POLYMORPHISM OF MTHFR A1298C, A MARKER IN NORTHERN INDIAN MOTHERS WITH DS BABIES AND ITS ASSOCIATION WITH BIOCHEMICAL RISK FACTORS AND CHD

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Background: Down syndrome occurs due to nondisjunction in maternal meiosis. Polymorphism of MTHFR due to low folate, high homocysteine are implicated as risk factors.

Objective: To evaluate A1298C polymorphism as a risk factor in DS babies and association with biochemical parameters and CHD.

Methods: 81 mothers(mean age 24.9±3.2yrs) with babies having free trisomy 21 and 99 mothers (mean age 26.9±4.6yrs) having no children with DS were evaluated . Fasting blood was collected for plasma homocysteine, folate (serum and RBC) and for PCR amplification.The MTHFR A1298C polymorphisms were done by allele specific polymerase reaction and enzyme digestion. Homocysteine quantified by liquid chromatography-TMS . Cardiovascular system examination and Echo was done to delineate CHD.

Results: The prevalence of A1298C polymorphism in cases and controls were 66.7% vs. 39.4% respectively. The heterozygous and homozygous genotype frequencies at 1298(AC and CC) among case and control were (38.3% vs. 22.2% and 28.4% vs. 17.25% respectively,OR=3.10, 95% CI 1.6-5.79, P=0.002).Low serum folate in 33.3% % of cases vs.8.0%% in controls(OR= 5.68, CI 95% 2.41-13.4, P= 0.0001).Low RBC folate was found in 28.3% of cases vs.11.1% in controls,(OR= 3.172, CI 95% 1.43-6.99 P=0.005).High homocysteine was found in 9.8% of cases vs. 2.0% in controls. The median intraquartile rangeof homocysteine in cases was10.2(Q1-Q3, 8.2-12.0) vs.7.6(Q1-Q3, 5.7-10.1) in controls. No relationship was observed among A1298C polymorphism and CHD.(Pvalue=0.601).

Conclusion: MTHFR A1298C polymorphism associated with 3 times more risk of developing DS. Low serum, RBC folate and high homocysteine association are significant. Periconceptional folate supplementation may lead to a decline in DS births and CHD.

MTHFR,A1298C	AA	AC	CC	P	Pa
CASES	27(33.3%)	31(38.3%)	23(28.4%)	0.001	0.002
CONTROLS	60(60.6%)	22(22.2%)	17(17.2%)		
AGE<25YRS	AA		AC/CC		
CASES	13(52%)		12(48%)	0.22	
CONTROLS	23(67.6%)		11(32.4%)		
AGE>25YRS	AA		AC/CC		
CASES	14(25%)		42(75%)	0.001	
CONTROLS	37(56.9%)		28(43.1%)		

[prevelence of homo and heterozygous genotypes]

RISK FACTORS	CASES	CONTROLS	OR	P	Pa
MATERNAL AGE AGE<25YRS AGE>25YRS	25(42.4%) 56(46.3%)	34(57.6%) 65(53.7%)	1.17(0.625-2.19)	0.621	
LOWS SERUM FOLATE	27(77.1%)	8(22.9%)	5.68(2.41-13.41)	0.0001	0.0001
LOW RBC FOLATE	23(67.6%)	11(32.4%)	3.17(1.43-6.99)	0.005	0.004
HIGH HOMOCYSTEINE	8(80%)	2(20%)	5.31(1.09-25.77)	0.04	0.036
COMBIND LOW SERUM AND RBC FOLATE	23(79.3%)	6(20.6%)	6.15(2.34-15.92)	0.0001	0.0001
POLYMORPHISM MTHFR A1298C	54(66.7%)	39(39.4%)	3.10(1.66-5.79)	0.001	0.001

[Association of biochemical parametres,gene polymor]