Table 1 SNP rs1076991 Genotype and Allele Frequencies in NTD Triad and Control Groups

Genotype	NTD Triad Group			Control Group
	Cases (n = 509)	**Mothers (n = 485)**	**Fathers (n = 439)**	**Controls (n = 966)**
CC	97 (0.19)[a]	98 (0.20)	66 (0.15)	198 (0.20)
CT	250 (0.49)	225 (0.46)	234 (0.53)	468 (0.48)
TT	162 (0.32)	162 (0.33)	139 (0.32)	300 (0.31)
TT vs. CT/CC OR (LL – UL)[b]	1.04 (0.82 – 1.31); $P = 0.37$	1.11 (0.88 – 1.41); $P = 0.76$	1.03 (0.81 – 1.31); $P = 0.82$	
Allele				
C	444 (0.44)	421 (0.43)	366 (0.42)	864 (0.45)
T	574 (0.56)	549 (0.57)	512 (0.58)	1068 (0.55)
T vs. C	$\chi^2 = 0.33$; $P = 0.57$	$\chi^2 = 0.45$; $P = 0.50$	$\chi^2 = 2.26$; $P = 0.13$	

[a] Population frequencies are shown in parentheses. Values might not add to 1 due to rounding.
[b] OR (Odds Ratio); LL (Lower Limit); UL (Upper Limit).

Table 2 Interactive Effect of *MTHFD1* SNP rs1076991 C→T with SNP rs2236225 G→A in NTD triad groups and controls.

	NTD Triad Group			Control Group
Genotype SNP rs1076991 C→T/ SNP rs2236225 G→A	**Cases**	**Mothers**	**Fathers**	**Controls**
CC/GG	41 (0.08) [a]	37 (0.08)	24 (0.06)	25 (0.06)
CC/GA*	43 (0.09)	46 (0.1)	23 (0.05)	60 (0.13)
CC/AA	11 (0.02)	12 (0.02)	11 (0.02)	11 (0.02)
CT/GG	71 (0.14)	55 (0.12)	83 (0.2)	59 (0.13)
CT/GA	142 (0.28)	107 (0.23)	104 (0.25)	109 (0.24)
CT/AA	36 (0.07)	58 (0.12)	38 (0.09)	45 (0.1)
TT/GG	32 (0.06)	36 (0.08)	30 (0.07)	39 (0.09)
TT/GA	69 (0.14)	70 (0.15)	72 (0.17)	75 (0.17)
TT/AA*	**55 (0.11)[b]**	**51 (0.11) [b]**	34 (0.08)	**23 (0.05)**
Maternal Interaction		**Genotype[c]**	**Allele[d]**	**Triads[e]**
		P = 0.14	P = 0.01	*P* = 0.10
Case Interaction		**Genotype[c]**	**Allele[d]**	**Triads[e]**
		P = 0.001	*P* = 0.001	*P* = 0.36

[a] Genotype frequencies are shown in parentheses. Values might not add to 1 due to rounding.

[b] The most significant differences in genotype combinations in Cases or Mothers versus controls are shown in bold.

[c] Genotype interactions were tested by logistic regression in Mothers or Cases versus Controls.

[d] Allele interactions were tested by logistic regression in Mothers or Cases versus Controls.

[e] Allele interactions were tested in a log linear model using triads.

* Odds Ratios were calculated using the combined genotype of lowest risk as the reference i.e., CC/GA in Cases or Mothers versus Controls. The highest risk was the case TT/AA genotype with an OR 3.34.