Salud, Ciencia y Tecnología. 2026; 6:2555
doi: 10.56294/saludcyt20262555

ORIGINAL

Elevated Urinary 3-OH-BaP Levels and CYP1A1 Enzyme Activity in Pediatric Acute Lymphoblastic Leukemia: A Case-Control Study in a High-Pollution Region

Niveles elevados de 3-OH-BaP en la orina y actividad de la enzima CYP1A1 en la leucemia linfoblástica aguda pediátrica: un estudio de casos y controles en una región de alta contaminación

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Cite as: Siagian LR, Handono K, Sujuti H, Ponco AY. Elevated Urinary 3-OH-BaP Levels and CYP1A1 Enzyme Activity in Pediatric Acute Lymphoblastic Leukemia: A Case-Control Study in a High-Pollution Region. Salud, Ciencia y Tecnología. 2026; 6:2555. https://doi.org/10.56294/saludcyt20262555

Submitted: 18-08-2025 **Revised:** 21-10-2025 **Accepted:** 27-11-2025 **Published:** 01-01-2026

Editor: Prof. Dr. William Castillo-González

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ABSTRACT

Introduction: pollutants related to acute lymphoblastic leukemia (ALL) include polycyclic aromatic hydrocarbons (PAHs), such as the carcinogenic benzo[a]pyrene (BaP). Urinary 3-hydroxybenzo[a]pyrene (3-OH-BaP) is a key biomarker for BaP exposure. Benzo[a]pyrene-7,8-dihydrodiol-9,10-epoxide (BPDE-dG), the ultimate metabolite of BaP, correlates with CYP1A1 activity. However, the correlation with urinary 3-OH-BaP remains unexplored in ALL. Exploring the relationship between urinary 3-OH-BaP and CYP1A1 enzyme levels in ALL patients, the present study makes a valuable contribution to global research, addressing the lack of non-Western data on urinary PAH biomarkers in pediatric ALL.
Method: this was a case-control study including 68 subjects (33 patients and 35 healthy controls). Urine was collected for 3-OH-BaP detection via HPLC, and isolate of peripheral blood mononuclear cell (PBMC) for CYP1A1 enzyme levels via an ELISA kit.
Results: mean urinary 3-OH-BaP levels were 623 ± 463 ng/mL in ALL cases vs. 286 ± 155 ng/mL in controls ($p = 0,000$). Mean CYP1A1 levels were 0,4817 ± 0,17 ng/mL in ALL cases vs. 0,3018 ± 0,03 ng/mL in controls ($p = 0,000$). A positive correlation was found between urinary 3-OH-BaP and PBMC CYP1A1 levels ($r = 0,417$, $p < 0,001$).
Conclusions: the association between elevated urinary 3-OH-BaP and PBMC CYP1A1 levels in ALL patients compared to healthy controls suggests a role of CYP1A1 in BaP detoxification during carcinogenesis in pollution-exposed children.

Keywords: Urinary 3-OH-BaP; CYP1A1; Acute Lymphoblastic; Leukemia.

RESUMEN

Introducción: los contaminantes relacionados con la leucemia linfoblástica aguda (LLA) incluyen hidrocarburos aromáticos policíclicos (HAP), como el cancerígeno benzo[a]pireno (BaP). El 3-hidroxibenzo[a]pireno urinario (3-OH-BaP) es un biomarcador clave para la exposición a BaP. El benzo[a]pireno-7,8-dihidrodiol-9,10-epóxido (BPDE-dG), el metabolito final de BaP, se correlaciona con la actividad de CYP1A1. Sin embargo, la correlación con el 3-OH-BaP urinario sigue sin explorarse en la LLA. Al explorar la relación entre los niveles urinarios de 3-OH-BaP y la enzima CYP1A1 en pacientes con LLA, el presente estudio hace una valiosa contribución

a la investigación global, abordando la falta de datos no occidentales sobre los biomarcadores de HAP urinaria en la LLA pediátrica.
Método: estudio de casos y controles que incluyó a 68 sujetos (33 pacientes y 35 controles sanos). Se recolectó orina para la detección de 3-OH-BaP a través de HPLC y se aisló de células mononucleares de sangre periférica (PBMC) para los niveles de enzima CYP1A1 a través de un kit ELISA.
Resultados: los niveles urinarios medios de 3-OH-BaP fueron de 623 ± 463 ng/mL en los casos de LLA vs. 286 ± 155 ng/mL en los controles (p = 0,000). Los niveles medios de CYP1A1 fueron de 0,4817 ± 0,17 ng/ml en los casos de LLA frente a 0,3018 ± 0,03 ng/ml en los controles (p = 0,000). Se encontró una correlación positiva entre los niveles urinarios de 3-OH-BaP y PBMC CYP1A1 (r = 0,417, p < 0,001).
Conclusiones: la asociación entre los niveles elevados de 3-OH-BaP en la orina y PBMC CYP1A1 en pacientes con LLA en comparación con controles sanos sugiere un papel de CYP1A1 en la desintoxicación de BaP durante la carcinogénesis en niños expuestos a la contaminación.

Palabras clave: 3-OH-BaP Urinario; CYP1A1; Linfoblástico Agudo; Leucemia.

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a hematological malignancy characterized by uncontrolled proliferation of immature lymphoid progenitors in the bone marrow.[1] Exposure to air pollutants like polycyclic aromatic hydrocarbons (PAHs) is an established risk factor for childhood ALL.[2] Benzo[a]pyrene (BaP), a prototypical PAH classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC), has been linked to childhood leukemia via residential exposure sources.[3] In addition to ALL, PAHs, along with 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), are carcinogenic materials with significant potential as risk factors for lung cancer.[3] Urinary metabolites like 3-hydroxybenzo[a]pyrene (3-OH-BaP) serve as sensitive biomarkers for BaP exposure and detoxification,[4,5] providing a non-invasive, integrated measure of recent exposure. However, they remain underexplored in pediatric ALL cohorts in highly industrialized areas.

Studies on the relationship between exposure to air pollutants and childhood leukemia have been widely conducted. A positive relationship was identified between PAH in house vacuum dust and the risk of ALL, as indicated by an increase in serum BaP concentrations.[3,6] Significant differences in serum PAH concentrations have been found between patients with leukemia and healthy controls[7,8] and the same study suggested the detection of carcinogenic substances in urine. Studies have shown that some organic carcinogens are present in urine but, to date, there has been no study on the carcinogenic substances excreted in the urine in ALL cases.

CYP1A1 metabolizes BaP in the human body. The CYP1A1 and AHRR genes play a major role in coding proteins involved in the detoxification of tobacco cigarette components containing PAHs.[9,10] Studies indicate that the CYP1A1 gene is a risk factor for ALL.[11] PAH-mediated DNA hypermethylation in the CYP1A1 promoter can downregulate enzyme expression in smokers,[12] but in pollution-exposed children, chronic low-dose exposure may induce compensatory upregulation, as observed in ALL[11,13] Hypermethylation in the promoter region of CYP1A1 is a major epigenetic mechanism that downregulates AhR activity in hematological malignancies such as ALL.[14,15] This downregulation leads to a decrease in CYP1A1 enzyme synthesis, resulting in an increase in 3-OH-BaP metabolites in the urine.

Benzo[a]pyrene-7,8-dihydrodiol-9,10-epoxide DNA adducts (BPDE-dG), as the final metabolite of BaP, have been correlated with CYP1A1 enzyme activity, but whether the level of urinary 3-OH-BaP correlates with CYP1A1 enzyme levels is still unknown.[16,17] This study fills a critical gap by examining urinary 3-OH-BaP-CYP1A1 correlations in Indonesian pediatric ALL cases from an oil-rich region, where ambient PAH levels exceed WHO limits. It aimed to determine the differences in urinary 3-OH-BaP and CYP1A1 enzyme levels between ALL subjects and healthy control subjects, as well as the correlation between urinary 3-OH-BaP levels and CYP1A1 enzyme levels.

METHOD

Research Sample. This was a case-control study. The study participants consisted of 68 subjects, comprising 33 patients from Kanujoso Djatiwibowo Hospital in Balikpapan and 35 healthy controls. The case subjects were children newly diagnosed with ALL aged <17 years and excluded if the patient was relaps. The control subjects were clinically healthy, with complete blood count results within normal limits. Controls were frequency-matched to cases by age (±2 years) and sex to minimize confounding. Sample size for Spearman correlation was calculated using G*Power software (v3.1). Assuming r = 0,4, α = 0,05, and power = 0,80, the minimum sample size was n = 60, and 68 subjects were recruited to account for 10 % dropout. Urine and blood specimens were taken from all subjects to determine the levels of 3 OH BaP and the CyP1A1 enzyme. Approval for the

study was obtained from the Health Research Ethics Committee of RSUD AW Sjahranie 09/KEPK/AWS/II/2023. The study period was from March 2023 to July 2024. The participants who agreed to participate in the study provided informed consent and completed a validated 20-item questionnaire that assessed proxy exposures (e.g., household smoking, proximity to industry, outdoor play hours), adapted from the California Childhood Leukemia Study.[3]

Detection of Urinary 3-OH-BaP and CYP1A1 Enzyme Levels

3-OH-BaP Analysis. A urine sample (20 mL) was obtained from each subject for the detection of 3-OH-BaP. Isolation of 3-OH-BaP from urine was conducted at the East Kalimantan Provincial Health Laboratory in Samarinda, and detection was performed at the Pharmacology Laboratory of the Faculty of Medicine, Universitas Brawijaya, Malang. The method for detecting 3-OH-BaP concentration was adapted from Barbeau[18] and modified for linearity. Urine samples were stored at −20 °C before processing. Storage stability was confirmed at −20 °C for 6 months (<5 % degradation). Urine (10 mL) was added to pH 4,6 buffer solution (10 mL) containing ß-glucuronidase enzyme (GLPBIOR, 20 µL) and the solution was incubated for 2 h at 37 °C. The mixture was then centrifuged at 4000 rpm for 10 min at 4 °C and the supernatant was separated. Solid phase extraction (SPE) was carried out using Bond Elut C18 cartridges (Agilent, 500 mg, 6 mL), first washing the tip of the needle and the outside of the tube with 2 mL of methanol. The SPE process comprised the following stages: a) SPE conditioning stage, adding 5 mL of methanol and 10 mL of methanol/water solution (1:1 v/v) at a flow rate of 5 mL/min; b) urine supernatant addition (15 mL) at a flow rate of 10 mL/min; c) SPE washing stage, adding 10 mL of methanol/water solution (1:1 v/v) at a rate of 10 mL/min; and d) elution stage, with 5 mL of methanol. To prepare the analytical sample, the methanolic fraction was evaporated in an automatic evaporator at 50 °C for 120 min. The obtained dry residue was dissolved in methanol (500 µL) and ultrasonicated for 5 min. The residue in methanol was dissolved in water at a dilution of 1:1 (v/v) to match the mobile phase for compatibility. The sample (20 µL) was injected into the chromatography system (SHIMPACK VP-ODS HPLC device) fitted with a C18 250 x 4,6 mm analytical column (Shimadzu) and a fluorescence detector at a wavelength of $\lambda ex/\lambda em$ = 380/430 nm, eluting with methanol/water (1:1, v/v; 1–5 min), followed by a linear gradient to 100 % methanol (5–25 min), and finally at 100 % methanol (5 min). The flow rate used was 1 mL/min, the column temperature was 40 °C, and the run time was 30 min.[11] The method was validated with the following characteristics: LOD = 0,5 ng/mL; LOQ = 1,5 ng/mL; linearity R2. > 0,99 (5–1000 ng/mL); intra/inter- assay CV < 10 %.

CYP1A1 Enzyme Analysis. Peripheral blood (3 mL, EDTA) was obtained from each subject for the detection of CYP1A1 enzyme levels. Isolation of peripheral blood mononuclear cells (PBMCs) from the blood samples was conducted at the Clinical Pathology Laboratory of Abdul Wahab Sjahranie Hospital (Samarinda), and CYP1A1 enzyme levels were determined at the Biomedical Laboratory of the Faculty of Medicine, Universitas Brawijaya (Malang). CYP1A1 enzyme levels were examined in PBMC isolated from EDTA blood specimens using the Ficoll-Hypaque solution. After PBMC cell isolation, the PBMC cell protein was extracted using Protease Inhibitor Cocktail (PIC) at a ratio of 1:100 with the suspension solution. Protein levels were normalized to 50 µg/mL total protein (BCA assay) to measure CYP1A1 protein concentration (intra/inter-CV < 8 %; range 0,1–10 ng/mL). The supernatant (200 µL) was examined for enzyme levels using the Human Cytochrome P450 1A1 CYP1A1 ELISA Kit (Bioassay Technology Laboratory, Shanghai, China).

Statistical Analysis. Descriptive data were analyzed using univariate statistics. For differences, the Mann-Whitney test was used, and Spearman's test was used for correlation. Bonferroni correction was applied for multiple comparisons (α = 0,025). Analyses were carried out in SPSS v27.

RESULTS

Sample Description. The study included 68 subjects (33 patients and 35 healthy controls), and the participant characteristics are listed in table 1. The case group had more male than female subjects, while the control group had more female subjects. Most of the subjects in the case study were in the age range 0–5 years (51,5 %) and 5–12 years (36,4 %), with a fairly large percentage in the age range 12–17 years (12,1 %). In contrast, the age range predominant in the control group was 5–12 years (97,1 %). Regarding vehicles, both case and control subjects mostly used motorcycles (42,4 % and 60 %, respectively) to go to school or outside the home. The duration of playing outside the home averaged 1–3 hours in both case and control groups (87,9 % and 60 %, respectively). Most subjects did not consume grilled food regularly. The distance from home to school was 1–3 km (42,9 %) for the control subjects, but a significant proportion of case subjects (42,4 %) were not yet of school age. Among the case subjects, 48,5 % had homes close to factories or mines, while 51,5 % were distant from these industries. In the control group, 100 % of the participants lived distant from these industries. Most case and control subjects lived with active smokers at home (69,7 % and 62,9 %, respectively). No significant differences were identified in matching variables (p > 0,05), but case subjects had a significantly higher proximity to industry than controls (p = 0,02; chi-square).

Table 1. Characteristics of ALL cases and healthy control study participants

		ALL cases (n = 33) (%)	Healthy controls (n = 35) (%)
Sex	Male	21 (63,6)	16 (45,7)
	Female	12 (36,4)	19 (54,3)
Age (years)	0–5	17 (51,5)	1 (2,9)
	5–12	12 (36,4)	34 (97,1)
	12-17	4 (12,1)	0 (0)
School transportation			
	Car	1 (3,1)	4 (11,4)
	Motorcycle	14 (42,4)	21 (60)
	Bicycle	0 (0)	3 (8,6)
	Walking	4 (12,1)	6 (17,1)
	Not yet in school	14 (42,2)	1 (2,9)
Transportation			
	Car	12 (36,4)	6 (17,1)
	Motorcycle	19 (57,6)	24 (68,6)
	Bicycle	1 (3,0)	2 (5,7)
	Walking	1 (3,0)	3 (8,6)
Duration of play outdoors per day			
	< 1 h	0 (0)	3 (8,6)
	1-3 h	29 (87,9)	21(60,0)
	> 3 h	4 (12,1)	2 (5,7)
	0 h	0 (0)	9 (25,7)
Consumption of grilled food (min 5x/week)			
	Yes	6 (18,2)	5 (14,3)
	No	27 (81,8)	30 (85,7)
Distance from home to school (km)			
	< 1	2 (6,1)	15 (42,9)
	1–3	10 (30,3)	15 (42,9)
	> 3	7 (21,2)	4 (11,4)
	Not yet in school	14 (42,4)	1 (2,8)
Distance from factories/mining to the domicile (km)			
	3	4 (12,1)	0 (0)
	> 3	12 (36,4)	0 (0)
	No industry	17 (51,5)	35 (100)
Active smokers in the house			
Yes		23 (69,7)	22 (62,9)
No		10 (30,3)	13 (37,1)
Average smokers per household		1	1

ALL = Acute Lymphoblastic Leukemia

Validation of Urinary 3-OH-BaP Levels. Using the modified Wang(19) analytical HPLC method, a standard solution of 3-OH-BaP was detected at 13,795 s. The standard solution of 3-OH-BaP at a concentration of 40 ppb exhibited a peak at 13,901 s (figure 1A). A blank urine sample (figure 1B) and urine samples spiked with 3-OH-BaP at concentrations of 11,090 and 21,060 ng/L (figures 1C and 1D) showed 3-OH-BaP peaks at retention times of 13,711, 13,759, and 13,688 s, respectively, corresponding to increasing concentrations of 3-OH-BaP. These results indicate that 3-OH-BaP was consistently detected at approximately 13,795 s, and that the peak height increased with higher standard concentrations.

Urinary 3-OH-BaP Levels. The mean levels of 3-OH-BaP in urine for the case subjects were 623 ± 463 ng/mL, while in the healthy control subjects, the mean levels were 286 ± 155 ng/mL (figure 2A), with median 3-OH-BaP levels of 550 and 280 ng/mL for case subjects and controls, respectively (IQR 400–800 vs. 200–350). There was a significant difference in 3-OH-BaP urinary levels between ALL patients and healthy control subjects (p = 0,000) (figure 2B).

CYP1A1 Enzyme Levels. The mean CYP1A1 enzyme levels in the case and control subjects were 0,4817 ± 0,17 and 0,3018 ± 0,03 ng/mL, respectively (figure 3A), with median CYP1A1 levels of 0,48 and 0,30 ng/mL. There was a significant difference in CYP1A1 enzyme levels between ALL patients and healthy control subjects (p = 0,000) (figure 3B).

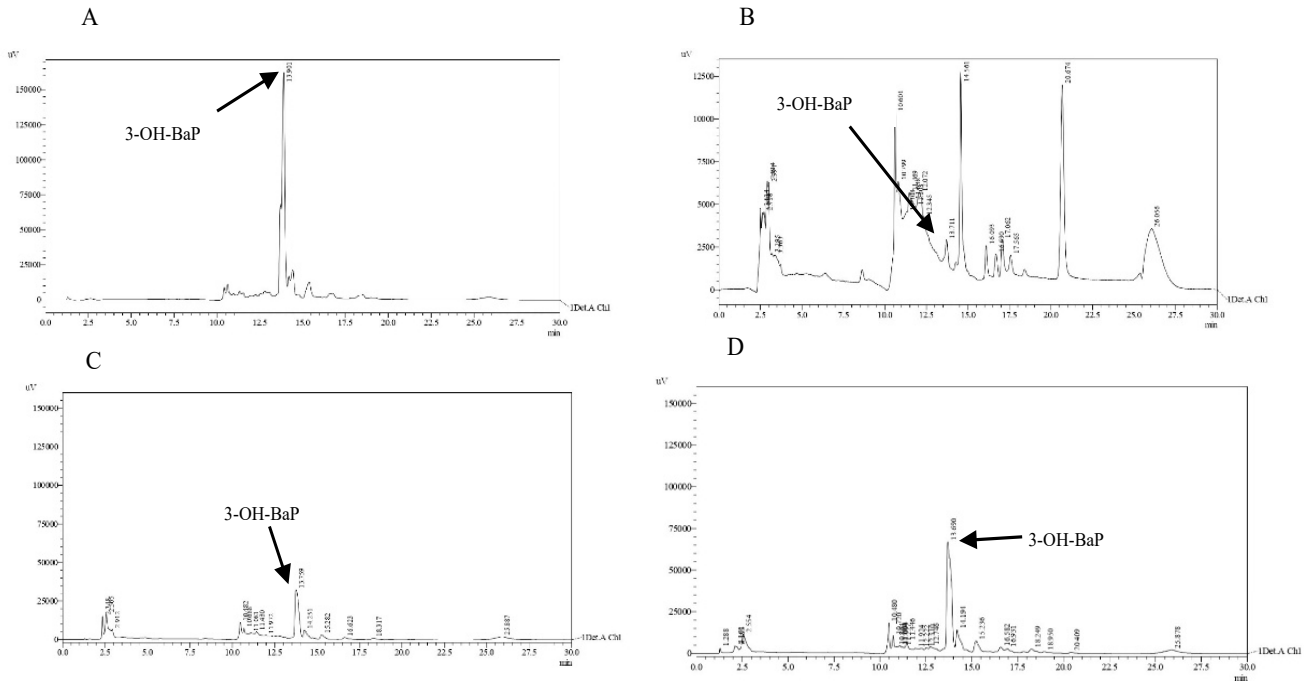

Figure 1. HPLC chromatograms with fluorescence detection of 3-OH-BaP: (A) standard 3-OH-BaP; (B) blank urine sample; (C) urine spiked with 3-OH-BaP (11,090 ng/L); (D) urine spiked with 3-OH-BaP (21,060 ng/L)

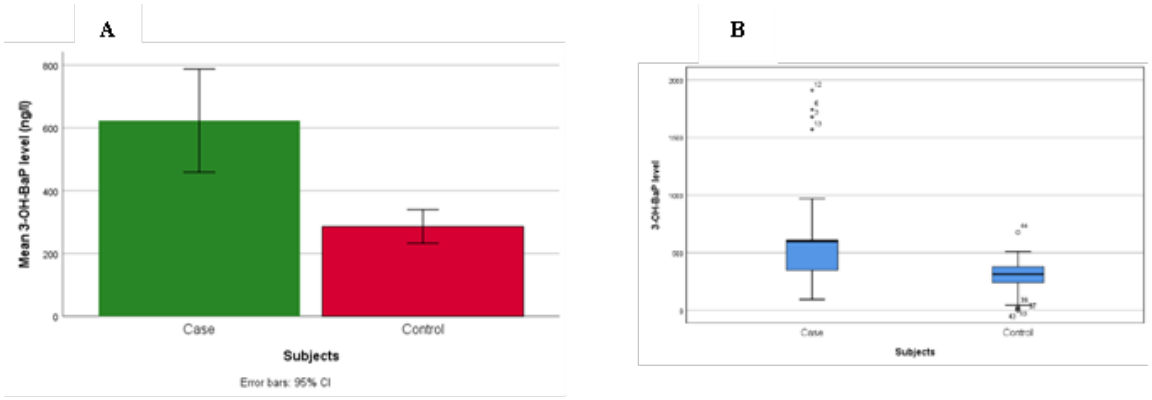

Figure 2. Urinary 3-OH-BaP levels in ALL cases and healthy control subjects: (A) mean and (B) difference, showing significance in the variable with p = 0,000

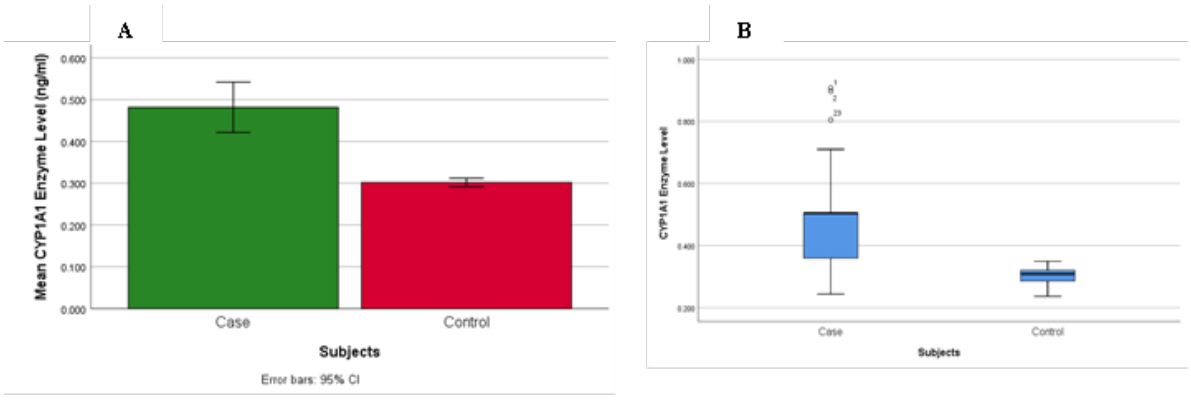

Figure 3. CYP1A1 enzyme levels in ALL cases and healthy control subjects: (A) mean and (B) difference, showing significance in the variable with p = 0,000

Correlation of Urinary 3-OH-BaP and CYP1A1 Enzyme Levels. There was a correlation between urine 3-OH-BaP and CYP1A1 enzyme levels (r = 0,417; p = 0,000). The scatterplot in figure 4 shows a linear fit (R2 = 0,174) and no influential outliers (Cook's D < 1).

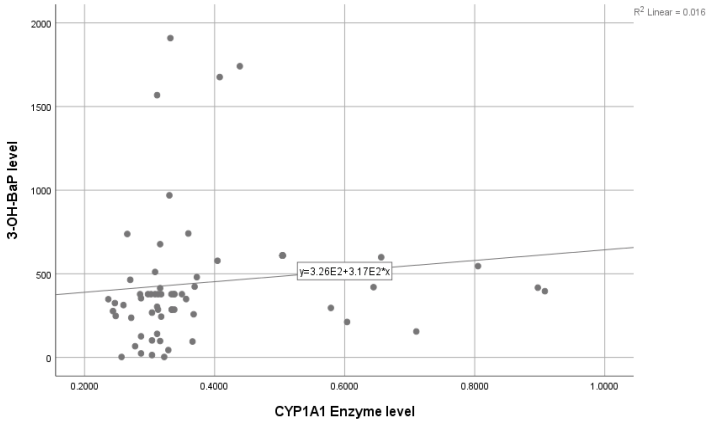

Figure 4. Correlation between urinary levels of 3-OH-BaP and CYP1A1 enzyme levels in PBMC (r = 0,417, p = 0,000)

DISCUSSION

Benzo[a]pyrene (BaP) is a carcinogenic and mutagenic polycyclic aromatic hydrocarbon (PAH) listed as a human carcinogen. Phase I metabolism of BaP by CYP1A1 leads to the generation of reactive intermediates such as BPDE, which subsequently form DNA adducts that can promote leukemogenesis.[19] Such DNA adducts may promote replication errors, modified promoter methylation, and altered transcription factor binding. These transient disruptions may lead, in turn, to cellular toxicity and transformation.[20] BPDE metabolites are mainly eliminated in feces, with a smaller fraction in urine as 3-hydroxybenzo[a]pyrene (3-OH-BaP). This urinary metabolite is considered a surrogate marker of carcinogenic PAH exposure. 3-OH-BaP in urine has been found to correlate strongly with adduct formation in human DNA marime.[21,22,23] and is therefore a potentially relevant biomarker for internal exposure and metabolic activation in humans.[24,25] Urinary levels of 3-OH-BaP are generally 2–4-fold lower than those of 1-hydroxypyrene (1-OHP). This is not only due to the relatively small proportion of BaP that is metabolized into urinary metabolites but also to the complex metabolic pathways of BaP.[25] Despite its low abundance, 3-OH-BaP serves as a useful biomarker reflecting the detoxification pathway of BaP metabolism.[26,27] A correlation has been established between urinary 3-OH-BaP levels and atmospheric BaP concentrations, supporting its relevance in environmental exposure assessment.[28] Our elevated 3-OH-BaP (623 ng/mL) aligns with high ambient PAH in industrial areas (> 2x non-exposed), though is lower than that in smokers due to pediatric non-tobacco exposure.

Further evidence has linked BaP exposure to health outcomes, particularly in vulnerable populations. Calderon-Hernandez[29,30] observed a positive association between increased BaP levels and the risk of acute lymphoblastic leukemia (ALL), whereas[7] found significantly higher serum PAH concentra tions in leukemia patients than in healthy controls. This condition is consistent with recent global burden data.[3,31] In the present study, urinary 3-OH-BaP concentrations were significantly elevated in patients with ALL compared to healthy controls, indicating increased BaP exposure in affected individuals. As the primary monohydroxyl metabolite of BaP, urinary 3-OH-BaP is a reliable indicator of BaP exposure in humans.[4]

Studies have demonstrated the formation of its carcinogenic intermediates. The CYP1 enzyme family, particularly CYP1A1 and CYP1B1, is highly expressed in lymphoid and myeloblastic cell lines, suggesting its potential role in hematopoietic carcinogenesis.[32,33] It has also been proven that DNA methylation of the CYP1A1 that CYP1A1 is essential for the detoxification of orally administered benzo[a]pyrene (BaP). In contrast, a reciprocal role has been reported between CYP1A1 and CYP1A2 in lung cancer: while CYP1A1 is involved in the activation of PAHs, CYP1A2 contributes to their detoxification.[20] CYP1A1 is recognized for its high bioactivation capacity toward environmental toxins, particularly PAHs, and serves as a key enzyme in converting these compounds into carcinogenic metabolites. Therefore, CYP1A1 is considered a potential biomarker for exposure to environmental carcinogens.[14,34] Supporting this, CYP1A1 is a central enzyme in both the formation and reduction of (±)-anti-benzo[a]pyrene-7,8-diol-9,10-epoxide (BPDE), the key carcinogenic intermediate of BaP.[35] In pollution-exposed neonates, CYP1A1 upregulation (3-fold) mirrors our findings.[36] These findings highlight the prenatal health risks associated with outdoor air pollution and underscore the importance of preventive measures to protect pregnant women and their infants. In the present study, CYP1A1 enzyme levels in peripheral blood mononuclear cells (PBMCs) were significantly higher in patients with acute lymphoblastic leukemia (ALL) compared to healthy controls.[37,38] This finding supports the role of CYP1A1 as a key enzyme

involved in tumorigenesis triggered by environmental carcinogens. Increased exposure to pollutants like BaP can induce CYP1A1 expression, which in turn enhances BaP metabolism and gene, mediated by PAH metabolism, is influenced by smoking.[22,39] In contrast, another study found that Wnt Inhibitory Factor 1 (WIF1) DNA methylation from the buffy coat could not be used as a nasopharyngeal carcinoma (NPC) marker or as a smoking behavior marker.[40] No association was found between smoking behavior and RASSF1A and CDKN2A methylation in NPC.[41] Methylation of CYP1B1 was associated with worse overall survival (OS) and disease-free survival in young adults with ALL and correlated with advanced disease.[32,42]

The correlation between 3-OH-BaP and CYP1A1 activity in response to BaP exposure has been extensively studied. This study found a direct relationship between urinary 3-OH-BaP levels and CYP1A1 enzyme activity in humans, suggesting that 3-OH-BaP is a reliable biomarker for CYP1A1-mediated BaP metabolism.[4,43] Occupational studies support this association. For example, researchers observed significantly lower urinary 3-OH-BaP levels in coking plant workers compared to refractory material plant workers, correlating with differences in CYP1A1 metabolic activity.[44,45] Another study further confirmed the crucial role of CYP1A1, showing that BaP-DNA adduct formation was 7-fold lower in hepatoma rats lacking cytochrome P450 enzymes compared to those expressing it, indicating that BaP activation in liver microsomes depends heavily on CYP1A1.[46,47] Additionally, studies in rats have demonstrated that urinary 3-OH-BaP is a valid indicator of CYP1A1 enzyme activity.[48,49] These findings suggest that individual variations in CYP1A1 activity can lead to differences in BaP metabolism rates, which are reflected in urinary 3-OH-BaP concentrations. Our r value of 0,417 supports CYP1A1 as a mediator, differing from occupational downregulation due to acute versus chronic exposure.[24] CYP1A1 variants increase ALL risk (OR = 1,5) in Asians.[11,50]

There are several limitations in our study. We have not yet linked the influence of cofounding factors such as BaP exposure intensity and liver clearance function in eliminating BaP to our variables. Furthermore, our cross-sectional study design cannot directly identify the relationship between our variables and the mechanism of carcinogenesis. Therefore, we recommend conducting a cohort study in children in areas with high levels of BaP exposure.

CONCLUSIONS

Elevated urinary 3-OH-BaP and serum CYP1A1 levels and their positive correlation suggest enhanced BaP bioactivation in pediatric ALL, highlighting CYP1A1 as a detoxification biomarker in high-pollution settings. Prospective validation with ambient monitoring could inform prevention strategies in vulnerable regions. In this study, the level of the pollutant BaP was not determined. However, urinary 3-OH-BaP can serve as a biochemical marker of exposure to environmental pollutants containing BaP. CYP1A1, an enzyme that metabolizes BaP, plays a significant role in BaP detoxification. CYP1A1 enzyme levels can be used to describe the activity of CYP1A1 in BaP metabolism. In ALL, the correlation between higher levels of urinary 3-OH-BaP and CYP1A1 enzyme indicates a role of the BaP detoxification mechanism by CYP1A1 in the carcinogenesis process.

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FINANCING

No financing.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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