Pregnancy in adolescence: Survival analysis of neonatal outcome in babies born to young mothers in Dhanusha, Nepal

INTRODUCTION: This analysis will utilize data from a trial in Nepal and address the characteristics and behaviour of adolescent mothers (12-19 years old), risk factors of neonatal mortality and most importantly the association between the two, conducting a survival analysis to examine whether neonatal outcomes differ between adolescent pregnancies and pregnancies in women of older age. Date of birth and death are in place for neonatal deaths, enriching the analysis with survival curve visualizations and regression models using hazard ratios – not only examining *if* neonatal mortality happens, but *when* it happens.

METHODS: *Origin of data set:* The data used is from a cluster-randomized trial conducted by Institute of Child Health at University College London (UCL) and Mother and Infant Research (MIRA) in Dhanusha district, Nepal. The analysis includes only the control group as well as the group where sepsis intervention was planned but not implemented. The study design was a cluster-randomized trial with the village development committee (VDC), a local administrative unit similar to a municipality, as the cluster unit. The study was conducted in the district of Dhanusha, in the Terai plains of South-Eastern Nepal.

*Outcome, exposure and covariates: The outcome is n*eonatal mortality, whether baby died before survived the neonatal period of 28 days. *The exposure is a*dolescent pregnancy, with age of the mothers being 12-19 or 20 and above. The data set has 23 covariates which span a number of topics including demographics, socio-economic status, reproductive health, pregnancy health, delivery care and postnatal care.

Process of data analysis: The data analysis was conducted in STATA 13 IC. The data set was adjusted for survey design to obtain correct estimates.. After taking account of requirements such as being in a non-intervention group, having a known age, a live birth (excluding stillbirths) and a complete date of birth for their newborn, the sample was narrowed down to 19 535 women. The data set was set for survival analysis (stset) by using

the date of birth and date of death of the newborn. If the child survived through the neonatal period it was assigned a survivor status and a date of death that was outside the survival analysis period, i.e. more than 28 days after birth. Babies who died on the same day they were born, were recoded with a date of death of [date of birth + 0.5], so it would still be included in the survival analysis.

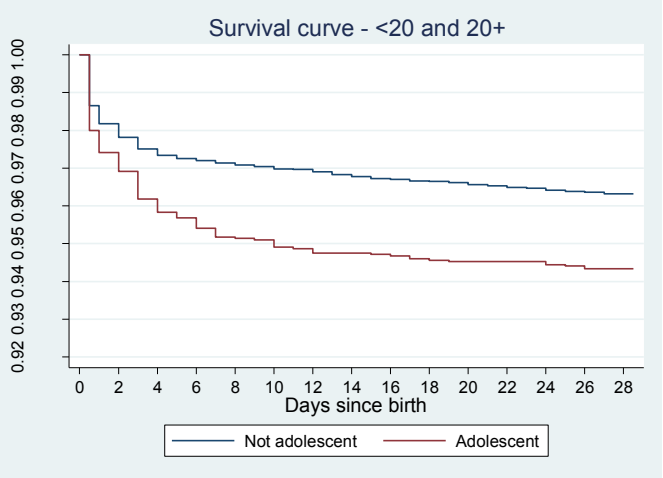
Bivariate and multivariate analysis: Risk factors and characteristics of adolescent pregnancies were established chi-square tests and logistic regression and Cox regression was used to assess hazard ratios and potential risk factors for neonatal mortality with a p-value of 0.05 as the cut off for statistical significance. The Cox regression model was then used to estimate hazard ratios (rate of dying) of neonatal mortality in relation to adolescent pregnancy, while controlling for identified potential confounders. Each variable was included in the model, and a 5 % change or more in the HR resulted in the variable being included in the final model. In addition, powerful a priori confounders were also included in final model.

RESULTS

Table 2. Bivariate analysis: Crude neonatal HR and NMR for adolescent pregnancies (p-value=0.002)

MATERNAL AGE	HAZARD RATIO	BIRTHS	DEATHS	PERCENTAGE (WEIGHTED)	NMR (WITH 95% CI)
ADOLESCENT (<20)	1.47 (1.16-1.87)	4174	201	4.82 %	48.2 per 1000 (41.03 – 56.54)
OLDER (20≤)	1 (baseline)	15 361	506	3.29 %	32.9 per 1000 (27.65 – 39.14)
TOTAL		19 535	707	3.62 %	36.2 per 1000 (31.57 – 41.43)

Fig 2. Survival analysis: Survival curve for babies born to adolescent mothers and primipara mothers



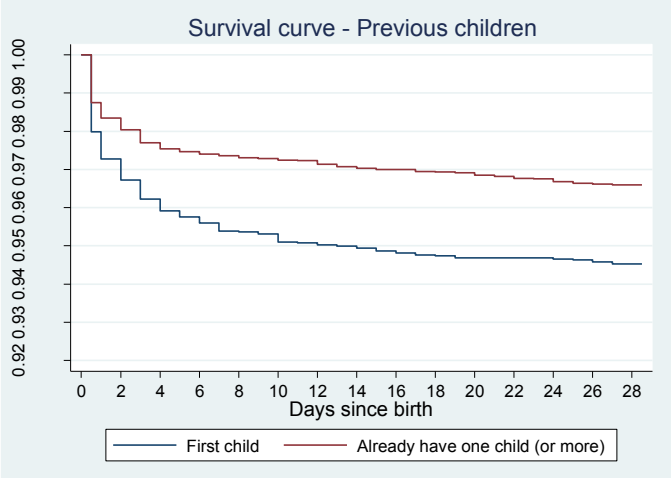


Table 3. Bivariate analysis: Significant characteristics and associations of adolescent pregnancies

VARIABLE	CATEGORY	ADOLESCENT (<20) (N= 4 174)	OLDER (20≤) (N=15 361)
SOCIO-ECONOMIC FACTORS			
READING SKILLS	Cannot read	67.21 %	74.70 %
(P=0.0001)	With difficulty	10.45 %	6.78 %
	Easily	21.44 %	17.52 %
	Missing	0.89 %	1.00 %
ANY STUDY	Yes	33.75 %	25.88 %
(P=0.002)	No	65.97 %	73.36 %
	Missing	0.28 %	0.76 %
ANY STUDY (HUSBAND)	Yes	58.62 %	53.71 %
(P=0.0042)	No	41.13 %	45.62 %
	Missing	0.26 %	0.66 %
REPRODUCTIVE FACTORS			
AGE AT MARRIAGE	5-15	40.24 %	36.80 %
(P=0.1391)	16+	58.91 %	62.47 %
	Missing	*0.86 %*	0.74 %
PRIMIPARITY – FIRST CHILD	Yes	87.52 %	16.47 %
(P<0.0001)	No	11.85 %	82.48 %
	Missing	0.63 %	1.06 %
PREGNANCY HEALTH			
GESTATION	<9 months	2.05 %	1.10 %
(P=0.0003)	9 months≤	97.93 %	98.81 %
	Missing	0.02 %	0.09 %
MULTIPLE BIRTHS	Singleton	98.79 %	97.55 %
(P=0.0032)	Twin/Triplet	1.10 %	2.32 %
	Missing	0.11 %	0.13 %

Table 4. Bivariate Cox regression analysis: Hazard ratios for factors of neonatal mortality

VARIABLE	CATEGORY	HAZARD RATIO	95 % CI
SOCIO-ECONOMIC FACTORS[1]			
READING SKILLS	Cannot read	1.58	1.11 – 2.24
(P=0.0150)	With difficulty	2.02	1.30 – 3.15
	Easily	1 (baseline)	
REPRODUCTIVE HISTORY			
AGE AT MARRIAGE	5-15	1.34	1.07 – 1.67
(P= 0.0128)	16+	1 (baseline)	
PRIMIPARITY	Yes	1.55	1.29 – 1.85
(P=0.0001)	No	1 (baseline)	
PREGNANCY HEALTH			
GESTATION	<9 months	30.80	22.93 – 41.36
(P<0.0001)	9 months≤	1 (baseline)	
MULTIPLE BIRTHS	Singleton	1 (baseline)	
(P<0.0001)	Twin/Triplet	7.32	5.47 – 9.81
SEX	Male	1.23	1.01 – 1.49
(P=0.0432)	Female	1 baseline	
DELIVERY CARE			
PLACE OF BIRTH	Home	1 (baseline)	
(P=0.0095)	Institution	1.41	1.10 – 1.80

From the bivariate analysis we identified nine potential confounders which we include in the Cox regression and assess the change in HR. Based on the adjusted HRs, we carry out the final Cox regression model, which now includes adolescent pregnancy, primiparity, gestation length and multiple births. Powerful a priori confounders were also included.

Table 7. Multivariate Cox regression analysis: Final model with adjusted hazard ratios

VARIABLE	CATEGORY	HAZARD RATIO	STANDARD ERROR	95 % CI	P-VALUE
MAIN EXPOSURE					
ADOLESCENT PREGNANCY	Adolescent	1.08	.14091	0.82 – 1.42	0.559
	Not adolescent	1 (baseline)			
SOCIO-ECONOMIC FACTORS					
READINGS SKILLS (LITERACY)[1]	Cannot read	1.44	0.23701	1.02 – 2.03	0.040
	With difficulty	1.74	0.34011	1.15 – 2.62	0.011
	Easily	1 (baseline)			
ASSET SCORE (SES)[1]	Increase in unit	0.95	0.02214	0.91 – 1.00	0.069
REPRODUCTIVE HISTORY					
AGE AT MARRIAGE	5-15	1.36	0.15776	1.07 – 1.73	0.016
	16 +	1 (baseline)			
PRIMIPARITY	Yes	1.56	.16375	1.25 – 1.94	<0.001
	No	1 (baseline)			
PREGNANCY HEALTH					
GESTATION	<9 months	22.85	3.49935	16.59 – 31.49	<0.001
	9 months≤	1 (baseline)			
MULTIPLE BIRTHS	Singleton	1 (baseline)			
	Twin/Triplet	3.60	0.92035	2.11 – 6.15	<0.001

[1] A priori confounders, identified by previous literature and research.

CONCLUSION: This analysis concludes that, in this sample population, there is no direct relationship between adolescent pregnancies and neonatal mortality, and that this instead increased hazard of neonatal mortality is explained by variables and influenced through channels like literacy, age at marriage, primiparity, gestation length and multiple births which are included in the.. The remaining confounders in the final model (with exception of SES) are all associated with neonatal mortality – independently, after controlling for the others - and illustrates the importance of addressing neonatal mortality in a holistic continuum of care – delaying adolescent pregnancies and child marriage, investing in girl's education, following up those in their first pregnancy closely, and reducing preterm births.