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Feasibility of introducing genetic services in the National Family Welfare Programme in India

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***Background & objective*: Genetic factors could play an important role in the outcome of pregnancy. This study was carried out to identify risk factors that result in adverse pregnancy outcome and to develop a system of screening and referral to a tertiary hospital equipped with facilities for diagnosis and management of such high risk pregnancies.**

***Methods*: District level hospitals close to the participating centers *e.g.* All India Institute of Medical Sciences, New Delhi, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, BJ Medical College, Pune, St. John Medical College, Bangalore and Genetic Research Center, (ICMR), Mumbai, were selected. Pregnant women < 28 wk gestation attending antenatal OPD of selected district hospitals were included. All eligible women who gave consent for participation in the study, were screened using a predesigned proforma based on family history, past pregnancy history, history of genetic disease/ congenital malformation in previous child and history of present pregnancy. Pregnancy outcome was noted.**

***Results:* There was statistically significant difference in the outcome of pregnancy in the following groups: (*i*) past pregnancy history of 3 or more spontaneous abortions (RR= 3.9; CI=1.17-9.02); (*ii*) still birth (RR= 2.5; CI= 1.41-4.48); (*iii*) previous child with neurol tube defect (NTD) (RR=2.3; CI= 1.22- 4.60); and (*iv*) previous child with congenital malformation (RR=2.2; CI = 1.11- 4.35).**

***Interpretation & conclusion*: A sample questionnaire may be used for screening of pregnant women at risk of having and adverse outcome. Also screening of pregnant women for thalassaemia carrier state and maternal serum α-foetoprotein (AFP) for NTD may be useful.**

Key words Genetic services - India - National Family Welfare Programme - pregnancy

The primary focus of antenatal care has been health of the mother during pregnancy and safe delivery of the child. Foetal medicine is now emerging as an equally important component of the antenatal care[1]. For this purpose not only the scope of antenatal care needs to be enlarged to include foetal health but also to add the concept of preconceptional clinic with genetic counselling.

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Adverse pregnancy outcomes comprise foetal loss (abortions and still birth), perinatal death, birth defects and a child born with genetic disorders. While state of mother's health and nutrition are important in determining birth weight and perinatal mortality, genetic factors play a major role in the causation of birth defects and foetal loss. Current estimates indicate that about 15-20 per cent of clinically recognized pregnancies end up in spontaneous abortion prior to 20 wk of gestation, while another 70 per cent of fertilized ova do not get implanted[2]. The major cause of spontaneous abortion and foetal loss is chromosomal anomaly and genetic defects; 40-60 per cent of first trimester abortuses and 10 per cent of second trimester abortuses have chromosomal anomaly while 5 per cent of perinatal deaths are due to chromosomal and other genetic disorders[2]. In developed countries with low infant mortality rates, this load is considerably higher[2,3].

Congenital malformations are present in 2-3 per cent of live births and in 10 per cent of still births[4,5]. Those who survive with malformations place a heavy burden on the society and affected families. Among malformations, neural tube defect (NTD) is a major malformation in the Indian subcontinent[3] which has become highly amenable to primary and secondary prevention[5-10]. Its prevalence is high in northern India, northern China, Egypt and Lebanon[11]. Anencephaly and spina bifida comprising a vast majority of NTD are common congenital abnormalities, which contribute substantially to morbidity and mortality in infancy and childhood. One out of four affected foetuses is stillborn and one out of two results in spontaneous abortion[12,13]. The risk of recurrence of NTD after birth of an affected child is 3-5 per cent which is 10 times higher than that of general population[14]. Other disorders need careful diagnosis and genetic counselling. There is paucity of information on women attending antenatal outpatient department of district hospitals who are at risk of having adverse outcome of pregnancy. This study was undertaken to determine the relative frequency of genetic risk factors which may result in adverse pregnancy outcome and to develop a system of screening and referral to a hospital equipped with management of such high risk pregnancies to improve pregnancy outcome.

Material & Methods

Selection of centres: The study was carried out at five tertiary level hospitals having genetic centres, namely the All India Institute of Medical Sciences (AIIMS), New Delhi, Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, BJ Medical College, Pune, St. John Medical College, Bangalore and Genetic Research Centre (ICMR), Mumbai. Each centre selected a district level or equivalent peripheral hospital, with active obstetric service. All pregnant women below 28 wk of gestation enrolled for antenatal care at these hospitals during the year 1995-1996 were taken up for the study. Mumbai centre selected the Thane Civil Hospital, and five primary health centres in the Thane district for the study. Bangalore centre selected one of the City Corporation Hospitals, which was, located 7 kilometers away from the St. John's Medical College. AIIMS selected the Faridabad Hospital, and the Lucknow centre selected the Mahila Hospital, Golaganj, which is a Government District Hospital. Approval of the study protocol by the Institutional Ethics Committee of all the participating institutions was obtained prior to initiation of the study.

Inclusion criteria: All women upto 28th wk of gestation, attending Obstetrics OPD of the chosen hospital for the first time were included in the study. Informed consent was obtained from those who agreed to participate in the study after being briefed about the purpose of the study. After consent, a pre-designed screening proforma was filled up (Annexure). Information was collected on age of women, family history of genetic disease, history of still birth, 3 or more spontaneous abortion in the past, 2 or more neonatal deaths, history of genetic disease in previous births (*e.g.,* NTD, Down syndrome, congenital malformation, mental or physical retardation, thalassaemia, bleeding diathesis or other genetic syndrome, *etc*.) and history of systemic illnesses/history of infection/exposure to radiation and drug intake in the first trimester during the current pregnancy.

Blood samples (2 ml of EDTA blood from NESTROF test and 3 ml of non-ox lood for MSAFP) were collected from a subgroup of women with known last menstrual period (LMP) between 13-16 wk of gestation for estimation of maternal serum alpha-foetoprotein (MSAFP) and NESTROFT test (Naked Eye Single Tube Osmotic Fragility Test) along with routine haemogram. MSAFP was estimated by ELISA technique using modification of the method of McDonald and Kelly[15] to assess the risk of neural tube defect and chromosomal abnormality (Down Syndrome). Those having MSAFP value of 2 or more multiples of median value (MOM) for the given gestational age were advised to have an ultrasound evaluation done to rule out presence of neural tube

Annexure

INDIAN COUNCIL OF MEDICAL RESEARCH
FEASIBILTY OF INTRODUCING GENETIC SERVICS IN NATIONAL FAMILY WELFARE PROGRAMM

SCREENING PROFORMA

(Screening should only be done in women ≤ 28 weeks of gestation)

Name of woman ……Husband's name ……

Address……...

Name of district hospital……

1. ICMR Job No. 1- 5 ☐☐☐☐☐

2. Study No. 6-10 ☐☐☐☐☐

3 Centre No. 11 ☐
1. Delhi 2. Bombay
3. Pune. 4. Bangalore 5. Lucknow

4. Subject No. 12-15 ☐☐☐☐

5. Date of Registration 16-21 ☐☐☐☐☐☐

6. Religion 22 ☐
1. Hindu 2. Muslim
3. Christian 4. Others

7. Age (years) 23-24 ☐☐

8. Age of Husband (years) 25-26 ☐☐

9.Presence of Consanguinity 27 ☐
1.No. 2. Yes

10. Source of Referral 28 ☐
1. Self 2. Gen Practitioner
3. Specialist 4. PHC 5. Sub Centre
6. Other Hospitals 7. Others

11. Date Of L.M.P. 29-34 ☐☐☐☐☐☐

12. Gestation (weeks) 35-36 ☐☐
1. Self 2. Gen Practitioner
3. Specialist 4. PHC 5. Sub Centre
6.Other Hospitals 7. Others

13. E. D.D. 37-42 ☐☐☐☐☐☐

14. Gravida (Number) 43-44 ☐☐

15. Parity (Number) 45-46 ☐☐

PRENANTAL GENETIC SCREENING
(Code 1=No , 2 = Yes)

16. Age greater than 35 Years 47 ☐

FAMILY HISTORY OF

17. Any disease affecting Multiple members 48 ☐

PAST PREGNANCY HISTORY
(Code 1= No, 2= Yes)

20. More than 3 Spontaneous abortions (<28wks) 51 ☐

21. Still birth(s)/Intra-uterine deaths 52 ☐

22. 2 or more neonatal death with similar problems 53 ☐

23. Treatment for Sub fertility/ Infertility 54 ☐

PREVIOUS CHILD WITH GENETIC DISEASE
(Code 1=No , 2= Yes)

24. Downs Syndrome 55 ☐

25. Neural tube defect 56 ☐

26. Bleeding Diatheses 57 ☐

27 Transfusion dependent anemia 58 ☐

28. Muscular dystrophy 59 ☐

29. Congenital malformations(s) 60 ☐

30. Mental Retardation 61 ☐

31. Other genetic disease Specify_____ 62 ☐

SIGNIFICANT MATERNAL ILLNESS
(Code 1. No 2. Yes)

32. Diabetes 63 ☐

33. Epilepsy 64 ☐

34. Thyroid disease 65 ☐

35 Heart disease 66 ☐

36. Chronic lung disease 67 ☐

37 Tuberculosis 68 ☐

38. Cancer (present or Past) 69 ☐

Contd....

18. Congenital Malformations (Specify) 49 ☐

19. Mental Retardation 50 ☐

b. Rash 71 ☐

c. Lymphadenopathy 72 ☐

d. Jaundice 73 ☐

e. Genital ulcer 74 ☐

40. Drug Intake in first 75 ☐

41. Exposure to X-Rays Radiation to pelvis Exclude Chest X-Ray 76 ☐
1. No. 2. Yes

Centre No ---------- Sub. No----------

LABORATORY INVESTIGATIONS

42. Single tube osmotic fragility test (Nestrof test) 77 ☐
1.Negative 2.Positive
3.Doubtful Positive
(if 2 or 3 are scored then do Hb A2 in woman)

43. Hb. A2 in woman 78 ☐
1. <3% 2. ≥ 3%)
(if Hb A2 scores 2 then do Nestrof test and A2 in husband)

44. Nestrof test in husband 79 ☐
1. Negative 2.Positive
3. Doubtful positive

45. A2 in Husband 80 ☐
1. <3% 2. ≥ 3%
(if scores 2 in 45 then enroll for risk)

PRESENT PREGNANCY

39. Infections
(code 1= No , 2= Yes)
a. Fever >103 C 70 ☐

46. High Risk for B-thalassemia fetus 81 ☐
1.No 2. Yes
(Yes only when 2 in item 43&45)

47**. SERUM ALFA FETOPROTINE**

(Assay only in women with gestation Of 13 to24 weeks and known LMP)
Result
1. 0.8 to 2 MoM 82 ☐
2. >2MoM
3. <0.8 MoM
(if scores 1 No further action
if scores 2 or 3 –Enroll for high risk and till MSAFP Action Form)

ACTION TAKEN BASED ON HISTORY
EXAMINATION AND LAB. INVESTIGATIONS

48. High Risk for genetic disease 83 ☐
No. 2. Yes

If yes, Enroll for detailed genetic study
(Fill Risk High Proforma)

Name of the_____
Medical Officer_____
Signature _____

defect. Those having MSAFP <0.8 times the median value were counselled for the risk of having Down syndrome and were offered antenatal diagnosis. NESTROFT was done to screen carrier status for beta thalassaemia, which was later confirmed by HbA_2 estimation by column chromatography method[16]. If a woman was found to be a carrier for beta thalassaemia, her husband was also screened. If the husband was also a carrier, the couple was considered at a risk of having a foetus with thalassaemia major. The couple was then offered antenatal diagnosis by chorionic villous sampling.

Exclusion criteria: Women who enrolled for delivery beyond 28 wk of pregnancy or who came as an emergency to the labour room were excluded from the study.

Women enrolled in the study were followed up till delivery to record the pregnancy outcome. They were advised to come for delivery in the same hospital where they were enrolled and those having risk factors on screening were given genetic counselling and referred to tertiary hospitals for delivery. In case of non availability of primary outcome, reply paid cards were sent, and home visits were made by social workers to collect information on outcome of pregnancy. Outcome of pregnancy and condition of newborn among liveborn babies was noted.

Women having one or more risk factors on screening were considered at increased risk for genetic disease and those who did not have any risk factor were considered low risk. When the outcome of pregnancy was spontaneous abortion, still birth, induced abortion for NTD, Down syndrome, or thalassaemia, or the newborn was found to have congenital malformation/ genetic syndrome, the outcome was considered as abnormal.

Statistical analysis: Data were analyzed using software EPI - info version 5 and SPSS version 12.0 Chicago, Illinois, USA. Univariate analysis was performed for all the variables considered as risk factors for screening. Z - test was used for comparing the outcome in the two groups *viz*., the increased risk vs non risk group. All variables that achieved significance on univariate analysis were identified, and subjected to step-wise logistic regression analysis to determine independent risk factors associated with adverse outcome of pregnancy.

Results

Demographic and obstetric profile: A total of 8,331 women were enrolled for the study at the five centres. Mean ± SD age of the women was 23.5±3.8 yr. Seventy four (0.8 %) women were below 18 yr of age and 39 (0.5%) above 35 yr. Majority (83.2%) of the women enrolled in the study were Hindus at all the centres; only at Bangalore centre about half (46.4%) of women enrolled were Muslims. Mean gestational age at the time of enrollment was 19.8 ± 5.1 wk (range 18.5 ± 5.8 to 20.8 ± 4.6 wk) at various centres. Frequency of consanguinity varied from centre to centre. It was high in Bangalore (41.6%) and Pune (27.5%) centres, while at Mumbai, Lucknow and Delhi centres it was 14.2, 5.8 and 0.7 per cent only.

Increased risk for genetic disease: Based on history, a total of 1167(14.0%) women were found to be at increased risk for genetic disease/abnormal outcome of pregnancy, while 7164 (86.0%) women did not have any of the listed risk factors. Proportion of women with one or more risk factors varied from 10.3 per cent in Lucknow to 23.0 per cent in Mumbai. In Delhi, Bangalore and Pune these percentages were 11.3, 12.6, and 19.4, respectively. Majority of the women (10.5%) had single risk factor, while 3.5 per cent had 2 or more risk factors (Table I).

Pregnancy outcome: Information on outcome of pregnancy was available for a total of 4041 (48.5%) women enrolled; others were lost to follow up. Of these, 794 (19.6%) cases were enrolled at Delhi, 878 (21.7%) at Mumbai, 459 (11.4%) at Pune, 443 (11.0%) at Bangalore and 1467 (36.3%) at Lucknow. In order to test whether loss to follow up could have introduced any bias, two groups *viz*., those with and without information on outcome were compared for the prevalence of risk factors. There was no statistically significant difference in the two groups indicating that loss to follow up was not selective. Of the 4041 women on whom outcome information was available, 570 (14.1%) had one or more risk factors on screening and 3471 (85.9 %) did not have any risk factor.

Laboratory investigations NESTROFT followed by HB A_2 estimation and MSAFP were carried out in 2548 cases. Of the 1526 couples screened, 17 (1.1%) were at a risk of having a foetus positive for beta thalassaemia major. On maternal serum alpha foetoprotein assay, 221 (8.7%) women were found to have MSAFP value < 0.8 MOM; and 170 (6.7%) had MSAFP >2 MOM indicating risk for neural tube defect.

Outcome of pregnancy in increased risk and low risk groups is given in Table II. Abnormal outcome of pregnancy was observed in 11.2 per cent (64/570) cases in increased risk group and in 4.9 per cent (171/3471) in low risk group, the difference was statistically significant (RR=2.3, CI 1.73-3.0). The occurrence of spontaneous abortion, induced abortion and still birth were 2.8, 3.5, 3.0 per cent respectively in high risk group and 0.7, 1.1 and 1.8 per cent respectively in low risk group. All the differences were statistically significant (P<0.05) except for still birth. Abnormal condition in foetus/newborn (presence of Down syndrome, congenital malformation and neural tube defect) was observed in a total of 54 cases, 17 (3.0%)

Table I. Centre-wise distribution of women having risk factor on basis of history

Centre	No. of risk factors				Total risk factor
	1	2	3	≥4	
Delhi (n=2029)	190 (9.4)	39 (1.9)	0 (0.0)	0 (0.0)	229 (11.3)
Mumbai (n=902)	136 (15.1)	58 (6.4)	14 (1.6)	0 (0.0)	208 (23.0)
Pune (n=1612)	215 (13.3)	64 (4.0)	22 (1.4)	12 (0.7)	313 (19.4)
Bangalore (n=1130)	109 (9.6)	27 (2.4)	5 (0.4)	2 (0.2)	143 (12.6)
Lucknow (n=2658)	223 (8.4)	45 (1.7)	5 (0.2)	1 (0.0)	274 (10.3)
Total (n=8331)	873 (10.5)	233 (2.8)	46 (0.6)	11 (0.1)	1167 (14.0)

Values in parentheses are percentages

in increased risk group and 37(1.1%) in low risk group. The differences in the outcome in the newborn in both groups were statistically significant (RR = 2.9, CI 1.65 - 5.14) (Table III).

Family history of any disease affecting multiple members, congenital malformation, mental retardation, treatment for sub fertility/infertility, history of previous child with mental retardation, bleeding diathesis, muscular dystrophy, transfusion dependant anaemia, other genetic diseases, significant maternal illnesses (diabetes, epilepsy, thyroid disease, heart disease, TB, fever, rashes lymphadenopathy, *etc*.), drug intake and exposure to radiation was not found to be risk factors for adverse outcome of pregnancy in this study probably due to small numbers in each category. Multivariate logistic regression analysis was applied for identifying risk factors for adverse pregnancy outcome. The risk factors identified for abnormal outcome of pregnancy were past history of 3 or more spontaneous abortion (RR= 3.9; CI=1.17-9.02), still birth (RR= 2.5; CI= 1.41-4.48), previous child with NTD (RR=2.3; CI= 1.22-4.60), previous child with congenital malformation (RR=2.2; CI = 1.11- 4.35) (Table IV). MSAFP level >2 (RR 7.1, CI 2.63-19.35) was also found to be independent risk factor for adverse outcome in the live births.

Discussion

It was observed that out of 8331 pregnant women attending OPD of five district hospitals screened, 1167(14.0 %) were at risk of having adverse pregnancy outcome. Genetic factors play a major role in adverse pregnancy outcome like foetal wastage and congenital malformations. Of the 42 variables used for screening for increased risk in pregnant women, past history of spontaneous abortion, still birth, previous child with NTD/congenital malformation were found to be risk factors for adverse outcome of pregnancy. Adverse outcome in the previous pregnancy has also been observed as most serious risk factor in other studies[17-20]. In a community based prospective study where 6275 deliveries (6084 live births, 167 neonatal deaths and 150 still births were followed up for a period of 3 yr, adverse outcome in the previous pregnancy was observed as most serious risk factor[18]. In a case control study based on the record of the epidemiological surveillance system of neural tube defect association between history of maternal reproductive loss and the risk of anencephaly was evaluated in three Mexican States. Mothers of 157 cases of anencephaly and 151 controls were interviewed about their reproductive history and other additional factors. After adjusting for confounders, women with a history of miscarriage in previous pregnancies were 4.58 times more at risk of having a child with anencephaly than those who did not have such a history (OR = 4.58, 95% CI 1.22-17.23)[19].

NTD is the most common congenital malformation of CNS. Its prevalence in US and worldwide is 1 in 1000[11]. Primary prevention of genetic diseases is emerging as an important area to improve quality of life and prevent disease burden. It requires targeting of preventive measures to entire population or to individuals with increased risk, if the increased risk individuals could be identified by suitable screening strategies. Screening for genetic diseases otherwise is very expensive if it is applied to whole population. Moreover, screening facilities are not always available or there is a lack of trained manpower to carry out the tests. In this study around half of women screened were not available for follow up inspite of maximum possible efforts made to obtain traceable address at the time of registration. It remained a major challenge to reach them through post, or even by personal visit to obtain the details of the pregnancy outcome.

Initially it was planned that during the first year both screening, and genetic counselling cum intervention if any, will be done by the Genetic team at the district/ peripheral hospital itself. In the second year it was proposed to continue screening at the selected hospital by the Genetic team but to refer the at risk women to the attached tertiary care hospital for counselling intervention if any. In the third year it was envisaged that screening will also be carried out by the local hospitals' obstetric team. In order to achieve the goal, creation of awareness and training of the local team was carried out systematically from the very beginning. But the experience proved to the contrary. During the second year a number of referred at risk patients did not reach the tertiary care hospitals, and in the third year local hospitals obstetric team did not continue with screening because of excess workload of routine hospital services. In the end, the genetic team continued to provide both the screening and counselling-cum-intervention services throughout the study period.

The study establishes both the need and utility of introduction of preventive genetic services in the National Family Welfare Programme. At present, it has remained as an add on vertical programme. The reasons for failure of integration are multiple, primary reason being lack of motivation of both pregnant women and medical practitioner to accept and adopt

Table II. Distribution of risk factors in relation to outcome of pregnancy

Variables	Status of risk factors	Total (n=4041)	Normal outcome (n=3806)	Abnormal outcome (n=235)	*P* value & 95% Confidence Interval (CI)
Consanguinity	A	3505 (86.7)	3300 (86.7)	205 (87.2)	0.89
	P	536 (13.3)	506 (13.3)	30 (12.8)	
I. Family history:					
Any disease affecting	A	4030 (99.7)	3797 (99.8)	233 (99.1)	0.26
multiple members	P	11 (0.3)	9 (0.2)	2 (0.9)	
Congenital malformation	A	4017 (99.4)	3783 (99.4)	234 (99.6)	1.00
	P	24 (0.6)	23 (0.6)	1 (0.4)	
Mental retardation	A	4016 (99.4)	3784 (99.5)	232 (98.7)	0.17
	P	25 (0.6)	22 (0.5)	3 (1.3)	
II. Past pregnancy history:	A	4002 (99.2)	3776 (99.2)	226 (96.2)	RR=4.86
3or more spontaneous abortions (<28 wk)	P	39 (1.0)	30 (0.8)	9 (3.8)	(CI 2.33-11.11)
Still birth	A	3934 (97.4)	3717 (97.7)	217 (92.4)	RR=3.26
	B	107 (2.6)	89 (2.3)	18 (7.6)	(2.01-5.34)
2 or more neonatal death	A	4005 (99.1)	3774 (99.2)	231 (98.3)	0.15
	P	36 (0.9)	32 (0.8)	4 (1.7)	
Treatment for subfertility/infertility	A	4022 (95.5)	3789 (99.6)	233 (99.1)	0.30
	P	19 (0.5)	17 (0.4)	2 (0.9)	
III. Previous child with genetic disease:	A	4001 (99.0)	3771 (99.1)	230 (97.9)	0.13
	P	40 (1.0)	35 (0.9)	5 (2.1)	
Down syndrome					
Neural tube defect	A	3964 (98.1)	3743 (98.3)	221 (94.4)	RR=3.60
	P	77 (1.9)	63 (1.7)	14 (6.0)	(2.05-6.33)
Bleeding diathesis	A	4040 (100.0)	3805 (99.9)	235 (100.0)	1.0
	P	1 (0.0)	1 (0.1)	0 (0.0)	
Transfusion dependent anaemia	A	4028 (99.7)	3794 (97.7)	234 (99.6)	0.54
	P	13 (0.3)	12 (0.3)	1 (0.4)	
Muscular dystrophy	A	4039 (99.9)	3804 (99.9)	235 (100.0)	>0.05
	P	2 (0.1)	2 (0.1)	0 (0.00)	
Congenital malformation	A	3964 (98.1)	3743 (98.3)	221 (94.0)	RR=3.60
	P	77 (1.9)	63 (1.7)	14 (6.0)	(2.05-6.33)
Mental retardation	A	4007 (99.2)	3776 (99.2)	231 (98.3)	0.26
	P	34 (0.8)	30 (0.8)	4 (1.7)	
Other genetic disease	A	3986 (98.6)	3757 (98.7)	229 (97.4)	0.18
	P	55 (1.4)	49 (1.3)	6 (2.6)	
IV. Significant maternal illness in current pregnancy:					
Diabetes	A	4039 (99.5)	3805 (99.9)	234 (99.6)	RR 16.2
	P	2 (0.5)	1 (0.1)	1 (0.4)	(CI 1.02-258.13)
Epilepsy	A	4036 (99.9)	3801 (99.9)	235 (100.0)	>0.05
	P	5 (0.1)	5 (0.1)	0 (0.0)	
Thyroid disease	A	4040 (100.0)	3805 (99.9)	235 (100.0)	>0.05
	P	1 (0.0)	1 (0.1)	0 (0.0)	
Heart disease	A	4038 (99.9)	3805 (99.9)	235 (100.0)	>0.05
	P	3 (0.1)	3 (0.1)	0 (0.0)	
Chronic lung disease	A	4038 (99.9)	3803 (99.9)	235 (100.0)	>0.05
	P	3 (0.1)	3 (0.1)	0 (0.0)	
Tuberculosis	A	4031 (99.7)	3796 (99.7)	235 (100.0)	>0.05
	P	10 (0.3)	10 (0.3)	0 (0.0)	
Cancer	A	4039 (100.0)	3805 (99.9)	234 (99.6)	RR 6.2
	P	2 (0.0)	1 (0.1)	1 (0.4)	(CI 1.02-258.13)

V. History in 1st trimester:					
Fever	A	3951 (97.8)	3724 (97.8)	227 (99.6)	0.30
	P	90 (2.2)	82 (2.2)	8 (3.4)	
Rash	A	4025 (99.6)	3791 (99.6)	234 (99.6)	0.61
	P	16 (0.4)	15 (0.4)	1 (0.4)	
Lymphadenopathy	A	4039 (100.0)	3804 (99.9)	235 (100.0)	>0.05
	P	2 (0.0)	2 (0.1)	0 (0.0)	
Jaundice	A	4030 (99.7)	3796 (99.7)	234 (99.6)	0.48
	P	11 (0.3)	10 (0.3)	1 (0.4)	
Genital ulcers	A	4038 (99.9)	3804 (99.9)	234 (99.6)	0.16
	P	3 (0.1)	2 (0.1)	1 (0.4)	
Drug intake	A	3988 (98.6)	3753 (98.6)	235 (100.0)	>0.05
	P	53 (1.4)	53 (1.4)	0 (0.0)	
Unprotected exposure to X-rays	A	4038 (99.9)	3803 (99.9)	235 (100.0)	>0.05
	P	3 (0.1)	3 (0.1)	0 (0.0)	

A, absence of risk factor; P, presence of risk factor
Values in parentheses denote percentages

Table III. Distribution of outcome of pregnancy in relation to the risk factors

	Increased risk (%) N=570	Low risk (%) N=3471	Total N=4041
Outcome of pregnancy:			
Live birth*	517 (90.7)	3346 (96.4)	3863 (95.6)
Still birth	17 (3.0)	62 (1.8)	79 (2.0)
Spontaneous abortion*	16 (2.8)	26 (0.7)	42 (1.0)
Induced abortion*	20 (3.5)	37(1.1)	57 (1.4)
Outcome in newborn/foetus:			
NTD/DS/ other malformation (foetus /newborn)*	17(3.0)	37(1.1)	54 (1.3)

*Statistically significant difference $P<0.05$

the programme in routine obstetric practice. Besides, motivation, lack of appropriate infrastructure at the participating hospitals and logistics of travel to the tertiary centres and its response also came in the way. In case of thalassaemia screening, tracing the husbands, their counselling and acceptance to be tested were also major hurdles.

Table IV. Results of multiple logistic regression : risk factor for adverse outcome of pregnancy (n=4041, 235 high risk and 3806 non risk)

Variable/ risk factor	Relative risk	95% CI
≥ 3 spontaneous abortion	3.9	1.77 - 9.02
H/O still birth	2.5	1.41 - 4.48
Previous child with NTD	2.3	1.22 - 4.60
Previous child with congenital malformation	2.2	1.11 - 4.35

(Adjusted for age, family history of disease affecting multiple members, previous child with genetic disease, present maternal illness, illnesses during first trimester of pregnancy)

In spite of these limitations, around 14.0 per cent women who were at risk of having adverse pregnancy outcome were identified in this study using a simple questionnaire for screening women for genetic diseases during pregnancy. Thus this study highlights the need and benefit of screening women during pregnancy for genetic diseases. In view of the fact that around 80 per cent of our population live in the rural area , this calls for evolving and implementing a national programme with emphasis on screening of all pregnant women for genetic diseases. First step could be to develop appropriate information, education and communication (IEC) materials, combined with genetic centres/ preconception clinics preferably with community extension activities.

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