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The association of endocrine-disrupting chemicals exposure, sociodemographic factors, and polycystic ovarian syndrome among reproductive-aged nonpregnant women at the Philippine General Hospital: A case–control study

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Abstract:

BACKGROUND: Polycystic ovarian syndrome (PCOS) is a prevalent condition affecting women of reproductive age, characterized by metabolic, endocrine, and reproductive disturbances including insulin resistance, abnormal uterine bleeding, infertility, and hyperandrogenism, and is associated with diabetes and cardiovascular disease. The etiology of PCOS is unclear and exposure to endocrine-disrupting chemicals (EDCs) present in everyday products may play a role by disrupting hormonal pathways.

OBJECTIVES: To determine the association between exposure to EDC-containing products, sociodemographic factors, and PCOS diagnosis among nonpregnant reproductive-aged women.

MATERIALS AND METHODS: A survey assessed the frequency of EDC exposure in homes and workplaces. The Rotterdam Criteria were used for the diagnosis of PCO features with clinical history and ultrasound. The association between PCOS and EDC exposure was determined using Chi-square and logistic regression analysis.

RESULTS: The study identified significant sociodemographic factors associated with PCOS ($P < 0.001$) including age, civil status, and household income. Increased likelihood of PCOS was linked to frequent use of scented candles (odds ratio [OR] = 2.07), cleaning sprays (OR = 2.28), and floor polish (OR = 2.07), exposure to new upholstered furniture (OR = 4.00), thermal receipts (OR = 2.16), and consumption of microwaved and processed foods (OR = 2.60), as well as water sourced from wells (OR = 7.69). Additional associations were found with access to public markets (OR = 0.26) and the use of paper food wrappers (OR = 1.72).

CONCLUSION: These findings suggest that frequent exposure to EDC-containing products and certain sociodemographic factors may contribute to the development of PCOS among women of reproductive age. Results underscore the importance of reducing exposure to EDCs to prevent or mitigate the development of PCOS and other reproductive consequences.

Keywords:

Endocrine-disrupting chemicals, females, nonpregnant women, PCOS

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Introduction

Polycystic ovarian syndrome (PCOS) is characterized by hyperandrogenism, oligomenorrhea, and polycystic ovaries on ultrasound and is associated with an increased risk of infertility, type 2 diabetes, and cardiovascular disease.^[1] Globally, this common endocrine disorder affects 4%–20% of reproductive-aged women.^[2] The etiology of PCOS is not well understood, but environmental factors, including exposure to common chemicals, have been suggested as a possible contributing factor.^[3]

Endocrine-disrupting chemicals (EDCs) are a diverse group of compounds found in common items such as plastics, pesticides, personal care products, and food packaging materials, now classified as environmental pollutants.^[3] Commonly studied EDCs are Bisphenol A (BPA), found in plastics and food containers, parabens, and phthalates, which are found in personal care products and upholstery, and 2,4-dichlorophenoxyacetic acid, which is a common component of highly toxic herbicides.^[4-7] Evidence shows that EDCs can bioaccumulate in the human body through dermal, oral, and respiratory pathways, leading to various adverse health outcomes, including reproductive, metabolic and endocrine disorders, obesity, and cancer.^[3,8-11] In addition, accumulating evidence suggests that prenatal exposure to EDCs can lead to lasting effects on offspring, such as anomalous brain development and function and abnormal genital development.^[12,13]

Despite emerging evidence of human exposure and bioaccumulation of EDCs and their association with several health effects, the Philippines falls behind in examining common EDCs in the general population. Therefore, the objective of the study is to describe the exposure to common products that may contain EDCs such as phthalates, parabens, BPA, and 2,4-dichlorophenoxyacetic acid, the sociodemographic factors, and determine their association with having a PCOS diagnosis among women aged 18–49 years.

Materials and Methods

Study design and setting

This case-control study determined risk factors in the development of PCOS in nonpregnant women with or without exposure to EDCs. This study was conducted at the University of the Philippines – Philippine General Hospital (UP PGH) Department of Obstetrics and Gynecology (OB-GYN). Participants provided informed consent before completing the Environmental Pollutants and Endocrine Disruptors Questionnaire Survey and having their pelvic ultrasound with clinical history. Sources of exposure were organized into different

materials and classified according to the possible EDC they contain. This study obtained an ethical review clearance from the UP-Manila Research Ethics Board (UPMREB Code 2019-300-01).

Target population and eligibility criteria

The inclusion criteria were nonpregnant, reproductive-aged (18–49 years old), nonmenopausal women with no known illness or comorbidity, and who were not using hormonal medications for more than 6 months before the study. Women aged <18 years old and more than 49 years old, menopausal women, individuals with any chronic illness, comorbidity, or persisting disease such as hypertension, endocrine disorder, or seizure on medications, and those diagnosed with any disease during the study were excluded from the study. The patients consulting at the UP PGH – OB-GYN through face-to-face and teleconsulting services from community health centers in Manila City from October 15, 2021, to May 14, 2022, were invited to participate in the study.

Sample size calculation

A logistic regression of a binary response variable ($Y = \text{PCOS}$) on a binary independent variable ($X = \text{exposure to EDCs}$) with a sample size of 706 observations achieves 80% power at a 0.05 significance level to detect a change in the odds of PCOS from the baseline value of 0.460 to 0.580. This change corresponds to an odds ratio (OR) of 1.62. An adjustment was made since a multiple regression of the independent variable of interest on the other independent variables in the logistic regression obtained an $R^2 = 0.20$.

Sampling, data collection, and management

Simple random sampling was done using random number-generating software. Participants who met the inclusion criteria accomplished the Environmental Pollutants and Endocrine Disruptors Questionnaire Survey, administered by a research assistant, to determine their EDC exposure. Participants underwent a pelvic ultrasound performed by a trained clinician to diagnose PCOS using the Rotterdam criteria, which confirm the condition if at least two of the following three features are present: Oligo/anovulation, hyperandrogenism, or polycystic ovaries observed on the ultrasound.^[1]

Adapted from Gerona *et al.*'s study^[14] on EDC exposure in pregnant women, the questionnaire has been revised for relevance in the Philippine context. It is organized into four sections: the first section contains 7 questions on basic demographics and socioeconomic status. The second section includes 24 questions that explore the use of industrial and factory materials. The third section, with 8 questions, addresses agricultural factors, such as proximity to pesticide-using facilities and the consumption of organic produce. The final section,

comprising 3 questions, focuses on other food items in the household, such as processed foods and similar products.

Data collected were managed with stringent confidentiality and security protocols. Participant information was anonymized by assigning a unique identification number to each dataset, with names replaced by these identifiers. Data entry and encoding were conducted by research assistants who entered the data into a secure, password-protected database, ensuring accuracy through verification procedures. Electronic data were stored on encrypted servers with regular backups, while physical documents were kept in locked filing cabinets within a secure facility. Access to the data was strictly limited to the principal investigator, authorized research team members, and, if necessary, the University of the Philippines Manila Research Ethics Board (UPMREB).

Statistical analysis

The population profile, such as sociodemographic factors and clinical information, was described using frequency and percentages. The association of the exposure to EDCs to the non-PCO and PCO diagnosis was determined using the Chi-square analysis. To determine the relationship between each significant exposure factor associated with having PCOS, logistic regression was performed. The OR for each factor was also determined. All statistical analyses were performed using STATA Version 14 (RRID:SCR_012763).

Results

Sample population profile

A total of 706 nonpregnant women participated in the survey, with 636 participant responses analyzed. The study had 106 participants (16.67%) who were diagnosed with PCOS using the Rotterdam criteria, whereas the remaining 530 (83.33%) had nonpolycystic ovary findings (controls).

Table 1 presents the characteristics of the nonpregnant PCO and nonpregnant non-PCO. Sociodemographic factors such as age, civil status, occupation, type of residence, and household income were examined. Age, civil status, and household income have a significant association with being diagnosed with PCO [Table 1].

Sources of endocrine-disrupting chemical exposures

Sources of EDCs include industrial and factory materials found in homes, agricultural products, and processed food [Table 2]. Industrial and factory materials associated with PCOS diagnosis include makeup, a certain brand of toothpaste, scented candles/incense, cleaning sprays, floor or furniture polish or wax, removing or installing

flooring, purchase or receipt of new upholstered furniture, exposure to thermal receipts, microwaved food in plastic containers, and scratched rice cooker. Moreover, access to public, processed food such as red meat, food wrapped in paper or cardboard, beer, canned soda or juice, and water sourced from a well are associated with PCOS.

Simple logistic regression showed significant associations between PCOS and the following factors: Being aged 20–29 or 40–49 years, being married, separated, widowed, or having a partner, earning at least Php 50,000, exposure to scented candles/incense, cleaning spray, or floor/furniture polish/wax for more than 24 h, recent flooring installation, new upholstered furniture, frequent handling of thermal receipts, using makeup <7 times a week, microwaving food in the last 24 h, drinking canned juice or soda thrice a week, uncertainty about scratched rice bowls, consuming fruits or vegetables from public markets, recent intake of red meat, eating food wrapped in paper/cardboard, drinking beer within the last week, and drinking well water [Table 3].

The odds of having PCOS were 4.6 times higher for those aged 20–29 years, whereas the odds were 66.67 times lower for those aged 40–49 years. Using cleaning spray within the past week increased the odds by 2.27 times and eating microwaved food in the last 24 h increased the odds by 2.60 times. Exposure to thermal receipts increased the odds by 2.16 times. Eating fruits and vegetables from public markets decreased the odds by 0.74 times. Consuming red meat in the past 24 h increased the odds by 1.66 times, whereas consuming red meat between 2 days and a week ago decreased the odds by 0.58 times. Eating food wrapped in paper or cardboard in the past 24 h increased the odds by 1.72 times. Drinking beer between 2 days and a week ago increased the odds by 2.30 times, and drinking well water increased the odds by 7.69 times.

Discussion

Several sociodemographic factors had a significant association with PCOS diagnosis. In this study, PCOS was found to be associated with civil status. Being married or in healthy relationships was found to have an association with a better quality of overall health.^[15] Logistic regression also shows that younger age groups have an increased probability of having PCOS. This is in line with other studies that showed the proportion of PCOS-diagnosed women to have increased in the last decade, with higher numbers in younger women.^[2] While there are debates in PCOS diagnostic criteria, limitations in the use of biochemical markers of PCOS remain clinical, especially in a low-resourced setting. In addition, PCOS is difficult to diagnose in women in their perimenopausal

Table 1: Association of sociodemographic factors and exposure to endocrine-disrupting chemical-containing items with polycystic ovarian syndrome diagnosis

Factors	PCOS status		χ^2	P
	Negative	Positive		
Sociodemographic factors				
Age group (years old) (n=636)				
10–19	19	14	92.05	<0.001
20–29	132	64		
30–39	175	27		
40–49	204	1		
Civil status (n=636)				
Single	306	94	36.24	<0.001
Married or have a partner	205	11		
Separated or widowed	19	1		
Household income (n=631)				
<P10,000	279	48	31.02	<0.001
P10,000–P29,999	190	34		
P30,000–P49,900	39	5		
P50,000 or more	18	18		
Personal care products				
Make-up (n=634)				
Past 24 h	160	39	7.04	0.030
More than 24 h	89	25		
Unexposed	280	41		
Popular brand toothpaste (n=635)				
Past 24 h	163	39	6.04	0.049
More than 24 h	29	11		
Unexposed	337	56		
Scented candles/incense (n=636)				
Past 24 h	15	5	6.81	0.033
More than 24 h	42	16		
Unexposed	473	85		
Cleaning sprays				
Past 24 h	24	5	8.84	0.012
More than 24 h	53	21		
Unexposed	452	78		
Floor or furniture polish or wax (n=634)				
Past 24 h	8	2	7.45	0.024
More than 24 h	48	19		
Unexposed	472	85		
Tasks are done in the timeframe specified				
Remove or install flooring including places other than your home (n=635)				
Past 7 days	12	9	15.08	0.001
Between 8 days and 1 month ago	32	7		
N/A	485	89		
Number of times touched a thermal receipt in the last 2 days (n=630)				
Once	101	12	12.80	0.002
More than once	118	40		
Unexposed	307	52		
Used makeup in a week (n=630)				
<7 times	171	49	7.90	0.019
7 times or more	65	12		
Unexposed	289	44		
Microwaved food (n=636)				
Yes, in the last 24 h	27	13	8.14	0.017
Yes, between 1 and 2 days ago	24	6		
No	479	87		

Contd...

Table 1: Contd...

Factors	PCOS status		χ^2	P
	Negative	Positive		
Drink canned soda or juice in a week (n=636)				
Once per week	92	16	11.88	0.018
Twice per week	67	14		
Thrice per week	36	17		
More than thrice per week	27	8		
No	308	51		
Processed foodstuff and similar items				
Red meat (beef, pork, or goat) (n=633)			15.89	0.001
Past 24 h	220	57		
Between 1 and 2 days	117	31		
Between 2 days and 1 week ago	107	10		
N/A	84	7		
Food wrapped in paper or cardboard (n=631)			8.36	0.039
Past 24 h	92	28		
Between 1 and 2 days	63	15		
Between 2 days and 1 week ago	116	26		
N/A	255	36		
Beer (n=625)			13.29	0.004
Past 24 h	29	9		
Between 1 and 2 days	27	6		
Between 2 days and 1 week ago	65	26		
N/A	399	64		
Others				
Scratched rice cooker (n=636)			7.86	0.049
None	39	5		
Yes	51	13		
Don't know	20	10		
Without nonstick bowl	420	78		
The public market as a source of fruits and vegetables (n=636)			22.62	<0.001
No	34	22		
Yes	496	84		
Well water (source of drinking water)			6.81	0.009
No	528	103		
Yes	2	3		

PCOS: Polycystic ovarian syndrome, N/A: Not available

and menopausal period as the criteria used in diagnosis get altered during these reproductive stages.^[16] Likewise, other gynecological conditions are seen in the older age groups that may underestimate PCOS.

Household income is associated with PCOS diagnosis. Most participants reported a monthly income of less than Php 10,000, which falls under the set poverty threshold by the Philippine Statistics Authority. A review in the United States indicated that lower socio-economic groups with certain ethnic/racial backgrounds are more exposed to EDCs that are diabetogenic such as polychlorinated biphenyls, organochlorine pesticides, multiple chemical constituents of air pollution, BPA, and phthalates.^[17]

This study found that among industrial, sanitary, and furniture products that may contain EDCs in the household,

frequent use of cleaning sprays, scented candles, and wax for furniture and floors was associated with PCOS. In addition, purchasing new upholstered furniture and being involved in floor removal or installation showed an association with PCOS. This study found that exposure to cleaning products in the past week can increase the likelihood of having PCOS. Cleaning products contain EDCs such as fragrances, parabens, and ethers.^[18] As cleaning sprays contain a mixture of these compounds, they present difficulties in managing the correlation of specific chemicals to PCOS diagnosis. One common group is phthalates, which are used as plasticizers. Phthalates have been associated with disturbances in reproductive development and hormone disruption in animal studies.^[19] Another group of concern is alkylphenols which are used as surfactants. These compounds have shown estrogenic activity, potentially interfering with hormonal balance, leading to its association with PCOS.^[20]

Table 2: Endocrine-disrupting chemicals and their sources of exposure

EDCs	Source of exposure
BPA	Thermal receipts, ^[14] plastic and food containers, ^[15] dental sealant ^[16]
Parabens	Cosmetics, ^[17] beverages, fruits, vegetables, dairy products, fats and oils, cereals, fish and shellfish, and meat ^[18]
Phthalates	Cleaning materials, ^[19] scented candles, ^[20] vinyl or linoleum flooring, ^[21,22] PET bottles and aluminum cans, ^[23] cosmetics, perfume, ^[17] carpet, furniture, mattresses, ^[24] vinyl ^[25]
2,4-dichlorophenoxyacetic acid	Herbicides, agricultural products ^[7]
Polybrominated diphenyl ethers	Upholstered furniture, carpet, ^[25] paint ^[26]
PFCs	Nonstick cookware, ^[27] wax, ^[28] cosmetics, ^[29] food packaging and other paper materials, ^[15] and well waters ^[30]

EDCs: Endocrine-disrupting chemicals, BPA: Bisphenol A, PFCs: Perfluorochemicals, PET: Polyethylene terephthalate

Results indicate that exposure to scented candles the day before the interview increases the likelihood of being diagnosed with PCOS. Scented candles contain fragrances that may come in the form of phthalates.^[21] As discussed, phthalates have been associated with disruption of hormone signaling. Exposure to furniture or floor wax also showed an association with PCOS. Waxes used to coat floorings and furniture to enhance shine and water resistance are commonly made up of long-chain perfluoroalkyl substances (PFAS).^[19] The association may be due to the presence of PFAS from these sources. This has also been previously detected among women diagnosed with PCOS.^[22]

Previous studies established the association of having PCOS with exposure to makeup or cosmetics. Other studies have found the presence of PFAS in most waterproof cosmetics.^[23] The purchase or receipt of new upholstered furniture is also associated with PCOS diagnosis. However, logistic regression indicates that exposure to new upholstered furniture within the past month decreases the likelihood of having PCOS. This is conflicting with other studies indicating that upholstered furniture may contain polybrominated diphenyl ethers.^[24] In rats, polybrominated diphenyl ethers have been found to increase lipolysis and decrease insulin-stimulated glucose oxidation, which are associated with obesity and insulin resistance that are symptoms of PCOS.^[25]

Simple logistic regression also showed that removal or installation of flooring including places other than the home in the past 7 days increases the likelihood of PCOS. Studies have found that phthalates

such as di-2-ethylhexyl phthalate (DEHP) and mono (2-ethylhexyl) phthalate (MEHP) in PVC flooring can migrate into house dust, which can be enhanced by heat.^[26,27] These may have a role in the development of PCOS as DEHP and MEHP are found to be associated with insulin resistance in adolescents with PCOS.^[28]

The number of times a thermal receipt has been touched in the last 2 days also showed a significant association with PCOS diagnosis using Chi-square analysis; however, logistic regression shows that frequent exposure to thermal receipts decreases the likelihood of having PCOS. This is in conflict with the assumption that thermal receipts contain BPA and may interact within the human body, eventually causing PCOS. A study has shown that PCOS-diagnosed market seller women who handle thermal receipts daily exhibit higher serum BPA content compared to the control group.^[29] In addition, it has also been found that hand sanitizers and other skin care products that contain penetration-enhancing chemicals enhance BPA absorption after handling thermal receipts.^[30] Due to the pandemic, the use of hand sanitizers has been widespread and may have caused increased BPA dermal absorption in PCOS-diagnosed Filipino women.

The consumption of microwaveable food in plastic containers has also shown an association with PCOS diagnosis. This may be attributed to the presence of plasticizers such as BPA in plastic containers that are known to migrate from containers to food. The association of possible BPA-containing microwaveable containers to having PCOS diagnosis is in line with other studies where female individuals diagnosed with PCOS had a higher mean of BPA concentration levels detected in their blood.^[31]

Scratched nonstick bowls of rice cookers have also been found to be associated with PCOS diagnosis. Perfluorochemicals, such as perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), are known to be involved in the manufacturing of nonstick cookware.^[32] Studies have found that women with elevated serum levels of PFOS and PFOA are at an elevated risk of PCOS development as the sera of women with PCOS exhibit elevated levels of PFOS and PFOA compared to non-PCOS women.^[33,34]

Access to public markets is also associated with PCOS diagnosis, with the odds of not having PCOS higher among women who consumed fruits and vegetables from the public market. In the Philippines, livestock, fruits, vegetables, and other agricultural products are commonly sold in public markets. Consuming fruits may have conferred health benefits and protected women from PCOS. However, there has been a growing concern

Table 3: Simple logistic regression of sociodemographic and exposure to endocrine-disrupting chemical-containing sources in association with having polycystic ovarian syndrome

Factors	OR	95% CI	P
Age group (years old) (<i>n</i> =636)			
10–19 (reference)	-	-	-
20–29*	4.59	2.97–7.11	<0.001
30–39	0.69	0.43–1.11	0.129
40–49*	0.02	0.002–0.11	<0.001
Civil status (<i>n</i> =636)			
Single	-	-	-
Married or have a partner separated or widowed*	5.73	3.07–10.71	<0.001
Household income (<i>n</i> =631)			
<P10,000	-	-	-
P10,000–P29,999	0.85	0.54–1.32	0.462
P30,000–P49,900	0.62	0.24–1.62	0.308
P50,000 or more*	5.84	2.92–11.66	<0.001
Scented candles/incense (<i>n</i> =636)			
Unexposed	-	-	-
Past 24 h	1.67	0.60–4.78	0.315
More than 24 h*	2.07	1.11–3.83	0.021
Cleaning sprays			
Unexposed	-	-	-
Past 24 h	1.06	0.40–2.85	0.905
More than 24 h*	2.27	1.30–3.96	0.006
Floor or furniture polish or wax (<i>n</i> =634)			
Unexposed	-	-	-
Past 24 h	1.70	0.60–4.78	0.315
More than 24 h	2.07	1.11–3.83	0.021
Remove or install flooring including places other than your home (<i>n</i> =635)			
N/A	-	-	-
Past 7 days*	4.00	1.64–9.75	0.002
Between 8 days and 1 month ago	1.27	0.57–2.83	0.563
Purchase or receive new upholstered furniture (<i>n</i> =625)			
N/A	-	-	-
Past 7 days*	4.00	1.64–9.75	0.002
Between 8 days and 1 month ago	1.26	0.57–2.83	0.563
Number of times touched a thermal receipt in the last 2 days (<i>n</i> =630)			
Unexposed	-	-	-
Once	0.55	0.29–1.04	0.066
More than once*	2.16	1.38–3.37	0.001
Used makeup in a week (<i>n</i> =630)			
Unexposed	-	-	-
<7 times	1.81	1.19–2.77	0.006
7 times or more	0.91	0.47–1.76	0.786
Microwaved food (<i>n</i> =636)			
No	-	-	-
Yes, in the last 24 h*	2.60	1.30–5.23	0.007
Yes, between 1 and 2 days ago	1.27	0.50–3.17	0.616
Drink canned soda or juice in a week (<i>n</i> =636)			
No	-	-	-
Once per week	0.85	0.48–1.51	0.571
Twice per week	1.05	0.57–1.95	0.873
Thrice per week*	2.62	1.41–4.87	0.002
More than thrice per week	1.52	0.67–3.45	0.315
Red meat (beef, pork, or goat) (<i>n</i> =633)			
N/A	-	-	-
Past 24 h	1.66	1.09–2.53	0.018

Contd...

Table 3: Contd...

Factors	OR	95% CI	P
Between 1 and 2 days	1.47	0.92–2.35	0.105
Between 2 days and 1 week ago*	0.41	0.21–0.82	0.012
Food wrapped in paper or cardboard (n=631)			
N/A	-	-	-
Past 24 h*	1.72	1.05–2.79	0.030
Between 1 and 2 days	1.23	0.67–2.25	0.512
Between 2 days and 1 week ago	1.16	0.71–1.90	0.544
Beer (n=625)			
N/A	-	-	-
Past 24 h	1.59	0.73–3.46	0.245
Between 1 and 2 days	1.11	0.45–2.75	0.827
Between 2 days and 1 week ago*	2.30	1.38–3.85	0.001
Scratched rice cooker (n=636)			
N/A	-	-	-
None	0.62	0.24–1.62	0.332
Yes	1.31	0.69–2.51	0.410
Don't know*	2.66	1.21–5.85	0.015
The public market as a source of fruits and vegetables (n=636)			
No	-	-	-
Yes*	0.26	0.15–0.47	<0.001
Well water as a source of drinking water			
No	-	-	-
Yes*	7.69	1.27–46.59	0.026

N/A: Not available, OR: Odds ratio, CI: Confidence interval, *All the categories with significant EDC exposures

about the use of chemicals, pesticides, herbicides, and insecticides in the Philippines.^[35] Farmers commonly use herbicides that are easy to use and inexpensive to protect their crops from weed growth and from insects and vermin that can decrease their crop yield and income.^[36] The frequent use of these substances may result in the accumulation of EDCs, such as 2,4-dichlorophenoxyacetic acid, in public markets, where a large volume of agricultural products is stored and sold.

Processed food is also associated with PCOS diagnosis. Processed meats are usually packaged in supermarkets in plastic food packaging containing BPA and are stored for lengthy periods of time in freezers. Low but continuous exposure to EDCs from red and processed meat has been shown to alter glucose metabolism, impair pancreatic β -cell function, and induce insulin resistance, which may contribute to the symptoms of PCOS. In line with this, it has also been found that diets, such as the Dietary Approaches to Stop Hypertension diet and alternative Mediterranean diet, which decrease red meat intake and increase fish and dairy protein intake result in reduced follicles and blastocysts.^[37]

Frequent beer intake also raises the odds of having PCOS. Beer contains more carbohydrates than other alcoholic beverages and its intake thus results in high carbohydrate levels and hyperglycemia, which contribute to the pathophysiology of PCOS.^[38,39] A study has found that

a high dietary glycemic index and glycemic load, which can be increased through beer intake, are significantly associated with PCOS.^[40] In addition, beer is also stored in packaging that contains EDCs. A study has found that high concentrations of phthalates are present in beer stored in PET bottles and aluminum cans.^[41]

Frequent consumption of canned juice or soda also raises the odds of having PCOS. BPA can migrate from the plastic lining of the can to the soda or juice; therefore, frequent consumption of canned juice or soda increases the BPA concentration that enters the body.^[42] In addition, frequent consumption of junk food and soda with high sugar content is associated with PCOS diagnosis and can exacerbate PCOS symptoms.^[43]

Consumption of food wrapped in paper or cardboard is also shown to have an association with PCOS diagnosis. Many food packaging materials, including baking paper, butter wrappers, paper plates, paper straws, and take-out food containers and wrappers, contain PFAS, which enhance resistance to degradation from heat, fat, grease, and humidity.^[44,45] Restaurants in the Philippines were closed to dine-in customers during the community quarantine, resulting in a high demand for take-out food.

Finally, people who drink well water are more likely to be diagnosed with PCOS. A meta-analysis found that well waters in South and Southeast Asia contain PFAs although the levels are still below the recommended

level.^[46] Heavy metals have also been detected in groundwater in the Philippines. In communities around Taal Volcano, arsenic levels are beyond the limit set by the World Health Organization.^[47] In Guagua, Pampanga, arsenic, manganese, and iron levels have been found to exceed the recommended 10 ppb limit.^[48] In Puerto Princesa, Palawan, chromium, manganese, and nickel levels were above the acceptable standards for drinking water.^[49] In addition, well waters located near agricultural sites are also at risk of contamination from chemical runoff.^[50]

The pathophysiology of EDCs and PCOS involves complex interactions between environmental exposures and hormonal dysregulation. Endocrine disruptors, such as phthalates, BPA, and PFAS, disrupt endocrine function by mimicking or interfering with natural hormones, thereby altering hormone levels and metabolic processes.^[18,21,31] Phthalates, used in various consumer products, have been linked to disturbances in reproductive development and hormone signaling.^[19] Similarly, BPA, commonly found in plastic containers and packaging, is known to disrupt endocrine signaling and insulin metabolism, which exacerbates insulin resistance – a key feature of PCOS.^[30] PFAS, present in nonstick cookware and some cleaning products, has also been associated with increased risks of PCOS due to their estrogenic effects and potential to induce metabolic disturbances. Chronic exposure to these EDCs can lead to hormonal imbalances, increased androgen levels, and insulin resistance, which are central to the pathogenesis of PCOS.^[36] In addition, the consumption of processed foods and beverages, exposure to certain cleaning products, and the use of personal care items containing EDCs further complicate the hormonal equilibrium, potentially aggravating PCOS symptoms.^[40-42] Understanding these mechanisms underscores the need for more research into how environmental exposures contribute to the development and progression of PCOS, as well as the broader implications for reproductive and metabolic health.

Despite being able to link an association of PCOS among nonpregnant women of reproductive age to diverse sources of exposure and sociodemographic factors, there are recognized limitations that were addressed. The survey is limited because it relies on the participants' self-reporting of frequency of exposure that has recall bias. Second, the diagnosis of PCOS relies on clinical and ultrasound parameters in a low-resourced setting. Furthermore, there is no actual testing of EDC compounds from several sources; therefore, the actual presence of these chemicals in declared sources of exposure at this stage is limited based on available literature indicating their existence. Hence, other chemicals or confounding factors inherent in declared sources of exposure that do not fall under the EDC category may also take influence

in the association of PCOS to said exposure. The measuring EDCs in women exposed to these items and the correlation of the geographical sites of participants where these sources of exposure happen are the next steps to linking these in the next research initiative.

Conclusion

Many sources and factors were revealed to have an association with PCOS. Sociodemographic factors that had a significant association with PCOS include age group, civil status, and monthly household income. Exposure to and frequent use of personal and household products shown to have an association with having PCOS include cleaning products scented candles, floor and furniture wax, upholstered furniture, and thermal receipts. Finally, access to public markets, consumption of well water, usage of paper or cardboard food wrappers, microwaved food, and processed food all showed an association with having PCOS diagnosis. These findings suggest that constant exposure to EDCs may pose a significant risk factor for developing PCOS. Reducing exposure to these chemicals is crucial for mitigating PCOS and its related reproductive consequences.

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Conflicts of interest

There are no conflicts of interest.

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