

Background

- Infants with congenital cytomegalovirus (cCMV) infection are at risk for neurodevelopmental impairment (NDI)
- Antiviral therapy may improve neurodevelopmental outcomes for some symptomatic infants but is not currently recommended for all infants with cCMV infection
- There are currently no predictive markers for NDI in infants with cCMV.

Objective

Compare neonatal T cell differentiation and memory phenotypes in infant with cCMV with and without subsequent NDI

Methods

- Single-center, prospective study including infants with cCMV infection and uninfected control infants
- Peripheral blood mononuclear cells were collected at diagnosis and analyzed by flow cytometry for CD4+ and CD8+ T cells expressing CD28, CD57, PD1, CD45RA and CCR7.
- Demographic and clinical data were collected on the infants.
- NDI was defined as Bayley III/IV testing below the average range in at least one domain (Adaptive Behavior, Cognitive, Language, Motor, Social-Emotional) and/or clinical diagnosis of cerebral palsy for infants with at least 12 months of follow-up.
- Isolated SNHL with language delay was excluded from NDI group
- Statistical analyses performed using GraphPad Prism version 9.0.0.

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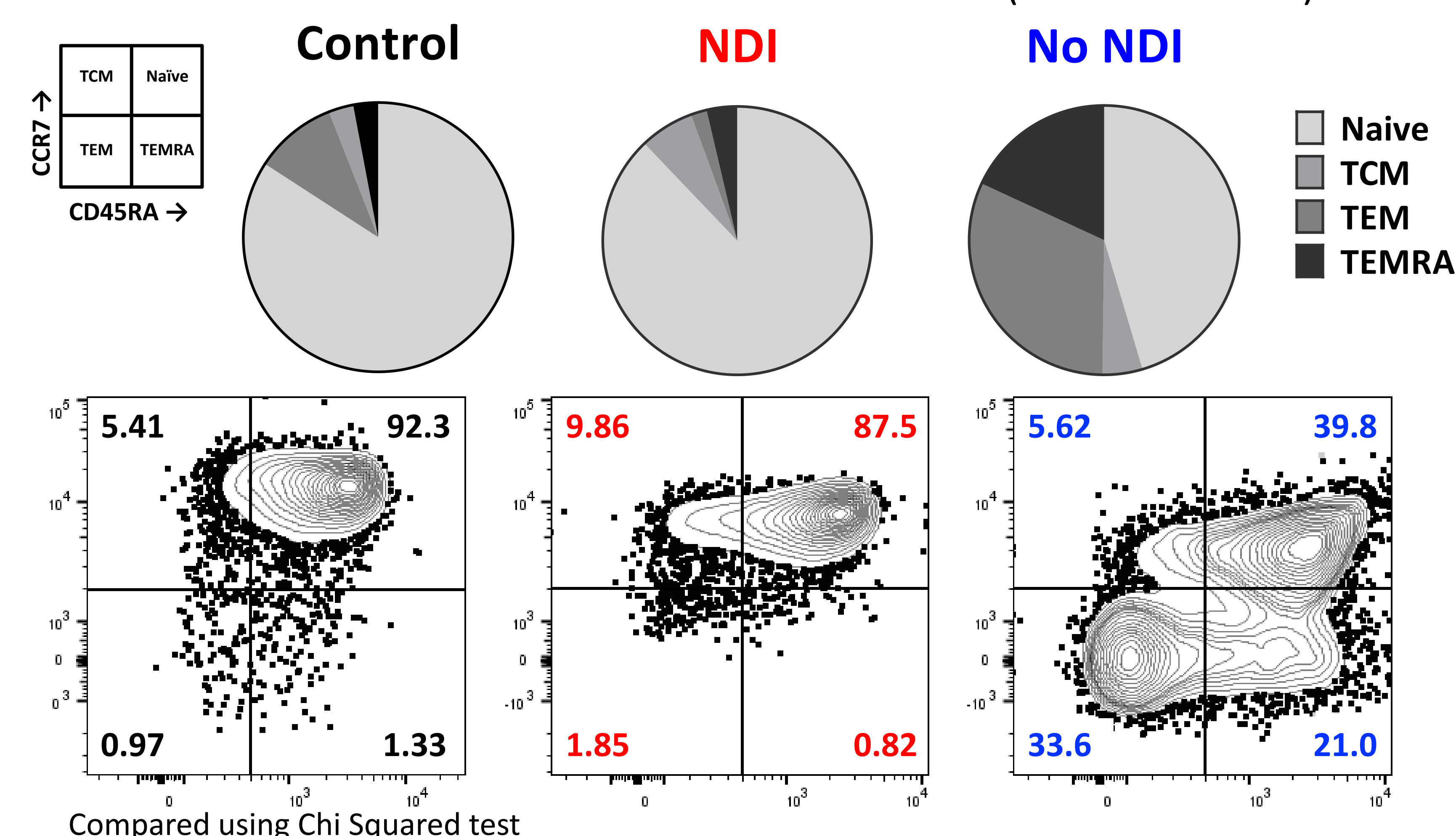
Results

Table 1. Demographic and clinical characteristics of cCMV and uninfected infants.

	NDI n = 4	No NDI n = 14	Control n = 5	p value*
Sex, n (%)				0.99
Male	4 (100)	9 (75)	1 (20)	
Female	0 (0)	3 (25)	4 (80)	
Gestational Age (weeks)	38	38	37	0.87
median[IQR]	[36-38]	[36-39]	[34-38]	
Birth Weight (g)	2225	2578	2620	0.32
median[IQR]	[2073-3135]	[2267-3249]	[3256-3100]	
Length (cm)	45	48	48	0.22
median[IQR]	[44-47]	[46-50]	[47-51]	
Head Circumference (cm)	31	32	34	0.22
median[IQR]	[30-32]	[31-34]	[32-34]	
Symptomatology, n (%)			N/A	
SGA/IUGR	3 (75)	8 (67)		0.99
Microcephaly	3 (75)	9 (75)		0.99
Hepatosplenomegaly	0 (0)	3 (25)		0.53
Thrombocytopenia	2 (50)	4 (33)		0.60
Direct Hyperbilirubinemia	1 (25)	1 (8)		0.45
Abnormal Head Imaging	3 (75)	4 (33)		0.26
Asymptomatic	1 (25)	3 (21)		0.99
Antiviral Treatment, n (%)			N/A	0.99
None	1 (25)	5 (42)		
vGCV and/or GCV	3 (75)	7 (58)		

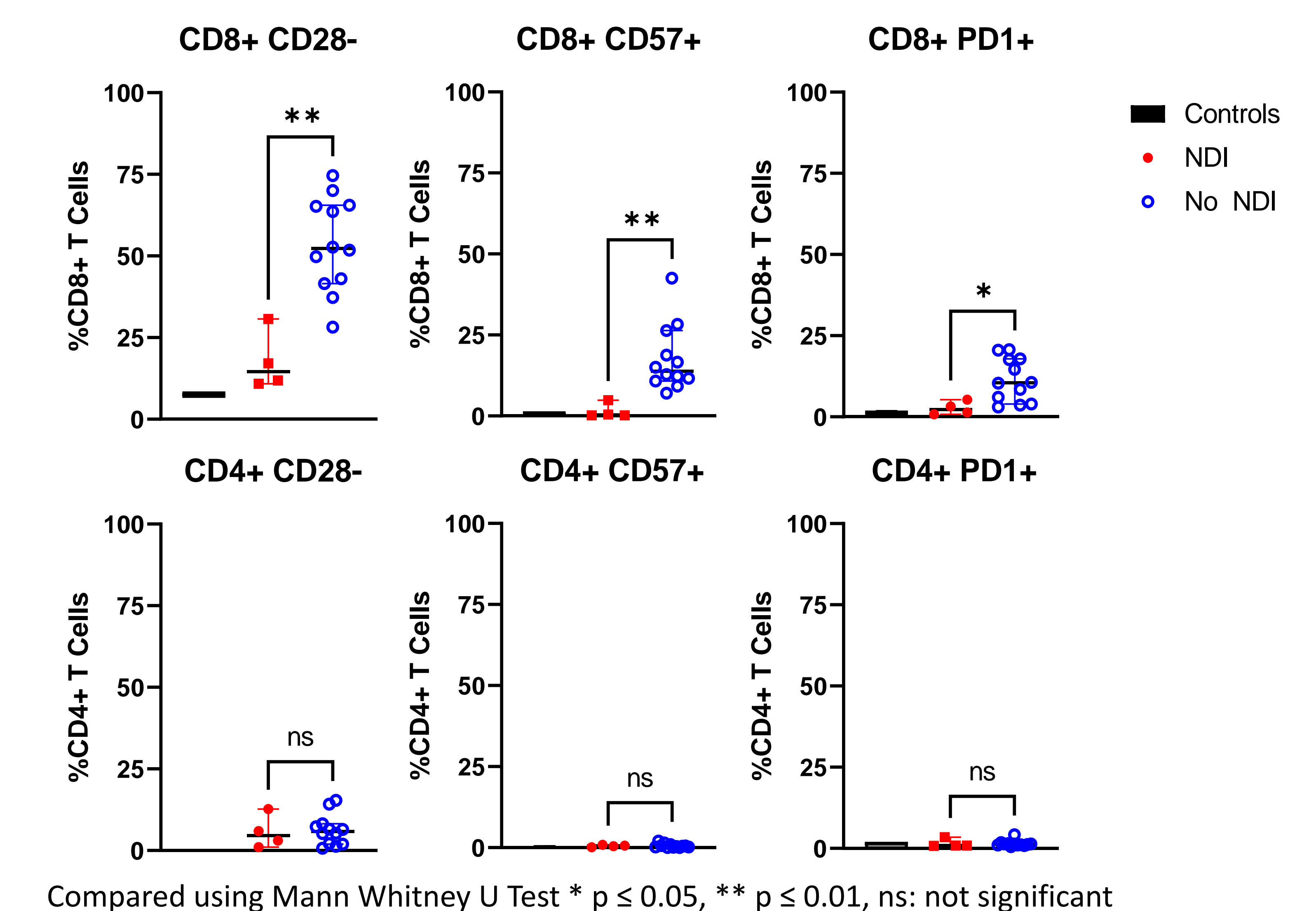
*Continuous variables compared using the Mann Whitney U Test and categorical variables with the Fischer's Exact test. Comparisons made between NDI and no NDI groups

Figure 1. CD8+ T cell memory subset distributions among cCMV and uninfected infants and representative flow plots. Infants with NDI had significantly lower proportions of TEM and TEMRA CD8+ T cells than infants without NDI and were not different from control infants. There was no difference between distributions of CD4+ T cells (data not shown).



Results

Figure 2. Frequencies of CD28-, CD57+ and PD1+ CD8+ and CD4+ T cells. Infants with NDI had lower frequencies of CD28-, CD57+ and PD1+ CD8+ T cells than those without NDI. Frequencies of all markers in infants with NDI were similar to control infants. There was no difference in expression of these markers in CD4+ T cells.



Conclusions

- Infants with NDI had memory cell subsets and frequency of CD8+ CD28-, CD57+ and PD1+ T cells similar to that of uninfected infants and different to those without NDI, suggesting that in this small cohort of infants a more differentiated CD8+ T cell phenotype may correlate with normal neurodevelopmental outcomes.
- One infant with asymptomatic infection at birth subsequently developed NDI and lacked CD8+ T cell differentiation similar to other infants with NDI.

