Gastroschisis and potential environmental risk factors in first trimester of pregnancy

Practicum presentation

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Introduction

- Gastroschisis is a congenital fissure in the abdominal wall usually accompanied by protrusion of abdominal viscera.
- A nationwide self-reported survey from Birth Defects Research for Children Inc. was used to identify cases and controls.
- 252 Gastroschisis cases and 229 Cleft palate controls were studied.
- Like many birth defects, the cause of Gastroschisis is still unknown.
- Insufficient environment exposure data is one of the biggest roadblock.
- National Birth Defects Prevention Study, one of the largest studies is still an undergoing work in 10 states of USA.

Why was the study necessary?

- The prevalence of Gastroschisis has been increasing all over the world with **0.29 (95% CI: 0.21,0.40) per 10,000 live births in 1974** to **1.66 (95% CI: 1.51,1.85) per 10,000 live births in 1998** (Di Tanna GL et al., 2002).
- Research studies for rare diseases gather less financial impetus and hence few hypothesis generating studies are performed .
- Birth Defects Research for Children Inc. is a non-profit organization and has developed its own survey system to enter information electronically, for parents and family members of children with congenital birth defects.
- Availability of vast environmental exposure data of all cases and controls from the “birthdefects.org” registry.

Hypothesis

- Hypothesis: To identify potential environmental risk factors in first trimester of pregnancy for gastroschisis.

Literature review

- Doing a scientific literature review of more than 20 articles through Pubmed and Google scholar, following risk factors were found to have statistically significant association with gastroschisis:
- **Maternal age <20 years** (aOR= 6.1; 95% CI: 4.8,8.0) (1) and (OR= 4.1; 95% CI: 1.4,12.0) (2)
- **Chest colds during first trimester** (OR= 16.77; 95% CI: 1.88,150.27) and **Sore throat during first trimester** (OR= 12.72, 95% CI: 1.32,122.52) (3) (a potential Ebola virus- infection mononucleosis)
- Decongestant drug **Pseudophedrine use during first trimester** (OR= 3.2, 95% CI: 1.3,7.7) *(4)*
- Vasoconstrictive **Recreational drug use - methamphetamine, cocaine, ecstacy** during first trimester (OR = 3.3, 95% CI: 1.0, 10.5) *(5)* and before pregnancy (OR= 4.46; 95% CI: 1.21-16.44) *(3)*

Literature review

- **Methamphetamine use before pregnancy** (OR=7.15; 95% CI: 1.35, 37.99) *(3)*
- Non-selective COX inhibitor drug **Aspirin use during first trimester** (OR= 20.4; 95% CI: 2.2,191.5) *(5)*
- **Cigarette smoking during first trimester** (OR= 1.7, 95% CI: 1.1, 2.6) *(5)* and (OR= 2.7; 95% CI: 1.1,6.8) *(6)*
- Agricultural ferilizer **Atrazine exposure to mothers < 25km radius** (OR, 1.6; 95% CI: 1.1–2.3)*(7)* and **Atrazine exposure to mothers ≥25 years** (OR= 1.97; 95% CI: 1.19,3.26) (8)

Methods

Methods

- Study population: 481 participants, 252 women delivering gastroschisis cases and 229 women delivering cleft palate controls
- Time-frame: Reported between 2004- 2012
- Source of data: National registry from Birth Defects Research for Children Inc., Florida

Risk factors studied:

- Maternal age at delivery
- Alcohol use
- Cigarette smoking
- Pesticide exposure
- Recreational drug use
- Acetaminophen use
- Pseudoephidrine use

Results

Table 1. Characteristics of Study Participants

Table 1: Selected lifestyle risk factor characteristics among women delivering Gastroschisis and Cleft palate newborns:
*exposure in first trimester of pregnancy

Characteristics		Gastroschisis Cases (n=252)		Cleft Palate Controls (n=229)		Total
		No.	%	No.	%	No.
Age at delivery (years)	16-20	45	83.3	9	16.7	54
	21-25	78	57.8	57	42.2	135
	26-34	40	38.1	65	61.9	105
	>34	4	23.5	13	76.5	17
	Missing	85	50	85	50	170
Alcohol glasses/week*	0	215	49.8	217	50.2	432
	1-2	22	84.6	4	15.4	26
	3-5	11	73.3	4	26.7	15
	6-10	2	66.7	1	33.3	3
	>10	2	40	3	60	5
Cigarette packs/day*	0	199	50.3	197	49.7	396
	1/4	4	66.7	2	33.3	6
	1/2	32	69.6	14	30.4	46
	≥ 1	17	51.5	16	48.5	33
Pesticide exposure*	Yes	28	63.6	16	36.4	44
	No	224	51.3	213	48.7	437
Recreational drug use*	Yes	27	81.8	6	18.2	33
	No	225	50.2	223	40.8	448
Acetaminophen use*	Yes	129	59.2	89	43.8	218
	No	123	46.8	140	53.2	263
Pseudoephidrine use*	Yes	25	62.5	15	37.5	40
	No	227	51.5	214	48.5	441

Table 2. Unadjusted Odds ratio (SPSS)

Table 2: Crude Odds ratios and 95% Confidence Intervals for Gastroschisis cases compared to Cleft palate controls

Risk Estimate		
Exposure	Crude Odds Ratio	95%Confidence intervals
Maternal Age at Delivery (≤ 20, >20)	5.53	2.60 - 11.79
Alcohol use (Yes, No)	3.11	1.58 - 6.13
Cigarette smoking (Yes, No)	1.64	1.0 - 2.65
Pesticide use (Yes, No)	1.66	0.88 - 3.16
Recreational drug use (Yes, No)	4.46	1.81 - 11.01
Acetaminophen use (Yes, No)	1.65	1.14 - 2.37
Pseudoephidrine use (Yes, No)	1.57	0.81 - 3.06

Table 3. Adjusted Odds Ratio (SPSS, WinPEPI)

Table 3: Association between Gastroschisis outcome and maternal age at delivery, recreational drug use and alcohol use with adjusted odds ratios and Mantel-Haenszel confidence intervals:

Birth defects	No. with exposure*	%	Total	Crude Odds ratio	95% confidence interval	Adjusted relative risk	M-H 95% confidence interval
Maternal age at delivery							
Gastroschisis cases	45	26.9	167	5.53	2.60-11.79	5.00**	2.37-10.55
Cleft palate controls	9	6.3	144	1.00	Referent	1.00	Referent
Recreational Drug use							
Gastroschisis cases	27	10.7	252	4.46	1.81-11.01	3.47**	1.41-8.55
Cleft palate controls	6	2.6	229	1.00	Referent	1.00	Referent
Alcohol							
Gastroschisis cases	37	14.7	252	3.11	1.58-6.13	4.73***	1.83-12.19
Cleft palate controls	12	5.2	229	1.00	Referent	1.00	Referent

*≤20 years for Maternal Age, Yes for Recreational drug use and Yes for Alcohol use
**Adjusted for Alcohol ***Adjusted for Maternal delivery age

Main Results (Stratified by Alcohol use)

- Maternal age at delivery (≤ 20, >20):
  - Crude OR = 5.53 (95% CI: 2.60 – 11.79)
  - Adjusted OR = 5.00 (95% CI: 2.37 – 10.55)

  The odds of mother with Gastroschisis newborn being less than or equal to 20 are 5.00 times greater than for mother with Cleft palate newborn.

- Recreational drug use(Yes/No):
  - Crude OR = 4.46 (95% CI: 1.81 – 11.01)
  - Adjusted OR = 3.47 (95% CI: 1.41 – 8.55)

  The odds of mother with Gastroschisis newborn using recreation drug during first trimester of pregnancy are 3.47 times greater than for mother with Cleft palate newborn.

Main Results (Stratified by Maternal Age at delivery)

- Alcohol use (Yes/No)
  - Crude OR = 3.11 (95% CI: 1.58 – 6.13)
  - Adjusted OR = 4.73 (95% CI: 1.83 – 12.19)

  The odds of mother with Gastroschisis newborn using alcohol during first trimester of pregnancy are 4.73 (1.83,12,19) times greater than for mother with Cleft palate newborn

Discussion

Effect modifiers and confounders

- Alcohol was found to be an effect modifier for Maternal age at delivery [Heterogeneity index: 3.6 (2.0,6.7)] and Recreation drug use in first trimester of pregnancy [Heterogeneity index: 2.3 (1.1,4.7)]

- Additionally, alcohol was also found to be a confounder for recreational drug use. Adjusting with other variables, no confounding was seen for Recreational drug use and Maternal age at pregnancy.

- Maternal age at delivery was found to be both an effect modifier and confounder for Alcohol use in first trimester with Heterogeneity index of 3.6 (2.0,6.7).

Comparison with previous studies

- In our study, Maternal Age at Delivery ≤ 20 years was to have significant association with Gastroschisis (aOR= 5.00; 95% CI: 2.37, 10.55). While in previous study, Maternal age <20 years (aOR= 6.1; 95% CI: 4.8,8.0).

- In our study, Recreational drug use in first trimester was found to have significant association with Gastroschisis (aOR= 3.47 ; 95% CI: 1.41,8.55). While in previous study, Recreational drug use - methamphetamine, cocaine, ecstacy during first trimester (OR = 3.3, 95% CI: 1.0, 10.5)

- In our study, Alcohol consumption in first trimester of pregnancy was to have significant association with Gastroschisis (aOR= 4.73; 95% CI: 1.83-12.19). While some previous studies have failed to find a significant association (10) others have found alcohol consumption during pregnancy to have significant association with Gastroschisis (OR = 1.40; CI: 1.17-1.67). (11)

Strengths and Limitations

- Strengths:
  - Calculation of multiple exposures
  - Time saving and inexpensive
  - Case control study – best preliminary study method to detect association of rare disease with exposure

- Limitations:
  - Recall bias
  - Healthy control group not used.
  - Self-reported exposures and disease used.
  - Relatively small sample size and power of the study

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Thank you.