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Bisphenol A levels among workers in plastic processing industry and their relations to thyroid hormones

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ABSTRACT

Bisphenol A (BPA) is widely used in the plastic processing industry. A cross-sectional study was conducted to measure BPA levels in the serum of workers as a biomarker of occupational exposure, investigate the thyroid hormone profile among BPA exposed workers, and identify the relationship between occupational exposure to BPA and thyroid hormones during. Our data indicate that the studied workers had higher BPA level than that reported for the Egyptian general population, with a median serum level of 15.6 ng/ml and ranged from 1.6 to 62.9 ng/ml while the interquartile range was 16.3 ng/ml, the highest concentration was among the workers of recycling followed by squeegees and PVC departments. As regards thyroid hormones, almost one-third of the studied workers had abnormal thyroid-stimulating hormone (TSH) levels and 12.2% had abnormal T4 levels. According to TSH and T4 levels, 64.4% of the studied workers had normal thyroid function and 35.6% were suffering from subclinical hypothyroidism. No significant correlation between BPA levels and subclinical hypothyroidism was statistically reported. However, our data reported a significant positive correlation between thyroid hormone T3 and serum BPA concentrations. As agonist or antagonist, BPA could bind to the thyroid hormone receptors indicating that remarkable endocrine disruption.

INTRODUCTION

One of the most volume chemicals produced globally is Bisphenol A (BPA), with more than 8 billion pounds produced annually and more than 1 million pounds released to the environment every year. Bisphenol A is a synthetic compound firstly recognized to be a potential synthetic estrogen then extensively utilized in plastic production (Repossi *et al*., 2016).

BPA is used to produce epoxy resins, polycarbonate plastic, as well as polyvinyl chloride plastics which are used to manufacture a variety of products. Therefore, various routes of human exposure to this substance have been reported; these include inhalation, oral, and transdermal. Exposure to BPA may occur due to occupational exposure or from environmental sources. Occupational exposure most likely is due to manual operating activities and low levels of automation (Wang *et al*., 2012). Commonly, environmental BPA exposure could occur through ingestion when food was stored or reheated in containers that lined with BPA. Many other sources of human exposure such as children's toys, thermal paper, dental materials, and medical devices were previously detected (Hoekstra and Simoneau, 2013).

A lot of recent evidence prove the effect of BPA on human health. The chemical structure of BPA promotes it to fit into the estrogen receptor and acts as an endocrine disruptor. This harmful effect was reported in some experimental animal studies (Acaroz *et al*., 2019). Previous experimental data revealed a direct effect of the exposure to BPA on the function of the thyroid hormones, as it may disrupt the action of thyroid hormones (TH) by interacting

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with the TH receptor directly, altering the metabolism of the thyroid hormones or affecting their normal delivery to target cells (Romano *et al*., 2015).

As regards humans, epidemiological studies have been equivocal. In US adult men's study, it was found that no associations of BPA with thyroid-stimulating hormone (TSH), free triiodothyronine (FT_3), and free thyroxin (FT_4) (Meeker *et al*., 2010). BPA concentrations were associated with lower total thyroxin (TT_4) in other experimental study (Meeker and Ferguson, 2011). Also, previous studies from China reported that exposure to BPA was associated with an elevation in the concentration of TSH, T_3, and T_4 (Wang *et al*., 2012; 2013).

Because of these inconclusive effects of BPA on thyroid hormones with limited studies of occupational BPA level, this study was performed to measure BPA level in the serum of workers in a plastic processing factory as a biomarker of occupational BPA exposure and to identify the relation between occupational exposure to BPA and thyroid hormones.

MATERIALS AND METHODS

The study was performed in a factory of plastic processing industry that is located at the 10th of Ramadan City, industrial zone A2, Al-Sharqiyah governorate, Egypt. This factory produces different products, such as cleaning tools, cookware as dishes, and many forms of plastics as baskets, tables, chairs, commodes, Shannon and turbo are also produced. The factory consists of many departments, including Moulding departments; Squeegees department; Breaker or granulator (crushing); Recycling department; PVC department; Decoration and finishing departments. The manufacturing processes were semiautomatic in which the raw materials and products were manually handled by the workers.

Study type and subjects: This study is a cross-sectional study, approved by the ethical committee of the National Research Centre (No.13-177), Egypt. All workers in the production line were included in the study (118 workers). According to exclusion criteria (Duration of work less than 1 year, pathological history of hyperthyroidism, thyroidectomy, thyroiditis, or hypothyroidism, taking medications affecting thyroid function, or antithyroid drugs, history of currently taking, or had previously taken thyroid hormones), 28 workers were excluded. Ultimately, 90 workers participated in the study distributed in different departments of the factory.

The study tools used were interview questionnaire that covered personal history, occupational history, and medical history. Venous blood sample was taken from each participant to measure serum BPA and thyroid hormones (TT3, TT4, and TSH) by using Enzyme-linked immunosorbent assay (ELISA) technique. BPA was assessed by using human bisphenol A ELISA kit (GSCIENCE Kit /USA) according to the method by Kodaira *et al*. (2000).

Statistical analysis

Data were presented as number and percentages for qualitative variables. Because serum BPA concentrations among the studied workers were not normally distributed, data will be presented as median and interquartile range. Non-parametrical Mann–Whitney *U* test and Kruskal–Wallis test were used to compare the differences in median serum BPA concentrations. BPA was log 10-normal-transformed to get normal distributions. Thyroid measures were presented as means and standard deviation (SD). We used Pearson correlation for thyroid hormones and logged BPA concentrations to find possible associations. The statistically significant level was set at $p \leq 0.05$.

RESULTS

The studied population includes 90 male workers, whose ages ranged from 21 to 54 years. The majority of the workers were married (85.6%) and from rural areas (91.1%). As regards education, almost two-thirds of the workers (67.8%) were secondarily educated. As regards the occupational characteristics of the studied workers, the manufacturing process was a semiautomatic process. More than half of the studied workers (56.7%) were machine operators (controlling the machine and retrieving the products), 12.2% were maintenance workers (changing the mold and maintaining the machine), and the same percentage of workers was in the finishing work (painting and packaging), while 18.9% were in the position of dealing with chemicals (Table 1).

Serum BPA concentrations among the studied workers were ranged from 1.9 to 62.9 ng/ml and the median BPA was 15.6 ng/ml and the interquartile range was 10.2–26.5 (Table 1). On studying the factors that may affect BPA concentration, we found no statistically significant difference in the concentrations of serum BPA as regards age, residence, marital status, education, nature of work, and the duration of work of the studied workers.

Table 2 shows thyroid hormones level among the studied workers; TSH levels were above the normal range, T3 levels were in the normal range while T4 levels were below the normal range.

According to TSH level and T4 levels, workers were classified into two categories: 1—Euthyroid group: that had normal TSH level with normal T4 levels and 2—Subclinical hypothyroidism group: TSH level higher than normal but less than 10 µIU\ml (American Thyroid Association, 2012). Based on this classification, 64.4% of the studied workers (n = 58) had normal thyroid function and 35.6% (n = 32) had subclinical hypothyroidism. To identify the relation between serum BPA concentration and thyroid function, comparison of serum BPA among the two categories of thyroid function (Euthyroid and subclinical hypothyroidism) was done, and found that the median and interquartile range of serum BPA were lower among those with subclinical hypothyroidism than the euthyroid workers without reaching the statistically significant level (Table 3).

For detecting possible associations between BPA concentration and thyroid hormones, the pearson correlation was used (Table 4) and found that there was a positive correlation between thyroid hormone T_3 and serum BPA concentration among the studied workers. Also, there was a negative correlation between TSH and serum BPA but statistically insignificant.

DISCUSSION

As countries develop and urbanize, production demands increase globally, so the exposure to BPA has steadily increased. Therefore, assessments of occupational exposure are needed to be performed, especially with the huge consumption and production of BPA containing materials and the elevation in the number of workers exposed to it worldwide (Corrales *et al*., 2015).

As regards bisphenol A, many studies measure BPA level among the general population in different countries,

Table 1. Serum BPA concentrations according to the general and occupational characteristics of the studied workers.

General characteristics	BPA (ng/ml) Mean ± SD 19.6 ± 14.3			Non-parametric tests*
	Median 15.6	Interquartile range 16.3 (10.2–26.5)	Range 1.9–62.1	
Age groups				
21–30 (*n* = 40)	18.4	18.3 (8.7–27.0)	2.3–62.1	*p* value = 0.75
31–40 (*n* = 37)	14.8	24.0 (6.4–30.4)	1.9–55.3	
41–54 (*n* = 13)	14.4	9.2 (11.6–20.8)	5.2–49.2	
Residence				
Urban (*n* = 8)	14.8	33.6 (12.5–46.1)	4.1–62.1	*p* value = 0.47
Rural (*n* = 82)	15.6	18.6 (7.7–26.3)	1.9–55.3	
Marital status				
Single (*n* = 13)	19.6	20.2(15.2–35.4)	3.6–52.1	*p* value = 0.12
Married (*n* = 77)	14.5	20.3 (6.4–26.7)	1.9–62.1	
Education				
Primary (*n* = 19)	14.5	23.0 (11.2–34.2)	1.9–46.2	*p* value = 0.95
Secondary (*n* = 61)	15.9	17.7 (9.2–26.9)	2.1–55.3	
High education (*n* = 10)	14.9	23.1(4.6–27.7)	2.1–62.1	
Nature of work				
Machine Operators (*n* = 51)	15.4	15.9 (6.5–22.4)	1.9–50.1	*p* value = 0.36
Maintenance workers (*n* =11)	14.5	25.9 (8.2–34.1)	4.8–55.3	
Deal with chemicals (*n* = 17)	19.7	25.9 (10.3–36.2)	4.2–47.2	
Finishing workers (*n* =11)	9.2	44.1 (5.1–49.2)	5.1–49.2	
Duration of work				
1–10 years (*n* = 61)	19.36	21.2 (7.3–28.5)	1.9–62.1	*p* value = 0.62
>10 years (*n* = 29)	14.4	10.6 (10.2–20.8)	2.1–55.3	

*Mann–Whitney test and Kruskal–Wallis test for median. BPA = bisphenol A.

Table 2. Serum thyroid hormones measures of the studied workers.

Thyroid Hormones	Reference normal range†	Studied workers	
		Range	Mean ± SD
TSH (µIU/ml)	0.35–4.5	0.4–9.5	4.1 ± 2.2
T_3 (ng\dl)	75–189	77–189	129 ± 26
T_4 (µg\dl)	4.5–12.5	3.3–12.5	7.7 ± 2.5

† Reference normal range according to the American Thyroid Association, (2012). TSH = thyroid-stimulating hormone.

Table 3. Serum BPA among the studied workers according to their thyroid function status.

Thyroid function status	Total = 90		BPA (ng/ml)		Mann–Whitney test
	N%		Median	Interquartile range	
Euthyroid	*N* = 58	64.4%	16.3	21.6 (11.0–32.6)	*p* value = 0.09
Subclinical hypothyroidism	*N* = 32	35.6%	13.8	17.6 (4.6–22.3)	

BPA = bisphenol A, TSH = thyroid-stimulating hormone.

Table 4. Correlation between serum BPA and thyroid hormones.

Thyroid hormones	Correlation coefficient	*p*-value
T_3	0.237	0.02
T_4	0.061	0.56
TSH	−0.122	0.25

Serum BPA was log 10-normal-transformed to achieve normal distribution. BPA = bisphenol A, TSH = thyroid-stimulating hormone.

(Calafat *et al*., 2008; Health Canada, 2010; Park *et al*., 2017; Wang *et al*., 2013), whereas only a few studies have measured exposures to BPA in the workplace. So, studies to investigate occupational exposure to BPA and its related hazards effect are urgently needed.

In the present work, BPA was detected in the serum of all participants. Serum BPA concentrations were ranging from 1.9 to 62.9 ng/ml and the median was 15.6 ng/ml. This is in accordance with Zhuang *et al*. (2015) who reported that the median serum BPA level was 18.75 ng/ml and the range was from undetectable up to 98.5 ng/ml in workers exposed to BPA in epoxy resin industry in China. On the other hand, Xiao *et al*. (2009) reported that the median serum BPA concentration was 101.9 µg/l among 20 occupationally exposed workers in China. On the contrary, Zhou *et al*. (2013) found that median serum BPA concentration was 3.19 µg/l in a study upon workers in a petrochemical company. These wide differences in BPA levels might be explained by the fact that some factories used BPA as pure raw materials, while others used it as additives. In addition, workers exposures are affected by different factors as whether industrial processes are manual or automatic, the existence, type and efficiency of protective measures used, also, in determining BPA levels, different analytical and measuring methods are used. In comparing the results of this work with other studies, Wang *et al*. (2012) reported a level ranged from 12.5 to 164.5 ng/ml of BPA in the urine of workers from two epoxy

resin factories in china. Recently, Kouidhi *et al*. (2017) found that the interquartile range of urinary BPA was 2.03–4.99 ng/ml among 70 workers of plastic injection moulding factory in Malaysia. Although these studies were among occupationally exposed workers, they cannot be compared with the results of this study because, in the current study, BPA was measured in serum while they measured BPA in urine with different measuring methods. However, these occupational studies concluded that the BPA level among occupationally exposed workers was higher than that of the general population.

Nature of the work and the duration of work are the important occupational characteristics that may influence the exposure at the workplace. In this study, serum BPA concentrations were insignificantly higher among the workers who worked for 10 years or less than those who worked for more than 10 years (Table 1). These come in accordance with Mohamed *et al*. (2012) who found that work duration was not related to urinary BPA level among the workers of the fiberglass pipe industry in Egypt. On contrary to this finding, Zhuang *et al*. (2015) reported that work duration had a significant positive association with serum BPA level. These controversial findings maybe because there is no final proof of the accumulation potential of BPA in the human body (Corrales *et al*., 2015). However, the findings in the current study may be explained by the pharmacokinetics of BPA, as BPA is rapidly metabolized and excreted through kidneys with approximately 6 hours biological half-life, within 24 hours of complete urinary excretion (Vandenberg *et al*., 2012).

As regards the abnormality of thyroid hormones among the studied workers, it was found that 32 workers (35.6%) had subclinical hypothyroidism. Human studies concerned with the prevalence of thyroid hormone abnormalities among occupational settings are much lacking. However, the prevalence of subclinical hypothyroidism reported in this research is much higher than that reported by Soliman *et al*. (2013), Metwalley and E-Saied (2014), and Unnikrishnan *et al*. (2013). So, the finding of the present study about the high prevalence of subclinical hypothyroidism (35.6%) acts as an alarming sign that evokes many questions like, is this high prevalence specific for the workers in the studied factory or involve the workers of other plastic processing industry? and if there is a causal relationship to chemicals involved in the plastic processing industry or related to environmental pollutants? also what about the general population? Further research on a large scale not only on plastic workers but also on the general population is urgently needed to answer these questions.

To identify the relation between serum BPA concentration and thyroid function, comparison of serum BPA among the two categories of thyroid function (Euthyroid and subclinical hypothyroidism) was done, and found that the median and interquartile range of serum BPA were lower among those with subclinical hypothyroidism than the euthyroid workers without reaching the statistically significant level (Table 4). This means that serum BPA has no effect on TSH levels among the exposed workers. This finding is in agreement with Sugiura-Ogasawara *et al*. (2005) who reported unchangeable BPA mean values between patients with and without hypothyroidism. Also, Wang *et al*. (2013) found a lower urinary BPA on subjects with overt or subclinical hypothyroidism in comparison with the euthyroid group. As in our study, no relation was detected between the levels of serum BPA and subclinical hypothyroidism among the studied workers of plastic processing industry, this hypothyroidism condition may be attributed to many other factors as plastic workers deal with different chemical compounds, some of them had endocrine disruptor effects as brominated flame retardants, phthalates, as well as BPA. Also, plastic workers are exposed to complex mixtures of chemicals whose combined effects on health may be more than their individual ones. In addition, plastic workers are also exposed to environmental pollutants which may affect thyroid function as dioxin, perchlorate, and some pesticides and heavy metals.

For further exploration of the relation between BPA and thyroid hormones, the correlation was done and found that there was a statistical significant positive correlation with T3 and an insignificant negative correlation with TSH among the studied workers. That is the same finding of Wang *et al*. (2012) who found that increasing urinary BPA levels in exposed workers was accompanied by rose of T3 and dropped in TSH levels, although this drop was not significant. Also, Wang *et al*. (2013) reported a positive association of urinary BPA and FT_3 and inverse association with TSH among 3,394 non-occupationally exposed Chinese population. On the contrary, Meeker *et al*. (2010) found a weak inverse association between BPA and TSH but they observed no association of BPA with total T3 in male patients from infertility clinics. Also, Meeker and Ferguson (2011) using data from US NHANES 2007–2008 reported no relation between BPA and TSH in 1,346 adults and they observed an inverse correlation between BPA and total T4.

These controversial results may be explained by the complex mechanism of action of BPA as endocrine disruptors. Because of the structural similarity of BPA to thyroid hormone, BPA binds to thyroid hormone receptors and acts as an agonist or antagonist of thyroid hormone receptor. Also, there is evidence from experimental studies indicating that BPA inhibits the secretion of TSH at the pituitary level and suppresses TSH release a way that is independent of the thyroid hormone feedback mechanism (Sriphrapradang *et al*., 2013). Such mechanism might be more difficult to understand, as the receptors of thyroid hormones might not be a direct target of BPA but instead another factor might be involved, as BPA was observed to have a direct effect on thyroid follicular cells and leads to inhibit transcriptional activity that promoted by T3 in a dose-dependent mechanism in the transient gene expression experiments (Chailurkit *et al*., 2006). xSo, it seems agreeable that BPA would not produce patterns of disorders that simulate thyroid hormone insufficiency or excess.

Although the studies did not provide a conclusive finding of the exact effect of BPA on thyroid hormones, they supported the evidence that BPA is thyroid disruptor.

CONCLUSION

The studied workers in that factory of the plastic processing industry had bisphenol A levels higher than that reported for the Egyptian general population. As regards thyroid function, it was found that almost one-third of the studied workers had subclinical hypothyroidism. However, this finding was not significantly related to BPA levels. There was a statistically significant positive correlation between thyroid hormone triiodothyronine (T_3) and serum BPA concentrations.

Consequently, we recommended that there is a great need for environmental and biological monitoring of BPA exposure not only in the present factory but also in all plastic processing industries, and occupations in which workers are suspected to

exposed to a high BPA level. Raise the awareness of the general population and environmental concerning agencies about BPA exposure, its health effects, and how to limit its danger. Further studies among the general population and occupationally exposed workers are needed for more identification of the effects of BPA exposure on thyroid and other body systems.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest in this article.

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