## Nickel Allergy Is a Risk Factor for Endometriosis : An 11-Year Population-Based Nested Case-Control Study

#### Jin-Sung Yuk<sup>1</sup>, Jong Seung Shin<sup>2</sup>, Ji-Yeon Shin<sup>3</sup>, Eunsuk Oh<sup>4</sup>, Hyunmee Kim<sup>5</sup>, Won I. Park<sup>6</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Gyeongsang National University Changwon Hospital, <sup>2</sup> Department of Obstetrics and Gynecology, Hyundai UVIS hospital, <sup>3</sup> Preventive medicine, Eulji University, <sup>4</sup> Internal medicine, Mizmedi hospital, <sup>5</sup> Family medicine, Mizmedi hospital, <sup>6</sup> Department of Obstetrics and Gynecology, Hallym University

## Endometriosis (EMS)



## Incidence



## 10% of women of childbearing age

Eskenazi and Warner 1997

## Regurgitation



## Leading hypothesis

Giudice and Kao 2004

## Immune response



Eisenberg, Zolti, and Soriano 2012; Poppe et al. 2002; Sinaii et al. 2002

## **Environmental substances**



Giudice 2004; Matarese et al. 2003; Olovsson 2011

## Allergic diseases



## HIRA-NIS



#### 2009-2011



1,000,000 National Inpatients Sample



## **EMS vs Control**



**n=7**,259

#### **n=535,818**

## EMS & Nickel allergy



#### Adjusted OR 1.167 (1.004~1.357)

## Nickel allergy

#### Prevalence 10~23%



Cheng et al. 2008, Thyssen et al. 2009, Darlenski et al. 2012

## Nickel



## Aim



# Method

## Data



#### 2009~2011 Cross-sectional data









## **Exclusion in EMS**



## Selection of EMS



## **EMS vs Control**



#### 1:4 matching

## Selection of Nickel allergy



## Result

## EMS & Nickel allergy



## EMS & Nickel allergy



#### Adjusted OR 2.474 (1.023~5.988)

# Discussion

## Nickel is metallo-estrogen



## Nickel & breast cancer



## Job & Nickel allergy



## Nickel in serum



## Hypothesis



## EMS & Nickel allergy



## Dx of Nickel allergy



## EMS & Nickel allergy

#### Prevalence 10~23%



## Limitations

# Inaccuracy of code



#### Indirect study



## **Further studies**



# Thank you for your attention!!





## High rate of nickel allergy in women with endometriosis: A 3-year population-based study

Jin-Sung Yuk<sup>1,2</sup>, Yong Jin Kim<sup>3</sup>, Kyong-Wook Yi<sup>3</sup>, Kim Tak<sup>3</sup>, Jun-Young Hur<sup>3</sup> and Jung-Ho Shin<sup>3</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, School of Medicine, Eulji University, Daejeon, Republic of Korea <sup>2</sup>Department of Obstetrics and Gynecology, Miz Medi Hospital, Seoul, Republic of Korea <sup>3</sup>Department of Obstetrics and Gynecology, Korea University College of Medicine, Seoul, Republic of Korea

## **Cross-sectional Study**



## **Cross-sectional Study**

Table 2Observed and expected numbers of cases of allergic diseases among women with and without endometriosis from 2009to 2011 obtained from the National Patients Sample provided by the Korean Health Insurance Review and Assessment Service

		Endometriosis ( $n = 7259$ )			Non-endometriosis ( $n = 535\ 818$ )			
		Observed†	Expected‡ (%)	SE (%)	Observed†	Expected‡ (%)	SE (%)	P§
Contact dermatitis¶	Yes	1004	16769 (13.9)	1016 (0.8)	68 008	2735826(13.0)	15 117 (0.1)	0.26
Nickel allergy	No Yes	6255 712	103 960 (86.1) 12 677 (10.5)	2523 (0.8) 904 (0.7)	$467810 \\ 46704$	18 256 860 (87.0) 1 867 741 (8.9)	31 504 (0.1) 12 601 (0.1)	0.02*
Allergic rhinitis	No Yes	6547 2789	108 053 (89.5) 48 684 (40.3)	2564 (0.7) 1759 (1.1)	489 114 197 291	19124945 (91.1) 8005038 (38.1)	31778 (0.1) 24338 (0.1)	0.05*
0	No	4470	72 046 (59.7)	2076 (1.1)	338 527	12 987 648 (61.9)	28769 (0.1)	
Atopic dermatitis	Yes	138	2630 (2.2)	420 (0.3)	11 663	457 004 (2.2)	6313 (0.0)	0.99
	No	7121	118 099 (97.8)	2686 (0.3)	524 155	20 535 681 (97.8)	32 122 (0.0)	0.01***
Drug allergy	Yes No	3 7256	23 (0.0) 120 707 (100.0)	13 (0.0) 2719 (0.0)	22 535 796	262 (0.0) 20 992 422 (100.0)	103 (0.0) 32 204 (0.0)	<0.01***

 $\pm$ Observed number of cases in the sample.  $\pm$ Expected number of cases in the population.  $\pm$ Cross-tabulations made with expected cases. *P*-values represent a  $\chi^2$ -test of the endometriosis group versus the non-endometriosis group.  $\parallel$ Contact dermatitis includes nickel allergy. SE, 95% standard error.

## **Cross-sectional Study**

**Table 3** Odds ratios among women with endometriosis from 2009 to 2011 obtained from the National Patients Sample providedby the Korean Health Insurance Review and Assessment Service

	No adjustments			Adjustment for aget			Adjustments for age and other diseases‡		
	OR	95%CI	Р	OR	95%CI	Р	OR	95%CI	Р
Contact dermatitis§	1.076	0.947-1.224	0.26	1.087	0.956-1.236	0.21			
Nickel allergy	1.201	1.036-1.393	0.02**	1.175	1.011-1.366	0.04**	1.167	1.004-1.357	0.04*
Allergic rhinitis Atopic dermatitis	1.096 1.001	1.001–1.201 0.728–1.376	0.05* 0.99	1.070 1.093	0.977–1.172 0.795–1.502	0.14 0.59	1.070 1.059	0.973–1.167 0.770–1.456	0.17 0.73

OR for drug allergy could not be properly calculated due to too few observations. †Adjustments for covariates, such as age (per 5 years) and data year. ‡Adjustments for covariates, such as age (per 5 years), data year, nickel allergy, allergic rhinitis and atopic dermatitis. §Contact dermatitis includes nickel allergy. CI, confidence interval; OR, odds ratios.



#### RESEARCH ARTICLE

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Department of Obstetrics and Gynecology, School of Medicine, Eulji University, Daejeon, South Korea,
Department of Obstetrics and Gynecology, MizMedi Hospital, Seoul, South Korea,
Department of Obstetrics and Gynecology, Hyundai UVIS hospital, Incheon, South Korea,
Department of Preventive Medicine, School of Medicine, Eulji University, Daejeon, South Korea,
Department of Internal Medicine, MizMedi Hospital, Seoul, South Korea,
MizMedi Hospital, Seoul, South Korea,
Department of Family Medicine, MizMedi Hospital, Seoul, South Korea

## Selection of subjects



**1:4 matching** 

## Demographics

#### Table 1. Characteristics of patients in the endometriosis group and the control group, 2002–2013.

	EMS group	Control group	Total	p-value
	997	3,988	4,985	
009 <sup>a</sup>	183			
010 <sup>a</sup>	198			
011 <sup>a</sup>	198			
012 <sup>a</sup>	201			
013 <sup>a</sup>	217			
	8.5±1.8	8.5±1.9	8.5±1.8	1
	42.6±9.2	42.6±9.3	42.6±9.3	
Mean group socioeconomic status <sup>d</sup>		6.0±2.9	6.0±2.9	1
				0.052 <sup>e</sup>
esent	8 (0.8%)	13 (0.3%)	21	
esent	989 (99.2%)	3975 (99.7%)	4964	
	009 <sup>a</sup> 010 <sup>a</sup> 011 <sup>a</sup> 012 <sup>a</sup> 013 <sup>a</sup> atus <sup>d</sup> esent	$\begin{array}{c c} & & 997 \\ \hline 009 \\ a & & 183 \\ \hline 010 \\ a & & 198 \\ \hline 011 \\ a & & 198 \\ \hline 012 \\ a & & 201 \\ \hline 013 \\ a & & 217 \\ \hline & & 8.5 \pm 1.8 \\ \hline & & 42.6 \pm 9.2 \\ \hline & & 42.6 \pm 9.2 \\ \hline & & atus \\ d & & 6.0 \pm 2.9 \\ \hline \\ esent & & 8 (0.8\%) \end{array}$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$997$ $3,988$ $4,985$ $009^{a}$ $183$ $4,985$ $010^{a}$ $198$ $100^{a}$ $011^{a}$ $198$ $100^{a}$ $012^{a}$ $201$ $201$ $013^{a}$ $217$ $8.5\pm 1.8$ $8.5\pm 1.8$ $8.5\pm 1.9$ $8.5\pm 1.8$ $42.6\pm 9.2$ $42.6\pm 9.3$ $42.6\pm 9.3$ $42.6\pm 9.2$ $6.0\pm 2.9$ $6.0\pm 2.9$ esent $8(0.8\%)$ $13(0.3\%)$ $21$

<sup>a</sup> First diagnosis of EMS was made in the year noted.

<sup>b</sup> Mean age groups per 5 years in 2013. 1; 0–4 years, 2; 5–9 years, ...., 17; 80–84 years, 18; 85 years+.

<sup>c</sup> The mean age was calculated from the mean age groups per 5 years.

<sup>d</sup> Mean socioeconomic status groups in 2013. 1; upper 0–9%, 2; upper 10–14%,....., 9; upper 90–94%, 10; upper 95%+.

<sup>e</sup> Fisher's exact test

Data are presented as numbers or means ± standard deviations

## EMS & Nickel allergy

#### Table 2. Multivariate logistic regression analysis of endometriosis and nickel allergy.

Adjustment	Adjusted OR	а
	OR (95% CI)	p-value
Age group per 5 years	1.001 (0.964~1.039)	0.977
Socioeconomic status group (decile)	1.000 (0.976~1.024)	0.977
Nickel allergy	2.474 (1.023~5.988)	0.044

<sup>a</sup> Covariates: Age group per 5 years, socioeconomic status group (decile), nickel allergy.
CI, Confidence interval; OR, Odds ratio