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RESEARCH ARTICLE

Mothers' Knowledge Regarding The Hazards Xenoestrogens Pose To Young Females: A Cross-Sectional Study in Western Saudi Arabia.

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Abstract

Background:-Xenoestrogens are endocrine-disrupting chemicals capable of altering or interfering with the natural actions of endogenous hormones. However, there is currently a paucity of data regarding the public's knowledge of the risks xenoestrogens pose, especially for young females, and regarding their knowledge of measures that can be taken to prevent such risks. This study aim to investigate mothers' knowledge of the hazards associated with xenoestrogen exposure in young females in western Saudi Arabia.

Methods:-This cross-sectional study was conducted at the pediatric ambulatory clinic at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, between June and August 2016. We randomly selected mothers with at least one daughter aged 6–15 years. In total, 794 mothers participated. Data were gathered on the participant demographics, beliefs about xenoestrogens, and knowledge of xenoestrogen-containing products and related risks.

Results:- The mean age of the participants was 38.4 ± 7.01 years. Most were of Saudi origin ($n = 625$, 78.7%). There were 378 (47.6%) mothers with a low/average level of education, whereas 416 (52.4%) were highly educated. Only 219 (27.6%) had received previous information regarding xenoestrogens; the remaining 575 (72.4%) had not. There was a significant association between the mothers' education level and their knowledge of xenoestrogen hazards.

Conclusions:- Our findings indicate that knowledge of xenoestrogens among mothers in Saudi Arabia is limited. Hence, programs and activities using social media, as well as educational campaigns, need to be established to increase awareness.

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Introduction:-

Xenoestrogens are endocrine-disrupting chemicals (EDCs) that are capable of altering or interfering with the natural actions of endogenous hormones [1]. Moreover, it has been recently reported that xenoestrogens can affect pubertal maturity in addition to modifying the behaviors and neurobiology of wildlife, laboratory animals, and humans [2].

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Specifically, there are claims that xenoestrogens can induce early development of pubertal characteristics in young girls. In addition, xenoestrogens are associated with increased risks of developing breast, ovarian, prostate, and endometrial cancers [3]. Hence, there is a need to evaluate the level of public awareness—especially among mothers—of the existence of environmental xenoestrogens and the effects of xenoestrogens on pubertal development in young girls. The most critical periods of human exposure to xenoestrogens, which occurs mainly through interactions with xenoestrogen-containing products such as domestic and consumer plastic products made from polybrominated biphenyls (PBBs), are during the antenatal, pre-pubertal, and post-pubertal periods

The xenoestrogens most commonly found in consumer and domestic products, and consequently in the environment, are bisphenol A (BPA), dioxin, PBB, phthalate esters, dichlorodiphenyltrichloroethane (DDT), and polychlorinated biphenyls [4]. In fact, many consumer and domestic products that contain chemicals that introduce xenoestrogens into the environment are used daily for beverage and food storage. Moreover, physical contact with certain products, such as pesticides, dry cleaning chemicals, industrial waste, and other environmental sources, is almost inevitable. Thus, it is important that the public is aware of xenoestrogens and their effects, as well as of any preventative measures to reduce exposure, such as not using plastic wrapping materials, replacing plastic food storage containers with glass packaging and plastic bottles with glass cups, avoiding the consumption of canned food, and using natural cleaning products [5]. In this study, we aimed to investigate mothers' knowledge of the hazards posed by xenoestrogens for young females in a western region of Saudi Arabia.

Methods:-

Study setting and participants:-

This was a cross-sectional study conducted at the pediatric ambulatory clinic at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, between June and August 2016. The Ethics Committee of King Abdulaziz University approved the study. We randomly selected mothers who had at least one daughter aged 6–15 years. The objective of the study was explained to each potential participant, and verbal consent was obtained before study enrollment. The personnel who assisted with data collection were informed regarding the strategy for the selection and recruitment of participants for the study.

For further analyses, the study participants were classified into two groups: mothers with low/average education (participants with a primary, middle, or high school education) and highly educated mothers (bachelor's degree or higher level of education).

The survey questions were divided into four parts to obtain data on the following: 1) Socio-demographic characteristics; 2) awareness of the participants regarding xenoestrogens and their effects on early puberty and health, including some cancer-related questions in the second part; 3) family exposure to xenoestrogen products; and 4) one specific question on whether they had previous knowledge of the term 'xenoestrogen'.

Statistical analysis:-

The data collected were entered, coded, and analyzed using SPSS version 16.0 (SPSS Inc., Chicago, IL). Pearson's chi-square analysis was performed to evaluate the relationship between each research question and the mothers' education level, and to quantify the strength of any relationship found. The dependent variable was set as the education level of the respondents, dichotomized as low/average and high education. The independent variables included a variety of factors that can affect the pubertal age of girls, such as ethnicity, genetic factors, consanguinity, and mother's age at puberty, father's age at puberty, nutritional status, and consumption of fast foods or foods that contain hormones. For all analyses, a p -value < 0.05 was considered statistically significant.

Results:-

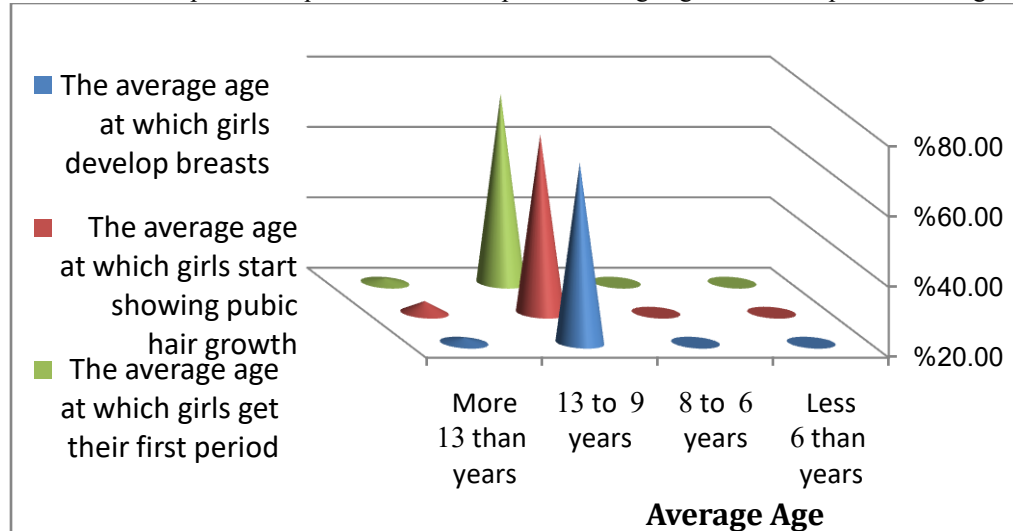
A total of 794 mothers were randomly selected to participate; of these, 625 (78.7%) were of Saudi nationality and 169 (21.3%) were non-Saudis. The mean age of the mothers was 38.4 ± 7.01 years. Low/averagely educated mothers comprised 47.6% ($n = 378$) of the sample, while highly educated mothers comprised the remaining 52.4% ($n = 416$).

To ascertain whether there was any relationship between the mothers' level of education and their previous level of awareness about xenoestrogens, the respondents were asked: 'Do you have any previous information regarding xenoestrogens?' Their responses were stratified by the level of education. There was no significant difference in the

proportion of positive responses to this question between those with a low/average education level ($n = 96$; 25.4%), and those with a high education level ($n = 123$; 29.6%).

The mothers surveyed were asked at what age they think certain pubertal characteristics (breasts, pubic hair, and menarche) normally develop; their responses (in percentages) are shown in Figure 1.

Figure 1:-Mothers' responses to questions on the expected average age at onset of pubertal changes in girls



The mother's responses regarding their awareness of factors related to the age of puberty in girls, such as ethnicity, genetic factors, consanguinity, mother's age at puberty, father's age at puberty, nutritional status, use of xenoestrogen-containing products, and consumption of fast foods or foods containing hormones are presented in Table 1. There were statistically significant relationships between the mothers' education level and their responses regarding the awareness of ethnicity ($p = 0.010$), genetic factors ($p = 0.010$), mother's age at puberty ($p = 0.008$), father's age at puberty ($p = 0.054$), use of xenoestrogen-containing products ($p = 0.016$), and eating foods containing hormones ($p = 0.013$) as factors influencing the age of puberty in girls.

Table 1: Mothers' responses regarding knowledge of factors that may affect the age at puberty of young females

	Low/average education				High education				P
	Yes	No	Maybe	Don't know	Yes	No	Maybe	Don't know	
Ethnicity	139 (36.8)	137 (36.2)	68 (18.0)	34 (9.0)	188 (45.2)	143 (34.4)	68 (16.3)	17 (4.1)	.0100
Genetic factors	230 (60.8)	59 (15.6)	77 (20.4)	12 (3.2)	293 (70.4)	60 (14.4)	58 (13.9)	5 (1.2)	.0100
Consanguinity	142 (37.6)	133 (35.2)	73 (19.3)	30 (7.9)	148 (35.6)	159 (38.2)	73 (17.5)	36 (8.7)	.7610
Mother's age at puberty	181 (47.9)	84 (22.2)	82 (21.7)	31 (8.2)	236 (56.7)	86 (20.7)	80 (19.2)	14 (3.4)	.0080
Father's age at puberty	83 (22.0)	158 (41.8)	82 (21.7)	55 (14.6)	108 (26.0)	174 (41.8)	98 (23.6)	36 (8.7)	.0540
Nutritional status	220 (58.2)	56 (14.8)	72 (19.0)	30 (7.9)	248 (59.6)	59 (14.2)	90 (21.6)	19 (4.6)	.2200
Using xenoestrogen-containing products	189 (50.0)	37 (9.8)	81 (21.4)	71 (18.8)	246 (59.1)	35 (8.4)	87 (20.9)	48 (11.5)	.0160
Eating fast food	209 (55.3)	51 (13.5)	83 (22.0)	35 (9.3)	261 (62.7)	47 (11.3)	79 (19.0)	29 (7.0)	.1890
Food containing hormones	238 (63.0)	23 (6.1)	78 (20.6)	39 (10.3)	303 (72.8)	19 (4.6)	71 (17.1)	23 (5.5)	.0130

Data are presented as n (%).

The mothers' responses to the questions regarding how height, short stature, an increase in body mass index, and estrogen hormones can affect the pubertal age of girls are shown in Table 2. In addition, the awareness of mothers about the effect of increases in estrogen hormones and the use of xenoestrogen-containing products on an increase in the risk of cancer was also recorded. There was a significant relationship between the mothers' education level and awareness of the facts that xenoestrogens have side effects ($p = 0.047$), increases in body mass can affect early puberty ($p = 0.059$), and estrogen hormones can affect the height of a child ($p = 0.046$).

Table 2: Mothers' general knowledge of xenoestrogens

Question <i>Do you think that:</i>	Low/average education				High education				P
	Yes	No	Maybe	Don't know	Yes	No	Maybe	Don't know	
Xenoestrogens have any side effects?	161 (42.6)	16 (4.2)	102 (27.0)	99 (26.2)	207 (49.8)	25 (6.0)	104 (25.0)	80 (19.2)	.0470
There is a relationship between height and puberty?	116 (30.7)	171 (45.2)	73 (19.3)	18 (4.8)	147 (35.3)	162 (38.9)	89 (21.4)	18 (4.3)	0.300
There is a relationship between short stature and early puberty?	181 (47.9)	84 (22.2)	87 (23.0)	26 (6.9)	210 (50.5)	87 (20.9)	101 (24.3)	18 (4.3)	0.409
Increases in body mass index can effect early puberty?	148 (39.2)	83 (22.0)	90 (23.8)	57 (15.1)	196 (47.1)	74 (17.8)	101 (24.3)	45 (10.8)	0.059
Estrogen hormones can affect the height of your child?	102 (27.0)	81 (21.4)	105 (27.8)	90 (23.8)	147 (35.3)	81 (19.5)	113 (27.2)	75 (18.0)	0.046
Increases in estrogen hormones can cause cancer?	131 (34.7)	46 (12.2)	115 (30.4)	86 (22.8)	172 (41.3)	51 (12.3)	113 (27.2)	80 (19.2)	0.238
Increased use of xenoestrogen can cause cancer?	38 (10.1)	32 (8.5)	252 (66.7)	56 (14.8)	52 (12.5)	34 (8.2)	283 (68.0)	47 (11.3)	0.390

Data are presented as n (%).

Finally, the mothers were asked about their awareness of xenoestrogen-containing products such as plastic bottles, plastic packaging materials, cosmetic products, food preservatives, and soap/shampoo. Their responses are shown in Table 3.

Table 3: Mothers' knowledge of products that may exert xenoestrogenic effects

Do these products have a xenoestrogenic effect?	Low/average education				High education				P
	Yes	No	Maybe	Don't know	Yes	No	Maybe	Don't know	
Plastic water bottles	69 (18.3)	130 (34.4)	92 (24.3)	87 (23.0)	89 (21.4)	132 (31.7)	117 (28.1)	78 (18.8)	0.239
Children's toys	83 (22.0)	104 (27.5)	114 (30.2)	77 (20.4)	104 (25.0)	116 (27.9)	114 (27.4)	82 (19.7)	.0190
Plastic packaging materials	91 (24.1)	108 (28.6)	97 (25.7)	82 (21.7)	115 (27.6)	97 (23.3)	137 (32.9)	67 (16.1)	.1640
Cosmetics	120 (31.7)	83 (22.0)	89 (23.5)	86 (22.8)	142 (34.1)	73 (17.5)	119 (28.6)	82 (19.7)	.1640
Food preservatives	99 (26.2)	102 (27.0)	90 (23.8)	87 (23.0)	112 (26.9)	85 (20.4)	129 (31.0)	90 (21.6)	.0570
Pesticides	85 (22.5)	122 (32.3)	86 (22.8)	85 (22.5)	84 (20.2)	117 (28.1)	121 (29.1)	94 (22.6)	0.197
Certain soaps and shampoos	85 (22.5)	238 (63.0)	32 (8.5)	23 (6.1)	96 (23.1)	263 (63.2)	36 (8.7)	21 (5.0)	.9350

Data are presented as n (%).

Discussion:-

Our findings in the present investigation on mothers' knowledge of xenoestrogen-related hazards for young females in western Saudi Arabia showed mixed results. There was a statistically significant association between the education level of the mothers and their knowledge regarding xenoestrogen-related hazards, specifically in terms of the following: ethnicity, genetic factors, mother's age at puberty, father's age at puberty, use of materials that contain xenoestrogens, and consumption of foods containing hormones.

Further, we attempted to determine whether any relationship existed between the mothers' level of education and their awareness of how height, short stature, increases in body mass index, and estrogen hormones can affect pubertal timing in girls. In addition, other variables, such as their awareness of the effects of increases in estrogen hormones and increases in the use of xenoestrogen-based products on the development of cancer were also evaluated, with mixed results.

Puberty is defined as a period of spontaneous transformation during which the body of a child undergoes a number of changes to attain the reproductive system of an adult [6]. The onset of puberty provides an opportunity to study individual differences in pubertal timing; this timing can differ by more than five years [7]. By studying the variations in pathological pubertal characteristics in female laboratory rodents and the hypothalamic actions that control the commencement of sexual development, a relationship between early pubertal onset and several genetic and environmental factors has been reported [8]. Specifically, possible links between the age of puberty onset and a number of factors such as ethnicity, genetics, nutrition, EDCs (both manufactured and naturally occurring), geographical area, stress, and prevailing socio-economic circumstances have been suggested [8,9]. Moreover, it has been claimed that the tendency of environmental factors to influence the actions of neuroendocrine structures in humans is greater during the fetal and early postnatal life than at the onset of pubertal development [7]. However, a recent study claimed that the effects of environmental factors on pubertal timing and characteristics are rather complex and confirmed that environmental factors can affect genetic elements and consequently affect the pubertal characteristics and the timing thereof [10]. Importantly, one of the main factors affecting the timing of puberty is the environment of the child, and endocrine disruptors—both natural and chemical-based—are important components of the environment.

Endocrine disruptors are exogenous chemical compounds with actions that are similar or antagonistic to those of endogenous hormones, thereby causing disturbances in the endocrine homeostasis. In the last five decades, the understanding of endocrine disruptors and their mechanisms of action has grown due to an increase in the number of research studies conducted on the topic. The increased interest in EDCs resulted from the realization of the effects of these chemicals in communities where the use of domestic and consumer products, such as plastic bottles and cosmetics, is high [11-13]. The mechanisms of action of EDCs in the human body include mimicking endogenous hormones such as estrogen, thereby antagonizing endogenous hormones by competing with the primary hormone for binding to its receptors, resulting in either enhanced or inhibited hormone stimulation, and interference with the metabolism and synthesis of endogenous hormones, for example by disturbing their metabolism in the liver, which increases the quantity of the primary endogenous hormones in the blood and results in abnormal effects [11-14]. Consequently, the related target organs are also affected by the exposure to EDCs. These chemicals exert their effects during three critical periods during which their toxicity has the greatest influence: in utero, before puberty, and in adulthood [4]. Although these chemicals are abundant in the environment, mothers who participated in the present survey had a limited knowledge of them.

Worldwide, there has been an increase in the production and consumption of a number of EDC-containing products, which are easily available at a low cost and, hence, are commonly used for domestic purposes. As the use of these products has increased, there has been a parallel rise in several diseases, such as disorders related to the development of the female breast, obesity, cancer, and reproductive and metabolic diseases [11-15]. DDT, an organochlorine pesticide, became popular and commonly used after 1939, and was globally recognized as a wonder chemical for controlling pests. However, its potential toxicity for animals and humans soon became apparent, and DDT was quickly recognized as a possible cause for the increase in health issues such as feminization, intersex in fish, precocious puberty, cancers, and thyroid hormone suppression. Consequently, DDT was subsequently banned in several countries, especially throughout Western Europe and in the USA [16,17]. Since then, dichlorodiphenyldichloroethylene, another important xenoestrogen compound that is a derivative of DDT, has also been discovered in the environment. It was found to affect the age of menarche in a retrospective study conducted in Belgium [18,19], while a cross-sectional study conducted in China in 2005 found an association between

DDT/dichlorodiphenyldichloroethylene and an earlier age at menarche and an increased risk of experiencing a shortened menstrual cycle [20]. Other xenoestrogen chemicals have also been found to affect sexual maturation. A 2013 French study that focused on premature thelarche reported an increase in estrogenic bioactivity in the blood of the analyzed females [21]. In 2000, a case-control study showed a possible link between phthalates with estrogenic and anti-androgenic activities and premature thelarche in females.⁵ A study on EDC compounds conducted in 2010 claimed that phthalates, along with phytoestrogens and phenols, exerted an effect on the early development of breasts and demonstrated a weak association with early onset of pubic hair growth [22]. In 2006, yet another study on PBBs showed a link between the effect of EDCs and earlier pubic hair development and age of menarche age in breastfed females with *in utero* PBB exposure [23]. In the present study, 59.1% of highly educated mothers acknowledged that xenoestrogens could affect puberty, as compared to 50.0% of mothers with a low/average education level.

Prior to 1971, xenoestrogens were used in diethylstilbestrol given to pregnant women to prevent miscarriage. Diethylstilbestrol has been associated with numerous adverse consequences later in adult life for daughters exposed to it *in utero*, including grade 2 or higher cervical intraepithelial neoplasia and breast cancer [24]. Further, BPA is a major xenoestrogen chemical found abundantly in the environment. It is one of the most commonly produced EDCs, used extensively in the manufacture of epoxy resins and polycarbonate plastics, which are found in reusable containers including water bottles, baby milk plastic bottles, plastic tableware, and many other commonly used plastic products. BPA has been linked to many health issues due to *in utero* exposure, leading to increases in body weight and the development of various cancers [4,25]. BPA has been reported to show a tendency to induce neoplastic changes by antagonizing the protective effect of the estradiol cascade in the colon; hence, BPA exposure is a potential risk factor in the development of colon cancer [26]. In addition, lung and lymphatic cancers, as well as cardiovascular diseases, have been linked to dioxin exposure [27,28], and a recent case-control study conducted in Spain observed an association between serum total xenoestrogen mixtures and breast cancer risk [29]. However, only 11.3% of the mothers who participated in the present survey were aware or believed that xenoestrogens could increase the risk of cancer.

This study had some limitations, most importantly, its relatively small sample size and the fact that the study was conducted in a small geographic area. Hence, it is difficult to generalize our results to other areas or populations.

In conclusion, the knowledge of xenoestrogens and their effects on puberty in young females among mothers in Saudi Arabia is limited. Among those surveyed, mothers with a high level of education tended to have superior knowledge regarding xenoestrogen hazards, indicating the importance of education in this population. Accordingly, programs and activities using social media, as well as educational campaigns, need to be established to increase awareness.

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