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REPORT

Health Effects of Benzene Exposure among Children Following a Flaring Incident at the British Petroleum Refinery in Texas City

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Human exposure to benzene is associated with multiple adverse health effects leading to hematological malignancies. The objective of this retrospective study was to evaluate the health consequences of benzene exposure in children following a flaring incident at the British petroleum (BP) refinery in the Texas City, Texas. The study included children aged <17 years who had been exposed and unexposed to benzene. Using medical charts, clinical data including white blood cell (WBC) counts, platelets counts, hemoglobin, hematocrit, blood urea nitrogen (BUN), creatinine, alkaline phosphatase (ALP), aspartate amino transferase (AST), alanine amino transferase (ALT), and somatic symptom complaints by the children exposed to benzene were reviewed and analyzed. A total of 312 subjects (benzene exposed, $n = 157$ and unexposed, $n = 155$) were included. Hematologic analysis showed that WBC counts were significantly decreased in benzene-exposed children compared with the unexposed children (6.8 ± 2.1 versus 7.3 ± 1.7, $P = .022$). Conversely, platelet (X 10^3 per μL) counts were increased significantly in the benzene-exposed group compared with the unexposed group (278.4 ± 59.9 versus 261.6 ± 51.7, $P = .005$). Similarly, benzene-exposed children had significantly higher levels of ALP (183.7 ± 95.6 versus 165 ± 70.3 IU/L, $P = .04$), AST (23.6 ± 15.3 versus 20.5 ± 5.5 IU/L, $P = .015$), and ALT (19.2 ± 7.8 versus 16.9 ± 6.9 IU/L, $P = .005$) compared with the unexposed children. Together, the results of the study reveal that children exposed to benzene experienced significantly altered blood profiles, liver enzymes, and somatic symptoms indicating that children exposed to benzene are at a higher risk of developing hepatic or blood related disorders.

Keywords benzene poisoning, blood disorders, chemical exposure, health impact, hematological toxicity, hepatotoxicity, petroleum refinery, urinary metabolites of benzene

INTRODUCTION

Petroleum refining industries are the major source of toxic chemicals such as benzene, toluene, nitric oxides, and carbon monoxide. Human exposure to benzene is associated with multiple adverse health effects; specifically its toxic effects on the blood and bone marrow. Exposure to benzene has been shown to increase the risk

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of developing carcinogenesis, specifically, leukemia, lymphoma, aplastic anemia, pancytopenia, and chromosomal aberrations [1–5]. In addition, benzene exposure can lead to several adverse respiratory effects including pulmonary edema, acute granular tracheitis, laryngitis, bronchitis, and massive hemorrhaging. Moreover, benzene exposure can affect a variety of organs such as the liver, kidney, and brain [6–8]. Thus, communities living near petroleum refineries have significant health risks due to the increased probability of being exposed to benzene.

Several studies have shown that benzene exposure can lead to deleterious health effects not only in adult subjects but also in children [9, 10]. In comparison to adults, children are more sensitive to the deleterious effects of benzene due to their incomplete metabolic systems, immature host defenses, high rates of infection by respiratory pathogens, and activity patterns [10, 11]. A meta-analysis showed that children have a higher susceptibility to environmental chemical exposures including benzene [12]. Although several studies have shown that benzene exposure causes childhood leukemia, its relationship with other lymphocytic malignancies remains unknown. Evidence from in vitro and in vivo studies on benzene metabolism, pharmacokinetics, hematologic toxicity, cytotoxicity, genotoxicity, and carcinogenicity is starting to converge on a small set of overlapping hypotheses about the most probable biological mechanisms of benzene carcinogenicity [13]. The generation of free radicals leading to oxidative stress, immune system dysfunction, and decreased immune surveillance have been described as the possible mechanisms underlying benzene-induced toxicity [2]. The toxic effects of benzene are thought to arise from its metabolites such as benzoquinone, phenol, hydroquinone, and catechol [14].

Recently, a flaring incident at the BP refinery facility led to the release of a massive amount of toxic chemicals into the skies of Texas City, Texas [15, 16]. The release of toxic chemicals from the BP refinery began on April 6 in 2010 and lasted 40 days until May 16, 2010. It is estimated that more than 500,000 pounds of toxic chemicals, including over 17,000 pounds of benzene were released into the air while BP was fixing the problem [15–17]. This flaring incident contaminated the air surrounding the refinery [16, 18] and threatened the residents of Texas City and the surrounding communities. The Galveston County District Clerk's Office estimated that over 50,000 people were affected as a result of the BP refinery flaring incident.

The purpose of this study was to investigate the health consequences of benzene exposure in children following a flaring incident at the BP's refinery in Texas City, Texas. Specifically, the clinical outcomes of children exposed to benzene were evaluated and compared with children who were not exposed to benzene.

MATERIALS AND METHODS

Subjects

This retrospective study was approved by the Institutional Review Board (IRB). Using medical charts, demographic and clinical data were reviewed for the pediatric subjects (<17 years) who underwent clinical and laboratory evaluation between June 2010 and October 2012.

Children exposed to benzene were referred to the clinic for medical evaluation by their legal representatives. A written consent was obtained from the subjects' legal representatives. The study was conducted according to the ethical principles of the Declaration of Helsinki. To comply with the Health Insurance Portability and Accountability Act (HIPAA), confidentiality of information was secured by utilizing text encryption, password protection, and limited personnel involvement.

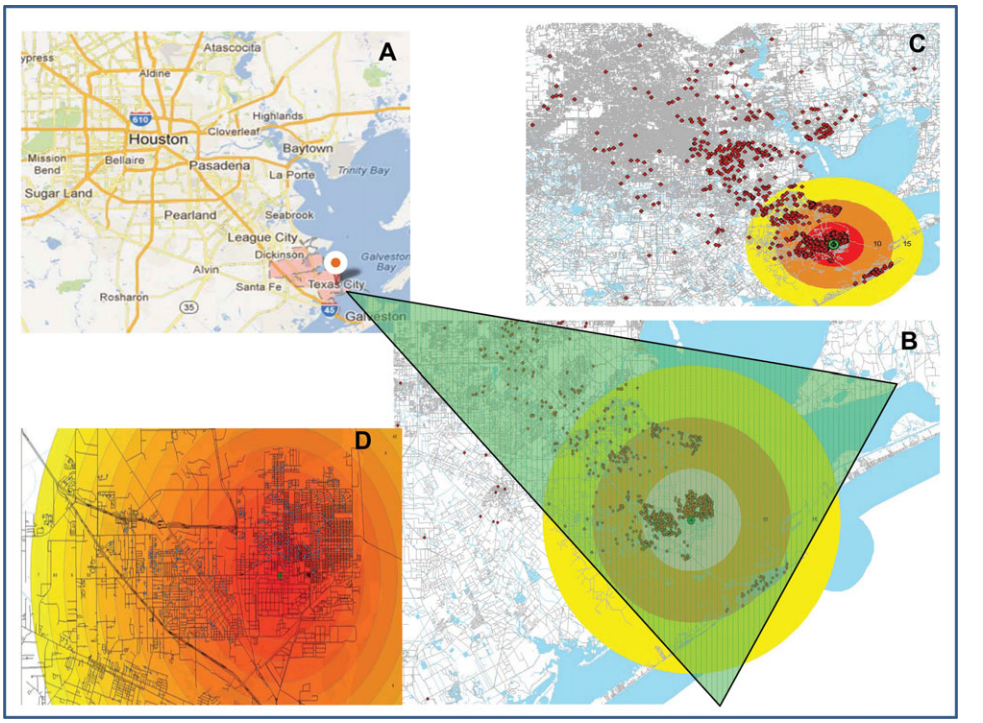

FIGURE 1 Map showing the location of the incident of British petroleum (BP) refinery that released hundreds of thousands of pounds of toxic chemicals including benzene and carbon monoxide into the skies of Texas City, Texas for 40 days from April 6 to May 16, 2010. During the incident, the wind originated from south to north and dispersed the discharged benzene impacting the people residing in the northern parts of the Texas City. (A) Location of Texas City, Texas. (B) The inset showing the location of the BP incident and the release of toxic chemicals. (C) The exposed region of Texas City to benzene and other toxic chemicals from where subjects were recruited for the study. The dots or marks represent the subjects that participated in the study. (D) Depicted intensity of benzene exposure from the BP incident into the surrounding neighborhoods of Texas City, Texas.

Selection of Pediatric Subjects

Children Exposed to Benzene

As illustrated in Figure 1, based on the residential addresses and zip codes, children who resided in the path of the toxic chemical release from the BP refinery emission event were identified and included in the study. All children in this group experienced involuntary exposure to benzene for 40 days following the flaring incident at the BP facility. The personal information of the subjects who participated in this study was redacted to exclude any identifiable personal information.

Unexposed Subjects

Children in the unexposed group were drawn from a pediatric care clinic that is located in another city approximately 30 miles away from the BP refinery in Texas city, Texas. The unexposed children included in the study had visited the clinic for their routine pediatric check up. The unexposed subjects were selected randomly by the pediatric physician and any identifiable personal information was redacted. Demographic and clinical data were collected from the subjects' medical charts and included in this study.

Chart Review and Evaluation

Medical charts of the exposed and unexposed children were reviewed and the clinical data were processed for statistical analysis. Clinical data such as white blood cell (WBC) counts, platelet counts, hemoglobin, hematocrit, blood urea nitrogen (BUN), creatinine, alkaline phosphatase (ALP), aspartate amino transferase (AST), and alanine amino transferase (ALT) levels were evaluated and compared between the unexposed children and those children exposed to benzene. In addition, data on urinary phenol was assessed as a benzene metabolite in the exposed children. Moreover, data on somatic symptoms were collected for children exposed to benzene and analyzed.

Statistics

Descriptive statistics were used to assess patient demographics and other variables. The statistics included means and standard deviations for the exposed and unexposed groups to benzene. The variables included were WBC, platelets, hemoglobin, hematocrit, creatinine, BUN, AST, ALT, and urinary phenol. Student's *t*-test was used to assess the differences between the exposed and unexposed groups to benzene. The significance level was predetermined at an alpha level of 0.05.

RESULTS

A total of 312 children aged <17 years were included in the study. Out of the 312 children, 157 were exposed to benzene and 155 were not exposed to benzene. The subjects' demographics are shown in the Table 1. The mean age of the exposed and unexposed children was 15.4 and 11.8 years, respectively. Among the benzene-exposed children ($n = 157$), there were 91 (58%) males and 66 (42%) females. In the unexposed group ($n = 155$), there were 91 (59%) males and 64 (41%) females.

The results presented in Table 2 show the differences in hematologic and hepatic markers between the exposed and unexposed children to benzene. Children who were exposed to benzene experienced a significantly reduced mean WBC count ($\times 10^3$ per μL) compared with the unexposed children (6.8 ± 2.1 versus 7.3 ± 1.7, $P = .02$). Conversely, the mean platelet count ($\times 10^3$ per μL) in the benzene exposed group was significantly higher when compared with the unexposed group (278.4 ± 59.9 versus 261.6 ± 51.7, $P = .005$).

Serum creatinine levels (mg/dL) were significantly increased in the benzene exposed children compared with the unexposed children (0.8 ± 0.2 versus 0.6 ± 0.2, $P = .000$). However, no significant alterations were observed in the mean hemoglobin (g/dL) or hematocrit or BUN levels between the exposed and unexposed children to benzene. Serum ALP (IU/L) levels were found to be increased in children exposed to benzene compared with the unexposed children (183.7 ± 95.6 versus $165 \pm 70.3 = 0.04$). Similarly, the mean AST (IU/L) levels were significantly higher in the

TABLE 1 Demographics of the Pediatric Subjects

Demographics	Unexposed	Exposed
Total subjects	155 (100%)	157 (100%)
Mean age	11.8 years	15.4 years
Gender		
Male	91 (59%)	91 (58%)
Female	64 (41%)	66 (42%)
Median time following exposure to the time of testing (range), days	–	143 (117–290)

TABLE 2 Comparison of Hematologic and Hepatic Indices Between the Exposed and Unexposed Pediatric Subjects to Benzene

Variable	Unexposed ($N = 155$)	Exposed ($N = 157$)	P Value
WBC ($\times 10^3$ per μL)	7.3 ± 1.7	6.8 ± 2.1	.022*
Platelets ($\times 10^3$ per μL)	261.6 ± 51.7	278.4 ± 59.9	.005**
Hemoglobin (g per dL)	13.9 ± 1.5	13.6 ± 1.4	.324$^{\psi}$
Hematocrit (%)	39.4 ± 3.9	39.9 ± 3.4	.1034$^{\psi}$
BUN (mg per dL)	12.5 ± 3.3	12.1 ± 2.6	.0856$^{\psi}$
Creatinine (mg per dL)	0.6 ± 0.2	0.8 ± 0.2	.000**
ALP (IU per L)	165 ± 70.3	183.7 ± 95.6	.0429*
AST (IU per L)	20.5 ± 5.5	23.6 ± 15.3	.0148*
ALT (IU per L)	16.9 ± 6.9	19.2 ± 7.8	.005**

*$P = .05$; **$P = .001$; ψ = did not reach statistical significance.
WBC = White blood cells; BUN = Blood urea nitrogen; ALP = Alkaline phosphatase; AST = aspartate amino transferase; ALT = Alanine amino transferase.

benzene exposed children compared with the unexposed children (23.6 ± 15.3 versus 20.5 ± 5.5, $P = .0089$). The mean serum ALT (IU/L) levels were increased significantly in the benzene-exposed group compared with the unexposed group (19.2 ± 7.8 versus 16.9 ± 6.9, $P = .005$).

The results presented in Tables 3 and 4 represent the differences in hematologic and hepatic markers between the benzene exposed and unexposed children according to gender. The mean WBC count ($\times 10^3$ per μL) was significantly decreased in male children exposed to benzene compared with the unexposed male children (6.3 ± 1.8 versus 7.3 ± 1.5, $P = .0002$). The mean hemoglobin (g/dL) levels were significantly increased in male children exposed to benzene compared with the unexposed male children (14.2 ± 1.1 versus 13.7 ± 1.6, $P = .005$). The hematocrit (%) levels were significantly increased in male children exposed to benzene compared with the unexposed male children (42.4 ± 3.1 versus 40.5 ± 5.0, $P = .001$). The serum creatinine levels (mg/dL) were significantly increased in male children exposed to benzene compared with the unexposed male children (0.9 ± 0.2 versus 0.6 ± 0.2, $P = .000$). The liver enzymes such as ALP, AST, and ALT were also found to be significantly higher in male children exposed to benzene compared with the unexposed male children ($P = .03$). Female children exposed to benzene had significantly higher levels of platelet counts, creatinine, AST, and ALT compared with the unexposed female children (Table 4).

TABLE 3 Comparison of Hematologic and Hepatic Indices Between the Benzene Exposed and Unexposed Male Children

Variable	Unexposed ($N = 91$)	Exposed ($N = 91$)	P Value
WBC ($\times 10^3$ per μL)	7.3 ± 1.5	6.3 ± 1.8	.0002**
Platelets ($\times 10^3$ per μL)	253.5 ± 49.1	261.7 ± 57.4	.1558$^{\psi}$
Hemoglobin (g per dL)	13.7 ± 1.6	14.2 ± 1.1	.0050**
Hematocrit (%)	40.5 ± 5.0	42.4 ± 3.1	.0010**
BUN (mg per dL)	12.9 ± 3.6	12.3 ± 2.6	.1062$^{\psi}$
Creatinine (mg per dL)	0.6 ± 0.2	0.9 ± 0.2	.000**
ALT (IU per L)	186.8 ± 68.9	212.1 ± 94.9	.0339*
AST (IU per L)	21.8 ± 5.4	23.8 ± 8.4	.0375*
ALT (IU per L)	17.7 ± 7.0	20.3 ± 9.3	.0319*

*$P = .05$; **$P = .001$; ψ = did not reach statistical significance.
WBC = White blood cells; BUN = Blood urea nitrogen; ALP = Alkaline phosphatase; AST = Aspartate amino transferase; ALT = Alanine amino transferase.

TABLE 4 Comparison of Hematologic and Hepatic Indices Between the Benzene Exposed and Unexposed Female Children

Variable	Unexposed ($N = 64$)	Exposed ($N = 66$)	P Value
WBC ($\times 10^3$ per μL)	7.2 ± 2.0	7.4 ± 2.2	.2964$^{\psi}$
Platelets ($\times 10^3$ per μL)	273.9 ± 53.5	302.0 ± 55.6	.0031**
Hemoglobin (g per dL)	14.2 ± 1.6	12.7 ± 1.3	.1604$^{\psi}$
Hematocrit (%)	37.5 ± 3.2	38.4 ± 3.5	.0659$^{\psi}$
BUN (mg per dL)	12.0 ± 2.8	11.7 ± 2.7	.2575$^{\psi}$
Creatinine (mg per dL)	0.6 ± 0.1	0.7 ± 0.1	.000**
ALT (IU per L)	135.3 ± 61.0	131.2 ± 71.9	.3929$^{\psi}$
AST (IU per L)	18.1 ± 4.4	23.3 ± 8.4	.0375*
ALT (IU per L)	15.4 ± 6.3	19.3 ± 10.9	.0123*

$^{*}P = .05$; $^{**}P = .001$; ψ = did not reach statistical significance.
WBC = White blood cells; BUN = Blood urea nitrogen; ALP = Alkaline phosphatase; AST = Aspartate amino transferase; ALT = Alanine amino transferase.

Urinary phenol is considered as an index of benzene exposure. Thus, we assessed the phenol excretion in the urine of benzene-exposed patients. The mean levels of urinary phenol in the benzene-exposed subjects was 8.0 (range 1–64.2) mg/L.

The principal somatic symptoms experienced by the benzene exposed children following the flaring incident are illustrated in Figure 2. Among somatic complaints, neurological symptoms such as unsteady gait, memory loss, and headaches were the most (80%) frequently reported symptoms by the benzene-exposed children (Figure 2A). Upper respiratory symptoms were reported by 48% of the benzene exposed children followed by cough (48%), nausea/vomiting (43%), dermatological (36%), shortness of breath (32%), wheezing (27%), dizziness (22%), chest pain (15%), painful joints (15%), and weight loss (13%). The results presented in Figure 2B reveal the differences in the occurrence of somatic symptoms by gender among the benzene exposed children. Male children had a lower frequency of neurological complaints compared with female children (71% versus 91%). Similarly, male subjects experienced a lower frequency of upper respiratory symptoms (44% versus 53%), nausea/vomiting (30% versus 61%), and dermatological symptoms including rash (26% versus 48%). Conversely, male children had a higher frequency of blurred vision compared with the female children (10% versus 6%). Other somatic symptoms appeared to be similar among the male and female children exposed to benzene.

DISCUSSION

Health consequences of benzene exposure have been studied less extensively in children than in adults, but current evidence indicates that benzene exposure may have similar health effects in children [9, 12, 19, 20]. Although epidemiologic studies in adults show clear evidence of causal relationship between benzene exposure and certain leukemias [21, 22], benzene induced carcinogenicity in children has not been clearly demonstrated [23–25]. Multiple factors could be responsible for potential health risks among children following their exposure to benzene. These include benzene metabolism, phackokinetics, and other biochemical processes that may differ in children when compared to adults [26, 27]. To understand the health consequences of benzene exposure in pediatric subjects, we performed a retrospective analysis of children less than 17 years of age who were exposed to benzene following BP's flaring incident in Texas City, Texas. According to our knowledge, this is the first study that specifically evaluated the health consequences among children following exposure to benzene.

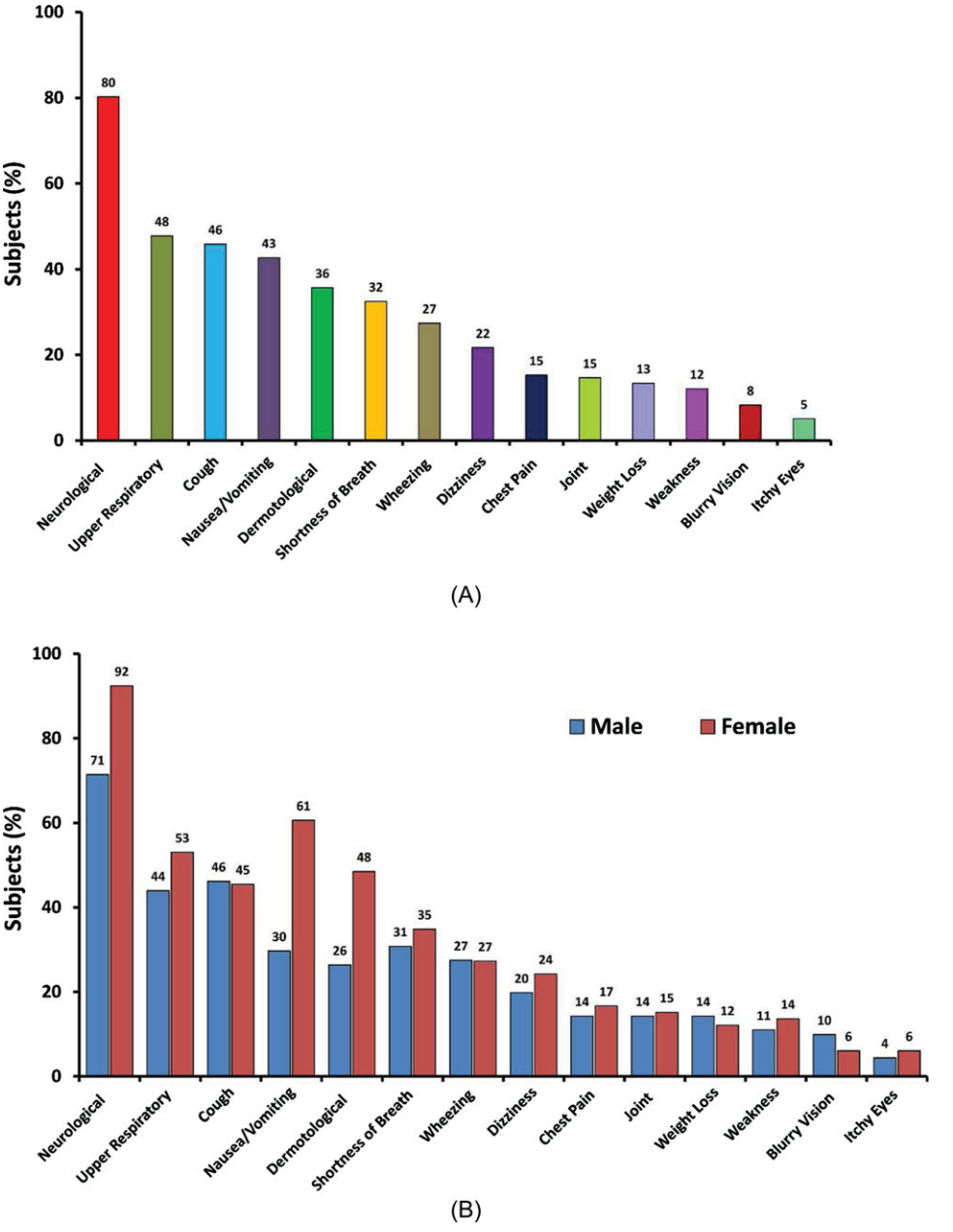

FIGURE 2 Principal somatic complaints by the subjects following a flaring incident that occurred at the BP refinery in Texas City, Texas. (A) The principal somatic symptoms experienced by the benzene-exposed children. (B) The differences in the occurrence of somatic symptoms by gender among benzene exposed children.

The results of this study indicate that children exposed to benzene had significant hematologic and hepatic toxicity. The mean WBC counts were significantly decreased in children exposed to benzene compared with the unexposed children. Conversely, the platelet counts were significantly increased in children exposed to benzene compared with the unexposed children. The hemoglobin, hematocrit, and BUN levels remained similar between the benzene exposed and unexposed children. An

epidemiologic study by Rothman and coworkers showed that adult Chinese workers (mean age of 35 years), exposed to benzene had significantly reduced total WBC and platelet counts compared with those other workers who had not been exposed to benzene [28]. Similarly, McHale et al. reported that adult subjects who were exposed to benzene had significantly reduced total WBC and platelet counts compared with those not exposed to benzene [29].

In contrary, Ray and coworkers reported significantly increased WBC and platelet counts in adult subjects exposed to benzene compared with the controls [30]. In our study, children who were exposed to benzene had significantly reduced WBC counts and had elevated platelet counts compared with those not exposed to benzene. These results suggest that thrombocytopenia may not occur in children exposed to benzene. Ceresa and coworkers reported that thrombocytopenia was not a constant finding in the majority of cases resulting from chronic benzene exposure in adult subjects [31]. Further studies are required to establish the effect of benzene exposure on platelets in children.

In general, serum levels of ALP, AST, and ALT are often measured to evaluate liver function [32]. Most organic solvents including benzene are well-known hepatotoxic compounds and known to affect these enzymes [33]. Therefore, in this study, serum levels of ALP, AST, and ALT were evaluated in children exposed to benzene and compared with those unexposed to benzene. In the present study, the serum levels of ALP, AST, and ALT were found to be increased among children exposed to benzene compared with the unexposed children. These serum enzymes levels have been considered indicators of hepatic damage [34]. Phosphatases, amino transferases, and dehydrogenases are important enzymes in biological processes. These enzymes are implicated in the detoxification, metabolism, and biosynthesis of energetic macromolecules for different essential functions. Any interference in these enzymes leads to biochemical impairment and lesions in the tissue and cellular function. The increased levels of these enzymes found in this study are consistent with other clinical and preclinical studies that reported on benzene hepatotoxicity. The elevated levels of these hepatic enzymes in the serum may be due to the impaired function of hepatic tissues following exposure to benzene, impairment of the function there by the liberation of these enzymes into the circulation.

Furthermore, the serum levels of ALP are often used as an indicator of not only hepatic function but also to evaluate the biliary tract function [35, 36]. Thus, the increased serum levels of this enzyme suggest biliary tract dysfunction in the benzene-exposed children. Traditionally, the excretion of phenol in the urine has been used as an index of benzene. In general, it is believed that subjects who are not exposed to benzene should excrete undetectable levels of phenol in their urine [37–39]. Therefore, we assessed the urinary phenol levels in children exposed to benzene. In this study, we lack information on urinary levels of phenol for the unexposed children to establish baseline values and to ascertain the differences from those children exposed to benzene. Despite this limitation, we found elevated phenol levels in the urine of benzene-exposed children. Additional studies are required to determine the association of urinary levels of phenol in relation to observed hematologic and hepatic changes in children exposed to benzene.

The somatic symptoms experienced by the benzene exposed children are consistent with a previously published report in which Tunsaringkarn and coworkers [40] reported that dizziness, headache, skin irritation, eye irritation, fatigue, sore throat, nausea, and depression were experienced by the subjects exposed to benzene. In our study, we found that children exposed to benzene experienced neurological, dermatological, and upper respiratory symptoms in additions to the symptoms reported by Tunsaringkarn and coworkers [40]. Furthermore, a subanalysis of somatic symptoms

suggests that gender appears to play some role in the occurrence of these somatic symptoms in children. Compared with male children, female children experienced a higher frequency of neurological symptoms, dermatological symptoms, and nausea, after benzene exposure. However, these gender differences in the prevalence of somatic symptoms need further evaluation.

We acknowledge that this study is subject to a number of important limitations. As with any cross-sectional study, the findings of this investigation should be considered carefully. Foremost among these limitations is our lack of our subjects' baseline data prior to the benzene exposure as the result of a flaring event at the BP refinery. Another shortcoming of this investigation was the retrospective nature of the study. Therefore, it is difficult to infer a causality using such a study design because the clinical outcomes were measured at one time point after exposure to benzene. Nonetheless, the results of this retrospective study does shed light on the health consequences among children exposed to benzene following a flaring incident at the BP refinery in Texas City, Texas.

CONCLUSION

The results of this retrospective study revealed that children exposed to toxic chemicals specifically benzene have significantly elevated health risks, specifically, alterations in their blood cells and liver enzymes, indicating that these children are at a high risk of developing hepatic or blood related disorders. Additional studies are underway to further understand the health consequences among subjects exposed to the benzene due to the flaring incident at the BP refinery facility in Texas City, Texas.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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