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Statins and other lipid-lowering therapy and pregnancy outcomes in homozygous familial hypercholesterolaemia: A retrospective review of 39 pregnancies

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ABSTRACT

Background and aims: Pregnancy in HoFH females is associated with further elevation of already markedly elevated low density lipoprotein cholesterol (LDL-C) levels, particularly if lipid-lowering therapy is discontinued, placing the mother and fetus at increased cardiovascular risk. Lipoprotein apheresis is the current recommended treatment for pregnant HoFH patients. However, this is costly, time consuming, and is not available in many countries. Alternative treatment strategies to control hypercholesterolaemia during pregnancy in HoFH patients are necessary.
Methods: This study was a retrospective review of 39 pregnancies from a cohort of 20 genotypically confirmed female HoFH patients.
Results: No maternal cardiac complications or deaths occurred during the pregnancies or during the first year postpartum. Twenty five pregnancies were exposed to lipid-lowering therapy, of which 18 were exposed to statin therapy, just prior to or during the pregnancy. Thirty three (84%) pregnancies carried to term, 3 (8%) premature deliveries and 3 (8%) miscarriages were observed. Complications associated with pregnancy in these HoFH patients, did not differ from those reported during pregnancies of otherwise healthy woman.
Conclusions: HoFH is a severe disease impacting significantly on life expectancy. However, for many females with HoFH, despite the high cardiovascular risk, pregnancy is not uncommon. In resource poor settings and when LA is not available, lipid lowering therapy, particularly statin therapy during pregnancy, appears to be safe for both mother and fetus and is an acceptable alternative for LDL-C reduction in these high risk patients.

1. Introduction

Homozygous familial hypercholesterolaemia (HoFH) is a rare but serious genetic disorder. HoFH is due to bi-allelic mutations in the low-density lipoprotein receptor (LDLR) gene resulting in marked LDLR dysfunction. The prevalence of HoFH is 1 in 160,000 to 1,000,000 worldwide but in founder populations, such as the Afrikaners in South Africa, the prevalence can be as high as 1 in 30,000 [1–3]. Patients with HoFH have elevated levels of low density lipoprotein cholesterol (LDL-C) from birth and often suffer from premature atherosclerotic cardiovascular disease and valvular and supra-valvular aortic stenosis which require surgical intervention [4,5].

Pregnancy in HoFH females is associated with further elevation of already markedly high LDL-C. In healthy patients, total cholesterol and LDL-C levels may increase by up to 40% during pregnancy [6]. This increase is exaggerated in HoFH patients, particularly if lipid-lowering therapy is discontinued, placing the mother at even higher cardiovascular risk [7]. Maternal hypercholesterolaemia

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Table 1
Clinical characteristics of cohort, arranged by maternal year of birth.

Year of birth of patient	Age at death	Age at diagnosis / initial presentation	Total cholesterol (mmol/L) at initial presentation[a]	LDL-C (mmol/L) at initial presentation[a]	Mutations		Age at surgical interventions	Maternal age at first and subsequent pregnancies
					Allele 1	Allele 2		
1933	62	42	18.90	17.90	c.681C > G	c.681C > G	CABG at 50 and 59	20, 23, 25, 29
1936	70	39	21.80	21.00	c.681C > G	c.681C > G	Cholecystectomy at 28; CABG at 47; AV replacement and CABG at 58	22, 25, 26
1944	–	54	18.60	16.60	c.917C > T	c.1690A.C, 2458_2466del	–	30, 32, 38
1954	54	44	20.30	18.70	c.681C > G	c.523G > A	CABG at 41; AV surgery at 47	24, 26
1962	–	42	11.58	9.75	c.681C > G	c.1444G > A	Portacaval shunt at 18; CABG at 42	22, 26, 29
1968	44	6	24.60	23.73	c.681C > G	c.662A > G	–	37, 39
1968	34	9	16.06	–	c.681C > G	c.681C > G	CABG and AV repair at 30; CABG and AV replacement at 34	18, 23
1969	30	18	16.08	14.84	p.47_48del DG	p.47_48del DG	MI at 30	27
1969	–	8	23.50	22.49	c.681C > G	c.662A > G	Partial ileal bypass at 13; Coronary artery stent inserted at 21,33,43,45; CABG at 24; Carotid endarterectomy at 24 and 26; Cholecystectomy at 30; Bilateral ileal angioplasty at 42 and AV surgery at 44	34
1969	–	35	–	–	c.681C > G	c.1444G > A	–	27, 29
1970	38	1	17.70	–	c.681C > G	c.681C > G	Portacaval shunt at 4; Partial ileal bypass at 11; Aortic endarterectomy at 15 and MI at 16	26
1975	–	14	17.70	–	c.2054C > T	c.2054C > T	CABG at 34	25, 27, 32
1975	–	7	20.80	19.59	c.681C > G	c.681C > G	CABG at 18; Coronary artery stenting at 24; CABG at 31	25, 32
1977	–	1.5	18.40	16.70	c.681C > G	c.681C > G	AV replacement at 33	30
1980	–	4	22.58	21.68	c.681C > G	c.662A > G	–	32
1982	29	4	21.05	20.41	c.662A > G	c.523G > A	Portacaval shunt at 5; CABG and Aortic root repair at 14; MI at 23	23
1984	–	4	18.80	17.80	c.681C > G	c.681C > G	AV replacement at 27	21, 25
1986	–	18	–	–	c.2054C > T	c.2054C > T	–	23, 25
1989	–	10	12.20	11.20	c.681C > G	c.681C > G	–	17, 23
1993	–	4	22.60	21.90	c.681C > G	c.681C > G	–	21

CABG, coronary artery bypass graft; MI, myocardial infarction; AV, aortic valve; LDL-C, low density lipoprotein cholesterol.
All ages are reported in years.
[a] Patients already using lipid lowering therapy at initial presentation included.