Birth Defects Research Group

Dr Anita Kar, Professor,
School of Health Sciences,
Savitribai Phule, Pune University,Pune 411007, India.
dranitakar@gmail.com;akar@unipune.ac.in

Our research focuses on understanding the epidemiology and public health implications of birth defects in India. The goal of the research is to identify components of a low-cost, contextual and ethical birth defects service, as a constituent of the existing maternal and child health programme in India. The research is placed in the milieu of a low public health interest in these conditions, as they are considered to be rare and too debilitating to constitute a significant health problem.

The underlying argument of our research is that birth defects are likely to be a significant problem in India due to the high annual number of births occurring in the country. With improving access to medical care, population prevalence of patients is also likely to be high [1-3]. Evidenced interventions are needed to design a birth defects service, including components of prevention, care, surveillance and competency

1. Epidemiology and public health implications of birth defects in India

Our ongoing studies are aimed at measuring the prevalence rates of birth defects, and identifying their public health impact.

We initiated these studies by conducting a systematic review and meta-analysis in order to derive a national estimate of birth defects in the country [4]. This data yielded a rate of 184.48 per 10 000 births (95% CI 164.74 - 204.21). Another meta-analysis estimated the magnitude of neural tube defects in the country [5]. In the background of the suspected Zika virus associated microcephaly, we have estimated the prevalence of microcephaly in India [6].

In order to validate the data from the meta-analysis, we conducted a maternal cohort study (PUBOs, Pune Urban Birth Defects study) to measure the prevalence of birth defects by type of defect. The results of the study identify a prevalence of 230 per 10 000 births, translating to over 500 000 babies born with birth defects in the country [7]. Analysis of defects by type identifies a significant magnitude of congenital heart defects. The contribution of birth defects to neonatal and perinatal mortality has been measured. Health service utilization indicators, such as termination of pregnancy due to detection of foetal anomaly, pediatric surgery rate and prenatal diagnosis prevalence have also been measured.

The periconception risk factors of the cohort have been studied, in order to identify the key components of preconception education [8]. We intend to explore this data to determine whether periconception interventions (eg pregnancy education, supplementation, screening) can benefit general maternal outcome indicators, as well as result in identifying parents with a family history

risk of a disorder.

We have created a population biobank for nearly 1700 pregnant women.The DNA is linked to outcome data (maternal complications and adverse pregnancy outcomes) as well as selected maternal exposures.

2. Birth defects and childhood disability

The study indicated that one of the consequences of birth defects was childhood disability. In order to identify the contribution birth defects on disability, the National Sample Survey 2002 Disability data was analyzed. The data identified that 5.6 million individuals reported the onset of disability since birth. Disability since birth was more common among males resident in rural areas. The years lived with disability was significantly higher among those reporting disability since birth, as compared to those with acquired disability.

A population based study is underway in urban slums of Pune city where we are measuring the prevalence of developmental delays and disabilities.

Earlier studies : epidemiology and public health implications of genetic disorders

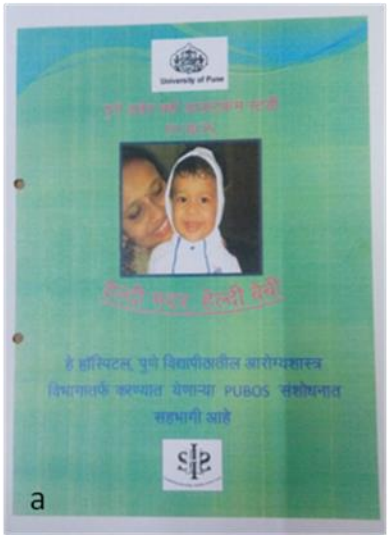
Our earlier research had aimed at asking whether single gene disorders were truly self limiting conditions or not. For the study, we had used haemophilia, an inherited bleeding disorder, as it is the only single gene disorder for which there is a national disease registry [9-10].

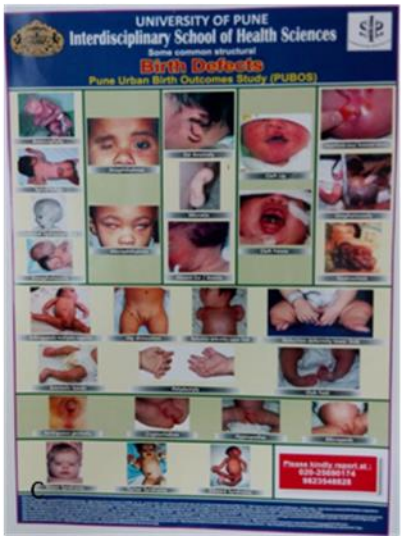
A database of haemophilia patients diagnosed over a twenty year period in the state of Maharashtra has been constructed. Using this database, we had reported that patients accrue over time, resulting in increasing population prevalence. We reported that India may have as many as 56000 – 74000 patients, constituting the largest magnitude of haemophilia globally [11].

The impact of lack of services on patients and families [12] was determined through a number of studies. The data indicated that families incurred extensive out of pocket expenditure, which was catastrophic to nearly 70% of families [13]. In order to circumvent this expenditure, patients did not access appropriate treatment [14] resulting in widespread disability [15]. The opportunity of NGO/parent patient partnership in service delivery was studied. The impact of referral of patients for genetic counseling by the NGO, and its correlation with declining haemophilia rates over a twenty year period in the state of Maharashtra has been reported [16-17]. The impact of education and psychosocial support intervention on the knowledge, home management of bleeding episodes and the quality of life of parents has also been studied.

Selected key publications:

1. Kar A (2015) Birth Defects: An emerging public health issue in the field of child health in India. In Public Health and Development in India . Ed SB Nimse and MK Agarwal. Northern Book Centre, New Delhi.
2. Kar A (2014) ***JKIMSU*** 3(2) : 7-16
3. Kar A (2011) ***EPW*** XLVI No 48,21
4. Bhide P and Kar A ***BMC Pediatrics*** (ms in press)
5. Bhide P et al. 2013 ***Birth Defects Res Part A: Clin and Mol Teratology***, 97: 437–443
6. Bhide P and Kar A Bull World Health Organ ms.submitted epub:23 Feb 2016
7. Bhide et al. PLoS ONE11(11): e0166408. doi:10.1371/journal.pone.0166408
8. Gund P et al. 2016 J of Womens Health Care (ms in press)
9. Kar A (2010) ***Haemophilia*** 16:952–954
10. Potnis-Lele M and Kar A (2001) ***Hemophilia*** 7: 561-567
11. Kar A and Potnis-Lele M (2004) ***Haemophilia*** 10:301-304
12. Kar A et al. (2014) ***Ind J Med Res*** 140, pp 19-31.
13. Kar A (2012) ***Lancet*** 38 :216- 217
14. Dharmarajan S et al. (2014) ***Haemophilia*** 20: 382-387
15. Dharmarajan S et al. (2012) ***Haemophilia*** :18 e27-29
16. Kar A et al (2007) ***Haemophilia*** 13, 398–404
17. Potnis Lele M and Kar A (2003) ***Int J Epid*** 32: 316-320
18. Nakade J and Kar A (2013) ***Haemophilia*** Aug 28. doi: 10.1111/hae.12255





The burden and prevalence of risk factors for congenital anomalies in Pune city, India

Prajkta Bhide, UGC-UPE JRF, Doctoral study (ongoing)

BACKGROUND

In India, congenital anomalies are the fifth largest cause of neonatal deaths, contributing to 9% of neonatal mortality. The true magnitude of the number of congenital anomaly affected births in India is unknown due to lack of a national birth defects surveillance.

OBJECTIVES

To determine the birth prevalence of congenital anomalies in India and to determine the prevalence of risk factors for congenital anomalies and their contribution to stillbirths and neonatal mortality

METHODOLOGY

Part A) Systematic review and meta-analysis of published literature to derive a national estimate of congenital anomaly affected births in India

Part B) Establishment of a cohort of pregnant women to measure the birth prevalence of congenital anomalies and their contribution to stillbirths and neonatal mortality

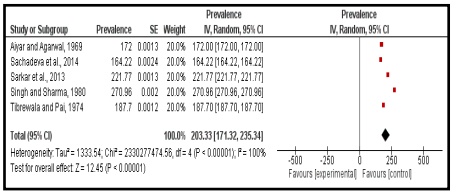
RESULTS (Interim)

Part A) Systematic review and meta-analysis

The pooled prevalence of congenital anomaly affected births was 184.48 per 10 000 births (95% CI 164.74 - 204.21), estimating that between **421 652 to 522 676** anomaly affected births may occur in India every year.

Central nervous system anomalies are the most commonly occurring anomalies, with anencephaly as the most frequently reported anomaly.

High burden of neural tube defects affected births at 4.1 per 1000 births (95% CI 3.1 - 5.4) annually in India.



Anomaly affected birth rates:

All anomalies: 1 in 45 births

CHDs: 1 in 182 births

Renal anomalies: 1 in 260 births

NTDs: 1 in 607 births

Part B) Birth prevalence of congenital anomalies

Estimated birth prevalence of 230.52 per 10 000 births.

Congenital heart diseases were the most commonly reported anomalies followed by renal anomalies.

Maternal DNA biobank: 1710 DNA samples linked toadverse pregnancy outcomes and risk exposure data

Publications;

1. Bhide P, Sagoo GS, Moorthie S, Burton H, Kar A. Systematic review of birth prevalence of neural tube defects in India. ***Birth Defects Res A Clin Mol Teratol***. 2013;97(7):437-443.
2. Bhide P and Kar A. A national estimate of the birth prevalence of congenital anomalies in India: systematic review and meta-analysis. ***BMC Pediatrics*** (ms accepted)
3. Bhide P, Digvi K and A Kar. Prevalence of *MTHFR* C677T gene polymorphism in pregnant Indian women (ms submitted ***Indian J Hum Genet***)
4. Bhide P, Gund P and A Kar Birth prevalence of congenital anomalies in a cohort of Indian women (ms submitted ***BMC Public Health***)

Abstracts presented in conferences:

1. Bhide P., Sagoo G., Moorthie S., Burton H., Kar A. A systematic review of birth prevalence of neural tube defects in India. Poster presented at Pune Public Health Conference 2013, Pune. Feb 11-12. Abstract # B-1.
2. Sagoo G., Nacul L., Schuler-Faccini L., Sanseverino M., Groisman B., Bidondo M., Barreiro C., Larrandaburu M., Bhide P., Kar A., Kroese M., Burton H. A Toolkit to assess health needs for congenital anomalies in low- and middle-income countries: An instrument for public health action. Poster presented at the 12th European Symposium on Congenital anomalies, Croatia. June 14. Abstract # P48.
3. Bhide P., Agrawal A., Narvekar P., Gund P., Bodhale S., Doiphode M., Kar A. A study on selected nutri-genetic risk factors for birth defects in pregnant women at first antenatal care visit. Poster presented at the Pune Public Health Conference 2014 – Joint State Conference of the IPHA-IAPSM (Maharashtra) Millenium Maternal and Child Health Goals: Post 2015 Strategies, Pune. Feb 25-26. Abstract # N12.
4. Bhide P., Kar A. A systematic review of the prevalence of folate deficiency in Indian women. Poster presented at the 2nd International Workshop on Micronutrients and Child Health, New Delhi. Nov 3-7, 2014. Abstract # 377.
5. Bhide P., Gund P., Kar A. Types and rates of congenital anomalies in an Indian pregnancy cohort. Poster presented at the Maharashtra IPHA & IAPSM Joint Conference 2015: Emerging Threats in Public Health, Pune. Jan 30-31. Abstract # P:10.13.

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Prevalence of selected risk factors for low birth weight, timing of birth and type of pregnancy outcome among pregnant women registered for antenatal care at government hospitals in Pune, India

Pooja Gund, UGC-UPE JRF, Doctoral study (ongoing)

Background: There is limited data on prevalence of periconception risk factorsamong women from low and middle-income countries. Furthermore, weight gain, haemoglobin levels and micronutrient exposures in pregnancy and their relationship withbirth outcomesremains less explored.

Objective: To measure the prevalence of selected risk factors for low birth weight, preterm birth and adverse pregnancy outcomes and to determine the relationship between these risk factors and low birth weight, preterm birth and adverse pregnancy outcomes in a cohort of pregnant women registering for antenatal care in government hospitals, Pune.

Methodology: Study design: Data being collected as part of prospective cohort study.**Study settings:** Study was conducted at 4 selected government hospitals in Pune city.**Participants:**Pregnant women below 16 weeks of gestation. **Data collection:** Risk factor data and anthropometric measures using a structured questionnaire at baseline. Data on weight gain, change in hemoglobin levels, micronutrient supplement use, maternal illness or infection during pregnancy, was collected through follow-up Data on pregnancy outcome was obtained from respondent and confirmed with hospital records.

Interim results

1 Spectrum of periconception risk factors

All women in the cohort reported at least one risk factor. Seventy percent women reported five or more risk factors.

Women from families who were below poverty line (OR, 1.3; 95% CI, 1.0-1.6) and with low education levels (OR, 1.4; 95% CI, 1.1-1.6) were more likely to report higher numbers of risk factors.

The most prevalent risk factors were nutritional (lack of preconception folic acid supplement use 99.7%, anaemia 61% and malnutrition 41%), followed by social (low education levels 62%, poor economic status 68%). High prevalence of chemical exposures in the household environment was also reported (household cleaners 76%, use of indoor insect repellents 64%).

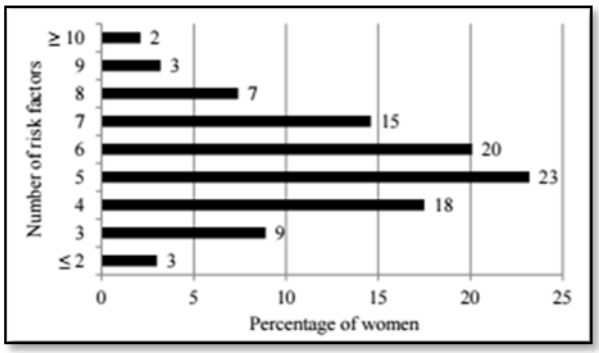

Figure1: Distribution of risk factorsamong women in the cohort (n = 2107)

2 Description of outcomes

- One amongst every 5 live births was born low birth weight (<2500gms)
- One preterm birth occurred amongst every 9 live births (<37 weeks)
- One in every 20 pregnancies resulted in spontaneous pregnancy loss.
- Still birth rate was 23 per 1000 births.
- Neonatal mortality rate was 11.4/1000 live births.

Paper communicated and abstracts presented in conferences based on the study

(1)Gund P, Bhide P, Kar A. Prevalence of Periconception Risk Factors for Adverse Pregnancy Outcomes in a Cohort of Urban Indian Women: Implications for Preconception Health Education. ***Journal of Womens Health Care*** (ms in press)

(2) Gund P., Bhide P., Kar A. First trimester nutritional status and birth outcomes: Interim data from the Pune Urban Birth Outcomes Study (PUBOs). Poster presented at the 2nd International Workshop on Micronutrients and Child Health, New Delhi. Nov 3-7, 2014. Abstract # 375

(3) Gund P., Bhide P., Kar A. Registration for antenatal services and place of delivery and its implications for the Maternal and Child Health Tracking System.Poster presented at the Maharashtra IPHA & IAPSM Joint Conference 2015: Emerging Threats in PublicHealth, Pune. Jan 30-31. Abstract # P:10.12.

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Beta thalassaemia: A public health problem

Sumedha Dharmarajan, DST INSPIRE fellow, Doctoral study

STUDY 1: SYSTEMATIC REVIEW AND META-ANALYSIS : PREVALENCE OF BETA THALASSAEMIA CARRIERS

Objective: To estimate the prevalence of beta thalassaemia carriers in India through a systematic review of existing literature

Methodology: A PubMed search with keywords "beta thalassaemia and India" identified 918 articles, which were assessed for relevance, diagnosis tests used, and methodologies.

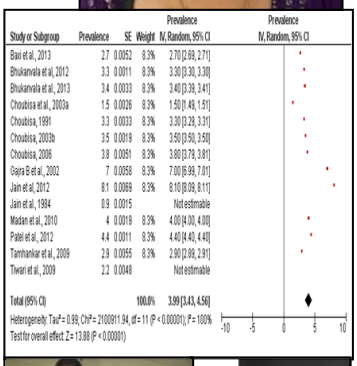
Results:

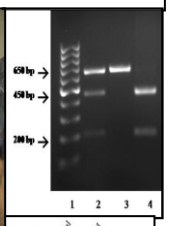
1.Pooled prevalence of beta thalassemia carriers in the general population was estimated to be 4.07% (95% CI 3.4- 4.6)

2. Pooled prevalence of thalassaemia carriers among suspected cases of anaemia was 21.5% (95% CI 19.0-23.9)

3. Heterogeneity in study methodologies and sampling procedures, incorrect use of diagnostic reference standards.

Conclusions: Need to conduct a well-designed study, with adequate consideration to sample size, representativeness and reference standards



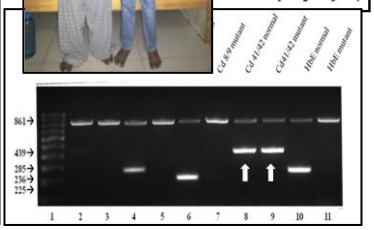


STUDY II : PREVALENCE OF BETA THALASSAEMIA CARRIERS

Objective : To determine the number of beta-thalassemia carriers in a random sample of pregnant women

Methodology: PUBOs DNA biobank is a repository of DNA samples from pregnant women recruited across four government hospitals in Pune city. 360 DNA samples were randomly selected and analysed by ARMS PCR for the five common beta thalassaemiua mutations.

Expected results: Prevalence of beta thalassaemia carriers amongst pregnant women accessing ante-natal services at government hospitals (ongoing study)



STUDY III: GENOTYPE-PHENOTYPE CORRELATION IN BETA THALASSAEMIA

Objective 1: To genotype patients with beta thalassemia for the primary, secondary and tertiary modifier genes

Objective 2: To characterize the phenotype (clinical parameters, anthropometric measures and transfusion history) of patients with beta thalassemia major and correlate phenotype to genotype

Methodology: 100 patients with beta thalassaemia major were genotyped using ARMS PCR, Gap PCR, PCR-RFLP and Real-time PCR methods. Further, 21 patients from this cohort were followed up for a period of one year to record the treatment pattern **Results:**

- The most common mutation in the *HBB* gene was the IVS 1-5 (G→C) allele (63%).
- The allele frequency of $-\alpha^{3.7}$ and $-\alpha^{4.2}$ ameliorating alleles at the *HBA* gene was 4.7% and 1% respectively, $\alpha\alpha\alpha^{anti3.7}$ allele in *HBA* gene that exacerbates the severity of the disorder was 2.5%.
- Allele frequency of the ameliorating 'T' allele at the *HBG2* gene was 28%.
- Allele frequency of the ameliorating 'T' allele at *rs11886868* in the *BCL11A* gene was 40%,
- Allele frequency of the ameliorating G allele at *rs4895441* in the *HBS1L-MYB* intergenic region was 10%.
- The median number of blood transfusions was 8 (range 0-23) per year.

Abstracts presented in conferences:

1. Vijayan G, Chandy R, Dharmarajan S, Munshi N and Kar A. Mutation analysis of fifty beta thalassemia patients from Pune city, Maharashtra. Abstract of the Pregnancy loss, birth defects and genetic disorders in India: Epidemiology, social costs and health system needs. ***Pune Public Health Conference;*** 2013 Feb 11-12; Pune, India. Abstract # C6:59
2. Dharmarajan S, Divgi K, Munshi N, Kar A. Out-of-pocket expenditure and health systems cost of management of beta thalassaemia. ***Abstract of Millenium maternal and child health goals: Post 2015 strategies*.** Abstract #HS1:93
3. Dharmarajan S, Divgi K, Munshi N and Kar A. A study to genotype the primary and secondary modifiers of beta thalassaemia among patients from Pune, India. Abstract of International symposium on "Genomics on Health and disease& 40th Annual Conference of Indian Society of Human Genetics, 2015 Abstract #P93: ***Ind J Hum Genet 2014***;20(1):S79

Other publications

1. Dharmarajan S, Gund P, Phadnis S, Lohade S, Lalwani A, Kar A. Treatment decisions and usage of clotting factor concentrate by a cohort of Indian haemophilia patients. ***Haemophilia*** 2012; 18
2. Dharmarajan, S, Phadnis S, Gund, P and Kar, A, Out-of-pocket and catastrophic expenditure on treatment of haemophilia by Indian families. ***Haemophilia*** 2014, 20: 382–387.
3. Kar A, Phadnis S, Dharmarajan S and Nakade J. Epidemiology and social costs of Hemophilia in India. ***Indian J Med Res*** 2014; 140:19-31.

Needs assessment of families with children with birth defects

Charuta Gokhale, doctoral study (Ongoing)

Rationale of the study:
There is lack of standard protocols for referral and support for children born with disabling conditions. There is limited research on the experiences of families of children diagnosed with disability due to birth defects. Such data are needed for guiding the health care system in India to identify the service needs of families of children born with birth defects.

Goal of the study:
This study will aim at identifying parent's perspectives on service needs of children born with disabilities due to birth defects. The study shall document the responses of parents to identification of a birth defect, access to information and care, satisfaction regarding interaction with professionals and the needs in terms of their children, siblings and for parents themselves.

Utility of the study:
The results from this study will contribute towards understanding the best practices and designing a protocol for referral for care from newborn or pediatric services to special care.

A review of needs and services available to families of children with disability in high and low and middle income settings

Objectives:

1. To document the needs and opinions of parents about the available services in high and low and middle income settings
2. To determine how family needs are influenced by available health and social services

Methodology: Systematic search was conducted using electronic databases ERIC, PubMed, PsycINFO and Google Scholar.

Terms used for search on databases- Family needs OR unmet needs OR parents needs OR health care needs OR chronic conditions needs **and** locomoter disability OR cerebral palsy OR spina bifida OR hearing impairment OR visual impairment OR speech disability OR cognitive disability OR intellectual disability OR autism OR mental retardation OR down syndrome

No time period was used for selecting the articles

Results:
Out of 75 relevant studies identified, only 15 studies were from developing countries suggesting limited data on family needs from these settings. Needs reported in the literature can broadly be classified as information needs, service and support needs, needs related to communication with relatives and health professionals, psychosocial support for dealing with parental stress and anxiety, needs of financial assistance and needs of guidance related to family relationships. **Information needs** were priority needs from low income countries while families from high income countries had more advanced needs in terms of **respite care, specialized schools and parent support groups**. These was a lack of contextualized validated scales for needs assessment in India

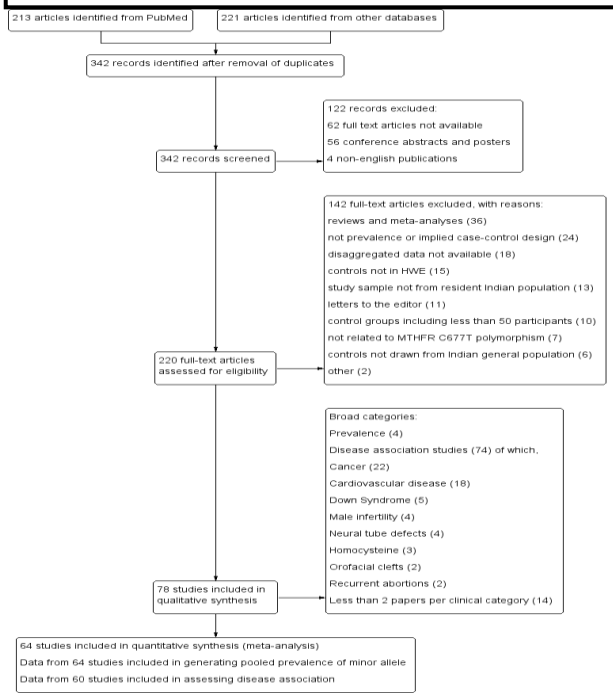
Conclusion:
Needs of families of children with disability in India remain underrepresented suggesting necessity to conduct such study for documentation of needs related to different types of disabling conditions.

MTHFRC677T polymorphism: A systematic review and meta-analysis to determine the disease association and public health implications in the Indian population

Kalyani Divgi and Anita Kar

Background:
The *MTHFR* C677T polymorphism has been implicated in increasing the risk for hyperhomocysteinemia, and the predisposition for non-communicable disease like cardiovascular disease, cancer, diabetes, psychiatric conditions, preeclampsia, recurrent pregnancy loss and birth defects like neural tube defects, orofacial clefts, congenital heart disease and Down syndrome. A plethora of disease association studies for the *MTHFR* C677T polymorphism are published from India each year. They are conducted from different parts of the country and thus have the potential to capture data representative of the entire Indian population. However, a meta-analysis of data presented by these studies is needed to understand the true population health implications.

Objectives:
To review data from prevalence and disease association studies on the *MTHFR* C677T polymorphism published in India and determine the prevalence of the *MTHFR* C677T polymorphism in the Indian population and its association with the increased risk of hyperhomocysteinemia, cardiovascular disease, cancer and selected birth defects.



Methodology:
A Pubmed search conducted in 2015 using the keywords 'methylenetetrahydrofolate', or 'MTHFR' and 'India' yielded 342 studies. Publications in English conducted in India with Indian participants resident in the country were selected. Cross-sectional studies were selected for determining prevalence and case-control studies with at least 50 cases and 50 controls were selected for determining disease-association.

Allele frequencies were computed from pooled data of prevalence studies and control data from case-control studies.

Strength of the association between *MTHFR* C677T genotype and risk of disease/disorder was computed using pooled odds ratios (OR) with 95% Confidence Intervals (CI) and *p*-values for significance using the Review Manager 5.3 software.

Heterogeneity between studies was tested using Cochran's Q test, $P<0.05$ and I^2 value >60% suggested lack of homogeneity between studies. Publication bias was measured with the funnel plot and Egger's test.

Results: The prevalence of the risk allele, T, from pooled data was found to be 13%. Genotype frequencies were found to be 74.5%, 22.9% and 2.6% for the CC, CT and TT genotypes respectively

The TT genotype of the *MTHFR* C677T polymorphism was strongly associated with an increased risk for:

- Cardiovascular disease (OR = 2.83, 95% CI = 1.83 – 4.36),
- Maternal risk of NTD (OR = 2.53, 95% CI = 1.28 – 5.01),
- Offspring risk of NTDs (OR = 3.78, 95% CI = 1.75 - 8.14)
- Orofacial clefts (OR = 1.36, 95% CI = 1.07 - 1.73)
- Male infertility (OR = 2.85, 95% CI = 1.65 – 4.90)

The TT genotype was found to be weakly associated with increased risk for cancer (OR = 1.32, 95% CI = 1.01 – 1.71, p=0.04).

Presence of T allele, either as CT or TT genotype, is weakly associated with the maternal risk for Down syndrome(OR 1.39, 95% CI = 1.07 – 1.82, p=0.02)

Conclusion: Use of this SNP for genetic diagnosis without medical or family history in the Indian general population is not appropriate due to multiple associations. Therefore, there is a need of regulation of genetic diagnostic services and guidelines for testing and counseling with reference to *MTHFR* C677T polymorphism as a tool for risk assessment.

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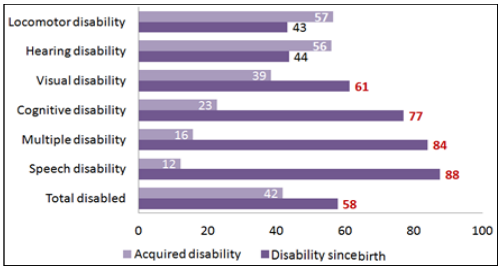
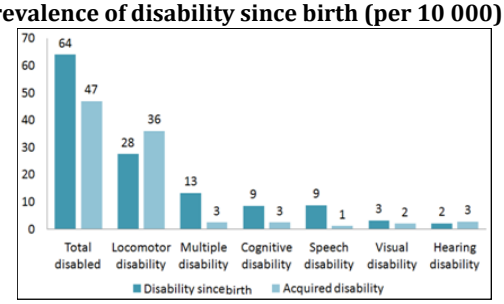
A study on childhood disability arising at birth: Magnitude and characteristics

Dr Amruta Gujar, Doctoral candidate

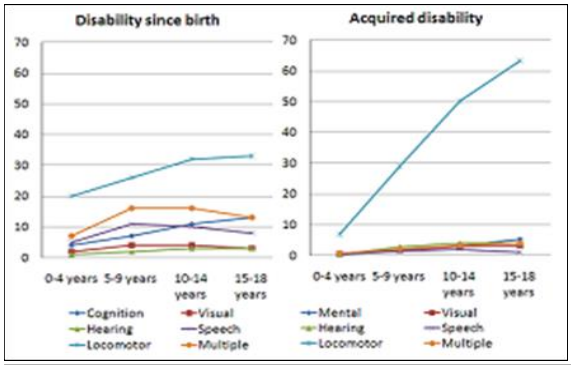
Proportion of childhood disability since birth (%)



Prevalence of disability since birth (per 10 000)



Age-specific prevalence (per 10 000)



Study I: Magnitude of childhood disability arising at birth

Background: There is a paucity of data on childhood disability since birth in India.

Objectives: Primary: i) to estimate the prevalence of childhood disability and disability since birth in India. ii) to estimate the person-years lived with disability. **Secondary:** todescribe the characteristics of children disabled since birth.

Materials and methods: Two national datasets for disability (National Sample Survey 2002 and Census 2011) were independently analyzed for children under eighteen years of age to calculate crude and age-specific prevalence rates.

Results: Childhood disability contributed about 30% in India. Almost 58% of childhood disability arose at birth. Among all types of disability, 88% of speech, 84% of multiple, 77% of cognitive impairment were present since birth. The largest causes of childhood disability since birth arose due to impairment in locomotion and multiple disability. Disability severity was more pronounced in children affected since birth (no perception to light (61%), deformity of limb (64%), unable to speak (32%) and severe hearing disability (40%)). The person years lived with disability since birth were almost double (30 million p-yrs) than that due to acquired causes.

Conclusions: Disabled children make up one third of all disabled individuals and impairment arising at birth contributes to a significant magnitude of childhood disability in India. The study suggests need for disability prevention and care programme.

Study II: Prevalence of developmental delays and disabilities among children under five years in urban slums of Pune, Maharashtra (ongoing study)

Objectives: To determine the prevalence of developmental delay and disability among children under five years in urban slums and to determine the characteristics and prevalence of selected risk factors.

Materials and methods: Population based cross-sectional study is being conducted in 35 randomly selected urban slums of Pune city. The data is being collected using a pretested structured questionnaire and the CDC checklist for developmental delays. The sample size of the study is 3500 children under five years of age. The data will be analyzed to calculate the prevalence rates and odds ratios (OR) will be calculated to determine associated risk factors.

Publications and Conference presentations

- Gujar A., Kar A. The epidemiology of childhood disability in India: Types, magnitude and characteristics of disabled children. (ms in preparation)
- Gujar A., Kar A. Magnitude and survival of persons with disability arising due to birth defects in India, 2002. Platform presentation at the Maharashtra IPHA & IAPSM Joint Conference 2015: Emerging Threats in Public Health, Pune. Jan 30-31. Abstract # 6.8
- Gujar A., Kar A. Magnitude and characteristics of congenital and acquired childhood disability in India. Presentation at International workshop on Identifying areas for translating disability research to primary care services under Indo-Norwegian Cooperation Programme 2015, Pune. Aug 17-19.

PUBOs maternal DNA biobank

The PUBOs maternal DNA biobank was set up as part of the Pune Urban Birth Outcomes study (PUBOs) linking the woman's DNA to her pregnancy outcome data, data on extrinsic risk exposures and pregnancy complications.

This DNA repository holds samples from 1710 pregnant women who have been recruited after obtaining informed consent in the first trimester of pregnancy and have been followed-up till pregnancy outcome.Till date, DNA samples are available for 1564 women with outcome data:

- 31 with major congenital anomalies,
- 32 with stillbirths, 76 with miscarriages,
- 150 with preterm births and
- 285 with low birth weight babies.

Methodology

Samples are also available for pregnancy complications:

- 24 samples of mothers who experienced pregnancy induced hypertension (PIH)
- 8 samples of gestational diabetes mellitus

and risk exposures:

- 79 women exposed to second hand smoke
- 263 women with severe/ moderate/ mild anemia.

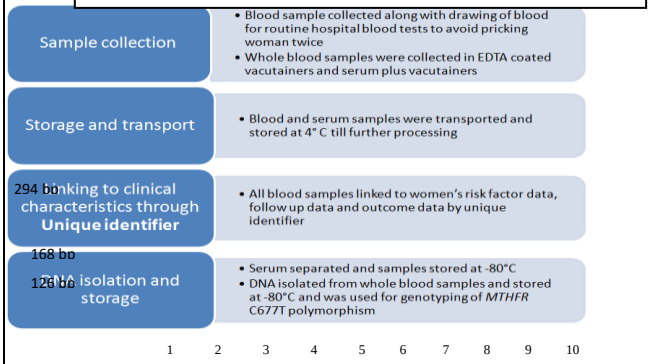
Prevalence of *MTHFR* C677T gene polymorphism

Bhide P, Digvi K and Kar A

Background: The methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism is associated with adverse pregnancy outcomes. There are no studies on the prevalence of the risk allele among pregnant women in India.
Aim: The aim of the present study was to determine the prevalence of the MTHFR C677T polymorphism among pregnant Indian women. We investigated whether there was any association with adverse pregnancy outcomes in this cohort.

Sample and Methods: Blood samples were collected from 1165 pregnant women. PCR-RFLP was used for genotyping of the MTHFR gene for the C677T polymorphism. Risk was reported as odds ratios with 95% confidence intervals.
Results: The genotypic frequencies of the MTHFR C677T polymorphism were 76%, 23% and 1% for the CC, CT and TT genotypes among 1165 women, with no difference in the distribution of genotypic frequencies between religious groups. Among 1041 women for whom pregnancy outcome data was available, there was no significant association of MTHFR C677T and adverse pregnancy outcome.
Conclusions: The low prevalence of the risk allele in the Indian population may provide a protective advantage for women against adverse pregnancy outcomes.

Figure: Bbanding pattern of different genotypes for MTHFR C677T polymorphism



Lane 10: 100 bp ladder.
Lane 1, 4-9: 294 bp band (no digestion) – CC genotype.
Lane 2: 168 bp and 126 bp bands (complete digestion)– TT genotype.
Lane 3: 294 bp, 168 bp and 126 bpbands(partial digestion) – CT genotype

Birth Defects Research Group

Out of pocket expenditure of families for the treatment of children affected with major and minor congenital anomalies

Supriya Phadnis, Research Associate, post doctoral study (on-going)

Objective: To determine the out of pocket expenditure incurred for the treatment of major and minor congenital anomalies

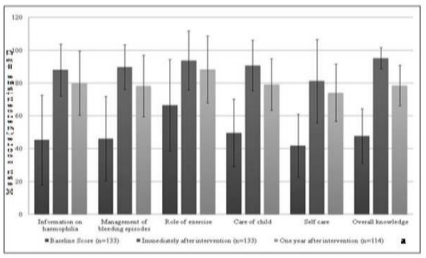
Methodology: Children with minor/major anomaly from the PUBOS birth cohort were contacted. Data is being collected using a structured questionnaire.

Four families of children detected with minor anomalies and one family of child detected with major anomaly did not seek treatment primarily due to inability to pay out of pocket

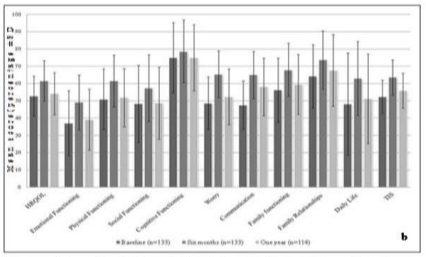
The impact of psychosocial support intervention on the quality of life of parents of children affected with haemophilia

Objective:
To develop a psychosocial support intervention using peer experiences and to test the impact of the developed psychosocial support intervention on parent's knowledge about haemophilia, its management and the HRQOL of parents

METHODOLOGY
Part A: Qualitative study to determine the psychosocial needs of parents
Part B: Quasi-experimental study to test the impact of developed psychosocial support intervention on parent's knowledge about haemophilia, its management and the HRQOL of parents from five haemophilia treatment centers across Maharashtra state



RESULTS
1. Significant improvement in the scores for parents' knowledge (47.7±1.4 at baseline,95.2±0.6 post intervention and 78.5±1.1 one year after intervention, e= 0.9 and 0.4)
2. Significant improvement in use of first aid for limiting the bleeding (6% at baseline,67% at six months and 63% one year after intervention)
3. No significant improvement in HRQOL one year after the intervention (54.2±1.1, e=0.4, 95% CI) as compared to the baseline score (52.8±1.0)



g.1. Impact of intervention. (a) Scores for knowledge at baseline, post-intervention and one year intervention. (b) TIS, HRQOL and family functioning scores at baseline, six months and one after intervention.

CONCLUSIONS
PSS resulted in improvement of knowledge, and practice of management of bleeding. However, a single psychosocial support intervention did not have any long term effect on the HRQOL of parents, suggesting the need for regular PSS for parents of patients with haemophilia in India.

PUBLICATIONS
1. Dharmarajan S., Gund P., Phadnis S., Lohade S., Lalwani A., Kar A. Treatment decisions and usage of clotting factor concentrate by a cohort of Indian haemophilia patients. Haemophilia 2012; 18
2. Kar A., Phadnis S., Dharmarajan S. and Nakade J. Epidemiology and social costs of Hemophilia in India. Indian J Med Res 2014; 140:19-31.
3. Dharmarajan, S., Phadnis S., Gund, P. and Kar, A, Out-of-pocket and catastrophic expenditure on treatment of haemophilia by Indian families. Haemophilia 2014, 20: 382–387.

Currently submitted and under revision
1. **Phadnis S.**& Kar A., 2016. The impact of psychosocial support on knowledge and health related quality of life of parents of Indian children with haemophilia. *Haemophilia*