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Original Article

Maternal nutrition and the risk of congenital malformations in the tea garden community of Assam, Northeast India

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ABSTRACT

Problem considered: There is a high prevalence of congenital malformations (CMs) in the tea garden community of Assam, Northeast India. The present cross-sectional study was carried out to assess if insufficiencies in maternal nutrition during the periconceptional period are associated with high incidence of CM in the said community.

Method: Over a period of 2 years, 156 pregnant women with a mean age of 25.7 years (SD 4.7) were enrolled. During an interview, anthropometric and obstetric data pertaining to periconceptional use of iron and folic acid (IFA) were collected. Adequate iodine intake during pregnancy was determined by measuring urinary iodine (UI) levels in each trimester.

Results: Malformations were noted in 16 babies, giving an uncorrected incidence rate of 102.5/1000 births. Among the participants, 87 (55.8%) were underweight and 6 (3.8%) were overweight. Periconceptional IFA supplementation was self-reported by 31 (19.8%). The median urinary iodine concentrations (MUICs) in the 1st, 2nd and 3rd trimesters were 170 µg/l (IQR 100 µg/l), 275 µg/l (IQR 166 µg/l), and 265 µg/l (IQR 160 µg/l), respectively. An analysis of maternal nutrition indicated that IFA supplementation reduced the risk of birth defects. However, a pre-pregnancy BMI > 23 kg/m² and a 1st trimester MUIC < 150 µg/l increased the odds of having an infant with CM. Maternal age < 20 years and illiteracy also elevated the risk.

Conclusion: Inadequacies in periconceptional maternal nutrition are associated with the high incidence of CM. Community members should also be sensitized against early pregnancy and educated to minimize the risk.

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1. Introduction

Congenital malformations (CMs) are one of the leading causes of high neonatal deaths in India,¹ and a high incidence of these malformations have been reported from the tea garden communities in Assam.² Apart from the genetic predispositions, the incidence of which is considered to be similar throughout the world,³ the regional variation in its prevalence can be attributed to other epidemiologic factors. Periconceptional maternal nutrition is an important determinant of pregnancy outcomes, as the availability and supply of essential nutrients to the developing fetus depends on maternal nutritional status. Iron and iodine are essential for development of the central nervous system, whereas folic acid and vitamins, such as A, B-6, and B-12, influence oxidative pathways and methylation.⁴ Although supplementation of diet with iron and folic acid (IFA) tablets, and iodized salt has been a part of the Ministry of Health and Family Welfare Program, their levels of intake have been low.⁵ In light of the above, the present study was conducted among a section of pregnant women, visiting the tertiary health care facility at Dibrugarh, to assess the relation between periconceptional maternal nutrition and risk of CMs in the community.

2. Methods

2.1. Study design

This cross-sectional study was conducted among pregnant mothers from the tea garden community attending a tertiary health care center in Assam. The sample size was calculated using an anticipated incidence rate of 12.6% for the tea garden community (based on retrospective review of our hospital records) and an overall incidence of CM, which was 1.2% at this facility.⁶ The study had a power of 80% and the values of α and β were 0.05 and 0.2, respectively. All pregnant women in their first trimester, who were reportedly from the tea garden community, were included in the study. Pregnant women suffering from any acute or chronic illness, thyroid disorders, or ingesting iodine-containing products like cough syrups were excluded from the study. To identify associated risk factors, participating pregnant women were classified into two groups. The cases were mothers who gave birth to babies with CM, while controls were mothers of children with no apparent CM at the time of birth. Overall, 156 pregnant women and 160 non-pregnant women were recruited in the study, spanning 2 years. The non-pregnant women were recruited to know the status of iodine nutrition in the community. All the participants provided written informed consent. Demographics, obstetric and dietary information were collected using a precoded questionnaire.

2.2. Sample collection

Sampling of urine for pregnant women was carried out during each trimester for each participant: first trimester (GW4–8), second trimester (GW14–19) and third trimester (GW27–30) during their antenatal visits to the facility. The urine samples of pregnant and non-pregnant women were stored at -80°C .

Urine iodine estimation was done using the Sandell–Kolthoff formula.

2.3. Definitions of variables

Preterm birth was defined as duration of pregnancy between 20 weeks 0 days and 36 weeks and 6 days.⁷ BMI (kg/m^2) was classified according to the criteria suggested by WHO for the Asian populations as follows: underweight ($<18.5 \text{ kg}/\text{m}^2$), normal-weight ($18.5\text{--}22.9 \text{ kg}/\text{m}^2$), overweight, and obese ($>23 \text{ kg}/\text{m}^2$) women.⁸ The iodine intake was classified as deficient, adequate, or excessive according to the WHO reference medians.⁹ Ministry of Health and Family Welfare, Govt. of India directs all pregnant women to consume 1 tablet containing 100 mg elemental iron and 0.5 mg folic acid daily for 100 days. Periconceptional IFA supplementation was self-reported, and based on the duration of supplementation, it was categorized into three groups: IFA intake ≥ 90 days, IFA intake < 90 days, and no supplementation.

2.4. Statistical analysis

Conditional logistic regression was used to describe the associations between the variables and CMs. The average concentrations of iodine in the urine were calculated as medians because of the skewed data distribution. Student's *t*-test was employed to compare data between pregnant and non-pregnant, primi- and multigravida women. All the statistical results were considered significant at $p < 0.05$ (two-tailed). IBM SPSS statistics 20 (SPSS Inc., Chicago, IL, USA) was used for the data analysis.

2.5. Ethical approval

This cross-sectional study was approved by the Institutional ethical committee.

3. Results

There were 12 preterm deliveries and a single stillbirth who had myelocoele with bilateral telepes. Malformations were noted in 16 babies. The anthropometric, obstetric, and socio-demographics characters of the 156 pregnant women who were recruited for the study are shown in Table 1. Within the study group, 87 (55.8%) pregnant women were underweight and 6 (3.8%) were overweight. Although all respondents reportedly used iodized salt, periconceptional IFA supplementation was self-reported by only 31 (19.9%) participants. The median urinary iodine concentrations (MUIC) of pregnant women in their 1st, 2nd, and 3rd trimesters were $170 \mu\text{g}/\text{l}$ (IQR $100 \mu\text{g}/\text{l}$), $275 \mu\text{g}/\text{l}$ (IQR $166 \mu\text{g}/\text{l}$) and $265 \mu\text{g}/\text{l}$ (IQR $160 \mu\text{g}/\text{l}$), respectively, as compared to $117.94 \mu\text{g}/\text{l}$ among non-pregnant women of the same community. A significant rise in UI was noted during the 2nd trimester (Fig. 1, Tables 2 and 3).

3.1. Risk factors associated with CMs

From Table 4, it is evident that the prevalence of CM was significant among pregnant women suffering from iodine

Table 1 – Characteristics of pregnant women participating in the study (n = 156).

Parameter	n	(%)
Age at enrolment (years)		
>20	5	3.2
20–29	115	73.7
≥30	36	23.1
IFA supplementation		
IFA tablets consumed ≥90	28	17.9
IFA tablets consumed <90	3	1.9
No supplementation	125	80.1
Consumption of iodized salt		
Yes	156	100
No	0	0
BMI (kg m ⁻²)		
18.5–22.9	63	40.4
<18.5	87	55.8
>23	6	3.8
Gravidity		
First	62	39.7
Second	39	25.0
Third	34	21.8
Fourth	16	10.3
Fifth	5	3.2
Literacy		
Literate	82	52.6
Illiterate	74	47.4
Knowledge of iodine		
Yes	44	28.2
No	108	69.2

BMI, body mass index; IFA, iron and folic acid.

Distribution of urinary iodine concentration (UIC) among primigravida by trimester of pregnancy **Distribution of urinary iodine concentration (UIC) among multigravida by trimester of pregnancy** **Fig. 1 – Distribution of iodine concentration among primi- and multigravida women by trimester of pregnancy.**

deficiency (MUIC < 150 µg/l) during the 1st trimester (OR 4.10, 95% CI: 1.39–12.10) and those having a BMI > 23 kg/m² (OR 1.90, 95% CI: 0.19–19.06). The incidence was also higher among pregnant women aged <20 years (OR 6.30, 95% CI: 0.95–41.89). In the community, consumption of IFA supplements for ≥90

days (OR 0.31, 95% CI: 0.04–2.42) and being literate (OR 0.27, 95% CI: 0.81–0.86) lowered the risk of having a child with an anomaly. Analysis of variables also indicated that maternal BMI < 18.5 (OR 2.68, CI: 1.25–5.74) and age <20 years (OR 1.39,

Table 2 – UI differences between primi- and multigravida women compared to non-pregnant women.

Non pregnant women	Mean UI (n) = 117.94 (160)		SD = ±45.26		–
Time of gestation	Primigravida (n = 61)		Multigravida (n = 83)		p value
	Mean UI (n)	SD	Mean UI (n)	SD	
1st trimester	181.70 (61)	±78.81	187.40 (83)	±77.01	0.67
2nd trimester	223.11 (59)	±83.00	254.20 (79)	±65.04	0.02*
3rd trimester	251.94 (36)	±78.70	235.95 (37)	±94.09	0.43

UI, urinary iodine; SD, standard deviation; Mean UI are in µg/l units.

* Statistically significant.

Table 3 – UI differences by trimester of pregnancy between two age groups.

Time of gestation	<26		≥26		Significance
	Mean UI (n)	SD	Mean UI (n)	SD	
1st trimester	185.11 (81)	±79.35	184.83 (63)	±75.82	0.98
2nd trimester	224.93 (78)	±85.70	252.04 (60)	±64.51	0.04*
3rd trimester	249.27 (41)	±81.80	236.88 (32)	±93.28	0.55

UI, urinary iodine; SD, standard deviation; Mean UI are in µg/l units.

* Statistically significant.

Table 4 – Non genetic risk factors associated with congenital malformations in the tea garden community.

Category	Cases ^a	Control ^b	OR (95% CI)	p-value
IFA supplementation				
No supplementation	14 (87.5)	109 (79.3)	Ref.	
IFA ≥ 90	1 (6.2)	27 (18.6)	0.31 (0.04–2.42)	0.26
IFA < 90	1 (6.2)	4 (2.1)	2.64 (0.26–27.18)	0.41
BMI				
18.5–22.9 kg/m ²	6 (37.5)	57 (40.7)	Ref.	
<18.5 kg/m ²	9 (56.2)	78 (55.7)	1.10 (0.37–3.25)	0.87
>23 kg/m ²	1 (6.2)	5 (3.6)	1.90 (0.19–19.06)	0.58
UIC of 1st trimester				
UIC ≥ 150 µg/l	6 (37.5)	91 (71.1)	Ref.	
UIC < 150 µg/l	10 (62.5)	37 (28.9)	4.10 (1.39–12.09)	0.01*
UIC of 2nd trimester				
UIC ≥ 150 µg/l	11 (68.8)	101 (83.5)	Ref.	
UIC < 150 µg/l	5 (31.2)	20 (16.5)	2.30 (0.72–7.33)	0.16
UIC of 3rd trimester				
UIC ≥ 150 µg/l	14 (87.5)	48 (82.8)	Ref.	
UIC < 150 µg/l	2 (12.5)	10 (17.2)	0.69 (0.13–3.50)	0.65
Maternal age (years)				
20–29	11 (68.8)	104 (74.3)	Ref.	
<20	2 (12.5)	3 (2.1)	6.30 (0.95–41.89)	0.05*
≥30	3 (18.8)	33 (23.6)	0.86 (0.23–3.27)	0.82
Literacy				
Illiterate	12 (75.0)	62 (44.3)	Ref.	
Literate	4 (25.0)	78 (55.7)	0.27 (0.08–0.86)	0.03*

IFA, Iron and folic acid; BMI, body mass index; UIC, urinary iodine concentration; OR, odds ratio; CI, confidence interval; Ref, Reference.

* Statistically significant.

^a Mothers who gave birth to babies with CM.

^b Mothers of children with no apparent CM.

Table 5 – Factors associated with UIC < 150 µg/l in the 1st trimester among pregnant women.

Category	UIC < 150 µg/l	UIC ≥ 150 µg/l	OR (95% CI)	p value
BMI				
18.5–22.9	13 (28.9)	49 (49.5)	1	
<18.5	32 (71.1)	45 (45.5)	2.68 (1.25–5.74)	0.01*
>23	0 (0.0)	5 (5.1)	–	–
Age				
20–29	35 (77.8)	73 (73.7)	1	
<20	2 (4.4)	3 (3.0)	1.39 (0.22–8.70)	0.73
≥30	8 (17.8)	23 (23.3)	0.73 (0.30–1.78)	0.48
Iodine awareness				
Yes	9 (20.5)	29 (30.2)	1	
No	35 (79.5)	67 (69.8)	1.68 (0.72–3.95)	0.23
Literacy				
Literate	21 (46.7)	49 (49.5)	1	
Illiterate	24 (53.3)	50 (50.5)	1.12 (0.55–2.30)	0.75

BMI, body mass index; UIC, urinary iodine concentration; OR, odds ratio; CI, confidence interval.

* Statistically significant.

CI: 0.22–8.70) elevated the risk of acquiring MUIC <150 µg/l during the 1st trimester (Table 5).

4. Discussion

Although the prevalence of CM in Assam is considerably low,² a high incidence has been reported from the tea garden communities.^{2,10} The tea garden communities are quite distinct from other communities of Assam. People are socioeconomically backward, illiterate, undernourished, and

live in unhygienic conditions. According to The District Level Household Survey (DLHS-3), in rural Dibrugarh, 15.3% girls were getting married before 18 and 44.6% had a birth order of 2 and above at the age of 20–24 years.¹¹ So, the present study was carried out to evaluate if these factors contribute to maternal undernourishment, which could be associated with the risk of CMs.

The role of iodine as a prerequisite for proper fetal development during early gestation is clearly illustrated by the association between MUIC < 150 µg/l and CM in our study. Within the cohort, 32.64% pregnant women were iodine

inadequate (MUIC < 150 µg/l) during the 1st trimester, which elevated to adequacy (MUIC ≥ 150 µg/l) during the 2nd (18.25%), and the 3rd trimesters (16.22%). Similar to findings by Grewal et al. in a north Indian cohort,¹² the UIC of pregnant women aged ≥26 years and in multigravida spiked in the 2nd trimester and dropped in the 3rd trimester (Tables 2 and 3). Although erstwhile studies by Majumder et al.¹³ and Habimana et al.¹⁴ suggested that a sliding MUIC during progression of pregnancy is consistent with increase in iodine requirement, our values clearly indicate that iodine is most essential during first half of gestation, when both the mother and the developing fetus depend completely on maternal thyroid hormones.¹⁵ An uphill swing in MUIC thereafter indicates the onset of fetal thyroid hormone production.

Supplementation with IFA before the time of conception reduces the risk of CMs, and it is generally recommended that women planning to become pregnant take a daily supplement. 17.3% participants visiting our center consumed IFA for ≥90 days, while 2.6% consumed for <90 days. Although we report a higher consumption as against the National Family Health Survey (NFHS-3)⁵ report of only 13.7% mothers in the rural Assam consumed IFA for ≥90, the overall consumption of IFA was very low. It was evident that in the community, consumption of IFA lowered the risk of CM. Low folate levels could also be associated with 12 preterm deliveries as good maternal folate status has implications on birth weight, placental weight, or length of gestation.¹⁶

Maternal BMI is one of the strongest predictors of physical parameters at birth.¹⁷ In our study, the overall prevalence of overweight was low (3.8%), given the fact that most of the participants were socioeconomically backward, but we still observed an association between pre-gestational overweight and CM. This is in consensus with previous reports that overweight and obese mothers have significantly increased risk of neural tube defects (NTD) and cardiovascular defects in the babies.^{18,19} According to Rankin et al. maternal obesity was associated with the increased risk of ventricular septal defect, cleft lips, and eye anomalies, and maternal underweight was associated with atrial septal defects, genital anomalies, and hypospadias.²⁰

Our study raises an important question whether the salt iodization program implemented by the Government of India can alone supplement the iodine requirement of pregnant women in all communities. In their recent review, Yadav et al. reported that 59.5–95% of pregnant women were consuming adequately iodized salt in India,²¹ but the condition is skewed in rural and tribal communities.^{22,23} While some studies indicate widespread iodine deficiency among pregnant women of India,^{13,23,24} others report of adequacy.^{12,25,26} While evaluating iodine adequacy among healthy women of the community, we observed an overall deficiency (117.94 µg/l). These differences could be attributed to food habits, which varies across India, across socioeconomic orders, and the quality of iodized salt available.

Authors' contribution

The study was conceived and designed by HKD and MB. MB and DB performed the experiments and compiled the data.

Data were analyzed by DB. The article was drafted by DB and revised by HKD.

Conflicts of interest

The authors have none to declare.

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