* *Corresponding author*. Department of Biochemistry, Cancer Biology, Neuroscience & Pharmacology, School of Medicine, Meharry Medical College, Nashville, TN 37208, USA

E-mail address: aramesh@mmc.edu (A. Ramesh).

Peer review under responsibility of Chang Gung University.

https://doi.org/10.1016/j.bj.2023.02.006

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

At a glance commentary

Scientific background on the subject

Intimate partner violence (IPV) is one of the public health issues. Some victims of IPV resort to smoking as a way of coping. Saliva serves as an ideal biomonitoring tool for toxicants such as benzo(a)pyrene (present in tobacco smoke and charbroiled meat) that may precipitate systemic disease in female victims of IPV.

What this study adds to the field

We report data for the first time on exposure to benzo(a) pyrene, a ubiquitous toxicant in the saliva of IPV patients. The exposures to PAHs in IPV-positive patients were high compared to IPV-negative patients and also with a high prevalence in African Americans compared to non-African American patients.

Oral health is a significant predictor of an individual's overall health and well-being. Research shows that poor oral health can be a sign of heart disease, stroke, diabetes, premature births, cancer and other systemic maladies. The physiologic and environmental stressors on the oral cavity consist of personal habits such as smoking, alcohol consumption and tobacco chewing, which aggravate the oral mucosa and accelerate the development of tumors in the oral cavity [1]. Nutritional preferences also contribute as risk predictors of oral disease. Grilling of meats can produce carcinogens called polycyclic aromatic hydrocarbons (PAHs). These compounds can be ingested directly or absorbed through the skin [2] mucus membranes in respiratory tract by breathing in aromas during food preparation [3] and smoking [4]. Studies measuring urine samples characterized the greatest exposure of PAH came from eating barbequed food, followed by inhalation of barbeque fumes [3,5,6].

Cigarette smoke contains several toxicants, some of which are carcinogenic and epidemiological studies have established a greater incidence of oral health issues among long-term smokers [7,8]. Monitoring the residue levels of these chemicals in body fluids has the potential to assess both individual and community risk to toxicant exposure [9]. One such important group of chemicals that are constituents of cigarette smoke are polycyclic aromatic hydrocarbons (PAHs [10]). These are a family of more than 100 compounds with fused aromatic rings and are released into the environment as a result of petrogenic (products such as asphalt, diesel, engine oil, kerosene, lubricants etc.) and pyrolytic (wildfires, residential wood and municipal refuse burning, automobile exhausts, industrial emissions, volcanic eruptions etc.) processes [11]. As products of combustion, these compounds are present in barbecued meat [12] as well. Benzo(a)pyrene [B(a)P] is one of the most prevalent PAHs in the environment and a widely studied compound in terms of its ability to cause toxicity and cancer. Human intake of B(a)P through inhalation and ingestion could potentially enhance risks associated with chronic exposure [13–19].

Certain populations can be predisposed to the adverse effects of these toxic exposures as a result of poor diet, social history coping strategies and prior stress-induced traumatic events. Each alone or in combination can precipitate/exacerbate physiologic responses to toxicant exposure with resultant heath consequences [20]. This population, as an example, are those who have been exposed to intimate partner violence (IPV). IPV is a global public health epidemic that initiates/exacerbates health consequences affecting a victim's lifespan. IPV can significantly predispose women to a lifetime risk of developing significant health consequences due to the effect of stress and inflammation [21]. A well-established cohort of women exposed to IPV and poor health outcomes has been previously studied [22,23]. Women who have experienced IPV engage in coping strategies that pose negative health consequences; i.e. smoking and poor nutritional choices, both of which potentiates a poor health-related quality of life [24–28]. Although some researchers theorize that inflammatory/hormonal insults are pivotal in the development of significant health disparities in victims of IPV, the exact mechanism(s) are still undetermined [22,24–26,28–31]. Women who have been exposed to IPV may be more susceptible to the deleterious effects of pro-inflammatory cytokines and impairment of endothelial function [31,32].

Biomonitoring studies using several body fluids have gained prominence to assess human exposure to a multitude of chemicals including PAHs [33–35]. Blood and urine samples are frequently used, yet require careful processing and chemical clean-up before the samples are analyzed. Previous studies using saliva as predictors of adverse clinical outcomes associated with IPV have been examined and as such, can provide an accurate and sensitive vehicle for biomarker profiling inflammatory mediators to assess the mechanisms of disease progression [22,23]. Saliva has the potential as a "diagnostic alphabet" to monitor disease progression in stress-related events [22,23,29,31,36–39]. It is an ideal matrix for biomonitoring as it is less invasive to obtain and sample processing is simple and could be collected and processed in a relatively shorter timeframe. It also contains blood derivatives from oral wounds with the potential to reflect the degree of toxicant exposure under normal and disease conditions [40,41].

The purpose of our study is to utilize whole samples of saliva to identify concentrations of total polycyclic aromatic hydrocarbons ($\sum$PAHs), B(a)P and their metabolites in a cohort of female patients exposed to IPV who frequent a dental clinic in a community hospital center (Nashville, TN). The specific aims of our study are: 1. To test the feasibility of using saliva as a non-invasive biomarker for detecting and measuring PAHs and their prototypical representative compound B(a)P along with its metabolites; and 2. To investigate whether victims of IPV have an increased risk of build-up of PAH residues when compared with a control group cohort (IPV negative).

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

Material & methods

Sample collection and processing

This study, which involves patient/volunteers were approved by the institutional ethics committee (Institutional Review Board: IRB) and informal consent was obtained from the participants. An IRB approved cross-sectional study design was used to recruit participants from the Meharry Medical College (MMC) School of Dentistry (SOD) Oral Surgery Clinic. Enrollees were female, whose ages ranged from 19 to 63 yrs. The total number enrolled for this pilot study were N = 63: 37 African Americans (AA), and 26 non-African Americans (NAA). Inclusion criteria: female participants, who were required to speak, read, and comprehend English, and be willing to consent for the study. Exclusion criteria: participants that were unable to speak English. Computer generated random clinic times were used to identify potential participants over a period of 10 months during the clinic hours of 8:00 AM. to 12 Noon, Monday through Friday. During the visit individuals that agreed to participate were asked to complete the questionnaire about demographics, health history, including history of injury to head, neck and face, and also asked to complete the Intimate Partner Violence Screening [42] form and during the follow-up visit, the Partner Abuse Symptom Scale questionnaire [43,44].

Saliva specimens were obtained using the passive drool method (unstimulated whole saliva [22,23,38]). Samples were from women whose health status varied from having no health issues to those suffering from asthma, bronchitis and other maladies that contribute to excessive mucus formation. Therefore, to utilize sputum free samples for analyses, sputolysin (EMD Millipore Corporation, MA) or Sputo-LR (GBiosciences, St. Louis, MO) reagents were used for liquefaction specimen preparation. Prior to use, these reagents were diluted (1:10) with deionized water. One milliliter of saliva was diluted with equal volume of the diluted lysis reagent. The samples were centrifuged immediately at 15,000×*g* for 15 min at 4 °C. Aliquots (1.0 mL) of each saliva sample was placed into in a 1 mL Eppendorf tube and stored at −80 °C until analysis.

Chemical extraction and chromatographic analysis

Standardization of extraction method for analytes

Prior to extraction and analysis of saliva samples collected from the IPV patients, the extraction procedure was optimized using artificial saliva (Sigma−Aldrich). The stock solutions of the analytes of interest [the EPA priority PAHs mixture, B(a)P parent compound, and B(a)P metabolites such as the B(a)P 4,5-diol, B(a)P 3,6-dione, and 3(OH) B(a)P] were dissolved in methanol at the concentration of 100 μg/ml and stored at 4 °C. The working solutions prepared from the stock solutions at the level of 0, 10, 25 and 50 μg/ml were used to spike the artificial saliva. To check the percent recovery of analytes of interest, the samples were subjected to the extraction protocol detailed below.

Sample analysis

On the day of analysis, samples were retrieved, thawed and transferred to a Corning® screw capped vial (Corning Inc., Glendale, AZ). A volume of 1 ml HPLC grade water was added to the lysate, followed by 3 ml of methanol and 1.5 ml of chloroform. The tubes were stirred using a vortex for 60 s and then centrifuged at 5000×*g* for 20 min. After centrifugation, the organic and aqueous layers were separated. The organic layer was carefully retrieved into another tube using a Pasteur pipette fitted to an electrical pipettor. The extraction procedure was repeated with the aqueous layer left in the tube. The organic layer was collected as mentioned above. Organic phases from both extractions were pooled and dried under N_2 using a Meyer Analytical Evaporator (Organomation Associates Inc., Berlin, MA). The residue was reconstituted in 300 μl of methanol, passed through Acrodisc filters (0.45 μm; 25 mm diameter; Gelman Sciences, Ann Arbor, MI) to prepare particulate free samples for chromatographic analysis. The ∑PAHs, B(a)P, and its metabolites were analyzed by a High-Performance Liquid Chromatograph (HPLC) Model 1200 (Agilent, Wilmington, DE) equipped with a variable wave length detector and programmable fluorescence detector as reported in Cioroiu et al. [45] for ∑PAHs and Harris et al. [18] for B(a)P metabolites.

Statistical analysis

Data on ∑PAHs, B(a)P parent compound residues and B(a)P metabolite concentrations in IPV positive and negative patients for each racial group were analyzed by one-way analysis of variance. The differences among means were determined by using Bonferroni's post hoc test with the criteria for statistical significance set at $p < 0.05$ (SPSS, Chicago, Illinois).

Results

Our extraction method standardized by using artificial saliva yielded reliable results. The analyte extraction efficiency (as calculated by percent recovery of spiked compound) showed no sample matrix-related interferences. The percent recoveries ranged from 88 to 96% for ΣPAHs, 89−100% for B(a)P parent compound, and 88, 89 and 93% for B(a)P 4,5-diol; B(a)P 3,6-dione and 3(OH) B(a)P metabolites respectively. The reagent/solvent blanks and sample matrix (saliva) blanks extracted and analyzed in parallel with the patient samples showed no traces of the analytes of interest.

The concentrations of 16 Environmental Protection Agency (EPA) designated PAH pollutants from representative cohorts are presented in Figs. 1 and 2. The mean concentrations of individual PAH compounds ranged from 0.04 to 0.54 ng/mL for IPV negative cases in Non-African Americans (NAA) and 0.04−1.10 ng/mL for IPV positive cases in this group. On the other hand, the mean concentrations of PAH compounds for African Americans (AA) ranged from 0.06 to 0.99 ng/mL for IPV negative cases, and from 0.12 to 2.04 ng/mL for IPV positive cases. Since not all PAHs are toxic and/or carcinogenic, our main focus is B(a)P, which is a confirmed carcinogen. The mean concentrations of B(a)P for IPV positive and negative cohorts for both AA and NAA are shown in Fig. 3. The mean concentrations of B(a)P ranged from 0.05 to 0.47 ng/mL for IPV negative cases NAA and 0.38−1.60 ng/mL for IPV positive cases in NAA. On the other hand, for AA, B(a)P concentrations ranged from 0.19 to 0.80 ng/mL for IPV negative cases and

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

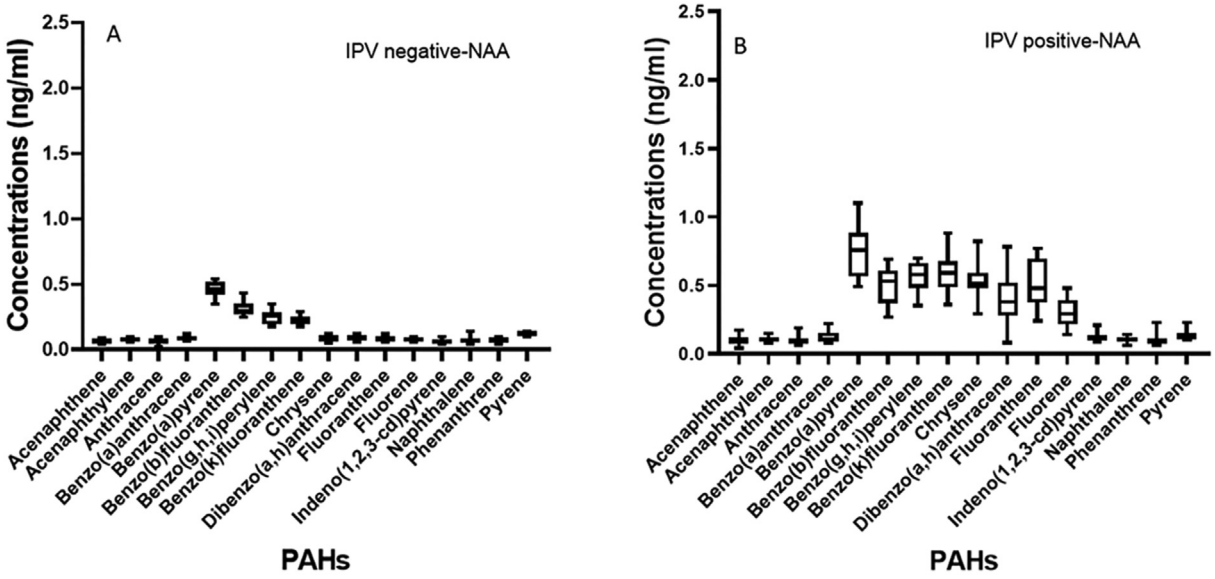

Fig. 1 Concentrations (ng/mL) of ∑PAHs in saliva samples from representative IPV positive (n = 17) and IPV negative (n = 9) dental patients from the non-African American (NAA) cohorts. The ∑PAHs are EPA priority PAH pollutants, which include naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, chrysene, benz(a) anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(a)pyrene, dibenz (a,h)anthracene, indeno (1,2,3-c,d)pyrene, and benzo (g,h,i)perylene. Data were not normalized for recovery of analytes from surrogate samples.

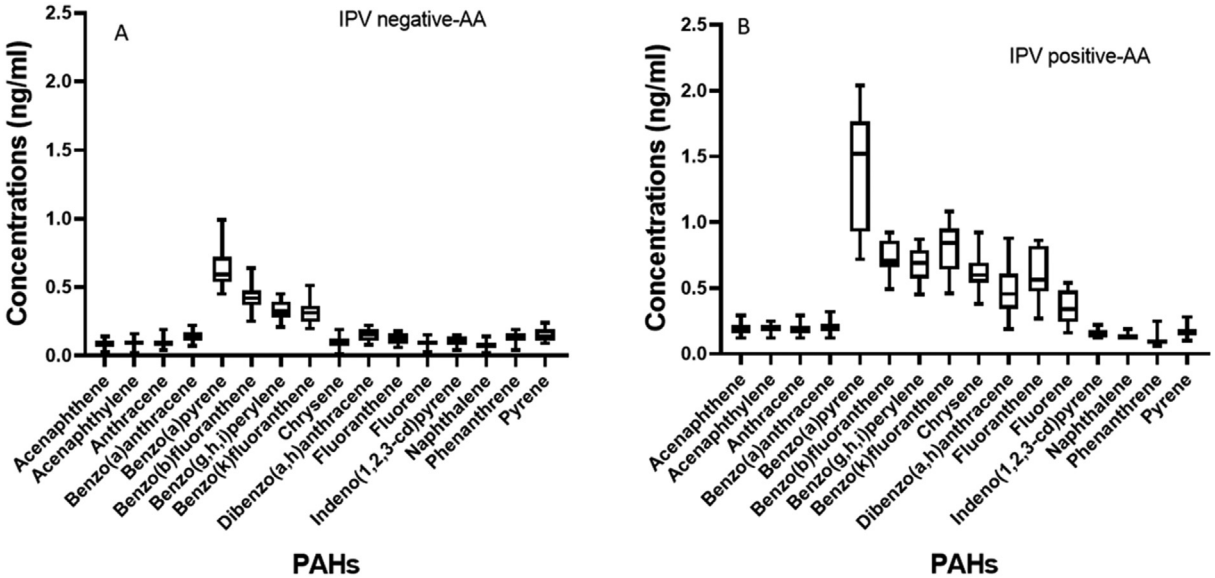

Fig. 2 Concentrations (ng/mL) of ∑PAHs in saliva samples from representative IPV positive (n = 19) and IPV negative (n = 18) dental patients from the African American (AA) cohorts. The ∑PAHs are EPA priority PAH pollutants, which include naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, chrysene, benz(a) anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(a)pyrene, dibenz (a,h)anthracene, indeno (1,2,3-c,d)pyrene, and benzo (g,h,i)perylene. Data were not normalized for recovery of analytes from surrogate samples.

1.06–4.30 ng/mL for IPV positive cases. The differences in B(a)P concentrations between IPV negative and positive cases both in NAA and AA were statistically significant ($p < 0.05$). Additionally, the differences between NAA and AA in IPV positive cases were statistically significant ($p < 0.05$). The total B(a)P metabolite concentrations are depicted in Fig. 4. The B(a)P metabolite concentrations reflected a trend similar to that of B(a)P parent compound. The B(a)P metabolite concentrations ranged from 0.45 to 0.81 ng/mL for IPV negative cases in NAA while 0.83–2.06 ng/mL for IPV positive cases in NAA. On the

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

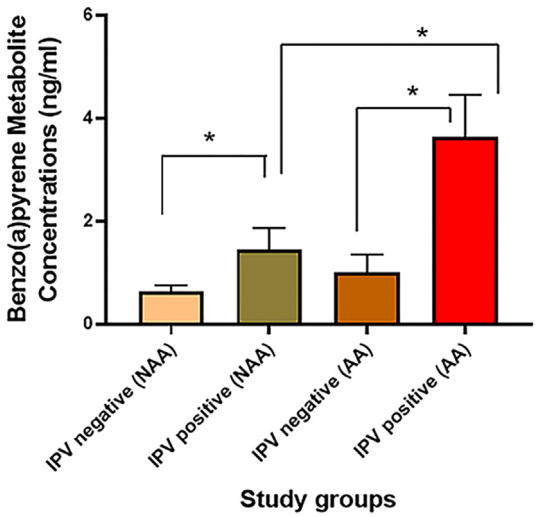

Fig. 3 Concentrations (ng/mL) of unmetabolized benzo(a) pyrene compound in saliva samples from IPV positive and IPV negative dental patients. Values represent mean ± SE (n = 18 for IPV- negative AA; n = 19 for IPV- positive AA; n = 17 for IPV- positive NAA; n = 9 for IPV negative NAA). Asterisks denote statistical significance ($p < 0.05$) in benzo(a) pyrene concentrations. Data were not normalized for recovery of analytes from surrogate samples.

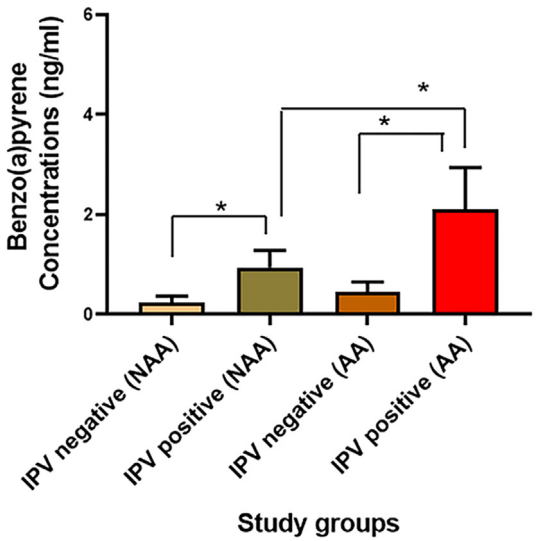

Fig. 4 Concentrations (ng/mL) of benzo(a)pyrene metabolites in saliva samples from IPV positive and IPV negative dental patients. Values represent mean ± SE (n = 18 for IPV-negative AA; n = 19 for IPV- positive AA; n = 17 for IPV-positive NAA; n = 9 for IPV negative NAA). Asterisks denote statistical significance ($p < 0.05$) in benzo(a)pyrene metabolite concentrations. Data were not normalized for recovery of analytes from surrogate samples.

other hand, for AA, the B(a)P concentrations ranged from 0.49 to 1.87 ng/mL for IPV negative cases and 2.32–4.36 ng/mL for IPV positive cases. As in the case of B(a)P parent compound concentrations, the B(a)P metabolite concentrations among the IPV groups in NAA and AA were statistically significant ($p < 0.05$). Using authentic B(a)P metabolite standards procured from the National Cancer Institute Chemical Carcinogen Repository, the B(a)P metabolites identified and quantified from our samples are shown in Fig. 5. The B(a)P metabolites detected in all the samples include B(a)P 4,5-dihydrodiol; B(a)P 7,8-dihydrodiol; B(a)P 9,10-dihydrodiol; B(a)P 3,6-dione; B(a)P 6,12-dione; 3(OH) B(a)P and 9(OH) B(a)P.

Discussion

The purpose of this cross-sectional cohort study was to report the use of a number of innovative tools and techniques to assess the presence of concentrations of ∑PAHs, B(a)P and its metabolites in the saliva samples in female patients exposed to IPV who frequent a dental clinic in a community hospital center in Nashville, TN. Based on results, we were able to successfully detect B(a)P in saliva samples of both IPV positive and negative participants. We hypothesized that previous exposure of IPV may increase the risk of exposure to toxicants from smoking and poor nutritional choices, both of which have the potential to exacerbate/precipitate poor health outcomes in this patient demographic. The ultimate goal is to apply salivary diagnostics for early identification of harmful toxicants and risk for carcinogenic diseases in populations affected by stress-induced traumatic events. Access to point of care salivary testing might potentially allow practitioners to initiate early monitoring that will help evaluate patients for a variety of toxicant exposures that could lead to poor health outcomes [46]. We suggest that this approach can provide useful diagnostic "rheostat" information that can be used to improve the overall health of not only patients exposed to IPV but all patients within that are chronically exposed to hazardous toxicants.

As PAHs comprise a family of more than 100 compounds, we screened the saliva for the United Stated Environmental Protection Agency (USEPA) designated 16 priority PAH pollutants. These PAHs were categorized based on their environmental occurrence, including hazardous waste sites, with the potential for human exposure and toxicity [47] and have been used for risk assessment purposes [48]. A saliva screen of our samples revealed not all but some of these priority PAHs registering high levels, one of which is B(a)P. Our data on PAH concentrations in saliva are mostly within the range of those reported by Martin Santos et al. [49] in saliva of firefighters (0.2–3 ng/ml), Marin Santos et al. [50] in saliva of non-smokers versus smokers (0.068–0.14 ng/ml), and Pena et al. [51] in saliva of non-smokers versus light smokers (0.037–0.16 ng/ml) and less than those reported by Carrizo et al. [52] in saliva of heavy smokers (100–1000 ng/ml). However, our salivary PAH concentrations measured for some IPV-positive cases ranged from 1.06 to 4.36 ng/ml. The duration of exposure to PAHs, total number of PAHs screened in saliva, characteristics of subjects, and differences in sample processing and analytical methods employed by us and other investigators could account for the differences in PAH concentrations in saliva.

Compared to NAA patients, the total PAH concentrations were significantly higher in their AA counterparts in screening of our samples. The B(a)P concentrations (unmetabolized parent compound) concentrations showed a similar trend.

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

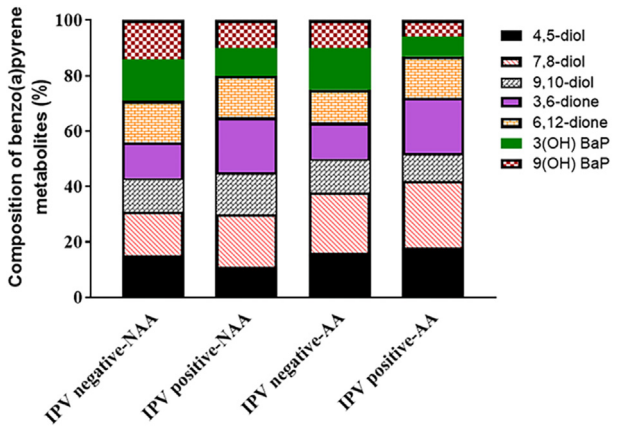

Fig. 5 Metabolite composition of benzo(a)pyrene in representative samples from IPV positive and IPV negative dental patients. AA stands for African American patients; and NAA stands for non- African American patients).

Regardless of the route of exposure, most of the B(a)P entering the body is rapidly metabolized and excreted [5,53] except in chronic (long-term) exposure scenarios. Even though the unmetabolized B(a)P concentrations were very low, compared to NAA patients, the concentrations were significantly higher in their AA counterparts. Our previous report on B(a)P and PAH levels in serum samples collected during post-mortem reiterate that environmental, dietary and smoking-related factors substantially contribute to the body burden of PAHs in AA [54]. Also, the effect of differences in B(a)P intake, biotransformation, half-lives and excretion rates depending on the route of exposure to B(a)P [50,53,55,56] could not be ruled out. Overall, the concentrations of B(a)P metabolites in saliva were greater in IPV positive patients, compared to IPV negative patients ($p < 0.05$). The results from this investigation support findings from other studies that correlates IPV exposure with immune dysfunction, chronic precipitation of inflammation and/or exacerbation of the metabolic syndromes. In addition, they show possible chronic cumulative effects along the inflammatory cascade which agrees with studies that suggests IPV as a severe stressor [23]. The differences seen with respect to the cross correlates of inflammatory mediators between the IPV + and IPV− cohort salivary samples follow findings seen in other studies [26,31,37,38,45]. Fernandez-Botran et al. [26] suggest that elevated levels of C-reactive protein (CRP) are more likely to be the result of a chronic cumulative effect of other mediators including the interleukins. Previous exposure to traumatic stress events such as facial trauma can result not only in elevated individual mediators, but their relationship to each other [26,45,57,58]. Stressors whether they be physical or psychological can both increase the systemic levels of acute phase reactants such as interleukin (IL)-6 and CRP as well as act as regulators of other mediators within the inflammatory cascades. This has its basis at the level of the Hypothalamic-Adrenal —Axis which then provides feedback loops that orchestrate inflammatory cascades. The exposure of IPV whether it be as an adult or through temporal timing from early trauma sets up the rhythm for disease progression. Our results with respect to the mediators measured also suggests a potential trend of heightened inflammatory status. In this context, it should be noted that a greater incidence of IPV has been reported in minority and impoverished populations [59], especially African Americans [60]. Our results therefore may support the correlation of inflammation with greater toxicant accumulation in AA and the significant differences between NAA and AA seen in our cohort samples.

Among B(a)P metabolites, the relative proportion of B(a)P 7,8-hydrodiol, B(a)P 3,6-dione and B(a)P 6,12-dione were greater in IPV positive cases compared to IPV negative cases. These metabolites are formed as part of regular biotransformation of B(a)P ingested either through diet or inhaled through cigarette smoke. Aside from metabolites generated through B(a)P biotransformation in lung and liver, some of the metabolites may have been generated through B(a)P metabolism in oral tissues. In addition to B(a)P metabolites, some of the ingested PAHs accumulate in the mucus lining of the oropharyngeal region where mucus-tissue partitioning of PAHs occur [61] facilitated by the mucin glycoproteins [62]. Kapoor et al. [63] and Vondracek et al. [64] found B(a)P metabolizing activity in human bronchial mucus, and buccal mucosa respectively. Human oropharyngeal mucosal biopsy samples incubated with the B(a)P metabolite, B(a)P 7,8-dihydrodiol 9,10-epoxide were found to have DNA damage induced by the diol metabolite [65]. Chen et al. [66] reported a preponderance of these DNA adducts (biomarkers of genotoxicity) derived from the diol metabolites of B(a)P and dibenzo [def,p]chrysene in oral buccal cells of smokers. Walle et al. [67] demonstrated transport, bioactivation and DNA binding of B(a)P in bioengineered human gingival tissue. These authors have shown B(a)P-induced cytochrome P450 (CYP)1A1 and 1B1 expression in those tissues. Chi et al. [68] also reported expression of B(a)P biotransformation enzymes in oral squamous epithelial tissues with a pronounced expression in smokers. The above-mentioned diol and quinone metabolites formed through epoxide and quinone pathways respectively of B(a)P metabolism evoke much interest in view of their involvement in various biochemical and molecular pathways involved in disease causation [69].

Our earlier studies [22,23] suggest that women who have experienced IPV engage in coping strategies that pose negative health effects, such as smoking and poor nutrition, which potentiate the long-term negative impact/risk for cardiovascular disease (CVD) and other chronic illnesses [24–28,70]. Although some researchers, including our team, theorize that inflammatory/hormonal cascades are pivotal in the development of significant health disparities such as CVD in victims of IPV, the exact mechanism(s) are still undetermined [22,24–26,28–31]. Women who have been exposed to IPV may be more susceptible to the deleterious effects of pro-inflammatory cytokines and impairment of endothelial function with subsequent cardiovascular breakdown [31,32,71]. The rupture of oral tissues or lacerations or other injuries caused during IPV contaminate the saliva with B(a)P residues released through blood into the oral cavity. If these patients happen to smoke as part of their lifestyle or to alleviate their stress arising from IPV [72], the net load of B(a)P residues in saliva are likely to

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

increase. Additionally, the damaged oral tissues could serve as portals of entry for B(a)P into the body, when these individuals ingest food tainted with B(a)P.

Aside from regular cigarettes, people who smoke menthol containing cigarettes or electronic cigarettes will have a relatively greater infusion of B(a)P into their system. Many people are drawn to the menthol cigarette due to the anesthetic, and analgesic effects of menthol [73]. Menthol was reported to enhance the flux of B(a)P across esophagus and help in B(a)P reservoir formation in the porcine esophageal mucosa model [74]. Published reports indicate that one third of female smokers are patrons of menthol cigarettes [75], with a prevalence among African American women smokers [76]. Since IPV victims also are addicted to alcohol to cope up with the trauma of IPV [77], the concomitant use of alcohol and tobacco smoke may have a deleterious effect on an individual's health.

The observed disparity in $\sum$PAH concentrations and B(a)P metabolite concentrations by race is consistent with published literature. Distinct associations between smoking and genetic polymorphisms in genes responsible for PAH metabolism [78] and smoking associated rise in PAH levels in urine [79] was reported in AA. As our study sample exclusively comprises women, some of them being in the child-bearing age group, even if they are non-smokers, their exposure to airborne PAHs, dietary habits (too much consumption of red meat), and body mass index (accumulation of PAHs in fat masses) may put their fetuses at an elevated risk resulting in PAH-induced adverse pregnancy outcomes [80].

To the best of our knowledge, there were no studies that explored the levels of toxicants in IPV victims. Our studies for the first time analyzed the levels of ubiquitous toxicants such as PAHs in saliva. Additionally, findings of our study provide some novel insights into the utilitarian value of salivary toxicants as not only biomarkers of exposure but also biomarkers of effect. IPV is a primary or psychosocial stressor, which could create a path for further insult from secondary stressors (environmental toxic chemical exposures and substance abuse such as tobacco, cannabis smoke etc.). The synergistic effect of these stressors on a chronic basis may have significant adverse effects [81,82]. In this regard, studies conducted earlier by our team [22,23] on IPV are worthy of mention. These studies revealed elevated levels of IL 1β, IL-6, tissue necrosis factor α, CRP, and matrix metalloprotease 9 in the saliva of IPV patients and considered as salivary biomarkers of stress, inflammation etc. Taken together, our prior studies on salivary markers of IPV, and current studies on salivary markers of tobacco smoke and food toxicant (PAHs) exposure in IPV patients suggests a potential benefit for monitoring nicotine, chemicals from tobacco smoke, and other toxicants particularly in individuals at risk for chronic psychosocial and/or environmental exposure. Biomonitoring studies like these maybe helpful for advancing our understanding of the relationship between existing trauma, exposure to environmental toxicants, and poor health outcomes.

Study limitations

Our study although quite encouraging does have limitations in data interpretation. The study design is cross-sectional; cause and effect studies can be prohibitive and the small sample size (N = 63) is of insufficient power to make any generalizations about CVD health and biomarker risk indices. Although there were significant differences between the number of IPV participants compared with the IPV negative cohort, due to the fear and stigma associated with IPV, the study may have been susceptible to false negative responses from participants. Also, while questionnaires, have been shown to be valid and have good test-retest reliability, victims may still report no abuse. In a study of this nature, victim misclassification is expected and should be taken into consideration as a potential confounder [83]. The health consequences from IPV may or may not exist after the abuse is discontinued and therefore our estimates may have missed a "window of opportunity".

Our sample size of NAA is modest and constitutes samples drawn from Caucasians, Hispanics, and Asians combined, limiting our ability to stratify data on the basis of exposure and putative biological effects individually in these races. Nonetheless, our study has implications for long-term biomonitoring of patients, who visit the dental clinics at least two times a year for dental clean-ups or some surgical procedures (capping, filling or root canal surgeries). Additionally, analysis of blood and urine samples from these patients may be helpful in validating the findings observed in the saliva samples and also provide valuable information on biomarkers of exposure not only for PAHs but other emerging pollutants of concern as well.

Conclusions/future directions

Our studies are corollary to the public health exposome concept that characterizes the whole gamut of individual exposure to environmental agents, coupled with endogenous factors [84]. While the saliva exposome studies published elsewhere [85] were able to capture the endogenous and therapeutic agent-derived compounds/metabolites, pollutants were not represented in detail in that report due to lack of sufficient data. Both the clinician and basic scientist continue to face challenges in assessing toxicant loads in the absence of comprehensive educational resources, definitive laboratory tests, established dose–response relationships or exposure history tools [86]. A timeline of exposure history will continue to be the most useful clinical tool for assessing toxicant exposures, until standardized assessment tools can be calibrated to be applied universally. Engaging all catchments of patients in community has the potential to integrate knowledge about toxicant exposures, individual susceptibility, genetic predisposition, and lifestyle. The latter support accountability for the impact of the environment on the health of populations and individuals. Future studies from our group and collaborators will focus on detecting and quantifying trace concentrations of emerging pollutants of concern such as endocrine disruptors, phthalates, nitrosamines, pharmaceuticals etc. in accessible oral tissues/cells of healthy individuals and patients in various disease states visiting dental clinics. Through these studies, we plan to embark on a toxicovigilance approach [87] to characterize biomarkers of exposure and, effect and susceptibility [88] for these toxicants from an environmental medicine standpoint.

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

Funding

This work was supported by the National Institutes of Health (NIH) [grant numbers 5U54MD007593-07, 5U54CA163069-04, G12RR003022], Robert Wood Johnson Foundation [grant numbers MMCRWJ#04-14-0021, MMCRWJ#04-16-0028] American Cancer Society (ACS) [grant number DICRIDG-21-071-01], US Department of Energy [grant number DE-EM0005266]. The content is solely the responsibility of the authors do not officially represent the views of the NIH, RWJF, ACS and DOE.

Conflicts of interest

The authors have none to declare.

Acknowledgements

We thank Drs. Mitchell Mascaro, Pratikkumar Patel, Douglas Reid, Yasser Obaid and Botros Aiyad for their assistance in sample collection, preservation and processing of some samples.

REFERENCES

[1] Chaturvedi AK, Freedman ND, Abnet CC. The evolving epidemiology of oral cavity and oropharyngeal cancers. Cancer Res 2022;82(16):2821–3.
[2] Lao JY, Wang SQ, Chen YQ, Bao LJ, Lam PKS, Zeng EY. Dermal exposure to particle-bound polycyclic aromatic hydrocarbons from barbecue fume as impacted by physicochemical conditions. Environ Pollut 2020;260:114080.
[3] Badyda AJ, Widziewicz K, Rogula-Kozłowska W, Majewski G, Jureczko I. Inhalation Exposure to PM-bound polycyclic aromatic hydrocarbons released from barbecue grills powered by gas, lump charcoal, and charcoal briquettes. Adv Exp Med Biol 2018;1023:11–27.
[4] Ding YS, Zhang L, Jain RB, Jain N, Wang RY, Ashley DL, et al. Levels of tobacco-specific nitrosamines and polycyclic aromatic hydrocarbons in mainstream smoke from different tobacco varieties. Cancer Epidemiol Biomarkers Prev 2008;17(12):3366–71.
[5] Oliveira M, Duarte S, Delerue-Matos C, Pena A, Morais S. Exposure of nursing mothers to polycyclic aromatic hydrocarbons: levels of un-metabolized and metabolized compounds in breast milk, major sources of exposure and infants' health risks. Environ Pollut 2020;266(Pt 3):115243.
[6] Duedahl-Olesen L, Ionas AC. Formation and mitigation of PAHs in barbecued meat - a review. Crit Rev Food Sci Nutr 2022;62(13):3553–68.
[7] Sadri G, Mahjub H. Tobacco smoking and oral cancer: a meta-analysis. J Res Health Sci 2007;7(1):18–23.
[8] Słowikowski BK, Jankowski M, Jagodziński PP. The smoking estrogens - a potential synergy between estradiol and benzo(a)pyrene. Biomed Pharmacother 2021;139:111658.
[9] Albertini R, Bird M, Doerrer N, Needham L, Robison S, Sheldon L, et al. The use of biomonitoring data in exposure and human health risk assessments. Environ Health Perspect 2006;114(11):1755–62.
[10] Vu AT, Taylor KM, Holman MR, Ding YS, Hearn B, Watson CH. Polycyclic aromatic hydrocarbons in the mainstream smoke of popular U.S. cigarettes. Chem Res Toxicol 2015;28(8):1616–26.
[11] Baldwin AK, Corsi SR, Oliver SK, Lenaker PL, Nott MA, Mills MA, et al. Primary sources of polycyclic aromatic hydrocarbons to streambed sediment in Great Lakes tributaries using multiple lines of evidence. Environ Toxicol Chem 2020;39(7):1392–408.
[12] Jakobsen LS, Georgiadis S, Nielsen BF, Bokkers BGH, Boriani E, Duedahl-Olesen L, et al. Probabilistic approach for assessing cancer risk due to benzo[a]pyrene in barbecued meat: informing advice for population groups. PLoS One 2018;13:e0207032.
[13] Jin Y, Xu P, Liu X, Zhang C, Tan C, Chen C, et al. Cigarette Smoking, BPDE-DNA adducts, and aberrant promoter methylations of tumor suppressor genes (TSGs) in NSCLC from Chinese Population. Cancer Invest 2016;34(4):173–80.
[14] Domingo JL, Nadal M. Human dietary exposure to polycyclic aromatic hydrocarbons: a review of the scientific literature. Food Chem Toxicol 2015;86:144–53.
[15] Chiang CF, Hsu KC, Cho CY, Tsai T, Hsu CH, Yang DJ. Comparison and establishment of appropriate methods to determine EU priority PAHs in charcoal-grilled chicken drumsticks with different treatments and their dietary risk assessments. Food Chem Toxicol 2020;142:111400.
[16] Hung YT, Lee YT, Inbaraj BS, Sridhar K, Chen BH. Analysis and formation of polycyclic aromatic hydrocarbons and cholesterol oxidation products in thin slices of dried pork during processing. Food Chem 2021;353:129474.
[17] Hakami R, Mohtadinia J, Etemadi A, Kamangar F, Nemati M, Pourshams A, et al. Dietary intake of benzo(a)pyrene and risk of esophageal cancer in north of Iran. Nutr Cancer 2008;60(2):216–21.
[18] Harris KJ, Subbiah S, Tabatabai M, Archibong AE, Singh KP, Anderson TA, et al. Pressurized liquid extraction followed by liquid chromatography coupled to a fluorescence detector and atmospheric pressure chemical ionization mass spectrometry for the determination of benzo(a)pyrene metabolites in liver tissue of an animal model of colon cancer. J Chromatogr A 2020;1622:461126.
[19] Cheng T, Chaousis S, Kodagoda Gamage SM, Lam AK, Gopalan V. Polycyclic aromatic hydrocarbons detected in processed meats cause genetic changes in colorectal cancers. Int J Mol Sci 2021;22(20):10959.
[20] WHO. Environment and health risks: a review of the influence and effects of social inequalities. WHO Report; 2010262pp.
[21] Gomez-Casillas A, Lozano M, Rentería E. Expected years lived with intimate partner violence: a new approach for public health. Glob Health Action 2021;14(1):1976442.
[22] Halpern L, Cho R, Rogers J, Padron V, Isaza S, Southerland J, et al. The impact of intimate partner violence exposure on orofacial and stress-related health consequences in female patients. Violence Gend 2017;3:181–8.
[23] Halpern LR, Shealer ML, Cho R, McMichael EB, Rogers J, Ferguson-Young D, et al. Influence of intimate partner violence (IPV) exposure on cardiovascular and salivary biosensors: is there a relationship? J Natl Med Assoc 2017;109(4):252–61.
[24] Breiding MJ, Black MC, Ryan GW. Chronic disease and health risk behaviors associated with intimate partner violence-18 US States/Territories. Ann Epidemiol 2008;18(7):538–44.
[25] Symes L, McFarlane J, Frazier L, Henderson-Everhardus MC, McGlory G, Watson KB, et al. Exploring violence against women and adverse health outcomes in middle age to promote women's health. Crit Care Nurse 2010;33:233–43.
[26] Fernandez-Botran R, Miller JJ, Burns V, Newton TL. Correlations among inflammatory markers in plasma, saliva,

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

and oral mucosal transudate in postmenopausal women with past intimate partner violence. Brain Behav Immun 2011;25(2):314–21.
[27] Kendall-Tackett KA. Inflammation, cardiovascular disease, and metabolic syndrome as sequelae of violence against women: the role of depression, hostility, and sleep disturbance. Trauma Violence Abuse 2007;8(2):117–26.
[28] Whiting K, Liu LY, Koyuturk M, Karakurt G. Network map of adverse health effects among victims of intimate partner violence. Bioinformatics 2017;2:324–35.
[29] Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon 3rd RO, Criqui M, et al. Markers if inflammation and cardiovascular disease and cardiovascular disease: application to clinical and public health practice: a statement for healthcare professionals from the centers for disease control and prevention and the American heart association. Circulation 2003;107(3):499–511.
[30] Scott-Storey K, Wuest J, Ford-Gilboe M. Intimate partner violence and cardiovascular risk: is there a link? J Adv Nurs 2009;65(10):2186–97.
[31] Newton TL, Fernandez-Botran R, Miller JJ, Lorenz DJ, Burns VE, Fleming KN. Markers of inflammation in midlife women with intimate partner violence histories. J Wom Health 2011;20(12):1871–80.
[32] Campbell J, Jones AS, Dienemann J, Kub J, Schollenberger J, O'Campo P, et al. Intimate partner violence and physical health consequences. Arch Intern Med 2002;162(10):1157–63.
[33] Martin Santos P, Del Nogal Sánchez M, Pérez Pavón JL, Cordero BM. Determination of polycyclic aromatic hydrocarbons in human biological samples: a critical review. Trends Anal Chem 2019;113:194–209.
[34] Vorkamp K, Castaño A, Antignac JP, Boada LD, Cequier E, Covaci A, et al. Biomarkers, matrices and analytical methods targeting human exposure to chemicals selected for a European human biomonitoring initiative. Environ Int 2020;2021146:106082.
[35] Marín-Sáez J, López-Ruiz R, Sobral M, Romero-González R, Garrido Frenich A, Ferreira I. Analytical methods for biomonitoring organic chemical hazards in saliva: a systematic review. TrAC, Trends Anal Chem 2023;158:116853.
[36] Pfaffe T, Cooper-hite J, Beyerlin P, Kostner K, Punyadeera C. Diagnostic potential of saliva: current state and future applications. Clin Chem 2011;57(5):675–87.
[37] Siervo M, Jackson SJ, Bluck JC. In-vivo nitric oxide synthesis is reduced in obese patients with metabolic syndrome: application of a novel stable isotopic method. J Hypertens 2011;29(8):1516–27.
[38] Punyadeera C. Human saliva as a tool to investigate intimate partner violence. Brain Behav Immun 2012;26(4):541–2.
[39] Foley JD, Sneed JD, Steinhubl SR, Kolasa JR, Ebersole JL, Lin , et al. Oral fluids that detect cardiovascular disease biomarkers. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;114(2):207–14.
[40] Vesell ES. Noninvasive assessment in vivo of hepatic drug metabolism in health and disease. Ann N Y Acad Sci 1984;428:293–307.
[41] Metcalf SW, Orloff KG. Biomarkers of exposure in community settings. J Toxicol Environ Health 2004;67(8–10):715–26.
[42] Feldhaus KM, Koziol-McLain J, Amsbury HL, Norton IM, Lowenstein SR, Abbott JT. Accuracy of 3 brief screening questions for detecting partner violence in the emergency department. JAMA 1997;277(17):1357–61.
[43] McHorney CA, Ware Jr JE, Lu JF, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Med Care 1994;32(1):40–66.
[44] Ford-Gilboe M, Wuest J, Varcoe C, Davies L, Merritt-Gray M, Campbell J, et al. Modelling the effects of intimate partner violence and access to resources on women's health in the early years after leaving an abusive partner. Soc Sci Med 2009;68(6):1021–9.
[45] Cioroiu BI, Tarcau D, Cucu-Man S, Chisalita I, Cioroiu M. Polycyclic aromatic hydrocarbons in lung tissue of patients with pulmonary cancer from Romania. Influence according as demographic status and ABO phenotypes. Chemosphere 2013;92(5):504–11.
[46] Out D, Hall RJ, Granger DA, Page GG, Woods SJ. Assessing salivary C-reactive protein: longitudinal associations with systemic inflammation and cardiovascular disease risk in women exposed to intimate partner violence. Brain Behav Immun 2012;26(4):543e5551.
[47] ATSDR. Toxicology profile for polyaromatic hydrocarbons. In: ATSDR's toxicological profiles on CD-ROM. CRC Press; 2005.
[48] Ju YR, Chen CF, Wang MH, Chen CW, Dong CD. Assessment of polycyclic aromatic hydrocarbons in seafood collected from coastal aquaculture ponds in Taiwan and human health risk assessment. J Hazard Mater 2022;421:126708.
[49] Santos PM, Del Nogal Sánchez M, Pérez Pavón JL, Cordero BM, Fernández RV. Liquid-liquid extraction-programmed temperature vaporizer-gas chromatography-mass spectrometry for the determination of polycyclic aromatic hydrocarbons in saliva samples. Application to the occupational exposure of firefighters. Talanta 2019;192:69–78.
[50] Santos PM, Campo L, Olgiati L, Polledri E, Del Nogal Sánchez M, Fustinoni S. Development of a method to profile 2- to 4-ring polycyclic aromatic hydrocarbons in saliva samples from smokers and non-smokers by headspace-solid-phase microextraction-gas chromatography-triple quadrupole tandem mass spectrometry. J Chromatogr, B: Anal Technol Biomed Life Sci 2020;1152:122273.
[51] Pena J, Laespada MEF, Pinto CG, Pavon JLP. Multiple headspace sampling coupled to a programmed temperature vaporizer – gas chromatograph-mass spectrometer for the determination of polycyclic aromatic hydrocarbons in water and saliva. Microchem J 2021;161:105822.
[52] Carrizo D, Domeño C, Nerín I, Alfaro P, Nerín C. Atmospheric pressure solid analysis probe coupled to quadrupole-time of flight mass spectrometry as a tool for screening and semi-quantitative approach of polycyclic aromatic hydrocarbons, nitro-polycyclic aromatic hydrocarbons and oxo-polycyclic aromatic hydrocarbons in complex matrices. Talanta 2015;131:175–84.
[53] Li Z, Romanoff L, Bartell S, Pittman EN, Trinidad DA, McClean M, et al. Excretion profiles and half-lives of ten urinary polycyclic aromatic hydrocarbon metabolites after dietary exposure. Chem Res Toxicol 2012;25(7):1452–61.
[54] Ramesh A, Kumar A, Aramandla MP, Nyanda AM. Polycyclic aromatic hydrocarbon residues in serum samples of autopsied individuals from Tennessee. Int J Environ Res Publ Health 2014;12(1):322–34.
[55] Chien YC, Yeh CT. Excretion kinetics of urinary 3-hydroxybenzo[a]pyrene following dietary exposure to benzo [a]pyrene in humans. Arch Toxicol 2012;86(1):45–53.
[56] Motorykin O, Santiago-Delgado L, Rohlman D, Schrlau JE, Harper B, Harris S, et al. Metabolism and excretion rates of parent and hydroxy-PAHs in urine collected after consumption of traditionally smoked salmon for Native American volunteers. Sci Total Environ 2015;514:170–7.

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006

[57] Suglia SF, Sapra KJ, Koenen KC. Violence and cardiovascular health: a systematic review. Am J Prev Med 2015;48(2):205–12.
[58] Shetty V, Yamaguchi M. Salivary biosensors for screening trauma related psychpathology. Oral Maxillofac Surg Clin NA 2010;22(2):269–78.
[59] Stockman JK, Hayashi H, Campbell JC. Intimate partner violence and its health impact on ethnic minority women [corrected]. J Womens Health (Larchmt) 2015;24(1):62–79.
[60] Lacey KK, Mouzon DM, Parnell RN, Laws T. Severe intimate partner violence, sources of stress and the mental health of U.S. Black Women. J Womens Health (Larchmt) 2021;30(1):17–28.
[61] Han M, Zhang R, Yu K, Li A, Wang Y, Huang X. Polycyclic aromatic hydrocarbons (PAHs) in corals of the South China Sea: occurrence, distribution, bioaccumulation, and considerable role of coral mucus. J Hazard Mater 2020;384:121299.
[62] Drug E, Landesman-Milo D, Belgorodsky B, Ermakov N, Frenkel-Pinter M, Fadeev L, et al. Enhanced bioavailability of polyaromatic hydrocarbons in the form of mucin complexes. Chem Res Toxicol 2011;24(3):314–20.
[63] Kapoor A, Batra JK, Luthra UK, Jain RC, Venkitasubramanian TA, Raj HG. Benzo(a)pyrene hydroxylase activity in human bronchial mucus. Eur J Drug Metab Pharmacokinet 1986;11(1):33–7.
[64] Vondracek M, Xi Z, Larsson P, Baker V, Mace K, Pfeifer A, et al. Cytochrome P450 expression and related metabolism in human buccal mucosa. Carcinogenesis 2001;22(3):481–8.
[65] Baumeister P, Reiter M, Kleinsasser N, Matthias C, Harréus U. Epigallocatechin-3-gallate reduces DNA damage induced by benzo[a]pyrene diol epoxide and cigarette smoke condensate in human mucosa tissue cultures. Eur J Cancer Prev 2009;18(3):230–5.
[66] Chen KM, Sun YW, Krebs NM, Sun D, Krzeminski J, Reinhart L, et al. Detection of DNA adducts derived from the tobacco carcinogens, benzo[a]pyrene and dibenzo[def,p] chrysene in human oral buccal cells. Carcinogenesis 2022;43(3):746–53.
[67] Walle T, Walle UK, Sedmera D, Klausner M. Benzo[a]pyrene-induced oral carcinogenesis and chemoprevention: studies in bioengineered human tissue. Drug Metab Dispos 2006;34(3):346–50.
[68] Chi AC, Appleton K, Henriod JB, Krayer JW, Marlow NM, Bandyopadhyay D, et al. Differential induction of CYP1A1 and CYP1B1 by benzo[a]pyrene in oral squamous cell carcinoma cell lines and by tobacco smoking in oral mucosa. Oral Oncol 2009;45(11):980–5.
[69] Luch A. The carcinogenic effects of polycyclic aromatic hydrocarbons. London: Imperial College Press; 2005.
[70] Wong SP, Chang JC. Altered eating behaviors in female victims of intimate partner violence. J Interpers Violence 2016;31(20):3490–505.
[71] Stubbs A, Szoeke C. The effect of intimate partner violence on the physical health and health-related behaviors of women: a systematic review of the literature. Trauma Violence Abuse 2022;23(4):1157–72.
[72] Crane CA, Pilver CE, Weinberger AH. Cigarette smoking among intimate partner violence perpetrators and victims: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. Am J Addict 2014;23(5):493–501.
[73] Ahijevych K, Garrett BE. Menthol pharmacology and its potential impact on cigarette smoking behavior. Nicotine Tob Res 2004;6(Suppl 1):S17–28.
[74] Azzi C, Zhang J, Purdon CH, Chapman JM, Nitcheva D, Hebert JR, et al. Permeation and reservoir formation of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and benzo[a]pyrene (B[a]P) across porcine esophageal tissue in the presence of ethanol and menthol. Carcinogenesis 2006;27(1):137–45.
[75] Giovino GA, Sidney S, Gfroerer JC, O'Malley PM, Allen JA, Richter PA, et al. Epidemiology of menthol cigarette use. Nicotine Tob Res 2004;6(Suppl 1):S67–81.
[76] Substance abuse and mental health services administration substance abuse and mental health services administration (SAMHSA)'s public online data analysis system (PDAS) national survey on drug use and health, . [accessed 5 September 2021].
[77] Rivera EA, Phillips H, Warshaw C, Lyon E, Bland PJ, Kaewken O. An applied research paper on the relationship between intimate partner violenceand substance use. Chicago, IL: National Center on Domestic Violence, Trauma & Mental Health 2015 [accessed 5 September 2021].
[78] Nock NL, Tang D, Rundle A, Neslund-Dudas C, Savera AT, Bock CH, et al. Associations between smoking, polymorphisms in polycyclic aromatic hydrocarbon (PAH) metabolism and conjugation genes and PAH-DNA adducts in prostate tumors differ by race. Cancer Epidemiol Biomarkers Prev 2007;16(6):1236–45.
[79] Patel YM, Park SL, Carmella SG, Paiano V, Olvera N, Stram DO, et al. Metabolites of the polycyclic aromatic hydrocarbon phenanthrene in the urine of cigarette smokers from five ethnic groups with differing risks for lung cancer. PLoS One 2016;11(6):e0156203.
[80] Choi H, Perera FP. Sources of greater fetal vulnerability to airborne polycyclic aromatic hydrocarbons among African Americans. J Epidemiol Community Health 2012;66(2):121–6.
[81] Shmool JL, Kubzansky LD, Newman OD, Spengler J, Shepard P, Clougherty JE. Social stressors and air pollution across New York City communities: a spatial approach for assessing correlations among multiple exposures. Environ Health 2014;13:91.
[82] Payne-Sturges DC, Scammell MK, Levy JI, Cory-Slechta DA, Symanski E, Carr Shmool JL, et al. Methods for evaluating the combined effects of chemical and nonchemical exposures for cumulative environmental health risk assessment. Int J Environ Res Publ Health 2018;15(12):2797.
[83] Hamby SL, Gray-Little B. Labeling partner violence: when do victims differentiate among acts? Violence Vict 2000;15(2):173–86.
[84] Juarez PD, Hood DB, Song MA, Ramesh A. Use of an exposome approach to understand the effects of exposures from the natural, built, and social environments on cardio-vascular disease Ooset, progression, and outcomes. Front Public Health 2020;8:379.
[85] Bessonneau V, Pawliszyn J, Rappaport SM. The saliva exposome for monitoring of individuals' health trajectories. Environ Health Perspect 2017;125(7):077014.
[86] Bijlsma N, Cohen MM. Expert clinician's perspectives on environmental medicine and toxicant assessment on clinical practice. Environ Health Prev Med 2018;23(1):19.
[87] Descotes J, Testud F. Toxicovigilance: a new approach for the hazard identification and risk assessment of toxicants in human beings. Toxicol Appl Pharmacol 2005;207(2 Suppl):599–603.
[88] Juarez PD, Matthews-Juarez P, Hood DB, Im W, Levine RS, Kilbourne BJ, et al. The public health exposome: a population-based, exposure science approach to health disparities research. Int J Environ Res Publ Health 2014;11(12):12866–95.

Please cite this article as: Ramesh A et al., Saliva as a diagnostic tool to measure polycyclic aromatic hydrocarbon exposure in dental patients exposed to intimate partner violence (IPV), Biomedical Journal, https://doi.org/10.1016/j.bj.2023.02.006