Clinical Pediatrics
2016, Vol. 55(12) 1143–1151

DOI: 10.1177/0009922816641463
cpj.sagepub.com
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Illness Symptoms Experienced by Children Exposed to Benzene After a Flaring Incident at the BP Refinery Facility in Texas City

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Abstract

Objective. To evaluate the illness symptoms experienced by children who were exposed to benzene following a flaring incident at the BP refinery in Texas City, Texas. *Methods*. A total of 641 children, aged <17 years, exposed to benzene were included. Using medical charts, data on the children's illness symptoms as well as the serum levels of β-2-microglobulin and the amount of urinary excretion of phenol were reviewed and analyzed. *Results*. A total of 1790 illness symptoms were reported in 641 children exposed to benzene. Upper respiratory symptoms were the most (67%) frequently reported, followed by neurological symptoms (57%), diarrhea (25%), and cough (24%). Logistic regression analysis indicated that neurological symptoms (R^2 = 0.75), chest pain (R^2 = 0.64), joint pain (R^2 = 0.57), and vision difficulty (R^2 = 0.54) were positively associated with increasing age. β-2-Microglobulin levels were significantly higher in children <5 years compared with those >5 year (P = .04). Conversely, urinary phenol levels were significantly lower in children <5 years compared with those >5 years (P = .00). *Conclusion*. Together, these findings reveal that children exposed to benzene experience a range of illness symptoms and an altered profile of urinary phenol indicating their vulnerability to potentially increased health complications.

Keywords

benzene poisoning, chemical exposure, health complaints, petroleum refinery, illness symptoms, urinary metabolites of benzene

Introduction

Benzene, a volatile organic compound, is one of the main contributors to air pollutants in the environment.[1,2] It occurs naturally in the environment as a contaminant from both natural processes and human activities.[3,4] Benzene is widely used for the production of petrochemical and hydrocarbon products such as styrene, paints, plastic materials, phenyl compounds, detergents, insecticides, and other commercial products. Benzene ranks in the top 20 most abundantly produced chemicals in the United States.[5] Over 98% of the benzene produced is derived from the petrochemical and petroleum refining industries.[6] Thus, petroleum refining industries are the main sources of benzene and other toxic chemicals leading to environmental contamination.

Exposure to benzene is associated with deleterious health effects including leukemia, lymphoma, aplastic anemia, pancytopenia, and chromosomal aberrations.[7-11] Moreover, multiple noncancerous adverse effects on function of vital systems such as hematological, hepatic, renal, cardiovascular, respiratory, nervous, and immune functions have been reported in individuals exposed to benzene.[2,12-16] Thus, communities living in close proximity to petroleum refineries have significantly increased health risks due to the increased probability of being exposed to benzene and other environmentally toxic pollutants.

In general, studies evaluating the health consequences of benzene exposure in children are scant. Earlier epidemiological studies suggest that environmental benzene exposure is associated with childhood leukemia.[17-19] When compared to adults, children's immune systems are more sensitive and are prone to develop more adverse reactions with toxic pollutants such as benzene because

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of their differences in physiology, immaturity of enzyme systems, and clearance mechanisms.[20-23] In particular, the pharmacokinetics of benzene may differ widely between children and adults. The incomplete metabolic systems, rapid tissue regeneration, immature host defenses, and activity patterns make children more vulnerable to the adverse effects of toxic pollutants and are susceptible to higher rates of infections caused by respiratory pathogens.[20,21] Moreover, children have a higher unit body weight exposure than adults due to their heightened activity patterns, different ventilation tidal volumes and frequencies, which increases their exposures to toxic pollutants. Furthermore, the toxicodynamic processes that determine exposure rates, absorption, metabolism, excretion, and tissue vulnerability all seem to be age related,[22] and thus, children are more susceptible to the effects of these toxic chemicals.

In Texas City, Texas, a 2010 flaring disaster occurred at the BP refinery facility. It lasted 40 days and led to the release of at least 500 000 pounds of toxic chemicals, including more than 17 000 pounds of benzene into the skies.[24-26] Environmentally, this massive toxic release polluted the air, threatening the health of local residents living in close proximity to the BP refinery facility. To understand the potential health effects of ambient benzene exposure resulting from the BP flaring incident, a series of studies were conducted examining the changes in hematological and hepatic functions in children and adults from the affected communities.[27-30] The findings of these studies demonstrated that benzene exposure resulting from the BP flaring incident significantly altered the hematological and hepatic indices in both children and adults. In this study, we investigated the occurrence of illness symptoms in children following their exposure to benzene as a result of the BP flaring incident.

Materials and Methods

Subjects

This retrospective study was approved by an institutional review board. Pediatric subjects aged 17 years or younger were included in this study. The details of the children' selection and the procedures employed for the clinical and laboratory evaluations were reported previously.[27,28] Briefly, residential areas affected by the BP refinery emission due to the flaring event were initially identified, and the children exposed to the emissions were selected from the affected areas of surrounding communities of Texas City, Texas (Figure 1). Specifically, these children experienced an involuntary exposure to benzene for up to 40 days following the BP refinery flaring incident that occurred on April 6, 2010, and lasted through May 16, 2010. Demographic and illness symptoms data were collected and included in this analysis. 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.

Assessment of Subjective Symptoms

A questionnaire survey was conducted to gather the information on illness symptoms in children exposed to benzene. The investigators developed a symptom questionnaire based on the possible adverse effects associated with benzene exposure. Illness symptoms included in the questionnaire survey were presented in Table 1. Although the questionnaire was self-administrable, it was carried out by face-to-face interview with children and their parents. The survey was conducted in a clinical interview by a member of the medical staff, reviewing all the questions in the set verbally. The survey included questions about illness symptoms, general characteristics, and past medical history.

Assessment of β-2-Microglobulin and Urinary Phenol

Blood and urine samples were collected from the children at the time of the health assessment. Serum β-2-microglobulin and urinary phenol were assessed by an accredited laboratory facility (LabCorp, Laboratory Corporation of America, Houston, TX). Urinary phenol was assessed as a benzene metabolite using Agilent 5980 GC system (Agilent Technologies, Wilmington, DE).[30]

Data Analysis and Statistics

Medical charts of benzene-exposed children were reviewed and the clinical data on illness symptoms were processed for statistical analysis. Descriptive statistics were used to assess patient demographics, which included means and standard deviations for each variable. Student's *t* test was used to assess the differences between the subgroups. Multiple logistic regression analysis was performed to assess the relationship between illness symptoms and subjects' age. The significance level was predetermined at an α level of .05.

Results

A total of 641 children, aged <17 years, who had been exposed to benzene were included in the study. The

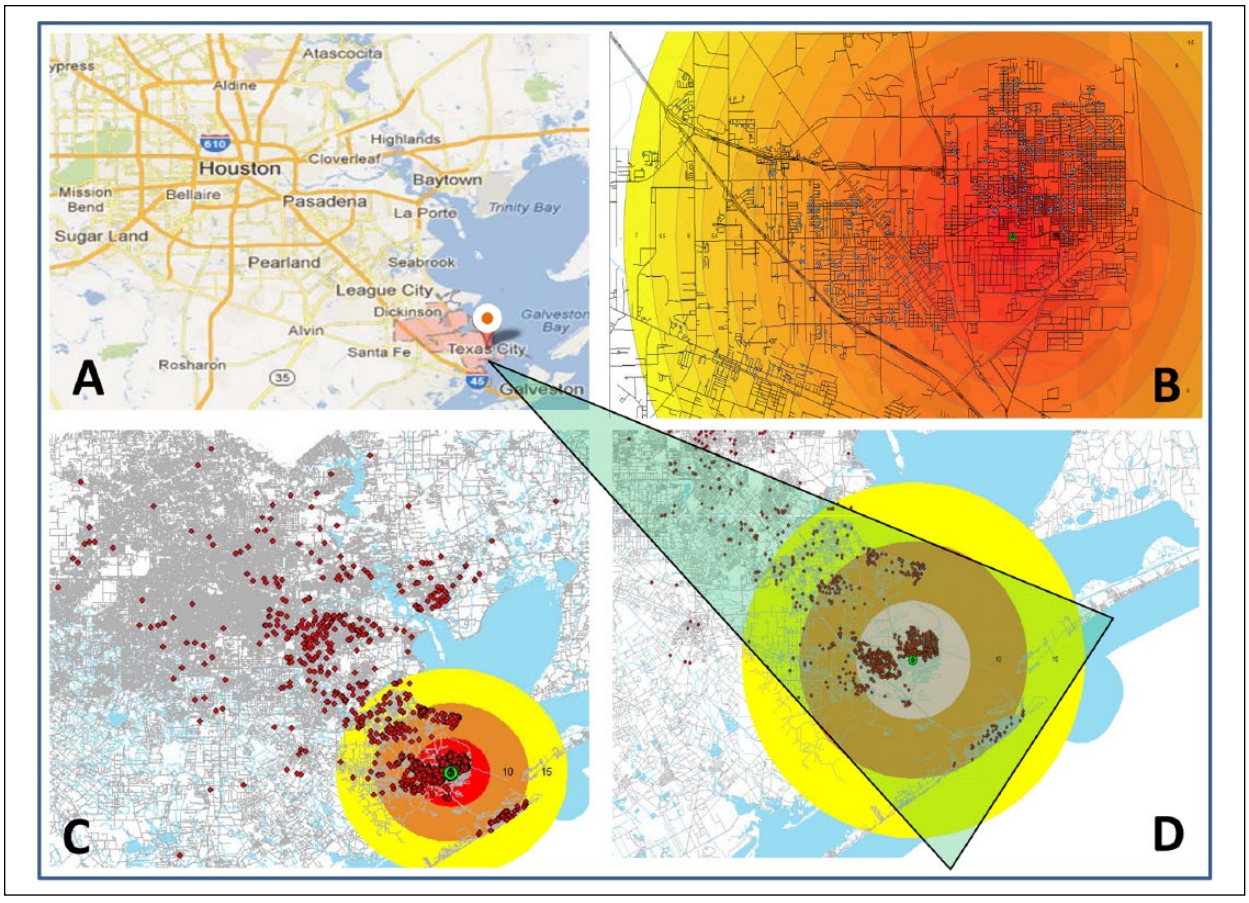

Figure 1. Map showing the location of the disaster of BP refinery facility in the northern parts of the Texas City. (A) Location of Texas City, Texas. (B) Depicted intensity of benzene exposure from BP incident surrounding neighborhoods of Texas City, Texas. The red, orange, and yellow colors depict the higher (red) to reduced (orange) to low (yellow) intensity of benzene exposure. (C) Scattered dots represent the location/address of the study participants who were exposed to benzene following a flaring incident at the BP refinery and surrounding areas. (D) A closer look at the affected area by the benzene exposure and the residential address of the study participants (scattered dots).

subjects' demographics are shown in Table 2. The mean age of the children was 9.5 years. There were 173 (27%), 200 (31%), and 168 (26%) children in ≤5 years, >5 to ≤10 years, and >10 to ≤15 years, respectively. Of the 641, only 100 (16%) children were in the age group of ≥15 years. There were 334 (52%) males and 207 (48%) females.

The principal illness symptoms experienced by the children exposed to benzene after the flaring incident are presented in Table 3. A total of 1790 illness symptoms were reported in 641 children exposed to benzene, indicating an average of 2.8 symptoms experienced by each child. Among these symptoms, upper respiratory symptoms such as shortness of breath, sore throat, difficulty in breathing, bronchitis, nose bleeds, hoarseness, and sinusitis were the most (67%) frequently reported symptoms by the benzene-exposed children. Neurological symptoms such as unsteady gait, memory loss, and headaches were the second most frequently reported symptoms (57%) among the children exposed to benzene. Diarrhea was experienced in 25% of the children, followed by cough (24%), dermatological (24%), nausea/vomiting (21%), gastrointestinal (12%), wheezing (9%), chest pain (6%), vision (6%), painful joints (6%), and urinary irritation (3%).

To evaluate the impact of gender, we assessed the differences in the incidence of illness symptoms between male and female children. A total of 899 subjective symptoms were reported among the 334 male children indicating an average of 2.7 symptoms experienced by each male child. In 307 female children, there were total of 891 subjective symptoms reported, indicating an average of 2.9 symptoms experienced by each female child. The incidence of individual subjective symptoms were similar between male and female children (Table 4).

Table 1. A Questionnaire Survey on Illness Symptoms in Children Exposed to Benzene.

Illness Symptoms	Yes	No
Upper respiratory		
Shortness of breath		
Difficulty in breathing		
Bronchitis		
Allergy		
Hoarseness		
Nose bleeds		
Post nasal drip		
Throat irritation		
Congestion/obstruction		
Respiratory infections		
Runny nose		
Sinusitis		
Wheezing		
Neurological		
Headache		
Memory loss		
Dizziness		
Ringing in ears		
Unsteady gait		
Seizures		
Dermatological		
Macules and papules		
Pruritic rash		
Nonpruritic rash		
Cough		
Gastrointestinal		
Poor appetite		
Black stools		
Heartburn		
Weight loss		
Diarrhea		
Nausea/vomiting		
Chest pain		
Chest pain		
Cardio irregular heart beats		
Cardio heart palpitations		
Vision difficulty		
Itchy eyes		
Water eyes		
Blurry vision		
Double vision		
Redness of eyes		
Urinary		
Urinary tract infection		
Burning during urination		
Increased frequency		
Joint pains		
Other		
Fever		
Night sweats		
Weakness		
Decreased energy		
Fatigue		

Table 2. Demographics of the Study Subjects.

Demographics	Benzene Exposed
Total subjects	641 (100%)
Mean age	9.5 years
Age group	
≤5 years	173 (27%)
>5 to ≤10 years	200 (31%)
>10 to ≤15 years	168 (26%)
≥15 years	100 (16%)
Gender	
Male	334 (52%)
Female	307 (48%)

Table 3. Illness Symptoms Experienced by the Children by Their Age Group Following Exposure to Benzene.

Symptoms	<5 Years (N = 173)	>5 to <10 Years (N = 200)	>10 to <15 Years (N = 168)	>15 Years (N = 101)
Upper respiratory	106 (61%)	136 (68%)	119 (71%)	66 (66%)
Neurological	44 (25%)	98 (49%)	126 (75%)	95 (95%)
Dermatological	54 (31%)	58 (29%)	28 (17%)	16 (16%)
Diarrhea	52 (30%)	51 (26%)	36 (21%)	21 (21%)
Cough	52 (30%)	45 (23%)	36 (21%)	22 (22%)
Nausea/vomiting	38 (22%)	35 (18%)	41 (24%)	19 (19%)
Gastrointestinal	25 (14%)	22 (11%)	13 (8%)	14 (14%)
Wheezing	17 (10%)	17 (9%)	18 (11%)	7 (7%)
Chest pain	4 (2%)	7 (4%)	14 (8%)	13 (13%)
Vision difficulty	4 (2%)	12 (6%)	13 (8%)	9 (9%)
Urinary	4 (2%)	6 (3%)	6 (4%)	4 (4%)
Joint pains	3 (2%)	8 (4%)	16 (10%)	11 (11%)
Other	31 (18%)	38 (19%)	41 (24%)	19 (19%)

Table 4. Illness Symptoms Experienced by the Children by Their Gender Following Exposure to Benzene.

Symptom	All (N = 641)	Male (N = 334)	Female (N = 307)
Upper respiratory	427 (67%)	230 (69%)	197 (64%)
Neurological	363 (57%)	183 (55%)	180 (59%)
Cough	156 (24%)	81 (24%)	75 (24%)
Diarrhea	159 (25%)	77 (23%)	82 (27%)
Dermatological	156 (24%)	73 (22%)	83 (27%)
Nausea/vomiting	133 (21%)	53 (16%)	80 (26%)
Gastrointestinal	74 (12%)	33 (10%)	41 (13%)
Wheezing	59 (9%)	35 (10%)	24 (8%)
Chest pain	38 (6%)	16 (5%)	22 (7%)
Vision difficulty	38 (6%)	25 (7%)	13 (4%)
Joint pains	38 (6%)	18 (5%)	20 (7%)
Urinary	20 (3%)	9 (3%)	11 (4%)
Other	129 (20%)	66 (20%)	63 (21%)

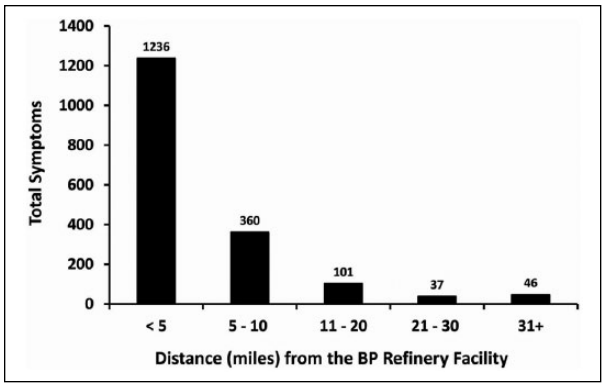

Figure 2. Illness symptoms experienced by children as measured by the distance from the BP refinery facility. Children living in a close proximity to the BP plant experienced majority of symptoms.

To evaluate if the children's age contributed to any observed health effects from the benzene exposure, a further analysis was performed by grouping children into 4 age groups (<5 years, ≥5 to <10 years, ≥10 to <15 years, and ≥15 years) and compared by their clinical outcomes between the 4 age groups. There were 434, 531, 507, and 318 total symptoms reported, respectively, in the following age groups of children: <5 years (n = 173), ≥5 to <10 years (n = 200), ≥10 to <15 years (n = 168), and ≥15 years (n = 101).

An increasing trend in neurological symptoms such as unsteady gait, memory loss, and headaches was seen with increasing age among the 4 age groups (Table 4). The lowest neurological symptoms were seen in the <5 years age group children (25%) followed by 49% in the ≥5 to <10 years, 75% in the ≥10 to <15 years, and 75% in the ≥15 years age group children. Conversely, the incidence of dermatological symptoms was highest in children (31%) in the <5 years age group followed by 29% in the ≥5 to <10 years, 17% in the ≥10 to <15 years, and 16% in the ≥15 years age group children. Similarly, the incidence of diarrhea was highest in children (30%) in the <5 years age group followed by 26% in the ≥5 to <10 years, 21% in the ≥10 to <15 years, and 21% in the ≥15 years age group children. Other illness symptoms appeared to be similar among the 4 age groups of children exposed to benzene.

The results presented in Figure 2 reveal the occurrence of illness symptoms in children as measured by the distance from the BP refinery facility. The results indicate that most symptoms were reported in children living in a close proximity to the BP plant. Of the 1790 total illness symptoms, 1236 were reported in children living within a 5-mile radius from the refinery facility. There were 360 illness symptoms reported in children living a distance of >5 to 10 miles radius from the refinery plant. The remaining 184 subjective symptoms occurred in children who were living a distance of more than 10 miles radius from the refinery facility.

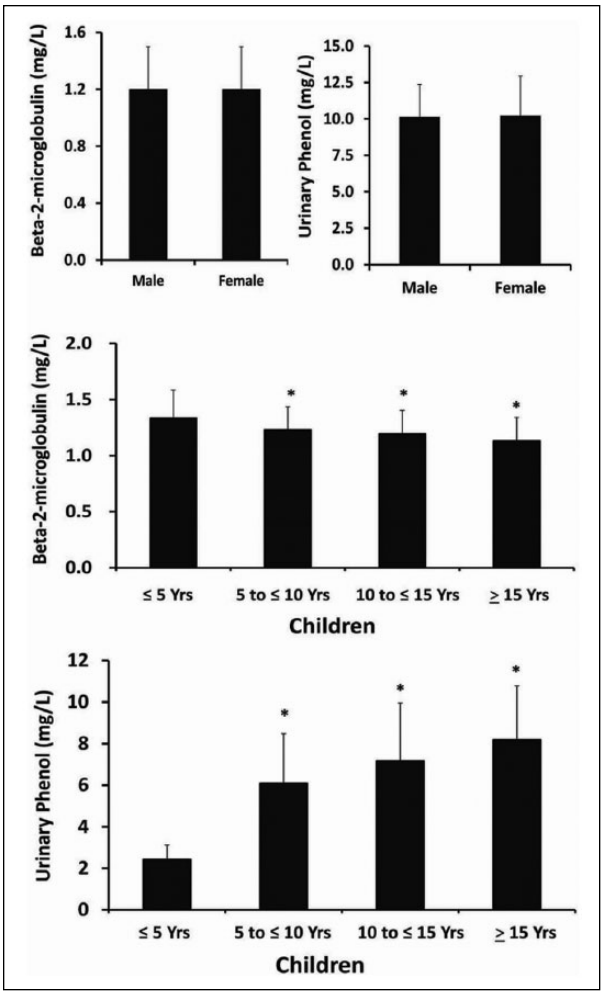

Figure 3. Beta-2-microglobulin and urinary phenol levels in children exposed to benzene according to their gender and among their age groups. (A) Beta-2-microglobulin and urinary phenol levels were statistically similar between male and female children after the benzene exposure ($P = .4$). (B) Differences in the serum levels of β-2-microglobulin among different age groups of children exposed to benzene ($P = .00$). (C) Differences in the urinary phenol levels among different age groups of children exposed to benzene ($P = .00$).

The findings in Figure 3 show the β-2-microglobulin and urinary phenol levels in children exposed to benzene according to their gender and among their age groups. β-2-Microglobulin and urinary phenol levels were statistically similar between male and female children after the benzene exposure ($P = .4$, Figure 3A). The serum levels of β-2-microglobulin were significantly reduced with increasing age among children exposed to

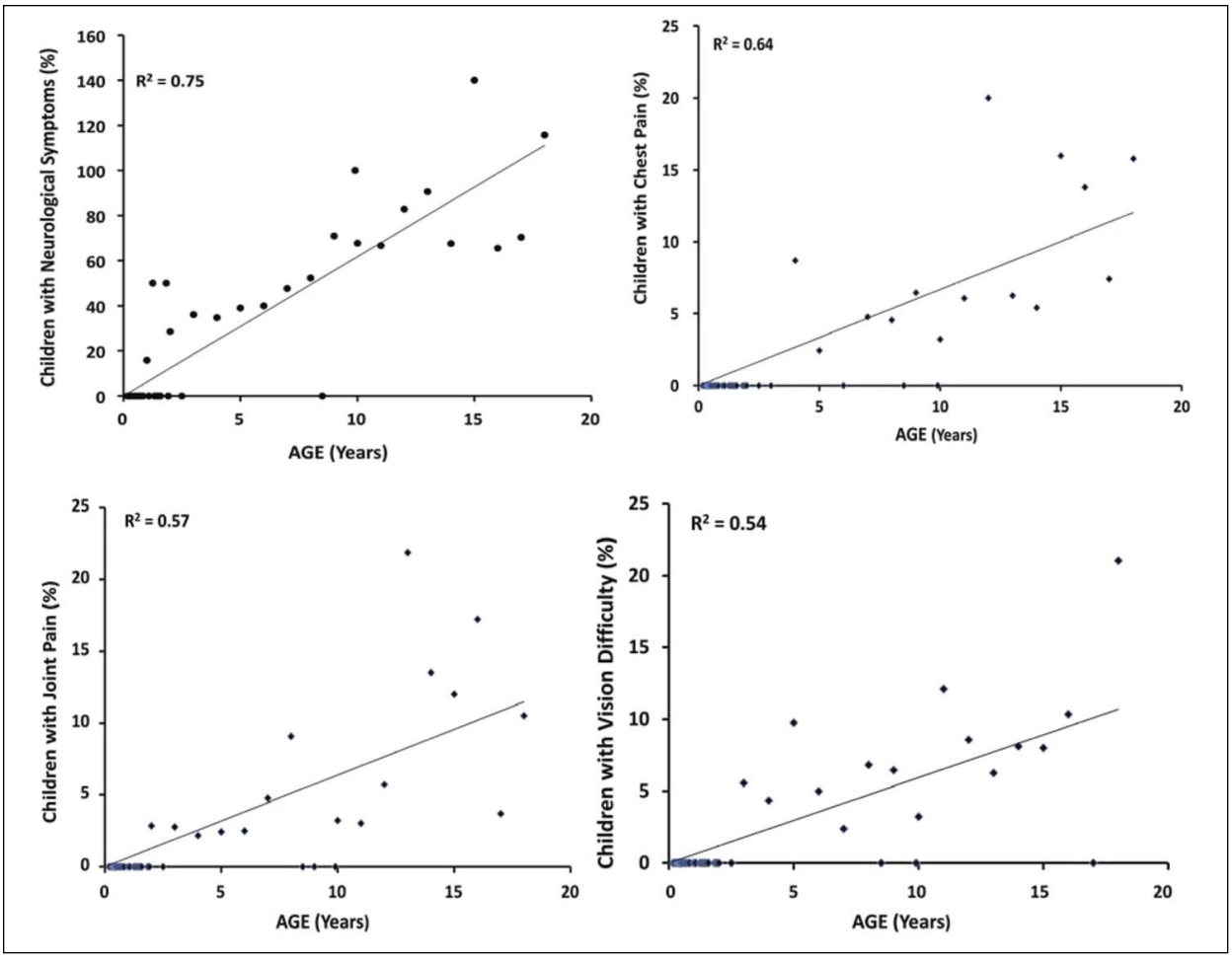

Figure 4. Multiple logistic regression analysis showing positive association of several illness symptoms with the children's age. (A) Correlation of neurological symptoms with the children's age (R^2 = 0.75). (B) Correlation of chest pain with the children's age (R^2 = 0.64). (C) Correlation of joint pains with the children's age (R^2 = 0.57). (D) Correlation of vision difficulty with the children's age (R^2 = 0.54).

benzene (P = .04, Figure 3B). Conversely, urinary phenol levels were significantly increased with increasing age among children exposed to benzene (P = .00, Figure 3C).

Multiple logistic regression analysis indicated that there were several illness symptoms positively associated with the children's age (Figure 4). In particular, neurological symptoms (R^2 = 0.75), chest pain (R^2 = 0.64), joint pain (R^2 = 0.57), and vision difficulty (R^2 = 0.54) were positively associated with the increasing age of the children following exposure to benzene.

Discussion

Benzene has long been recognized as a toxic pollutant that exerts both carcinogenic and noncarcinogenic effects in affected communities. Currently, several studies have established clear evidence of a causal relationship between benzene exposure and carcinogenesis in adults.[31,32] However, its link with the development of childhood cancer is still evolving.[4,33,34] In fact, studies evaluating the adverse effect of benzene exposure in children are very limited. Available research suggests that benzene exposure is associated with an increased risk of childhood leukemia.[19] Furthermore, it has been shown that children exposed to benzene experience noncancerous somatic abnormalities such as asthma,[35,36] deteriorated lung function,[37] pulmonary infections,[38] and bronchitis.[37] In our previous studies, we found that benzene exposure significantly altered the hematological and hepatic functions in children. To further advance current understanding of the adverse health effects of benzene, we assessed the illness symptom profiles in children who were exposed to benzene following BP's flaring incident in Texas City. To the best of our knowledge, this is the first and largest study that has assessed illness

symptom profiles experienced by the children following their exposure to benzene from this incident.

The results of this study reveal that children exposed to benzene experienced several illness symptoms including upper respiratory, neurological, dermatological, gastrointestinal, and a host of other symptoms. Over two thirds of the children experienced upper respiratory symptoms such as shortness of breath, sore throat, difficulty in breathing, bronchitis, nose bleeds, hoarseness, and sinusitis following benzene exposure. Neurological symptoms such as unsteady gait, memory loss, and headaches were seen in more than 50% of the children exposed to benzene. Although there is sparse literature to compare our findings with those previously published studies, Tunsaringkarn and coworkers[39] reported that dizziness, headache, skin irritation, eye irritation, fatigue, sore throat, nausea, and depression were frequently seen illness symptoms in children exposed to benzene. Our findings are comparable with these findings in that significant proportions of children experience these illness symptoms following their exposure to benzene.

To evaluate whether the children's gender contributed to the observed findings, we assessed the incidence of illness symptoms in both male and female children exposed to benzene. The overall frequency of illness symptoms was higher in female children (2.9 symptoms per female child) compared with male children (2.7 symptoms per male child). These results are consistent with our earlier findings where we reported that female children had a higher frequency of illness symptoms compared with the male children following exposure to benzene. Multiple regression analysis was performed to evaluate the association between the subjects' age and individual illness symptoms among the benzene-exposed children. The findings indicated that only neurological symptoms, blurred vision, chest pain, and joint pains were associated positively with the subjects' age among the benzene-exposed children. All other individual illness symptoms had no association with the subjects' age.

The measurement of serum β-2-microglobulin is considered as a marker for the activation of the cellular immune system, as well as a tumor marker in certain hematologic malignancies.[40] Therefore, in this study we assessed the β-2-microglobulin levels in the serum of children exposed to benzene. Our findings indicate that the serum levels of β-2-microglobulin were within the normal range (0.6-2.4 mg/L) in the children exposed to benzene. However, children <5 years had significantly higher levels of β-2-microglobulin levels in their serum compared with either 5 years to <10 years or above 10 years. Further studies are required to examine the role of β-2-microglobulin levels among children exposed to benzene.

Phenol is one of the well-known metabolites derived from the metabolism of benzene. The excretion of phenol in the urine of subjects exposed to benzene has a linear relationship to the degree of exposure. Thus, in the current study, we assessed the urinary excretion of phenol as an index of benzene exposure in the exposed children. We found that a significant amount of phenol was excreted in the urine of the children exposed to benzene. It should be noted that in healthy subjects (not exposed to benzene), only traceable or undetectable amounts of phenol is expected to be found in the urine.[41-43] In addition, our findings also indicate the urinary phenol levels were significantly increased with increasing age among children exposed to benzene. However, additional studies are warranted to determine the health consequences of benzene exposure and the significance of the elevated urinary levels of phenol in children exposed to benzene.

Several limitations are taken into consideration when interpreting our study findings. As with any cross-sectional study, the findings of this investigation should be considered carefully. A cross-sectional study design allows only for generating a hypothesis for further investigation, and not causality to be investigated. One important limitation is the lack of baseline data prior to the 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. Regardless of this study's limitations, the findings suggest that benzene exposure from the refinery incident is associated with significant adverse health effects among children. There is significant scientific evidence that clearly links benzene exposure with an increased risk of carcinogenesis in exposed subjects. Therefore, children who were exposed to this benzene flaring incident should be followed periodically over time to detect any long-term abnormalities and health complaints. Periodic health checkups, routine laboratory blood, pulmonary, cardiac, neurologic, and other organ function tests should be performed in these children to monitor the long-term health consequences of their benzene exposure. Thus, longitudinal studies are warranted to explore the importance and nature of the health effects of benzene exposure among children.

Conclusion

The findings of this study revealed that children exposed to benzene experienced a broad range of illness symptoms including neurological, respiratory, gastrointestinal, and dermatological symptoms. In addition, these

children had nausea/vomiting, diarrhea, cough, chest pain, joint pain, and other illness symptoms following their exposure to benzene. Moreover, a considerable proportion of these children excreted significantly elevated amounts of phenol in the urine, after their exposure to benzene from the BP flaring incident. These findings support our previous study findings in which we reported that children exposed to benzene experienced significant alterations in their hematological and hepatic functions. It is, therefore, crucial to monitor these children on a long-term basis to detect further long-term toxicities of benzene, especially the development of secondary malignancies. Additional studies are warranted to understand the potential health consequences of the benzene exposure from the flaring incident at the BP refinery facility in Texas City, Texas.

Acknowledgments

The authors thank Pradheeth Reddy for the data computing and processing and June Lyliston for her valuable assistance in editing the manuscript.

Author Contributions

Mark D'Andrea conceptualized the study, carried out the initial analyses reviewed and edited the initial manuscript, and approved the final manuscript as submitted. G. Kesava Reddy conceptualized and designed the study, gathered the data, carried out the data analyses, drafted, reviewed, and revised the manuscript, and approved the final manuscript as submitted.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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