Extended Abstract

Maternal age at conception. Effects on intrauterine development, disease predisposition and gene frequencies.

Gloria-Bottini F.[1], Cosmi E.[2], Meloni G.F.[3], Cosmi E.V.[4],Bottini E.[5]

1. Deparment of Biopathology and Imaging Diagnostics,University of Rome Tor Vergata, Rome,Italy
2. Department of Gynecology and Human Reproduction, University of Padua, Padua,Italy
3. Department of Pediatrics, University of Sassari, Sassari, Italy
4. Department of Obstetrics and Gynecology, University of Rome La Sapienza, Rome Italy
5. Department of Neurosciences, University of Rome Tor Vergata, Rome,Italy

Most western industrialized nations have undergone in the second part of the last century the so-called “fertility transition” characterized by a reduction of fertility below replacement level and by a delay in age at initiation of childbearing. Experimental data and clinical observations suggest that age of childbearing influences the biology of maternal-fetal relationship with important effect on fetal development and disease predisposition. Modifications of reproductive organs due to aging and changes of hormonal activity may bear a direct relationship with placental and fetal development and with disease predisposition. Unfavourable changes of maternal environment may interfere with intrauterine selection resulting in adaptive genetic modification at population level.

In the present note we review data by our group showing that delay of childbearing has important effects on fetal development, predisposition to type 1 diabetes and on gene frequencies.

The following samples were studied:

-5454 consecutive puerperae along with their newborns from Sardinia population (Sassari province).

-679 consecutive puerperae from the population of Central Italy . All women were White Caucasians.

-187 children with type 1 diabetes from Sardinia population (Sassari province

The results are shown in the following tables.

Table 1. Mean value of gestational age and birth weight in relation maternal age and neonatal sex

		maternal age			
		≤ 19	≥20≤39	>39	p
Gestational age	*mean*	38.9	38.9	38.5	<0.001
	SE	0.016	0.02	0.11	
	n°	179	5030	245	
Centlile class	*mean*	45.4	53.1	55.2	<0.001
	SE	2.04	0.40	1.94	
	n°	179	5030	245	

Table 2. Correlation between neonatal growth parameters in relation to maternal age. Probability refers to the difference between correlation coefficients in mothers with an age ≤ 19 years and in mothers with an age > 39 years

	Maternal age			
	≤ 19	≥20≤39	>39	p
	r	r	r	
Birth Weight / Placental Weight	0.29	0.19	0.11	<0.05
Birth Weight / Gestational Age	0.66	0.54	0.41	<0.001
Placental Weight / Gestational age	0.14	0.03	-0.10	<0.02
N°	179	5030	245	

Table 3. Distribution of maternal age at neonatal consecutive births and at birth of children with type 1 diabetes from the same population

Maternal Age	Consecutive Newborns	Type 1 diabetes Children
< 15 ≤ 22	10.2%	0.0%
> 22 ≤ 32	57.1%	10.7%
> 32 ≤ 42	31.6%	42.8%
> 42 ≤ 50	1.1%	36.9%
> 50 ≤ 55	0.0%	9.6%
N°	5454	187

Chi square test of independence *p<<0.001*

Table 4. Proportion of Hp phenotype in relation to maternal age

	Maternal age		
	≤ 22	> 22≤ 36	> 36
Hp phenotype			
Hp1	21.9%	12.4%	8.9%
Hp2-1	48.2%	3.0%	42.8%
Hp2	29.8%	44.6%	48.2%
N°	114	509	56

Chi square test of independence *p<0.01*

Table 5. Joint distribution of PGM_1ed RhC phenotypes in relation to maternal age

	Maternal age		
	≤ 22	> 22≤ 36	> 36
Proportion of phenotypes carriers of *C e PGM_1*1	60%	74.6%	92.9%
N°	35	173	14

Chi square test of indipendence *p = 0.017*

Table 1 shows that a delay of maternal age at childbearing is associated with a decrease of gestational age and with an increase of birth weight. Moreover, as shown in table 2, a delay of the maternal age at childbearing is associated with a decrease of bivariate correlation coefficients among birth weight, placental weight and gestational age suggesting a disharmony in intrauterine growth.

Table 3 shows that a high proportion of children with type 1 diabetes have been conceived by mothers aging more than 42 years, while in the general population only a very small proportion of children are conceived by mothers aging more than 42 years.

Several studies have shown that Haptoglobin (Hp) system plays an important role in modulating the maternal reaction against the implantation of the zygote and in particular that Hp*1/*1 genotype, producing more protein with a molecular weight lower than that of other genotypes, can spread more easily into the tissues favouring intrauterine implantation and growing of the zygote. Table 4 shows that in aging pueperae the proportion Hp1 phenotype decreases while that of Hp2 phenotype increases.

On the short arm of chromosome 1 there are genes influencing fetal growth. We have studied Rh system and Phospho-Gluco-Mutase locus 1 (PGM1) gene. Table 5 shows that in aging pueperae the proportion of carriers of Rh*C and PGM1*1 increases.

In natural primitive conditions the zygote is best adapted to a maternal environment corresponding probably to an age around twenty years. A displacement of maternal age to 30 years and beyond as it is happening in contemporary Western Population represents a drastic change that may have a negative effect on survival and development of zygote and on disease predisposition. In the course of generations this may bring about adaptive changes of gene frequencies at population level.