

ADVANCED MATERNAL AGE IN PREGNANCY: THE MATERNAL AND THE FETAL RISKS

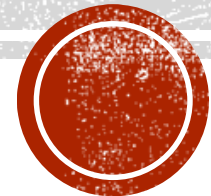
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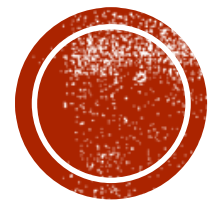
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CSIM PEI October 14th 2015





NO CONFLICT OF INTEREST

CSIM 2015

OBJECTIVES

At the end of the conference, the participant will be able to:

- Perform a preconception consultation for woman with advanced maternal age (AMA)
 - Evaluate her health status and comorbidities that can have an impact
- Counsel the patient with AMA about maternal risks in pregnancy including preeclampsia, gestational diabetes, obstetrical risks and fetal risks.



CASE 1

- 47 year-old women
- G0
- No medical condition
- Body index mass (BMI) of 20 and is active.



CASE 2

- 42 year-old woman
- G1P1
- G1 10 months ago in vitro fertilisation (IVF) + egg donor
 - Gestational diabetes (GDM)
 - Ceasarian section at 38 weeks
- Chronic hypertension
- BMI 39



OVERVIEW

- Introduction
- Maternal and fetal complications
- Preventive measures
- Conclusion



INTRODUCTION

- **Definition:**
 - No clear definition: continuum
- Spontaneous pregnancy described in a 57 year-old woman
- IVF in a 70 year-old woman
- In the USA 14 % of pregnancies in women > 35 years old
 - 3% of pregnancy in Great-Britain > 40 year-old
 - 4.6% in Germany
- In Canada the mean age for the first pregnancy is 29.6 years.

Fretts, UpToDate 2015.

Kenny et al. PLoS one 2013

Lui et al. J Obstet Gynaecol Can 2011



FERTILITY

- Declines from age 32
- More pronounced reduction after age 37
- If ovarian reserve is diminished, < 5% of chance of pregnancy

Rate of fertility with IVF with non-donor egg

Age	Success per cycle %
< 35	36
35-37	28
38-40	18
41-42	10
> 42	4

EARLY COMPLICATIONS

Rate of miscarriage increases

Age	Spontaneous loss	IVF with FH + at 9 wks.
< 30	12%	5-9%
30-34	15%	8-11.4%
35-39	25%	13-19.8%
40-44	51%	22-29.9%
> 45	93%	36.6%

Nybo Andersen et al BMJ 2000
Farr et al, Am j Epidemiol 2007.



EARLY-ONSET COMPLICATIONS

- Rate of ectopic pregnancy is increased 4-8x
- Congenital malformation is increased
 - Odds ratio varies 1.7-2.0
 - Cardiac anomaly
 - Club foot
 - Diaphragmatic hernia

Fretts, UptoDate 2015.



OBSTETRICAL COMPLICATIONS

- Related to maternal age
 - The risk is higher even if no comorbidity and no risk factors
- Presence of comorbidities
 - Cancer, diabetes, hypertension, obesity, etc.,
- Multiple pregnancy
- Primiparous VS multiparous



LITERATURE REVIEW: BASED ON DATABASE OR META-ANALYSIS

- Suggest increased risk in
 - Placental complication (Previa, abruptio)
 - Intra-uterine growth restriction (IUGR)
 - GDM
 - Prematurity
 - Ceasarian
 - Preeclampsia and gestational hypertension
 - Stillbirth
 - Depend on parity
 - Associated with gestational age
- Little data on IVF, BMI and other important counfounding factors
- Contradictory: birth weight under the 10th percentile and pre-eclampsia

Ludford et al. Australian and NZ J Obst and Gyn 2012.

Schoen et and Rosen.Maturitas 2009.

Kenny et al. PLoS one 2013.

Lamminpaa et al. BMC Pregnancy and Childbirth 2012

Waldenstrome et al. Obetric and Gynecol. 2015.



IS ADVANCED MATERNAL AGE ASSOCIATED WITH MATERNAL AND FETAL COMPLICATIONS? A RETROSPECTIVE COHORT STUDY AT THE CHUM

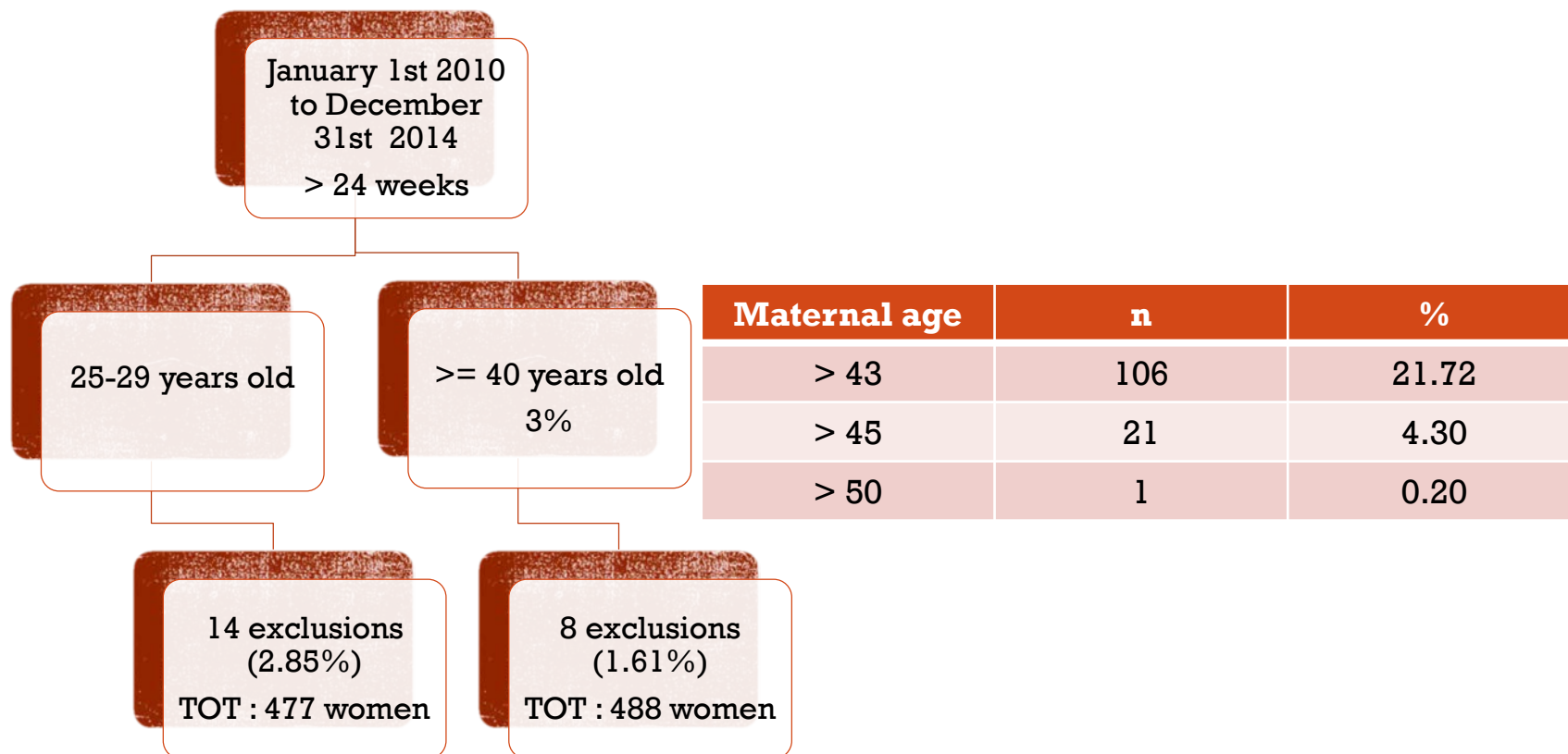


TABLE 1 : Maternal characteristics

	25-29 y/o n=477		> = 40 y/o n=488		p value
	n	%	n	%	
Multiparity	175	36.7	327	67.0	<0.001
University degree	230	48.2	283	58.0	0.002
Obesity pre-pregnancy	22	4.6	38	7.8	0.046
Smoking	56	11.7	33	6.8	0.008
Assisted reproductive technology (ART)	16	3.4	97	19.9	<0.001
ASA	9	1.9	87	17.8	<0.001
Prophylaxis with heparin or LMWH	7	1.5	14	2.9	0.85
Previous caesarean	30	6.3	104	21.3	<0.001
Previous preeclampsia	6	1.3	18	3.7	0.021
Previous GDM	22	4.6	70	14.3	0.000
Type 2 or 1 diabetes	5	1.0	70	14.3	0.025
Chronic hypertension	3	0.6	28	5.7	<0.001



TABLE 2: Maternal outcomes

	25-29 y/o n=477	>= 40 y/o n=488	OR (CI95%)	OR adjusted (CI95%)
	n (%)	n (%)		
Combined maternal outcomes	134 (28.1)	309 (63.3)	4.4 (3.4;5.8)	2.9 (2.1;3.9)
Preeclampsia	10 (2.1)	32 (6.6)	3.3 (1.6;6.7)	1.9 (0.8;4.3)
Gestational Diabetes	55 (11.5)	186 (38.1)	4.7 (3.4;6.6)	4.5 (3.0;6.7)
Cesarean	82 (17.2)	193 (39.9)	3.2 (2.4;4.3)	3.6 (2.4;5.4)
Gestational Hypertension	19 (4.0)	36 (7.4)	1.9 (1.1;3.4)	2.5 (1.3;4.8)
Induction	84 (17.6)	146 (30.3)	2.0 (1.5;2.8)	2.2 (1.6;3.1)
Assisted vaginal delivery	50 (10.5)	38 (7.9)	0.7 (0.5;1.1)	1.2 (0.8;2)
Postpartum hemorrhage	46 (9.7)	49 (10.2)	1.1 (0.6;1.6)	1.1 (0.7;1.8)
Placenta Previa	1 (0.2)	11 (2.3)	10.0 (1.4;85.2)	
Abruptio placentae	15 (3.2)	13 (2.7)	0.9 (0.4;1.8)	
Mortality	0 (0)	0 (0)		



TABLE 3: Fetal outcomes

	25-29 y/o n=477	40 y/o + n=488		OR adjusted (CI 95%)
	n (%)	n (%)	OR (CI 95%)	
Combined fetal outcome	74 (15.5)	109 (22.3)	1.6 (1.1;2.2)	1.5 (1.04;2.1)*
Macrosomia	29 (6.1)	43 (8.9)	1.5 (0.9;2.5)	1.5 (0.9;2.1)#
Low birth weight <5th perc.	34 (7.1)	31 (6.4)	0.9 (0.5;1.5)	0.9 (0.6;1.6)*
Prematurity <37 weeks	24 (5.0)	49 (10.0)	2.1 (1.3;3.5)	1.7 (1.003;2.9)*
Neonatal admission	53 (11.1)	66 (13.7)	1.3 (0.9;1.9)	0.9 (0.6;1.4)#
Fetal distress	5 (1.1)	6 (1.2)	1.2 (0.4;3.9)	
Malformation	4 (0.8)	4 (0.8)		
Stillbirth	3 (0.6)	4 (0.8)		

- *Adjusted for caesarian
- # Adjusted for pour caesarian et prematurity



CONCLUSION OF OUR STUDY

- Maternal age is associated with combined maternal and combined fetal outcomes
- Maternal age is associated with a higher rate of caesarean, gestational hypertension and GDM
 - Confirms pertinence of early screening for gestational diabetes irrespective of BMI
- Maternal age was not associated with preeclampsia and IUGR
 - PE was associated with the use of assisted reproductive technology and with the presence of hypertension
- ASA did not demonstrate benefits for AMA ♀ in our study



LIMITS OF OUR STUDY

- Retrospective study
- Only one centre
- Pregnancy >24 weeks
 - Earlier outcomes not included
- Age is a continuous variable
- Under-power to study effect of age on preeclampsia



ASSISTED REPRODUCTIVE TECHNOLOGY EFFECTS ON PREGNANCY COMPLICATIONS

- Increase rate of caesarean delivery RR 1.8
- No effect on rate of GDM, gHTN, prematurity
- Use of donor egg is an important factor:
 - Independent of age
 - IVF and egg donor = 20% PE

Schoen et and Rosen. Maturitas 2009

Le Ray et al. Human Reproduction 2012



OTHER COMPLICATIONS

- Rate of hospitalization 2-3X
- Maternal mortality
 - 25-29 y/o 9/100 000
 - > 40 y/o 46/100 000

Fretts, UptoDate 2015.

Kenny et al. PLoS one 2013

Dielt et al. Pregnancy and Obstetrical. 2015



PATERNAL ADVANCED AGE IN PREGNANCY

- **Decrease in fertility rate**
 - Decrease in quality of sperm
- **Increase in autosomal dominant mutations**
 - Increase in congenital malformation (small effect)
 - Increase in spontaneous abortions
- **Increase in neural development abnormality**
 - Increase in schizophrenia
 - Increase in autism spectrum disorder

Lui et al. J Obstet Gynaecol Can 2011



PREVENTION AND MANAGEMENT

- Guidelines
 - SOGC recommends pre-conception evaluation for women ≥ 40 y/o
 - Screening for:
 - Hypertension
 - Diabetes
 - Discussion of optimal weight

Lui et al. J Obstet Gynaecol Can 2011



PREVENTION AND MANAGEMENT

- Normal BMI
 - BMI < 40 for IVF
- Screen and assess for co-morbidities
 - 75g OGTT
- Smoking
- Folic acid
- Mammography if > 45 y/o
- Counselling for
 - Egg donor recipient > 40 y/o or any patient receiving egg donation ?
- ASA ???
- Induction in the 39th week



CASE 1

- 47 year-old women, G0 healthy
 - Screen and assess for co-morbidities
 - 75g OGTT
 - Assess smoking status
 - Folic acid 0.4 mg
 - Mammography screening
 - Refer for fertility assesement
 - ASA
 - Risk of GDM 20-30%
 - Risk of preeclampsia 10 %
 - If egg donor 20%
 - Induction in the 39th week



CASE 2: 42 YEAR-OLD WOMAN

- Screen and assess for co-morbidities
 - 75g OGTT
 - Assess for end-organs damage related to HTN
 - Assess medication
- Assess smoking status
- Refer for dietician for weight loss
- Folic acid 1-5 mg
- Counselling for:
 - Preeclampsia: egg donor > 40 y/o = 20%
 - Recurrence of GDM 70-100%
 - Ceasarian 100%
 - Prematurity 20%
- ASA
- Induction in the 39th week



CONCLUSION

Complications	Women 25-29 y/o (%)	Women >40 y/o (%)	WHAT DO I TELL THEM
Congenital malformation	2-3%	OR 1.7-2	Increase
Preeclampsia and gHTN ^{8,12,13,14}	4-11.0%	12-33%	15-20%
Gestational diabetes ^{8,12,13,14}	3.3%	5-38%	40%
Prematurity ^{2,8,12,13,14}	6-7%	6-29%	10%
Cesarean ^{2,8,12,13,14.}	15-29.4%	34-79%	40%



CONCLUSION

- The risk depends on the presence of:
 - Medical conditions
 - Obesity
 - Parity
 - Use of assisted reproductive technology
 - Use of egg donor



QUESTIONS



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