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Epidemiological Appraisal of Neonatal Mortality in India: Conventional vs. Hierarchical Models

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Abstract:

Nowadays multilevel regression is being often preferred in epidemiological and public health research mainly for the consideration of hierarchical structure of related data. The very few multilevel applications on neonatal mortality have not addressed the measures of area level variation. The aim of this study was an epidemiological appraisal of neonatal mortality using conventional and different multilevel models with a focus on the interpretation of district level variability and district level risk factors. The area level variance has been assessed by different epidemiological measures such as median odds ratio, 80% interval odds ratio, and intra-class correlation. The performance of the models was assessed by the area under the ROC curve, median odds ratio and the rank correlation of observed and model predicted neonatal mortality among the districts.

Eight socio-demographic variables (caste, toilet status of the household, cooking fuel used in the household, age of the mother at delivery, father's educational achievement, mother's educational achievement, birth order of the newborn, and the newborn's sex); six pregnancy related variables (swelling status, foetus movement, malaria, excessive vaginal discharge, supplementary nutrition status and jaundice during the pregnancy); and 2 delivery related variables (number of problems during delivery and feeding newborn with colostrums) turned out to be significantly associated with the NMR. Only two district level variables (proportion of mothers belonging to religions other than Hindu & Muslim; and mothers' average education) showed to be significant with NMR. Mothers belonging to other religions explained considerable area level variations.

Performance indicators clearly demonstrated the utility of multilevel models in complex data with hierarchical data structure.

Keywords: Multilevel Model, Median Odds Ratio, Neonatal mortality, intra-class correlation, 80% interval odds ratio, proportional change in variance, logistic regression

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1. Introduction

In many areas of the social, medical and other sciences data arises in complex multilevel structures in which responses from individuals grouped together in districts or communities are studied. Applied researchers should have an understanding of the appropriate analytical methods for data having complex multilevel structure. When the outcome is binary, ordinary logistic regression is inappropriate for data involving hierarchical structure, as it assumes that all events are independent {See Bryk and Raudenbush (1992) and Goldstein and Healy (1995)}. All individuals within a given hierarchy or a cluster such as a district tend to be similar than the individuals across different districts, both in measured and unmeasured characteristics associated with the outcome of interest. For example, all persons living in a cluster might share the environment such as polluted air or a pollution free environment and so are equally prone for or protected from a specific morbidity. Ignoring this clustering as is done in ordinary logistic regression, results in an artificially inflated number of independent observations leading to underestimation of the standard error of the parameters being estimated.

Multilevel modelling accounts for this hierarchical nature and the correlations present within the cluster with reference to the outcome and associated factors.

1.1 Why neonatal mortality?

One of the important components of reproductive health is child survival. The major public health interventions during the last two decades focused on the reduction in infant and child mortality (World Health Organisation, 2005; United Nations, 1995). In India, though there is a gradual decline in both under5 mortality and infant mortality, analysis indicates that neonatal mortality as a proportion of infant mortality is gradually rising. Neonatal mortality formed about 60% of infant mortality during the 1960s, but gradually increased to form more than 75% of infant mortality during 2006. Similarly, NMR as a proportion of under5 mortality increased from 45% in the year 1990 to 54% in 2010 {see Rajaratnam et al. (2010)}. These observations indicate a slower reduction in neonatal mortality compared to post-neonatal mortality in India. This is consistent with the fact that the focus on the health care of newborns has been mainly on the prevention of infections, malaria, diarrhoea and improvements in the general sanitation, immunization coverage, vaccine-preventable diseases {see Bhargave, SK (2004)}. Mortality during the neonatal period may be more associated with antenatal, perinatal and immediate post natal care along with the conduct of the child delivery, prematurity, low birth weight and neonatal infections etc {see Baqui et al. (2007), Tinker et al. (2005) and Mercer et al. (2006)}, which can be addressed better at an institutional level. The fact that more than 75% of IMR is NMR suggests that IMR cannot be reduced without substantial reduction in the NMR.

Most of the literature indicates that many of studies dealing with the identification of factors associated with neonatal mortality have been on either small scale and/or hospital based. Further, even when the data has a hierarchical structure, such structure has not been considered in the analyses. Ignoring the clustering of data within hospitals/villages/districts would under-estimate the standard error associated with the estimates leading to inflated significance of various factors. A suitable statistical method for analyzing grouped or clustered data is multilevel modeling, which has the following advantages: correction of standard error underestimation, examination of cross-level interactions, estimation of the variability at group level, and analysis of contextual effects after adjusting for individual variables, while also accounting for the non independence of within-group observations.

1.2 Use of Multilevel Models

Multilevel statistical techniques have been developed to deal with the data involving natural hierarchy {see Snijders and Bosker (2012), Godlstein (2011) and Austin et al. (2001)}. There are two possible scenarios for such natural clustering. Firstly, individuals such as patients or students can be nested in a hospital or standard which, in turn are nested in a community or school and these communities/schools are nested in geographic regions. Another possible scenario is multiple observations over time nested within an individual patient. In a more complex situation, repeated observations are nested within an individual who in turn is nested in different levels as indicated in scenario 1. In this type scenario, the covariates may vary either at occasion level (time dependent covariate) or vary at higher level (time independent covariate) {see Twisk Jos WR (2006)}.

The specialty of the multilevel models is in partitioning the variance at different levels (e.g. neighbourhood and individual). Such a partitioning is useful not only in improved estimation of the relevant parameters but also for better epidemiologic understanding of the role of the neighbourhoods in the occurrence of individual events {see Merlo (2003), Merlo J., Chaix B. et al. (2005)}. However, such partitioning of variance is not that straight forward when we are dealing with binary response variables, unlike in quantitative response variables. Yet, some epidemiological indices are available to assess the area level variance and clustering within areas {see Larsen and Merlo (2005), Larsen et al. (2000), Goldstein et al. (2002) and Rasbash et al. (2003)} for binary outcome variables. Some newer indices include the median odds ratio (MOR) {see Larsen and Merlo (2005) and Larsen et al. (2000)} and 80% interval odds ratio (IOR-80%) {see Larsen and Merlo (2005) and Larsen et al. (2000)}. These measures are helpful in the integration and presentation of fixed as well as random effects.

This paper presents the comparative analytical results of multilevel analysis using logistic regression models for the neonatal mortality in India from a multistage cluster survey. The aim of this study was an epidemiological appraisal using conventional and different multilevel models to 28-days death outcome of a large group of neonates in order to compare the performance of these models with the focus on the interpretation of district level variability and district level risk factors.

2. Data and Methods

2.1 Data

Data from the third round of the District Level Household Survey (DLHS-3) conducted during 2007–08 is used for this study. This is a large scale nationally representative survey aimed to provide information on family planning, maternal and child health, reproductive health of ever married women and adolescent girls, utilization of maternal and child healthcare services at the district level in India. The survey adopted a multi-stage stratified probability proportional to size (PPS) sampling design ((International Institute for Population Sciences (IIPS), 2010).

Unlike DLHS-1 and DLHS-2, detailed information on the specific aspects of the last delivery (in the preceding 4 years from the date of survey) that a woman had, has been collected in the DLHS-3. Such data has not been available at the community level till date. Analysis on these aspects may give insight into the factors associated with neonatal mortality. Neonatal death, defined as any death during the completion of first 28 days of neonate life, is considered as an outcome variable in this study. Only live births were considered and other births (still births and abortions) were disregarded.

After exploration of the available data in the original form of collection, a set of explanatory variables was selected for the analysis. Some of them were retained in their existing form while some of the variables were categorized for more practically meaningful and stable estimates.

Individual level characteristics studied are broadly under 3 categories, namely socio-demographic, pregnancy related and delivery related. Place of residence (rural/urban), religion, caste, treatment status of drinking water, toilet status as to shared or unshared, cooking fuel used in the household, possession of Below Poverty Line (BPL) card, type of house as to pucca, kutcha or semi pucca, age of the mother at the last child birth, father's years of schooling, mother's years of schooling and mother's age at marriage formed the socio-demographic group of variables. Pregnancy related characteristics were total number of pregnancies the mother had, birth order of the index newborn, sex of the index newborn, registration of the last pregnancy, who registered the pregnancy, details of antenatal care (ANC), details of iron and folic acid intake, tetanus injection, pregnancy problems, supplementary nutrition received. Delivery related characteristics were identified as problems during delivery, type of delivery, delivery place, who conducted the delivery, use of disposal delivery kit, wiping of the newborn, use of sterilized blade and feeding of colostrums to the newborns.

At the higher level of district, proportion of mothers following a religion other than Hinduism and Islam (≤ 10% or > 10%), mothers' average years of education (> 5 or ≤ 5), mothers' average age at last child birth (> 24 years or ≤ 24years), proportion of mothers with a minimum of three ANC visits (≤ 42% or > 42%), proportion of households with treated drinking water supply (> 30% or ≤ 30%), proportion of SC/ST population (≤ 30% or > 30%) were considered. These variables were aggregated from the survey data. The threshold level for each variable was chosen as the median of the respective values for all districts.

2.2 Ethics statement

We used the survey data available for academic use in the public domain (http://www.rchiips.org/), for which no ethics approval is required.

2.3 Multilevel Analysis

Traditional logistic regression model with individual and area level variable

When we have only two levels, we fit a usual binary logistic regression model with both individual level and district level variables. But the district level variables are disaggregated at the individual level. The model estimates the probability p_{ij} that the i^{th} neonate in the j^{th} district dies before the completion of 28 days, as a function of the predictor variables considered. This can be defined as {see Cox, DR (1958)}:

$$\log_e\left(\frac{p_{ij}}{1-p_{ij}}\right) = \beta_0 + \beta_1 x_{ij} + \lambda_1 y_{ij} + e_{ij}$$

where
i = 1 to n_j; j = 1 to j;
β_0 is the intercept; β_1 is the vector of the coefficients for individual level covariates indicated as the vector *x*.
λ_1 is the vector of coefficients for the second level covariates (disaggregated at individual level) indicated as the vector *y*.
e_{ij}'s are the residuals at individual level.
Also, $e_{ij} \sim N(0, \sigma_{ij}^2)$ where 0 is mean and σ_{ij}^2 is variance.

A two level empty model (Random intercept model without covariates)

When there only two levels of data, p_{ij} the probability of neonate's death can be defined in the empty model as

$$\log_e\left(\frac{p_{ij}}{1-p_{ij}}\right) = \beta_{0j} + e_{ij}$$

where i = 1 to n_j; j = 1 to j; n_j is the size of jth cluster
β_{0j} is the random intercept; and
$\beta_{0j} = \beta_{00} + \mu_{0j}$, where β_{00} is the fixed part of the intercept and μ_{0j} is the unique increment to the fixed part of intercept associated with the higher level unit *j*; and $\mu_{0j} \sim N(0, \sigma_{00}^2)$ where 0 is the mean and σ_{00}^2 is the unconditional variance in the individual level intercepts; e_{ij} are the individual level residuals which are $\sim N(0, \sigma_{ij}^2)$

A Two level Random Intercept Model with individual and area level variables

A two level random intercept model can be defined by adding two more terms in the empty model {see Bryk AS et. al (1992) and Goldstein H (2011)}:

$$\log_e\left(\frac{p_{ij}}{1-p_{ij}}\right) = \beta_{0j} + \beta_1 x_{ij} + \lambda_1 y_{ij} + e_{ij}$$

Where i = 1 to n_j; j = 1 to j; n_j is the size of jth cluster
β_{0j} is the random intercept; and
$\beta_{0j} = \beta_{00} + \mu_{0j}$, where β_{00} is the fixed intercept and μ_{0j} is the unique increment to the intercept associated with the higher level unit j; and $\mu_{0j} \sim N(0, \sigma_{00}^2)$, where 0 is the mean and σ_{00}^2 is the unconditional variance in the individual level intercepts.
The additional terms - β_1 is the vector of fixed coefficients for individual level covariates *x* and λ_1 is the vector of fixed coefficients for second level covariates *y*;
e_{ij} are the individual level residuals and

$$e_{ij} \sim N(0, \sigma_{ij}^2)$$

A Two level Random Intercept and Slope Model with individual and area level variables

A two level random intercept and slope model can be defined by adding two more terms in the empty model {see Bryk AS et al. (1992) and Goldstein H (2011)}:

$$\log_e\left(\frac{p_{ij}}{1-p_{ij}}\right) = \beta_{0j} + \beta_1 x_{ij} + \lambda_{1j} y_{ij} + e_{ij}$$

Where i = 1 to n_j; j = 1 to j; n_j is the size of j^{th} cluster
β_{0j} is the random intercept; and
$\beta_{0j} = \beta_{00} + \mu_{0j}$, where β_{00} is the fixed intercept and μ_{0j} is the increment to the intercept associated with the higher level unit j; and $\mu_{0j} \sim N(0, \sigma_{00}^2)$, σ_{00}^2 being the unconditional variance in the individual level intercepts
The additional terms, β_1 are the fixed coefficients for individual level covariates *x* and λ_{1j} are the random coefficients for second level covariates *y*.
$\lambda_{1j} = \lambda_{11} + \varphi_{1j}$, where λ_{11} is the fixed slope (coefficient) and φ_{1j} is the increment to the slope associated with the higher level unit j; and $\varphi_{1j} \sim N(0, \sigma_{11}^2)$, σ_{11}^2 being the unconditional variance in the individual level slopes (coefficients).
e_{ij} are the individual level residuals and

$$e_{ij} \sim N\left(0, \sigma_{ij}^2\right)$$

Further, the variance of second level random effects is described in the form of variance covariance matrix:

$$Var\begin{bmatrix} u_{0j} \\ \varphi_{1j} \end{bmatrix} = \begin{bmatrix} \sigma_{00}^2 & \sigma_{01} \\ \sigma_{10} & \sigma_{00}^2 \end{bmatrix}$$

Where,
σ_{00}^2 and σ_{11}^2 are the unconditional variance in the first level intercepts and slopes respectively;
$\sigma_{01} = \sigma_{10} = \text{cov}(u_{0j}, \varphi_{1j})$ is unconditional covariance between the intercept associated with second level unit j and the slope associated with second level unit j.

2.4 Method of Estimation

Stepwise logistic regression procedure was adopted for traditional multivariable regression technique. All the individual and community level characteristics found significant at 5% level of significance in univariate analysis were retained as candidates for stepwise multivariable logistic regression model. An entry probability of 0.05 and an exit probability of 0.051 were used for the stepwise model building with maximum likelihood approach for parameter estimation.

To build the multivariable models with random intercept alone and random intercept with slope, similar approach as in building the multiple logistic model was adopted. District level variables were included both for fixed effects and well as for random effects. To build the multivariable models, a manual stepwise procedure was adopted by deleting the least significant variable one at a time till all the variables in the model were significant.

To build the mixed effects models, the xtmelogit command in Stata was used. The fixed effects are akin to the standard regression coefficients which are estimated directly. However, the random effects are expressed in terms of estimated variances and covariances of the concerned coefficients. The assumptions that go with mixed effects logistic regression are that the random effects follow a Gaussian distribution and the response given the random effects follows Bernoulli distribution. The probability of the event is determined by the cumulative logistic distribution function. The log likelihood for this model is approximated by maximum likelihood estimation with adaptive Gaussian quadrature with 7 integral points.

This is necessary because the log likelihood has no closed form. To check the adequacy of 7 integral points, the model was also refitted with a larger number of quadrature points (results not shown) and it was observed that the model parameter are substantially the same. Hence 7 integral points were considered to be adequate for this analysis. All the analysis was implemented on Stata software (version 12.1).

2.5 Interpretation of the odds ratio in ordinary and multilevel logistic regression

In the ordinary logistic regression model, odds ratios characterize the effect of covariates at neonate level on the population as a whole, averaged over the increments associated with the intercept μ_{0j} or slope φ_{0j} or both, rather than on a district.

In the multilevel set up, the interpretation of an odds ratio associated with the covariate at neonate level compares within the same district, averaged over all districts. For example, effect of a new born sex on mortality may be explained as an odds ratio between a male neonate and female neonate belonging to the same district and with the same sets of other covariates.

The odds ratio for a district level covariate in an ordinary logistic regression can be explained as the odds of death for a neonate of a district with one value of the covariate compared to the odds of death of a neonate of a district with another value of the same covariate. For example, the odds of a neonatal death for a newborn from the districts with mothers' average education of ≤ 5 years compared to the neonates from districts with mothers' average education of > 5 years.

On the contrary, in a multilevel set up the odds ratio for a district level variable measured as a fixed effect is interpreted differently. It is interpreted as the odds of death for the districts with one value of a covariate compared to the districts with another value of the same covariate but with the same value of random effect. For example, the odds of a neonate's death within 28 days for the districts with mothers' average education of ≤ 5 years compared to the districts with mothers' average education of > 5 years, limited to the districts with the same value of random effect i.e. the intercept μ_{0j} or slope φ_{0j} or both, depending upon the type of multilevel model used. Additionally these random effects also adjust the odds ratios for unobserved district-level covariates in a multilevel model.

2.6 Measures of Area Level Variance and Clustering in Multilevel Logistic Regression

2.6.1 Intra class correlation coefficient (ICC)

People residing in the same area share a common set of social, economic, health facilities and other characteristics as compared to the people residing in another area. The multilevel model facilitates the special statistical technique to identify the intra-class (intra-district) correlation arising from the similar neonates' death risk within the same district compared to the other districts.

The individual level and the area level variance are not directly comparable in multilevel logistic regression, unlike in multilevel linear regression. This is because of the different scales of measurement. The model gives the area level variance V_A on logistic scale and individual level variance V_I on probability scale. Also, V_I is equal to P_I (1 - P_I) and therefore depends on the prevalence of the outcome. To overcome this difficulty, it was suggested {see Snijders and Bosker (2012)} the linear threshold model method, also known as latent variable method, which converts the individual level variance from probability scale to logistic scale, so that the scale is consistent with that of area level variance. The individual level unobserved variance V_I in logistic scale is equal to $\pi^2/3$ (i.e., 3.29). Hence the ICC based on the linear threshold model method is only a function of area level variance and is statistically more consistent. Another method explained by Goldstein {see Goldstein et al. (2002) and Rasbash J et al. (2003)} for computing the ICC is based on the simulation for dichotomous outcome which directly depends on the prevalence of the outcome, contrary to the linear threshold method.

2.6.2 The Median Odds Ratio (MOR)

As the area level variance and intra class correlation are difficult to understand in the case binary outcome, another index called the Median Odds Ratio (MOR) is proposed {See Larsen & Merlo (2005)}. It transforms the area level variance to the odds ratio scale which is easier to interpret and that expression can also be compared with the effects of other covariates on the same scale. MOR is defined as the median value of the distribution of odds ratios between the persons belonging to an area at highest risk and the persons belonging to an area at lowest risk with identical individual level covariates identified for all possible pair of areas, i.e. different in area level random effect values. For each model built there can be a MOR.

The MOR is the simple function of area level variance σ^2 and can be easily computed with the following formula:

$$MOR = \exp[\sqrt{(2 \times V_A)} \times 0.6745$$
$$\approx \exp(0.95\sqrt{V_A})$$

Where V_A is the area level variance and 0.6745 is the 75^{th} centile of the cumulative distribution function of the standard normal distribution. If the MOR is 1, the area level variation is close to zero. On the contrary, if there is substantial cluster level variation, the MOR will be large.

2.6.3 The 80% Interval Odds Ratio

Another index that can improve our understanding of the area level variability is the 80% Interval Odds Ratio (IOR-80) {See Larsen & Merlo (2005)}. For a given district level variable, we can imagine all possible pairs of subjects in which one subject is from a district with lower risk and another from a district with higher risk of the event associated with the district level covariate being considered. For each such pair, we can compute the OR between the subject from lower risk district and the subject from higher risk district, taking into account the level of the district level variable and the residual of these districts. The IOR-80 is the range of these odds ratios in which the middle 80% lies.

Practically, we can calculate the IOR-80 as:

$$IOR_{lower} = \exp[\beta + \sqrt{(2 \times V_A)} \times (\text{-}1.2816)]$$
$$\approx \exp(\beta - 1.81\sqrt{V_A})$$

$$IOR_{upper} = \exp[\beta + \sqrt{(2 \times V_A)} \times (1.2816)]$$
$$\approx \exp(\beta + 1.81\sqrt{V_A})$$

Where β is the regression coefficient for the district level covariate, V_A is the district level variance, and the values –1.2816 and +1.2816 are the 10^{th} and 90^{th} centiles of the standard normal distribution.

If the IOR-80 is wide, it implies that the contribution of the specific district level covariate in explaining the area level variability is minimal, and such an IOR-80 contains unity. Similarly when the contribution of the district level covariate is substantial, the IOR-80 is likely to be narrow and will not contain unity. One can also consider IOR-90 or IOR-70 instead of IOR-80.

2.6.4 The Proportional Change in Variance (PCV)

The addition of new variables in a model can be assessed through the proportional change in variance, which can be computed as

$$\text{PCV} = \frac{(\text{V}_\text{A}\text{-V}_\text{B})}{\text{V}_\text{A}} \times 100$$

where V_A is area level variance of the initial model and V_B is the area level variance of the model with additional terms.

2.7 Prediction of Explained Multilevel Model

2.7.1 Discriminating ability of a Model

The discriminating ability of any model can be examined through a receiver operating characteristic (ROC) curve analysis, using the predicted probabilities of the event. The area under the curve is also known as the c statistics of the model. The c-index ranges from 0 to 1, with higher values indicating better discrimination, indicating that the model is able to discriminate well between the event and non-event.

2.7.2 Response Probabilities from Logit Models

Response probability for i^{th} individual in j^{th} district can be calculated for the multilevel logistic regression model as

$$\Pi_{ij} = \frac{\exp(\beta_{0j} + \beta_1 x_{ij} + \lambda_1 y_{ij})}{1 + \exp(\beta_{0j} + \beta_1 x_{ij} + \lambda_1 y_{ij})}$$

Where $\beta_{0j} = \beta_{00} + \mu_{0j}$ and $\lambda_j = \lambda_1 + \varphi_j$ as defined previously so that

$$\Pi_{ij} = \frac{\exp(\beta_{00} + \mu_{0j} + \beta_1 x_{ij} + \lambda_1 y_{ij} + \varphi_j y_{ij})}{1 + \exp(\beta_{00} + \mu_{0j} + \beta_1 x_{ij} + \lambda_1 y_{ij} + \varphi_j y_{ij})}$$

Substituting the estimate of β_{00}, β_1, λ_1, μ_{0j} and φ_j in the above equation, the predicted probabilities can be obtained

$$\hat{\Pi}_{ij} = \frac{\exp(\hat{\beta}_{00} + \hat{\mu}_{0j} + \hat{\beta}_1 x_{ij} + \hat{\lambda}_1 y_{ij} + \hat{\varphi}_j y_{ij})}{1 + \exp(\hat{\beta}_{00} + \hat{\mu}_{0j} + \hat{\beta}_1 x_{ij} + \hat{\lambda}_1 y_{ij} + \hat{\varphi}_j y_{ij})}$$

However, the estimated or predicted values of random component should not be used for model diagnostics because their distribution is not known if the model is true. In general, the values should also not be used to obtain cluster-specific predicted probabilities. However, they can be used to obtain cluster-specific log-odds and hence ranking of clusters. The ranking of probabilities is the same as the ranking of log odds {See Hesketh SR and Skrondal A (2008)}. The average predicted probability in each cluster is calculated and appropriate rank is given based on these averaged predicted probabilities.

Accordingly the ranking of the districts by both the observed and predicted neonatal mortality levels can be compared.

3. Results

As mentioned earlier, the results are based on the last delivery a woman has had at the time of the survey. A total of 643,944 women were surveyed, out of which 415,657 had no child delivery during the preceding 4 years of the survey. Among the 228,287 women who reported a delivery in the preceding four years, 12,317 had still births, multiple births, induced abortions etc. Therefore a total of 215,970 newborns, including 1980 multiple births formed the study subjects. Each of the newborn in a multiple birth was considered as belonging to a separate mother. The survey registered 3,692 neonatal deaths among the 215,970 newborns.

The association of different study factors with the neonatal mortality was examined by the Odds Ratios estimated through the logistic regression. Table 1-a. shows the details of the 15 socio-demographic factors at the neonate level and their association with the NMR. As can be seen, all the 15 variables showed significant association with NMR ($P < 0.05$) by the usual univariate logistic regression.

Table 1-a. Association of Neonatal Mortality Rate (NMR) with individual socio-economic & demographic factors.

Characteristic		Live Births (N)	NMR (Per 1000)	OR (95% CI)
All Respondents		**215970**	**17.1**	
Area	Urban	40449	13.2	1.00
	Rural	175521	18.0	1.37 (1.25 – 1.50)
Religion	Hindu	162572	17.8	1.00
	Muslim	30942	17.4	0.98 (0.89 – 1.07)
	Others	22456	11.2	0.62 (0.55 – 0.71)
Caste	General	46555	13.7	1.00
	Schedule Caste	40272	20.5	1.51 (1.36 – 1.67)
	Schedule Tribe	39143	14.0	1.02 (0.91 – 1.15)
	OBC	85916	18.8	1.38 (1.26 – 1.52)
Drinking water status	Treated	66991	13.1	1.00
	Not treated	148979	18.9	1.46 (1.35 – 1.57)
Toilet status	Not Shared	65154	11.1	1.00
	Shared	150816	19.7	1.78 (1.64 – 1.93)
Fuel	Purchased	37324	09.9	1.00
	Other	178646	18.6	1.89 (1.69 – 2.10)
BPL card possession	Yes	67288	18.4	1.00
	No	148682	16.5	0.89 (0.83 – 0.96)
House type	Pucca	54288	12.4	1.00
	Semi Pucca	72860	18.8	1.53 (1.39 – 1.67)
	Kutcha	88821	18.6	1.51 (1.38 – 1.66)
Age of mother	25 – 29 yrs	59804	13.6	1.00
	20 – 24 yrs	87240	16.4	1.20 (1.10 – 1.31)
	< 20 yrs	31778	24.0	1.78 (1.61 – 1.96)
	≥ 30 yrs	37148	18.4	1.36 (1.22 – 1.50)
Father's education (years)	≥ 10 yrs	68862	12.6	1.00
	5 – 9 yrs	75018	17.3	1.38 (1.27 – 1.51)
	< 5 yrs	72090	21.1	1.69 (1.55 – 1.84)
Mother's education (years)	>= 10 yrs	40741	09.4	1.00
	5 – 9 yrs	61890	16.1	1.72 (1.53 – 1.94)
	< 5 yrs	113289	20.4	2.20 (1.97 – 2.45)
Mother's age at marriage	>=20 yrs	56440	12.1	1.00
	15 – 19 yrs	124255	17.7	1.47 (1.34 – 1.60)
	< 15 yrs	35275	23.0	1.92 (1.73 – 2.13)
Total pregnancies	1 – 2	112066	18.2	1.00
	3 – 4	64413	14.2	0.78 (0.72 – 0.84)
	> 4	39491	18.9	1.04 (0.95 – 1.13)
Birth order of the newborn	One	60745	21.9	1.00
	Two	59907	13.8	0.62 (0.57 – 0.68)
	Three	38336	13.9	0.63 (0.57 – 0.70)
	Four	56982	17.7	0.80 (0.74 – 0.87)
Sex of newborn	Male	115782	18.4	1.00
	Female	100170	15.6	0.84 (0.79 – 0.90)

The association of pregnancy related characteristics at the individual level with the NMR is presented in Table 1-b. A total of 25 pregnancy related factors at the individual level were assessed and out of these, 23 showed significant association with NMR. For example, if a pregnancy was registered, the odds of NMR for a newborn was 0.80, compared to a pregnancy which was not registered. In other words, a 20% reduction in the odds of NMR occurred when the pregnancy was booked. Similarly, if a mother had jaundice during the pregnancy, the odds of a neonatal mortality was 1.81 (95% CI: 1.46 2.24), compared to a mother who did not have jaundice during pregnancy.

Table 1-b. Association of Neonatal Mortality Rate (NMR) with individual pregnancy related factors.

Characteristic		**Live Births (N)**	**NMR (Per 1000)**	**OR (95% CI)**
Pregnancy registration	Not registered	75041	19.5	1.00
	Registered	140929	15.8	0.80 (0.75 – 0.86)
Who registered the pregnancy	Not registered	75041	19.5	1.00
	Other than doctors	59328	18.7	0.96 (0.88 – 1.03)
	Doctors	81601	13.7	0.70 (0.64 – 0.75)
ANC status	Received	155247	16.0	1.00
	Not received	60723	20.0	1.25 (1.17 – 1.34)
When ANC received	Not rec. /3rd Trim.	66769	20.1	1.00
	2nd Trimester	57918	18.4	0.91 (0.84 – 0.99)
	1st Trimester	91283	14.1	0.69 (0.64 – 0.75)
Number of ANC	Not Received	60723	20.0	1.00
	1 – 3	88639	18.9	0.94 (0.87 – 1.02)
	> 3	66628	12.1	0.60 (0.55 – 0.66)
Iron and Folic acid	Not Taken	97521	20.5	1.00
	Taken	118449	14.3	0.69 (0.65 – 0.74)
Days IFA taken	Not Taken	97521	20.5	1.00
	0-90 days	84723	15.1	0.73 (0.68 – 0.79)
	> 90 days	33726	12.2	0.59 (0.53 – 0.65)
Tetanus injection	Not Taken	61903	20.4	1.00
	Taken	154067	15.8	0.77 (0.72 – 0.82)
Total Tetanus injections	Not Taken	61903	20.4	1.00
	1 – 2	121927	16.5	0.81 (0.75 – 0.86)
	> 2	32140	12.9	0.63 (0.56 – 0.70)
Swelling status	No	164658	15.5	1.00
	Yes	51312	22.1	1.43 (1.33 – 1.54)
Paleness/ Giddiness	No	138906	15.8	1.00
	Yes	77064	19.4	1.23 (1.15 – 1.32)
Visual disturbances	No	185311	16.5	1.00
	Yes	30659	20.9	1.28 (1.17 – 1.39)
Excessive fatigue	No	162393	16.5	1.00
	Yes	53577	18.9	1.15 (1.07 – 1.23)
Convulsions	No	201411	16.9	1.00
	Yes	14559	20.3	1.21 (1.07 – 1.36)
Foetus movement	Strong	199024	16.9	1.00
	Weak	16946	18.8	1.11 (0.99 – 1.25)
Foetus position	Normal	210015	16.9	1.00
	Abnormal	5955	25.4	1.52 (1.29 – 1.79)
Malaria	No	209221	16.8	1.00

	Yes	6749	25.6	1.54 (1.32 – 1.79)
Excessive vomiting	No Yes	166269 49701	17.0 17.4	1.00 1.02 (0.94 – 1.10)
Hypertension	No Yes	205722 10248	17.0 19.0	1.00 1.12 (0.97 – 1.30)
Jaundice	No Yes	213056 2914	16.9 30.2	1.00 1.81 (1.46 – 2.24)
Excessive bleeding	No Yes	212368 3602	16.9 28.6	1.00 1.71 (1.40 – 2.09)
Excessive vaginal discharge	No Yes	209079 6891	16.9 23.9	1.00 1.43 (1.22 – 1.67)
Total pregnancy problems	No Problem 1 – 2 > 2	88692 71996 55282	14.6 17.5 20.6	1.00 1.20 (1.11 – 1.30) 1.42 (1.31 – 1.54)
Supplementary nutrition	Not Received Received	152367 63603	18.1 14.7	1.00 0.81 (0.75 – 0.87)
Treatment sought for preg. problems	No Yes	147981 67989	16.6 18.1	1.00 1.09 (1.02 – 1.17)

A total of 8 delivery related problems at the individual level, collected in the survey were analysed and 7 of these factors showed significant association with the NMR. Delivery place whether institutional or home showed similar odds of NMR (OR = 1.03). Similarly, if a disposable delivery kit was used during the delivery, the odds of NMR decreased by 20% (OR = 0.80; 95% CI: 0.70 0.91). Details can be seen in Table1-c.

Table 1-c. Association of individual delivery related factors with Neonatal Mortality Rate (NMR)

Characteristic		**Live Births (N)**	**NMR (Per 1000)**	**OR (95% CI)**
Problems during delivery	No Problem One ≥ Two	118385 58260 39325	15.1 17.7 22.2	1.00 1.17 (1.08 – 1.26) 1.48 (1.36 – 1.60)
Delivery type	Normal Cesarean Assisted	194586 17491 3893	17.0 16.9 21.6	1.00 0.99 (0.88 – 1.12) 1.27 (1.02 – 1.58)
Delivery place	Institution Home	93625 122345	16.8 17.3	1.00 1.03 (0.96 – 1.10)
Person conduct -ing delivery	Untrained Person Trained Person	110158 12164	17.5 15.3	1.00 0.87 (0.75 – 1.01)
Use of disposal delivery kit	No Yes	103596 18730	17.8 14.4	1.00 0.80 (0.70 – 0.91)
Baby wiping	No Yes	54084 68250	20.0 15.2	1.00 0.76 (0.69 – 0.82)
Sterilized blade	Not Used Used	14216 108121	18.0 17.2	1.00 0.96 (0.84 – 1.09)
Feeding colostrums	No Yes	43791 170146	20.5 07.9	1.00 0.38 (0.35 – 0.41)

Regarding the district level variables, the available data at individual level from the survey was examined for the possible factors that can have an association with the NMR at the district level. Six factors were identified to be likely to have association with NMR at a higher level and district level data was aggregated from the individual data. For example, mother's educational achievement was considered to have influence on NMR at the district level. Accordingly, the average level of mothers' education for each district was computed and the median of average level for all districts was taken as a threshold for categorization of each district. Similar approach was adopted for the other district level covariates, namely, percentage of mothers with religious belief other than Hinduism & Islam, average age of mothers at delivery, proportion of mothers receiving at least 3 ante natal care (ANC) visits, proportion of households with treated drinking water supply and proportion of scheduled castes and scheduled tribes population.

The association of district level variables with NMR was examined by univariate logistic regression and the respective ORs with 95% CI were calculated (Table 1-d). As can be realised, all the 6 variables showed at least marginally significant association ($P < 0.10$). For example, a neonate from a district with mothers' average educational achievement ≤ 5 years had 77% excess odds of NMR as compared to a newborn from a district with mothers' average education of > 5 years.

Table 1-d. Association of district level factors with Neonatal Mortality Rate (NMR)

District characteristic		**Number of Live Births**	**NMR (Per 1000)**	**OR (95% CI)**
% of population other than Hindu & Muslim	≤ 10%	174487	18.4	1.00
	> 10 %	41483	11.5	0.62 (0.56 – 0.68)
Average education of mothers	> 5 years	78759	11.6	1.00
	≤ 5 years	137211	20.3	1.77 (1.64 – 1.91)
Average age of mothers	> 24 years	164213	17.3	1.00
	≤ 24 years	51757	16.5	0.95 (0.88 – 1.03)
% of mothers with ≥ 3 ANC visits	≤ 42 %	106481	20.7	1.00
	> 42 %	109489	13.6	0.65 (0.61 – 0.69)
% of HHs with treated water supply	> 30 %	89731	13.5	1.00
	≤ 30 %	126239	19.7	1.47 (1.37 – 1.58)
Percentage of SC/ST population	≤ 30 %	104,288	18.3	1.00
	> 30 %	111,682	15.9	0.87 (0.81 – 0.93)

All the individual variables showing at least marginally significant association with NMR in the univariate analysis were put into a stepwise multiple logistic regression as the traditional method. Thus 45 variables were considered as candidates and only 18 were retained in the final model (Model A) and the results are presented in Table 2-a.

All individual (fixed effects) and district level characteristics (both fixed and random effects) with a promise of significant association in the univariate analysis are included for the multivariable multilevel regression models. Two types of multilevel models were considered, namely random intercept (Model B) and random intercept with random slope model (Model C). The comparison of the three models with respect to the individual level covariates is shown in Table 2-a. Models B & C did not show 3 individual level variables as significant that have been shown as significant in the Model A. One variable which is not picked up in Model A has been shown to be significantly associated with NMR in Models B & C.

Table 2-a. Multivariable association of individual study variables with neonatal mortality

Characteristic		Model A OR (95% CI)	Model B OR (95% CI)	Model C OR (95% CI)
Caste	Others	1.00	1.00	1.00
	SC	1.22 (1.05 – 1.41)	1.21 (1.05 – 1.40)	1.22 (1.06 – 1.40)
	ST	0.99 (0.83 – 1.18)	1.04 (0.89 – 1.23)	1.09 (0.93 – 1.29)
	OBC	1.10 (0.96 – 1.25)	1.09 (0.97 – 1.24)	1.09 (0.96 – 1.24)
Toilet status	Not Shared	1.00	1.00	1.00
	Shared	1.24 (1.09 – 1.42)	1.21 (1.07 – 1.37)	1.19 (1.05 – 1.35)
Cooking fuel	Purchased	1.00	1.00	1.00
	Other	1.26 (1.06 – 1.50)	1.23 (1.04 – 1.44)	1.22 (1.04 – 1.44)
Age of mother	25 – 29 yrs	1.00	1.00	1.00
	20 – 24 yrs	1.07 (0.95 – 1.20)	1.06 (0.94 – 1.20)	1.06 (0.94 – 1.20)
	< 20 yrs	1.15 (0.98 – 1.34)	1.15 (0.98 – 1.34)	1.15 (0.98 – 1.34)
	>= 30 yrs	1.22 (1.07 – 1.39)	1.22 (1.06 – 1.40)	1.22 (1.06 – 1.41)
Father's education	>= 10 yrs	1.00	1.00	1.00
	5 – 9 yrs	1.03 (0.92 – 1.16)	1.04 (0.92 – 1.18)	1.04 (0.92 – 1.18)
	< 5 yrs	1.20 (1.06 – 1.36)	1.23 (1.08 – 1.41)	1.24 (1.08 – 1.41)
Mother's education	>= 10 yrs	1.00	1.00	1.00
	5 – 9 yrs	1.50 (1.26 – 1.78)	1.48 (1.25 – 1.77)	1.49 (1.25 – 1.78)
	< 5 yrs	1.65 (1.37 – 2.00)	1.59 (1.32 – 1.92)	1.59 (1.32 – 1.92)
Birth order	One	1.00	1.00	1.00
	Two	0.67 (0.59 – 0.76)	0.67 (0.60 – 0.76)	0.67 (0.60 – 0.76)
	Three	0.60 (0.52 – 0.70)	0.60 (0.52 – 0.70)	0.60 (0.52 – 0.70)
	Four	0.59 (0.50 – 0.70)	0.59 (0.51 – 0.69)	0.59 (0.50 – 0.69)
Newborn's sex	Male	1.00	1.00	1.00
	Female	0.88 (0.81 – 0.95)	0.88 (0.81 – 0.96)	0.88 (0.81 – 0.96)
Pregnancy status	Not registered	1.00		
	Registered	1.15 (1.02 – 1.31)		
Tetanus injection	Not taken	1.00		
	Taken	0.83 (0.73 – 0.94)		
Swelling status	No	1.00	1.00	1.00
	Yes	1.36 (1.24 – 1.49)	1.34 (1.22 – 1.47)	1.34 (1.22 – 1.47)
Foetus movement	Strong	1.00	1.00	1.00
	Weak	0.84 (0.71 – 0.99)	0.83 (0.71 – 0.98)	0.83 (0.70 – 0.98)
Malaria	No	1.00	1.00	1.00
	Yes	1.33 (1.08 – 1.64)	1.29 (1.06 – 1.59)	1.30 (1.06 – 1.59)
Jaundice	No	1.00	1.00	1.00
	Yes	1.41 (1.04 – 1.92)	1.39 (1.04 – 1.86)	1.39 (1.04 – 1.86)
Excessive bleeding	No	1.00		
	Yes	1.32 (1.01 – 1.71)		
Excessive vaginal discharge	No	1.00	1.00	1.00
	Yes	1.27 (1.03 – 1.55)	1.26 (1.02 – 1.56)	1.27 (1.03 – 1.57)
Supplementary nutrition received	No	1.00	1.00	1.00
	Yes	0.88 (0.78 – 0.96)	0.88 (0.79 – 0.97)	0.88 (0.79 – 0.98)
Problems during delivery	Nil		1.00	1.00
	One		1.08 (0.97 – 1.19)	1.08 (0.97 – 1.19)
	≥ Two		1.20 (1.06 – 1.34)	1.19 (1.06 – 1.34)
Feeding colostrums	No	1.00	1.00	1.00
	Yes	0.43 (0.39 – 0.47)	0.42 (0.38 – 0.46)	0.42 (0.38 – 0.46)

The odds ratios associated with the variables common to all three models were almost same with similar confidence intervals. Eighteen individual level variables in Model A (traditional multiple logistic regression), 16 individual level variables in both Model B (Random intercept only) and Model C (Random intercept with random slope) turned out to be significant. Models B and C showed same variables as significant.

Of the 6 district level covariates considered, only one variable (average education of mothers) in Model B and two variables (average education of mothers and the proportion of mothers belonging to other than Hindu & Muslim) in Model C emerged as significantly associated with NMR (Table 2-b). Newborns belonging to a district with more than 10% population of other religions (other than Hindu & Muslim) had an odds ratio of 0.75 (95% CI: 0.60 0.93) for NMR as compared to newborns from a district with ≤ 10% population of other religions, as emerged in the random intercept and random slope model (Model C). Similarly, districts with mothers' average education of≤ 5 years showed significantly higher odds ratio of NMR as compared to districts with mothers' average education of > 5 years (OR 1.19 in Model B and 1.17 in Model C).

Table 2-b. Association of District level variables with NMR

Characteristic		**Model B OR (95% CI)**	**Model C OR (95% CI)**
Percentage of population	≤ 10%		1.00
other than Hindu & Muslim	> 10 %		0.75 (0.60 – 0.93)
IOR-80			(0.54 – 1.04)
District with Mothers'	> 5 years	1.00	1.00
average education	≤ 5 years	1.19 (1.04 – 1.36)	1.17 (1.01 – 1.34)
IOR-80		(0.52 – 2.75)	(0.85 – 1.61)

The 80% interval odds ratio for the district level variable of mothers' average education is wide and includes the unity, in both Models B (0.52 2.75) and C (0.85 1.61). It indicates that though the mothers' average educational achievement at district level is significantly associated with NMR, it contribution for the district level variation in NMR is not substantial. However, the district level covariate of proportion belonging to other religions shows the IOR-80 as 0.54 – 1.04, which barely crosses the unity. It is an indication that this variable is contributing to the area level variations significantly. Thus, the proportion of population belonging to religions other than Hindu & Muslim showed significant association with the NMR and further it also contributes to the district level variations in the NMR.

Table 2-c shows the relative performance of different models. An empty model without any covariates is also considered for the facilitation of these comparisons. As is expected, the log likelihood improved form empty model to model A to model B to model C, the incremental improvement being significant at each stage. As the log likelihood increased, there is a concurrent reduction in the area level variance and the intra class correlation (ICC). Model A being the usual fixed effects logistic regression, the area level variance is presumed to be zero and so is not shown. Taking the empty model as a reference, random intercept model (Model B) lead to a 16% reduction in the area level variance, while the random intercept with random slope reduced it by 32%. By taking the Model B as a reference, Model C led to a 19% reduction in the area level variance. The median odds ratios that convey the area level variation gradually decreased from 1.60 in the empty model to 1.49 in the random intercept with random slope model. Though it reduced, yet the MOR in Model C remained significant, the lower limit of 95% CI is far from unity. This is an indication that even with

random slope and random intercept model with 16 individual level characteristics and 2 district level variables, there is substantial between district variability.

Table 2-c. Comparison of models Measures of district level variation for the neonatal death in India

Parameter	Empty Model	Model A	Model B	Model C
Log Likelihood	-18520.60	-11748.59*	-11694.71*$	-11688.74*$#
Area Variance	0.25		0.21	0.17
PCV[1]	reference		- 16%	-32%
PCV[2]			reference	-19%
ICC	0.07		0.06	0.05
MOR (95% CI)	1.60 (1.52 – 1.69)		1.55 (1.46 – 1.66)	1.49 (1.26 – 2.11)
AUROC curve	67.4	66.8	72.7	72.8
Rank correlation		68.1%	85.8%	84.9%

*: significant compared to empty random intercept model
$: significant compared to conventional logistic regression model
#: significant compared to random intercept model with individual and area level covariates
AUROC: Area Under the Receiver Operating Characteristic Curve

The overall discriminating ability of the models as assessed by the area under the ROC curve shows a improvement in the discrimination of neonatal deaths and survivors with the random effects models (Models B & C) as compared to the empty model and Model A. The improvement in the discrimination is negligible from Model B to Model C, though there is improvement in other indicators. The rank correlation of the observed and predicted NMR among the 601 districts clearly shows the advantage of adopting a multilevel model in the data of hierarchical structure. The rank correlation was 68% with the ordinary logistic regression which, improved to 85% when the multi level structure of the data was considered in the analysis.

4. Discussion

This paper examined the application and interpretation of ordinary, two level random intercept and two level random slope logistic regressions for explaining between district heterogeneity in neonatal mortality in India.

Very few studies on multilevel analysis were done in India more so on community based neonatal deaths. Review of literature revealed that the results of available limited studies focused mainly on fixed effect for all the covariates with still fewer showing the variations at different levels. One study applied a two level logistic regression model and focussed only on the determinants of neonatal mortality in rural India, but did not talk about the area level variation {see Singh et al. (2013)}. Another study with two level {see Dwivedi et al. (2012)} and three level {see Dwivedi et al. (2013)} multilevel models to identify the determinants of infant mortality in rural India shown the variability at district level as well as at state level but a detailed explanation on this variability was not explained in detail. Magnitude of these variances between areas is very useful to explain association between contextual factors and the outcome.

A study from Ghana reported the individual and community level determinants of NMR. Only one community level variable – socio-economic disadvantage explained all the area level variation, with the MOR reaching to unity after including this community level variable. The individual level variables included mostly socio-demographic factors only {See Kayode GA et al. (2014)}. A study on 15,952 neonates from Indonesia attempted to identify determinants of NMR using multilevel modelling. Though area level variables were analysed, this study did not explain the area level variation and its association with the area level characteristics studied {See Titaley CR et al. (2008)}.

Also all such studies have not attempted the performance assessment of different models. The present communication compares the random intercept model and random intercept with random slope model with the traditional logistic regression model. The discriminating ability as assessed by the area under the ROC curve in the present communication, clearly demonstrated the advantage of multilevel models in estimating the parameters of interest. The same is reiterated when we compared the rank correlation of district-wise observed and model predicted NMRs.

The strength of this study is that it is based on a large sample of 215,000 neonates covering 601 districts among 34 states of the country. This study has provided the risk of neonatal mortality associated with some factors that have not been studied earlier, more so at a community level. The feeding of colostrums to the newborn is highly protective against the neonatal mortality. Other variables that have not been studied or reported earlier but assessed in this study are jaundice and malaria of the mother during pregnancy, supplementary nutrition to the mother and swelling status during pregnancy, mother’s perception about the foetus movement, excessive vaginal discharge, type of cooking fuel used in the household toilet status in the household. Results of some of these variables have public health relevance.

Though we could identify 6 district level variables for possible role in the area level variations, only two showed to be significantly associated with the NMR and of these two, only one (proportion of mothers belonging to religions other than Hindu & Muslim) showed to be able to explain the district level variations considerably. This observation is consistent with the general belief that the ‘other’ religions mainly include the Christians and the Sikhs in India. These ‘other’ religions are reported to have high literacy and generally well-to-do communities. Our observation of these ‘other’ religions having a lower risk of NMR (OR = 0.75, 95% CI: 0.60 – 0.93) and it explaining considerable area level variance is perhaps a reflexion of the literacy and socio-economic status and regional spread of these communities.

The observation of substantial residual area level variance even after the two significant district variables were included in the model, indicates that there are many other factors responsible for area level variations. For example, such variables could be the availability of doctors, health care personnel and health care facilities per 100,000 population, accessibility of these to the needy etc., apart from the individual beliefs, traditions and attitudes about the pregnancy among different communities of a large country like India. Such data at the district levels in the country is not readily available and so could not be studied in the multi level models.

The present study has some limitations too. All the limitations associated with the DLHS-3 are equally applicable for our results as we used the secondary data from it. The neonatal mortality as observed in the DLHS-3 is not concordant with NMR from other surveys in the country. The DLHS-3 relied on the recall of pregnancy and other details of the newborns by the mothers in the preceding 4 years. Therefore, the dissimilarity of NMR estimate from DLHS-3 and the recall bias of mothers, if any, present in the survey is equally applicable for this study also.

5. Conclusions

In this communication, we described the application and interpretation of the multilevel models with special focus to the area level variation and indices related to it. A detailed list of socio-demographic, pregnancy related and delivery related characteristics at the individual level were examined for their association with NMR, using a large number of neonates spread across the country. Eight socio-demographic variables (caste, toilet status of the household, cooking fuel used in the household, age of the mother at delivery, father's educational achievement, mother's educational achievement, birth order of the newborn, and the newborn's sex); six pregnancy related variables (swelling status, foetus movement, malaria, excessive vaginal discharge, supplementary nutrition status and jaundice during the pregnancy); and 2 delivery related variables (number of problems during delivery and feeding newborn with colostrums) turned out to be significantly associated with the NMR. Only two district level variables (proportion of mothers belonging to religions other than Hindu & Muslim; and mothers' average education) showed to be significantly associated with NMR. Mothers belonging to other religions explained considerable area level variation. Performance indicators (Median Odds Ratio, proportional change in variance, area under the ROC curve and rank correlation of observed and model predicted NMRs in the districts clearly demonstrated the utility of multilevel models in complex data with hierarchical data structure.

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