

Increased Nuchal Translucency and Developmental Delay in Fetuses with Normal Karyotype and Normal Anatomy: A Systematic Review and Meta-analysis

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Objective: To pool published data regarding the association of increased nuchal translucency (NT) with neurodevelopmental delay in fetuses with normal karyotype and normal anatomy.

Methods: Literature search of PubMed, Web of Sciences, Scopus, and Cochrane Library were performed from their inception to January 2022 to identify eligible studies on increased NT with neurodevelopmental outcome. The search included the combination of terms "nuchal translucency" and "outcome". Only fetuses with increased nuchal translucency with normal karyotype and no structural defects or syndromic abnormalities were analyzed. Between-studies heterogeneity was assessed using the I² statistic.

Result: The total prevalence of neurodevelopmental delay in 25 studies was 356/9274 (3.8%). Eleven studies (n=3100) used NT>99th centile as the cut-off; 58 children (1.8%; 95% CI, 0.001-0.036) were evaluated as having neurodevelopmental delay (I²=85.1%). Nine studies (n=6461) used the 95th centile as the cut-off; 275 children were diagnosed with neurodevelopmental delay (4.2%; 95% CI, 0.012-0.041; I^2 =81.8).

Study	Events	Total		Weight,	F-T, Random, 95% Cl				
Brady 1997	1	67		8.69%	0.015 [0.000, 0.063]	Conclusion		wata	- 6
Adekunle 1999	2	26	·	5.48%	0.077 [0.001, 0.218]	Conclusion:	Ine	rate	OT
Souka 2001	5	980	•	13.41%	0.005 [0.001, 0.011]				
Senat 2002	4	58	→ →	8.21%	0.069 [0.015, 0.151]	neurodevelonmental		delav	in
Senat 2007	2	142	6 -1	10.85%	0.014 [0.000, 0.042]	neuroacveropri	icittai	uciay	
Scott 2009	1	3	lI	1.1%	0.333 [0.000, 0.941]				
Miltoft 2012	1	96		9.8%	0.010 [0.000, 0.044]	Children with i	ncreased	tetal	

0.037 [0.008, 0.083]

0.004 [0.001, 0.009]

0.051 [0.035, 0.070]

0.103 [0.014, 0.246]

0.014 [0.001, 0.036]

Mula 2012	4	108	€ =- 1	10.13%
Lehner 2015	4	980	•	13.41%
Hellmuth 2017	31	611	-	13.09%
Stuurman 2021	3	29		5.84%
T-1-1 (05% CI)		2100	•	
lotal (95% CI)	58	3100		
Heterogeneity: $\tau^2 = 0.01$, $\chi^2 = 70.82$, df	=10 (P < 0.000)	L) I ² =85.1		
D				

Α

Study	Events	Total		Weight, F-T, Random, 95% CI	_
Baumann 2005	З	39	⊢	5.21% 0.077 [0.010, 0.186]	
Bilardo 2007	4	359		13.48% 0.011 [0.002, 0.025]	
Axt-Fliedner 2009	2	227	+ = - 1	12.1% 0.009 [0.000, 0.026]	
Vieira 2013	2	31	F	4.43% 0.065 [0.001, 0.185]	
Luculano 2016	10	270	·	12.66% 0.037 [0.017, 0.063]	
Äyräs 2016	29	691	- 	14.88% 0.042 [0.028, 0.058]	
Ranjit 2018	2	103	⊢ ∎1	9.08% 0.019 [0.000, 0.058]	
Buffin 2021	1	203	B -1	11.72% 0.005 [0.000, 0.021]	
Hellmuth 2017	222	4538	•	16.44% 0.049 [0.043, 0.055]	_
Total (95% CI)	275	6461	•	0.025 [0.012, 0.041]	
Heterogeneity: $\tau^2 = 0$, $\chi^2 = 42.8$, df=8	$P < 0.0001$ $P^2 = 8^2$	1.8			
			0 0.1 0.2		
			Dressertier		
			Proportion		

karyotype and normal normal structure seems to be higher than the general population. However, there is high heterogeneity across studies, which largely remains even in subgroup analysis of studies of apperantly similar design potentially indicating the presence of some residual unidentified bias.

Figure 1: Forest plots of neurodevelopmental delay in children with increased NT. Studies that used

NT>99th centile as cut-off (A) and studies that used NT>95th centile as cut-off (B).