10th POSTGRADUATE COURSE IN TRAINING IN REPRODUCTIVE MEDECINE & REPRODUCTIVE BIOLOGY

ASSOCIATION OF FETAL SEX AND PRE-ECLAMPSIA/ECLAMPSIA ?

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INTRODUCTION 1

- Pre-eclampsia/eclampsia (PE/E) : Hippocrates ;
- Its etiology and pathophysiology remains enigmatic
- This pregnancy-specific syndrome: 20th week as BP, proteinuria and/or edema. Eclampsia is a state of pre-eclampsia with convulsions and/or coma.
- Pre-eclampsia : 3-7% of human pregnancies; eclampsia is a major cause of maternal mortality in the developed countries as well as in developing countries (13%, WHO) .
- Several authors attempted the explanation of the pathogenesis of this " disease of theories " Chesley in 1968, still controversial.
- Studies : fetal gender may play an important role in the development of this disorder results are contradictory: M>F, F>M; M~F

INTRODUCTION 2

- Question: " Is there any association between fetal sex (gender) and pre-eclampsia/eclampsia ? "

- In fact, the histo-incompatibility of the fetus and the mother due to an antigen dependent on the Y-chromosome may play a role in the pathogenesis of PE/E.

If proven that there exists an association between a particular fetal gender and PE/E, this information could help to characterize a specific subgroup of women particularly at risk of PE/E by implementing systematic antenatal ultrasonography, to determine if the fetus is of the incriminated sex ; then a special follow-up could be given.

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OBJECTIVES

1. General objective:

- To determine if the fetal sex (gender) is associated with the development of pre-eclampsia/eclampsia.

2. Specific objectives:

- To establish a review of all publications on fetal gender and pre-eclampsia/eclampsia.
- To determine the sex ratio in the offspring of pre-eclamptic/eclamptic patients
- To compare the sex ratio of the offspring of pre-eclamptic/eclamptic patients to that of the normotensive patients (Case-control study)
- To review the possible mechanisms of pathogenesis of pre-eclampsia/eclampsia.

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NULL HYPOTHESIS

" There is no association between fetal sex and pre-eclampsia/eclampsia".

METHODS 1

- Period: 4th September to 4th October 2000
- 2 research engines: *Knowledge finder* & *Medline* 1955 to 2000
- 4 documentation centers:
- "Centre Medical Universitaire" (CMU)'s library,
- World Health Organization (WHO)'s library,
- Maternity's library of the Geneva University Hospital
- "Bibliothèque Publique Universitaire" (BPU).
- The non available reviews (3 of them) : Zurich and United Kingdom;

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METHODS 2

- **CASES:**

  INCLUSION CRITERIA:

- All relevant reviews that reported on sex ratio in the offspring of pre-eclamptic/eclamptic women.
- All cases of pre-eclampsia/eclampsia, well documented from studies where hypertensive diseases of pregnancy were treated as a whole
- Definition:
- Pre-eclampsia
- Edema wasn't considered as a criterion in this definition.
- Eclampsia
- Sex ratio: number of males/numbers of females

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METHODS 3

- ***EXCLUSION CRITERIA***:
- All meta-analysis studies
- Any study that has been repeated by the same author in a larger sample with similar conclusions.
- Any study that considered pre-eclampsia as high blood pressure in pregnancy associated with edema of fingers and/or pedal edema without proteinuria.
- Reported cases of essential hypertension in pregnancy and pregnancy induced hypertension were not considered in the analysis of our data.
- Any study that didn't specify the exact fetal gender in the various group.

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METHODS 4

- **CONTROLS:**
- All new-borns from normotensive women reported in the selected reviews.

- **DATA ANALYSIS:**

- Statistical analysis was performed using the chi-square test calculated by the EPI-INFO program (version 6) and a p- value of < 0.05 was considered to be the level of significance. The relative risk and its confidence interval were used as well in the analysis of our data.

RESULTS

- 13 Studies: 10620 offspring
- 7 Case-controls*
  - 7687 cases & 71750 controls
- 5 Cross-sectional
- 1 Cohort
- Suggested pathogenesis: 1-immunological; 2-genetical; 3-hormonal

TABLE II: THE OVERALL SEX RATIO OF OFFSPRING OF WOMEN WITH PRE-ECLAMPSIA/ECLAMPSIA IN ALL SERIES

Authors & years of the studies	MALES	FEMALES	Total
Salzmann[16] 1955	231	202	433
Toivanen et al.[17] 1970	588	473	1061
Juberg et al.[24] 1976	182	191	373
Scott et al.[9]1976	25	22	47
Campbell et al.[18]1983	2567	2226	4793
Naeye et al.[19]1987	440	440	880
Lopez Llera [21]1990	429	348	777
Arngrimsson et al.[8] 1993	46	72	118
Obed et al.[23]1994	77	67	144
Hsu et Witter[25]1994-Oct.	655	667	1322
Sanchez et al.[26]1996	154	172	326
Makhseed et al.[29]1998	92	91	183
Riethmuller et al.[30] 1999	76	87	163
TOTAL	5562	5058	10620
SEX RATIO	1.09		

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TABLE III: *THE SEX RATIO OF OFFSPRING OF WOMEN WITH PRE-ECLAMPSIA/ECLAMPSIA IN ALL CASE-CONTROL STUDIES*

Authors & years of the studies	Pre-eclampsia/Eclampsia		Controls	
	males	females	males	females
Toivanen et al.[17] 1970	588	473	4196	4061
Scott et al.[9] 1976	25	22	177	166
Campbell et.al.[18] 1983	2567	2226	4306	4333
Arngrimsson et al.[8] 1993	46	72	185	168
Hsu et witter[25] 1994-Oct.	655	667	12432	11912
Makhseed et al.[29] 1998	92	91	4992	4578
Riethmuller et al.[30] 1999	76	87	10489	9755
Total	4049	3638	36777	34973
Sex ratio	1.11		1.05	

X^2 : Chi-square: 5.57**; P-value : 0.018** : This is well above the conventionally statistically significant level ; Thus, null hypothesis is disproved.

RR: 1.05 (CI: 1.01-1.10).RR: Relative risk of males versus females. CI: Confidence Interval.

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TABLE IV: *THE SEX RATIO OF OFFSPRING IN WOMEN WITH PRE-ECLAMPSIA IN ALL CASE-CONTROL STUDIES*

Authors & years of the studies	Pre-eclampsia		Controls	
	males	females	males	females
Scott et al.[9] 1976	11	12	177	166
Campbell et.al.[18] 1983	2559	2217	4306	4333
Arngrimsson et al.[8] 1993	46	72	185	168
Hsu et witter[25] 1994 Oct.	655	667	12432	11912
Makhseed et al.[29]1998	92	91	4992	4578
Riethmuller et al.[30] 1999	76	87	10489	9755
Total	3439	3146	32581	30912
Sex ratio	1.09		1.05	

X^2: Chi-square: 1.98; P-value : 0.159 : Statistically not significant ; Thus null hypothesis not disproved.
RR: 1.03 (CI:0.99-1.08)

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TABLE V: *THE SEX RATIO OF OFFSPRING IN WOMEN WITH ECLAMPSIA IN ALL CASE-CONTROL STUDIES*

Authors & years of the studies	Eclampsia		Controls	
	males	females	males	females
Scott et al.[9] 1976	14	10	177	166
Campbell et. al.[18] 1983	8	9	4306	4333
Total	22	19	4483	4499
Sex ratio	1.15		0.99	

X^2 = Chi-square :0.23; P-value : 0.623: Statistically not significant .

→ This absence of statistical significance despite the clear difference in the sex ratios in the two groups is likely due to the very small number of eclamptic cases in these two studies.

RR: 1.16 (CI: 0.63-2.14)

Conclusion

The fetal gender probably plays no or a very small role in the pathogenesis of this ‘ disease of theories ’.

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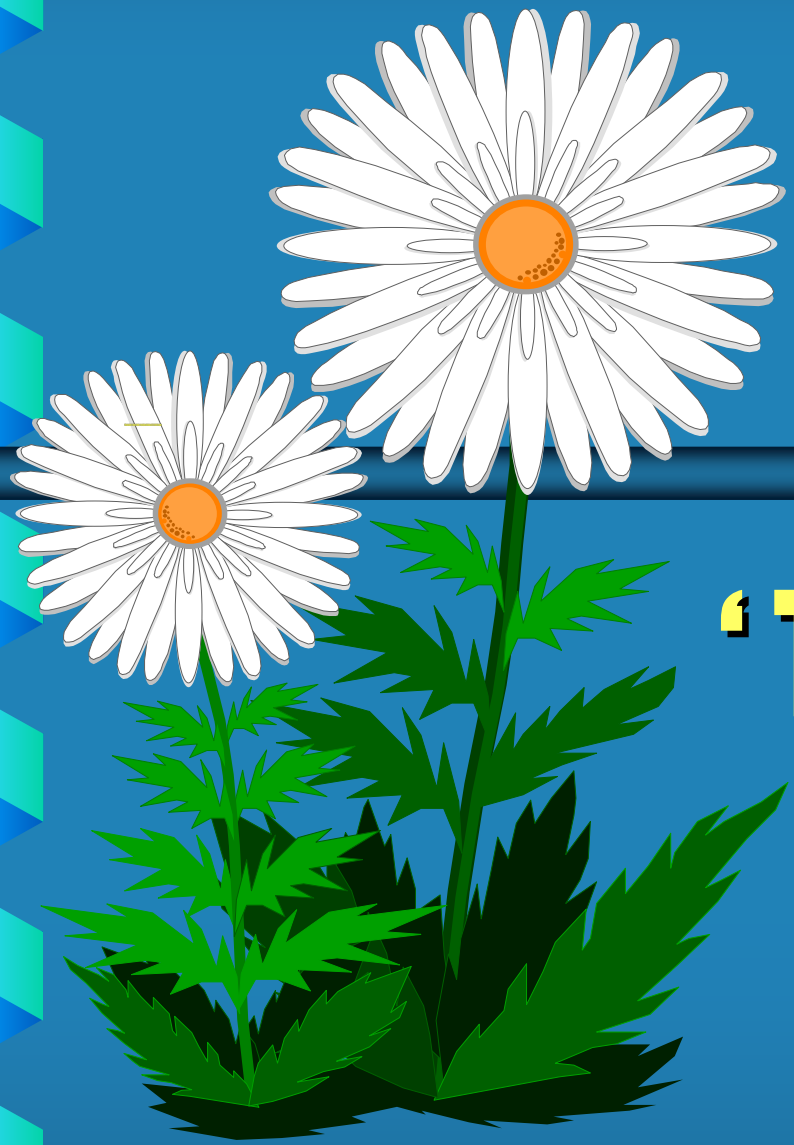

‘ THANK YOU FOR YOUR KIND ATTENTION’

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