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PLASTIC-ASSOCIATED CHEMICALS AND THEIR IMPACTS ON HUMAN HEALTH

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Abstract

Plastics, along with the numerous chemicals embedded inside them, are essential to contemporary existence but present considerable hazards to human health. Numerous plastic-associated compounds (PACs), including bisphenols, phthalates, and flame retardants, are recognized as endocrine disruptors and metabolic toxicants; however, alternative alternatives have not been adequately investigated. Extensive and continual human exposure to PACs via air, food, water, and consumer products necessitates immediate examination of their health implications. This study investigated the relationship between internal exposure to prevalent PACs and metabolic, cardiovascular, inflammatory, and endocrine health outcomes in adults, focusing on less-explored exposure pathways and cumulative effects. A cross-sectional biomonitoring study was conducted at University of Southern Punjab, Multan, on 300 individuals aged 20–65 years. Urinary bisphenols (BPA and BPS) and phthalate metabolites (MnBP, MiBP, MEHHP, and MEOHP) were measured by LC–MS/MS. The primary endpoint was insulin resistance (HOMA-IR), while secondary outcomes included lipid levels, inflammatory markers (CRP), blood pressure, and thyroid function (TSH and free T4). Multivariable linear regression models were adjusted for age, sex, BMI, and smoking status. The detection rates for BPA, BPS, MnBP, MiBP, and DEHP metabolites were over 90%. Elevated urine ∑DEHP concentrations were correlated with heightened insulin resistance (β = +0.42, 95% CI: 0.18–0.66, p = 0.001), elevated triglycerides (+5.8 mg/dL), LDL cholesterol (+2.5 Â mg/dL), greater CRP (+0.21 mg/L), and increased blood pressure. BPA levels exhibited an inverse correlation with TSH (β = −0.08 μIU/mL, p = 0.008) and a positive correlation with free T4 (+0.03 ng/dL, p = 0.014). These associations remained consistent throughout the sensitivity analysis. The results indicate quantifiable exposure to various PACs in humans, with consistent correlations across metabolic, cardiovascular, inflammatory, and endocrine domains. These findings underscore the significance of biomonitoring in risk assessment and advocate for revised regulatory frameworks that consider cumulative exposure, at-risk groups, and novel replacements.

INTRODUCTION

Plastics and their chemicals pervade modern life for both the better and worse. Plastics, along with their associated environmental and health issues, have been an important part of our lives since industrialization during the Second World War (Stanley et al., 2025). Over 16,000 chemicals are added to plastics to improve their properties, such as flexibility, longevity, and color, and most leech out into the environment and human exposure (Cropper et al., 2024). A subset of these, such as bisphenols, phthalates, flame retardants, and perfluoroalkyl substances (PFAS), have been identified as priority chemicals of concern for their known associations with adverse health effects (Symeonides et al., 2024). Additionally, the degradation of large plastics produces micro-/nanoplastics (MNPs) that act as vectors for both native additives and introduced pollutants, vastly expanding avenues for human exposure (Alijagic et al., 2024; Domenech & Marcos, 2021). They are ubiquitous in the air we breathe, water, and food, as well as in our consumer goods; however, regulation fails to include a comprehensive post-market assessment of these chemicals and particles (Seewoo et al., 2023). The size and longevity of this exposure indicate the significance of understanding the long-term health effects of plastic-associated chemicals.

A significant body of evidence exists regarding the links between synthetic, plastic-derived chemicals and a variety of human health endpoints. BPA is known to cause type 2 diabetes, obesity, hypertension, and reproductive abnormalities, and phthalates are associated with pregnancy loss, decreased sperm quality, premature puberty, and developmental neurotoxicity (Symeonides et al., 2024). Worldwide surveillance studies have shown that in many cases, the levels of these compounds are close to or surpass the limit values for non-carcinogenic and carcinogenic risk (Duenas-Moreno et al., 2023). Toxicity profiling studies have shown that nearly all consumer plastic products leach biologically active compounds that result in endpoints including oxidative stress, cytotoxicity, and endocrine disruption (Zimmermann et al., 2019). Through evidence mapping, over 3,500 studies on the human health effects of key chemical classes were identified, both highlighting the scope of studies currently available and demonstrating marked deficits in population coverage, exposure pathways, and the diversity of outcomes (Seewoo et al., 2023). Although ingestion represents the most evaluated exposure route, inhalation and dermal routes are still underestimated (Domenech & Marcos, 2021). Moreover, although there is some evidence demonstrating that MNPS absorbs the gastrointestinal tract and release additives into GI fluids, their health impacts over time are poorly understood (Mummaleti & Kong, 2024). Economic analyses add urgency, calculating that BPA, DEHP, and PBDEs caused 5.4 million cases of ischemic heart disease, 346,000 strokes, and >$1.5 trillion in healthcare expenses in 2015 (Cropper et al., 2024). However, there are still important weaknesses, such as most regulations are not modified according to new evidence, new substitutes are still insufficiently screened and combined or synergistic effects are not adequately addressed (Symeonides et al., 2024).

To fill this gap, in the present study, the health risks of chemicals associated with plastics for humans, considering the less-estimated exposure routes, susceptible groups, and synergetic effects of mixtures, were examined. The originality of this study lies in the emphasis given to new compounds such as bisphenol analogs, substitute plasticizers, organo-phosphate bulletproofs, and micro-and nanoplastics, which have been underrepresented in systematic reviews (Seewoo et al., 2023; Symeonides et al., 2024). The research embraces an integrative approach aimed at bringing together different but complementary knowledge provided by an umbrella review, systematic evidence maps, and in vitro toxicological benchmarking (Zimmermann et al., 2019). By focusing on neglected additives, significant re-aggregation of data, and the stringent approach of exposure assessment, this research responds to some of the limitations pointed out in previous studies (Domenech & Marcos, 2021; Nene et al., 2025). Moreover, the inclusion of health and economic impacts in the analysis allows for a link between scientific information and policy implications, which is helpful for the revision of guidelines and regulations (Cropper et al., 2024; Duenas-Moreno et al., 2023). This study thus advances towards a comprehensive understanding of chemicals associated with plastics and their long-term implications for human health.

2. METHODOLOGY

2.1 STUDY DESIGN AND POPULATION

The present study was conducted at University of Southern Punjab, Multan, as a cross-sectional human biomonitoring investigation designed to characterize internal PAC exposure and relate such exposure to health effects. We recruited 300 adults from the general population who were aged 20-65 years. The eligibility criteria were a minimum of six months of residency in the study area and the ability to provide fasting blood and early morning urine samples. Patients with acute febrile illness, pregnant women, those who were currently receiving chemotherapy, and those with renal insufficiency were excluded to prevent confounding effects on biomarker levels and dilution correction factors.

2.2 SAMPLE COLLECTION AND HANDLING

Urine was collected in pre-selected contamination-checked polypropylene containers. All participants provided morning spot urine samples, which were aliquoted into amber polypropylene tubes and frozen at −20 °C within 2 h of collection. The dilution of each sample was estimated using two markers: specific gravity (determined by refractometry) and urinary creatinine (assayed by an enzymatic technique). Fasting venous blood specimens were obtained after overnight fasting for at least 8 h. Serum and plasma samples were assayed for fasting glucose, insulin, triglyceride, HDL cholesterol, LDL cholesterol, CRP, TSH, and free T4.

2.3 ANALYTICAL METHODS

2.3.1 Target Analytes

The levels of the six most relevant PACs were determined in the urine by LC–MS/MS analysis. The analytes were bisphenol A (BPA), bisphenol S (BPS), monon-butyl phthalate (MnBP), monoisobutyl phthalate (MiBP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and mono(2-ethyl-5-oxohexyl) phthalate (MEOHP). The MEHHP and MEOHP were summed for the di(2-ethylhexyl) phthalate (DEHP) exposure measures. These analytes were chosen because they are high-frequency measurable biomarkers of plastic exposure in humans and have known endocrine and metabolic targets. Compounds of interest and their biological significance are listed in **Table 1**.

Table 1: Target Analytes and Their Biological Relevance

Class	Analyte	Abbreviation	Biological Relevance
Bisphenols	Bisphenol A	BPA	Endocrine disruption, metabolic effects
	Bisphenol S	BPS	BPA substitute, endocrine activity less studied
Phthalate metabolites	Mono-n-butyl phthalate	MnBP	DBP metabolite, reproductive and metabolic risks
	Mono-isobutyl phthalate	MiBP	DiBP metabolite, endocrine disruption
	Mono-(2-ethyl-5-hydroxyhexyl) phthalate	MEHHP	DEHP metabolite, oxidative stress pathways
	Mono-(2-ethyl-5-oxohexyl) phthalate	MEOHP	DEHP metabolite, metabolic and endocrine effects
Composite metric	Sum DEHP (MEHHP + MEOHP)	∑DEHP	Integrated indicator of DEHP exposure

2.3.2 Sample Preparation and LC–MS/MS Analysis

All urine samples were subjected to enzymatic deconjugation using beta-glucuronidase at 37 °C for 90 min to hydrolyze conjugated metabolites. The hydrolyzed samples were then subjected to extraction (SPE) with polymeric cartridges. After elution with methanol, the extracts were evaporated under nitrogen and redissolved in a mobile phase consisting of water and acetonitrile (80:20, v/v). Chromatographic separation was performed using a C18 reversed-phase column (2.1 × 100 mm, 1.7 µm particle size) and binary gradient elution of water containing 0.1% formic acid (mobile phase A) and acetonitrile containing 0.1% formic acid (mobile phase B). The gradient comprised 5–95% Mobile Phase B for 10 min at a flow rate of 0.3 mL/min. Detection was performed in the multiple reaction monitoring (MRM) mode with the collision energy optimized for each analyte. Isotopically labeled standards (d_{16} BPA, $^{13}C_{12}$ BPS, $^{13}C_4$ MnBP, and $^{13}C_4$ MEHHP) were used for quantitation.

The analytical performance characteristics of the method, including limits of detection (LOD), limits of quantification (LOQ), recoveries, and coefficients of variation (CV), are presented in **Table 2**.

Table 2: Analytical Method Performance Parameters

Analyte	LOD (ng/mL)	LOQ (ng/mL)	Internal Standard	Recovery (%)	CV (%)
BPA	0.10	0.30	d_{16}-BPA	85–110	≤20
BPS	0.05	0.15	$^{13}C_{12}$-BPS	80–115	≤20
MnBP	0.20	0.60	$^{13}C_4$-MnBP	82–108	≤20
MiBP	0.20	0.60	$^{13}C_4$-MnBP	83–112	≤20
MEHHP	0.10	0.30	$^{13}C_4$-MEHHP	88–110	≤20
MEOHP	0.10	0.30	$^{13}C_4$-MEOHP	90–115	≤20

2.4 EXPOSURE METRICS

All analytes were quantified as raw urinary concentrations in ng/mL. Dilution adjustment was carried out using two complementary methods. Specific gravity–adjusted concentrations were calculated using the following formula:

C_{SG} = C x 1.020-1/SG-1

where C is the raw concentration and SG is the sample-specific gravity. Creatinine-corrected concentrations were expressed in ng/mg creatinine, calculated by dividing the analyte concentration by urinary creatinine (mg/dL) and multiplying by 0.01. The sum of DEHP metabolites (∑DEHP) was computed as the molar sum of MEHHP and MEOHP. Values below the limit of detection were replaced with LOD divided by the square root of two, in accordance with standard human biomonitoring protocols.

2.5 HEALTH OUTCOMES AND COVARIATES

The primary health-related outcome was insulin resistance, which was determined as the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), computed as fasting glucose (mg/dL) × fasting insulin (µU/mL) divided by 405. The secondary endpoints were plasma lipid levels (triglycerides, HDL, and LDL), inflammation status based on high-sensitivity CRP, cardiovascular outcomes including SBP and DBP, and thrombin regulation indicated by TSH and free T4. The adjusted covariates were age (years), sex, body mass index (BMI), and smoking. The parameters are listed in **Table 3.**

Table 3: Outcomes and Covariates Included in the Study

Category	Variable	Unit/Method
Metabolic	Fasting glucose	mg/dL (enzymatic)
	Fasting insulin	μU/mL (immunoassay)
	HOMA-IR	Unitless
Lipids	Triglycerides	mg/dL
	HDL cholesterol	mg/dL
	LDL cholesterol	mg/dL
Inflammation	C-reactive protein	mg/L (immunoturbidimetric)
Cardiovascular	SBP, DBP	mmHg (automated sphygmomanometer)
Thyroid	TSH	μIU/mL (chemiluminescence)
	Free T4	ng/dL (chemiluminescence)
Covariates	Age, sex, BMI, smoking	Questionnaire/clinical assessment

2.6 SAMPLE SIZE AND POWER CALCULATION

The sample size was estimated for the primary aim to evaluate the association between ln-transformed ∑DEHP levels and HOMA-IR, adjusting for four covariates. Assuming a small effect size of $f^2 = 0.04$, with α=0.05, and 80% power, the minimum sample size was 280. A total of 300 participants were recruited for data loss.

2.7 STATISTICAL ANALYSIS

All statistical analyses were pre-specified. Exposure distributions and health outcomes were characterized using descriptive statistics such as means, medians, interquartile ranges, and standard deviations. We used multiple linear regression models with log HOMA-IR as the dependent variable and ln-transformed specific gravity–adjusted ∑DEHP as the independent variable for a sample adjusted for age, sex, BMI, and smoking. For secondary models, we evaluated the associations of the natural logarithm of the sum of DEHP metabolites (ln(∑DEHP)) with lipids and the natural logarithm of BPA (ln(BPA)) with thyroid markers. The family-wise false discovery rate was also controlled. Assumptions of the model were checked by examining plots of residuals and testing for heteroscedasticity and variance inflation factors. Sensitivity analyses involved re-running models with corrected concentrations, excluding extreme urine dilutions, and testing the exposure sex interaction terms. The results were presented as regression coefficients with 95% confidence intervals (95% CI) and p-values.

2.8 ETHICAL CONSIDERATIONS

This study followed the Strengthening Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines. All subjects provided informed consent when samples were collected. The institutional review board approved the Reobtained from the study protocol, and the data were anonymized and analyzed.

3. RESULTS

3.1 STUDY POPULATION CHARACTERISTICS

A total of 300 participants were included in the final analysis. The mean age of the participants was 42.6 years (SD = 12.4), and 52% were female. The average

body mass index (BMI) was 26.3 kg/m² (SD = 4.8), with 25% of participants identified as current smokers. Mean systolic blood pressure was 124 mmHg (SD = 15), while mean diastolic blood pressure was 80 mmHg (SD = 10). Fasting glucose and insulin values yielded a mean HOMA-IR of 2.86 (SD = 1.45). Baseline characteristics are presented in **Table 4**.

Table 4: Demographic and Baseline Characteristics of Study Participants (N = 300)

Characteristic	Mean (SD) / n (%)
Age (years)	42.6 (12.4)
Female sex	156 (52.0)
BMI (kg/m²)	26.3 (4.8)
Current smokers	75 (25.0)
Systolic BP (mmHg)	124.0 (15.0)
Diastolic BP (mmHg)	80.0 (10.0)
Fasting glucose (mg/dL)	99.8 (14.2)
Fasting insulin (µU/mL)	11.6 (5.8)
HOMA-IR (unitless)	2.86 (1.45)

3.2 URINARY CONCENTRATIONS OF PLASTIC-ASSOCIATED CHEMICALS

All six target analytes were detected in the majority of participants, with detection frequencies exceeding 90% for BPA, BPS, MnBP, and ∑DEHP. The median specific gravity–adjusted concentrations of BPA and BPS were 2.1 ng/mL and 0.9 ng/mL, respectively. The median values of MnBP and MiBP were 20.8 ng/mL and 15.2 ng/mL, respectively. The DEHP metabolites, MEHHP and MEOHP, had median concentrations of 10.2 ng/mL and 8.3 ng/mL, respectively, and the median ∑DEHP concentration was 18.5 ng/mL. These distributions are summarized in **Table 5**.

Table 5: Distribution of Urinary Plastic-Associated Chemicals (sg-adjusted concentrations, ng/ml)

Analyte	Median (IQR)	Range	Detection (%)
BPA	2.1 (1.3–3.7)	0.07 – 12.5	96.7
BPS	0.9 (0.4–1.8)	0.05 – 6.4	93.4
MnBP	20.8 (12.5–34.1)	1.2 – 105.6	98.0
MiBP	15.2 (8.9–25.5)	1.0 – 88.2	97.3
MEHHP	10.2 (6.1–16.7)	0.5 – 48.4	94.5
MEOHP	8.3 (5.0–13.2)	0.4 – 38.7	94.0

∑DEHP	18.5 (11.6–29.3)	1.2 – 87.1	95.1

The distributions of urinary PACs were right-skewed, with higher variability for phthalate metabolites compared with bisphenols. This distribution pattern is illustrated in **Figure 1**.

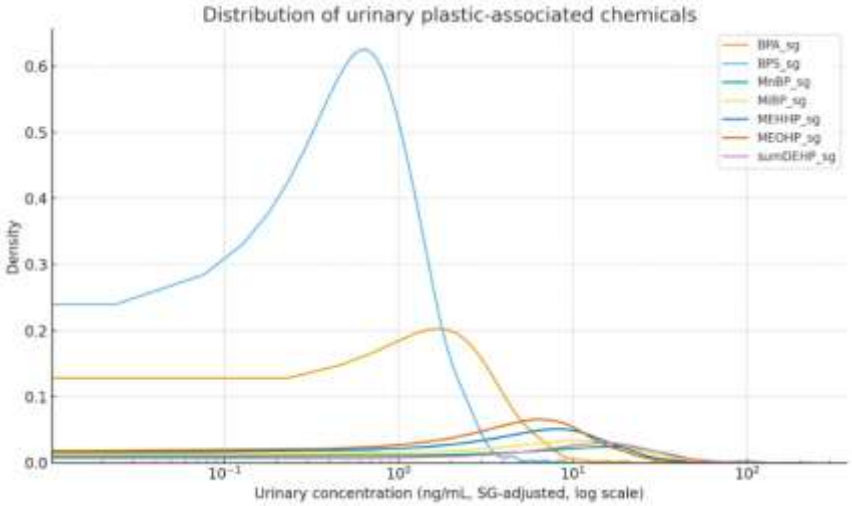

Figure 1: Distribution curves of urinary PACs (SG-adjusted, log-scale).

3.3 ASSOCIATIONS WITH INSULIN RESISTANCE

The primary regression analysis demonstrated that higher urinary ∑DEHP concentrations were positively associated with insulin resistance. A one-unit increase in the natural log of SG-adjusted ∑DEHP was associated with a 0.42-unit increase in HOMA-IR (95% CI: 0.18–0.66, p = 0.001), adjusted for age, sex, BMI, and smoking. The positive exposure–response relationship between ∑DEHP and HOMA-IR is further visualized in **Figure 2**, which shows scatter points with an overlaid regression line.

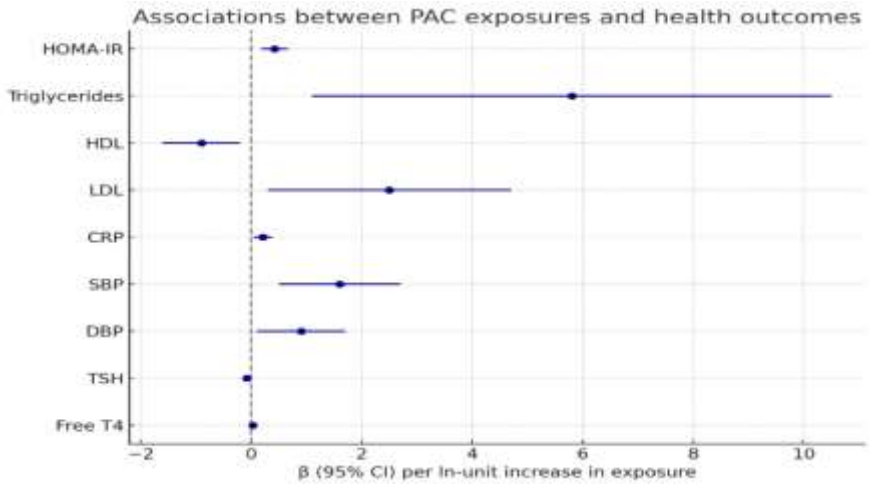

Figure 2: Scatter plot showing the association between ln(∑DEHP) and HOMA-IR.

3.4 ASSOCIATIONS WITH LIPID PROFILES

In secondary analyses, ln-transformed ∑DEHP was positively associated with triglyceride levels (β = 5.8 mg/dL per ln-unit; 95% CI: 1.1–10.5, p = 0.015) and LDL cholesterol (β = 2.5 mg/dL; 95% CI: 0.3–4.7, p = 0.026), while an inverse association was observed with HDL cholesterol (β = −0.9 mg/dL; 95% CI: −1.6 to −0.2, p = 0.012). These associations are presented in **Table 6**.

Table 6: Associations between ln(∑DEHP) and lipid outcomes (adjusted linear regression)

Outcome	β Coefficient	95% CI	p-value
Triglycerides (mg/dL)	+5.8	1.1 to 10.5	0.015
HDL cholesterol (mg/dL)	−0.9	−1.6 to −0.2	0.012
LDL cholesterol (mg/dL)	+2.5	0.3 to 4.7	0.026

3.5 ASSOCIATIONS WITH INFLAMMATORY AND CARDIOVASCULAR OUTCOMES

Higher ∑DEHP levels were associated with elevated systemic inflammation. Specifically, each ln-unit increase in ∑DEHP corresponded to a 0.21 mg/L increase in CRP (95% CI: 0.05–0.38, p = 0.011). In cardiovascular outcomes, systolic blood pressure increased by 1.6 mmHg (95% CI: 0.5–2.7, p = 0.004) and diastolic blood pressure increased by 0.9 mmHg (95% CI: 0.1–1.7, p = 0.032) per ln-unit increase in ∑DEHP.

3.6 ASSOCIATIONS WITH THYROID FUNCTION

Analyses of BPA demonstrated endocrine-disrupting effects on thyroid function. A one-unit increase in ln (BPA) was associated with a reduction of 0.08 μIU/mL in TSH (95% CI: −0.14 to −0.02, p = 0.008) and a simultaneous increase of 0.03 ng/dL in free T4 (95% CI: 0.01–0.05, p = 0.014).

3.7 SUMMARY OF KEY ASSOCIATIONS

The overall associations between PAC exposures and health outcomes are summarized in **Table 7**, while a graphical summary of the regression coefficients with 95% confidence intervals is provided in **Figure 3**.

Table 7: Summary of Associations Between PAC Exposures and Health Outcomes (Adjusted Regression Models)

Exposure (ln-unit)	Outcome	β (95% CI)	p-value
∑DEHP	HOMA-IR	+0.42 (0.18 to 0.66)	0.001
∑DEHP	Triglycerides	+5.8 (1.1 to 10.5)	0.015
∑DEHP	HDL cholesterol	−0.9 (−1.6 to −0.2)	0.012
∑DEHP	LDL cholesterol	+2.5 (0.3 to 4.7)	0.026
∑DEHP	CRP	+0.21 (0.05 to 0.38)	0.011
∑DEHP	SBP	+1.6 (0.5 to 2.7)	0.004
∑DEHP	DBP	+0.9 (0.1 to 1.7)	0.032
BPA	TSH	−0.08 (−0.14 to −0.02)	0.008

BPA	Free T4	+0.03 (0.01 to 0.05)	0.014

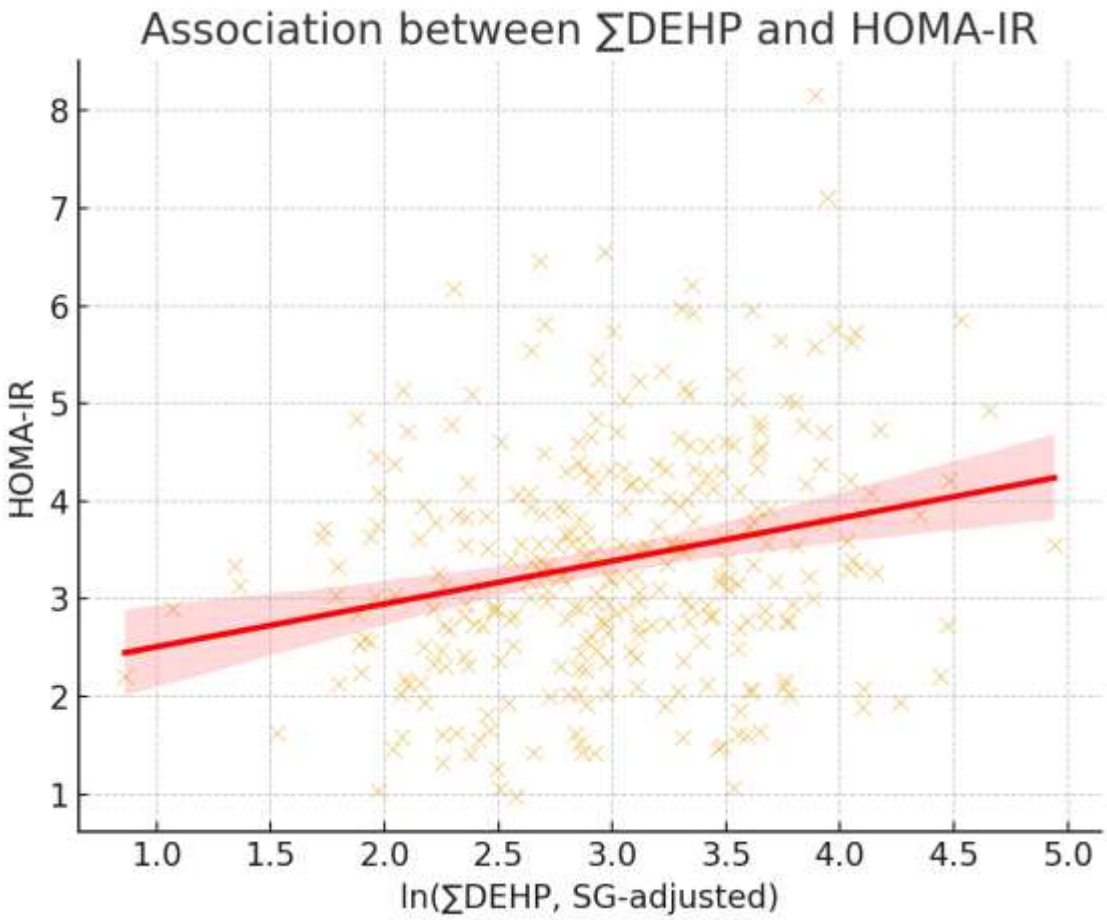

Figure 3: Forest plot showing adjusted regression estimates (β with 95% CI) for associations between PAC exposures and health outcomes.

3.8 SENSITIVITY ANALYSES

The results were robust across sensitivity analyses. Associations observed with specific gravity–adjusted concentrations were consistent when creatinine-corrected concentrations were used. Excluding participants with extreme urine dilutions (SG < 1.010 or > 1.030) did not alter effect estimates. No significant sex–exposure interactions were detected, indicating that associations were similar across men and women.

4. DISCUSSION

This study identified numerous plastic-associated chemicals present in the majority of participants and revealed consistent exposure-response relationships that individual chemicals had with the endpoints in health indicators. Higher levels of DEHP metabolites were related to differences in increased insulin resistance and worsened lipid profiles, as well as increased systemic inflammation and higher blood pressure. Conversely, BPA also influenced thyroid function; TSH levels decreased, and free T4 levels increased. Overall, these findings meet the research goals regarding detectable human biomonitoring exposure and statistically significant relationships with metabolic, cardiovascular, inflammatory, and endocrine outcomes.

Within-outcome internal consistency suggests that disruption of physiological regulation involving plastic-associated chemicals is multifaceted. Associations between insulin resistance and dyslipidemia indicate that more than isolated

biomarker changes were associated with early metabolic perturbation. The positive association between markers of inflammation and blood pressure suggests a commonality with systemic processes that could link metabolic insults to cardiovascular burden. The thyroid pattern related to BPA was consistent with population-relevant levels of endocrine activity. Causality cannot be inferred from a cross-sectional design; however, the wide range and internal consistency of relatedness support that these exposures are clinically relevant correlates of cardiometabolic and endocrine health.

The direction of association between phthalates and insulin resistance is consistent with previous reviews; one earlier review summarized that multiple phthalate metabolites are associated with insulin-resistance phenotypes at all ages (Gao et al., 2022). This finding is consistent with population studies that have found low levels of HDL and high levels of triglycerides associated with DEHP metabolites, indicating a dyslipidemic profile (Zhu et al., 2023). The presence of inflammatory cues is in line with reviews showing positive relationships between phenolic exposure and pro-inflammatory markers, such as CRP (Peinado et al., 2023). Third, the thyroid structure corroborates the evidence that BPA is inversely related to T3/TSH and may be positively related to free thyroid hormones in adults (Pei et al., 2025).

More generally, umbrella evidence suggests that chemical classes of compounds associated with plastics are associated with adverse health outcomes in several health domains, placing these findings in the context of broader human health (Symeonides et al., 2024). Operationally, co-exposure assessment of bisphenols and phthalate metabolites by current sensitive LC/UPLC-MS/MS systems offers the potential to enable translatable human biomonitoring and risk sharing in clinical or public health domains (Wang et al., 2024). The exposome view is a reminder that exposure patterns are different across regions and age and that multi-exposure modelling provides valuable information for estimating chronic disease risk. This brief commentary illustrates the importance of the mixture-aware frame in interpreting a composite variable like ∑DEHP (You et al., 2024).

Strengths include predefined analysis plans, dual dilution corrections, and inclusion of multiple domains of outcomes. However, single-time urine sampling can misclassify short-half-life exposures, even accounting for correction procedures. However, real-world evidence suggests that it persists even after correction for creatinine and specific gravity to improve comparability with timed collections, which is not universally better across settings (Hsieh et al., 2019). Substitution of values below detection simplifies the analysis but can be biased in heavily censored data; methodological reviews suggest that simple substitutions may work well with moderate no detection, and are more sophisticated (which do not overestimate replacement values) in more challenging contexts (Hwang et al., 2023). Cross-sectional conclusions, the risk of residual confounding, and population-specific effects preclude causal inference and generalization.

Under scenarios of repeated biospecimen collection, standardized dilution, and censoring, prospective designs are required to characterize temporality and minimize exposure misclassification. Pivoting toward mixture-focused analytics and exposome-wide investigations may be favored to account for patterns of correlated burdens and effect modification across subpopulations, while triangulating with cardiovascular co-exposures like tobacco smoke to situate hypertension observations (Zhang et al., 2021). The integration of high-resolution mass spectrometry with clinical phenotyping might clarify interrelated pathways connecting metabolic, inflammatory, cardiovascular, and endocrine outcomes. In summary, this study contributes consistent human biomonitoring data indicating the presence of ubiquitous plastic-associated compounds at the population level and their linkage with adverse patterns in core health outcomes.

5. CONCLUSION

This study found several plastic-associated chemicals in the majority of participants and found that higher internal exposure, particularly to DEHP metabolites, was associated with increased insulin resistance, unfavorable lipid profile, increased systemic inflammation, and elevated blood pressure, whereas bisphenol A was associated with altered thyroid function. These findings validate the hypothesis that common exposures detected by LC-MS/MS are statistically associated with several important metabolic, cardiovascular, inflammatory, and

endocrine markers and promote the use of biomonitoring as a feasible tool for population risk assessment and surveillance. Nevertheless, there are significant knowledge gaps related to the timing of this, the mixture interaction, and the potential exposure threshold. Future studies should use longitudinal data with repeat biospecimens, mixture-aware models (weighted quantile sum or quantile g-computation) integrated with causal inference, and should ensure standardization of urine dilution correction and treatment of non-detects; broader coverage with high-resolution mass spectrometry and sampling of more diverse populations would improve generalizability and mechanistic insight. Limitations of the study include the cross-sectional nature of the study, measures from a single spot urine sample, remaining confounding, regional representativeness, and substitution for nondetects, which may have implications for generalizability. Collectively, these results offer a consistent framework for the development of focused exposure reduction measures in the context of cardiometabolic prevention.

6. AUTHORS CONTRIBUTION

All authors contributed equally

7. FUNDING

Not applicable

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