British Journal of Nutrition, page 1 of 11 doi:10.1017/S0007114524002009

British Journal of Nutrition

Maternal dietary practices during pregnancy and obesity of neonates: a machine learning approach towards hierarchical and nested relationships in a Tibet Plateau cohort study

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(Submitted 13 November 2023 – Final revision received 6 June 2024 – Accepted 25 June 2024)

Abstract

Studies on obesity and risk factors from a life-course perspective among residents in the Tibet Plateau with recent economic growth and increasing obesity are important and urgently needed. The birth cohort in this area provides a unique opportunity to examine the association between maternal dietary practice and neonatal obesity. The study aims to detect the prevalence of obesity among neonates, associated with maternal diet and other factors, supporting life-course strategies for obesity control. A cohort of pregnant women was enrolled in Tibet Plateau and followed till childbirth. Dietary practice during pregnancy was assessed using the Chinese FFQ – Tibet Plateau version, food items and other variables were associated with the risk for obesity of neonates followed by logistic regression, classification and regression trees (CART) and random forest. Of the total 1226 mother–neonate pairs, 40·5 % were Tibetan and 5·4 % of neonates with obesity. Consuming fruits as a protective factor for obesity of neonates with OR (95 % CI) = 0·61 (0·43, 0·87) from logistic regression; as well as OR = 0·20 (0·12, 0·35) for consuming fruits (≥ weekly) from CART. Removing fruit consumption to avoid overshadowing effects of other factors, the following were influential from CART: maternal education (more than middle school, OR = 0·22 (0·13, 0·37)) and consumption of Tibetan food (daily, OR = 3·44 (2·08, 5·69). Obesity among neonates is prevalent in the study population. Promoting healthy diets during pregnancy and strengthening maternal education should be part of the life-course strategies for obesity control.

Keywords: Neonates obese: Maternal dietary practice: Tibetan food: Machine learning

The long history of the agricultural economy has fostered a social norm in China that it is desirable for mothers to have large and heavy babies. Birthweights are even used to name a newborn if the weight is high. For example, 'Ba Jin', a traditional Chinese weight unit equivalent to 4000 grams, has been a common first name for many Chinese. This traditional culture is now challenged in China because of the growing obesity epidemic. Along with a four-decade-long economic growth, obesity has

Abbreviations: CART, classification and regression trees; CFFQ-TP, The Chinese FFQ – Tibet Plateau version; PI, ponderal index; SHAP, Random Forest SHapley Additive Explanation.

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become a new public health challenge[1,2] The obesity of neonates has long been recognised as a risk factor for subsequent obesity and related health consequences (such as metabolic syndromes, CVD and cancer) during adolescence and adulthood[3–5]. Research indicates that higher neonatal adiposity correlates with elevated BMI and an increased likelihood of overweight or obesity during early childhood[6].

Maternal diets during pregnancy can affect the birth weight of neonates through fetal programming or epigenetic mechanisms[7]. The ponderal index (PI) provides the best measure of the adiposity of neonates[8]. From literature research, we found that maternal and infant health studies focus on low birth weight for women with low socio-economic status[9,10], and few studies if any examined the dietary factors associated with neonates with obesity (PI > 90 percentile). One cohort study with 570 mother–infant dyads from Dublin, Ireland reported a positive association between nutrition intake during pregnancy and neonatal birthweight, but the risk of obesity was not examined[11]. A recent cohort study of 937 mother–child dyads from Shenyang, an industrial city in northeast China observed a negative relationship between diet with more fruits and vegetables during pregnancy and infants' BMI[12]. However, the study's participants were mainly Han Chinese, resulting in a homogeneous diet due to the population's geographical and ethnic uniformity[12]. While some studies have explored outcomes related to babies with large gestational age or high birth weight, which may serve as indicators of neonatal obesity to some extent, their relationship with maternal diet remains elusive. For instance, a cohort study identified a positive association between a high intake of milk, vegetables and sweets during pregnancy with large gestational age births[13]. Conversely, research conducted in Iran revealed that high consumption of sugar, fruit juice, candy and desserts was positively correlated with low-birth-weight infants[14]. Additionally, studies have investigated the impact of maternal carbohydrate intake on total gestational weight gain and neonatal birth weight[15]. However, the results appear to be contradictory, as higher carbohydrate intake in early pregnancy has been linked to lower birth weight[16].

After decades of overall economic growth in China, the remote Tibet Plateau area experienced rapid economic growth recently[17]. Along with increases in food supply and improvements in education, many mothers may have altered their dietary practices when they become pregnant. For example, some women may start adding fruits and protein-rich foods to their table; while others may still stick to the traditional Tibetan food, a typical example is samba, a traditional Tibetan food of a mixture of roasted barley, butter and sugar, featuring high calories and fat[18–20]. Furthermore, it is noteworthy that Tibetan religious and cultural practices discourage fish consumption, but with the urbanisation of Tibetan areas, Han Chinese dietary influences are permeating and enriching traditional Tibetan diets, particularly among the younger generation[21,22]. The recent economic growth and improved infrastructure in the Tibet Plateau area have led to the diversification and transition in diets among pregnant women, offering a unique opportunity to study dietary practices during pregnancy and factors associated with neonatal obesity. The Tibetan region's distinct geography and culture lead to a unique diet and lifestyle compared with other regions. Additionally, health challenges brought by the high-altitude environment and remoteness contributed to the inferior health status in Tibet areas. Evidence suggests that high-altitude hypoxia may contribute to lower birth weight and length, thereby leading to an increased PI in newborns. There is currently no evidence supporting the notion that obesity in newborns in high-altitude areas offers protective effects on future health outcomes[23,24]. Thus, studies on the association between diets and birth outcomes have important public health implications.

In this study, we focused on the relationship between maternal dietary practice during pregnancy and the risk of obesity among newborns with a large cohort of mother–newborn dyads in the Tibet Plateau area. Our goal is to detect the prevalence of obesity in neonates and related factors and to provide evidence supporting the development of life-course strategies to control the growing obesity epidemic in China[25].

Materials and methods

Study design and participants

This cohort study targeted maternal–neonate dyads from the Tibet Plateau area in Qinghai Province where Tibetan and Han Chinese dominate. Pregnant women were recruited from two typical maternity hospitals serving all women in the region. Of the two hospitals, one provides care mainly for urban areas and another for rural areas. We completed participant recruitment during 2019–2020 when pregnant women visited the hospital for routine pre-delivery exams; we then followed them up till child delivery. The following inclusion criteria were used for enrollment: (1) legal local residence; (2) determined ethnicity of Tibetan or Han; (3) singleton pregnancy; (4) live birth without obvious congenital diseases and (5) agreed to participate by signing the informed consent. The following criteria were used to exclude unqualified participants: (1) mothers who were non-local residents, (2) undetermined ethnicity, (3) stillbirth and (4) neonates with congenital diseases such as Down syndrome. Of 1593 eligible women approached, 1518 met the criteria and were enrolled by signing the informed consent.

After enrollment, trained investigators interviewed the participants face to face to collect baseline survey data on demographic factors, socio-economic status and data on dietary practice. After the baseline assessment, all participants were followed until childbirth. After child delivery in the hospital, neonatal data were retrieved from the medical records, including gestation age, sex, birth status, Apgar scoring, congenital diseases, birth weight and length. After completion of data collection, 292 participants were excluded, including congenital diseases (7), stillbirths (10), no birthweight (56), no birth length (10), incomplete medical record (11), incomplete survey (120) and incomplete food frequency (78). Further analysis indicated that the incompleteness and missingness were related to difficulties in transportation and follow-up assessments despite tedious efforts by the study team. Online Fig. S1 summarises the recruitment and follow-up assessment using a flowchart.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures

https://doi.org/10.1017/S0007114524002009 Published online by Cambridge University Press

involving human subjects were approved by the Ethics Committee of the Medical College at Qinghai University, Qinghai Province, China (Approval No: 2018–36). Written informed consent was obtained from all subjects.

The study focuses on neonatal obesity as the primary outcome of interest. This variable was assessed based on the PI for newborns[26–28]. The PI was calculated as: PI = birth weight (kg)/(birth length (m))^3. A neonate was scored 1 (with obesity) if his/her PI > the 90th percentile, or 0 (with no obesity). This classification was made following the gender and gestational age-specific PI percentiles developed for Chinese newborns[29]. Of various weight status measures for neonates, we elected to use PI because of the greater validity of this measure than others such as BMI in measuring adiposity[8,30,31].

Maternal dietary practice during pregnancy

The Chinese FFQ – Tibet Plateau version (CFFQ-TP) was used to assess maternal dietary practices during the third trimester of pregnancy. With difficulties in locating a measurement tool for assessing the dietary practice of the study population, we developed the CFFQ-TP following the Chinese Dietary Guideline in four steps. Step 1, obtaining the food items common for Chinese by a careful review of the Chinese Dietary Guideline. Step 2, obtaining food items specifically for the study population and verifying which food items for Chinese in general were also common in the study population. This was achieved through intensive focused-group studies with the residents in local mountain villages and towns. Step 3, forming a draft CFFQ-TP by including both Chinese food and Tibetan food that were common in the study area for pilot testing. Step 4, generating the final version for use after revising based on the result from pilot tests. This instrument has adequate reliability and validity in predicting outcome variables[32].

The CFFQ-TP contained fourteen items (including refined carbohydrates, multigrain and roots, samba and butter, vegetables, fruits, red meats, poultry, fish and sea food, eggs, dairy products, beans and related products, pickles and other processed foods, soda and sugar beverages and snacks), reflecting the local dietary practice, including the consumption of samba, traditional high calories and high fat Tibetan food (roasted Tibetan barley, mixed with butter and sugar). We administered the CFFQ-TP in the hospital setting when the enrolled mothers were waiting for care, the average gestational age was 38 weeks, with a minimum of 28 weeks and a maximum of 43 weeks. Following the pilot-tested protocol, our trained investigators asked the mothers to rate the frequency of consuming individual foods during the past month. We assessed the reported frequencies using a four-point scale with 0 (less than monthly), 1 (monthly), 2 (weekly) and 3 (daily) for statistical analysis. The Cronbach alpha of CFFQ-TP was 0·704 in our study.

Covariates

Demographic factors for mothers were age (in years), education (< 9 years, 9–12 years *v.* more than 12 years), pre-pregnancy BMI and residential status (rural *v.* urban). Demographic factors for neonates were sex (male, female), ethnicity (Tibetan or Han) and birth order (if first-born).

Statistical analysis

Descriptive statistics were used to obtain estimates of the study sample. We constructed logistic regression models to assess the relationship between food items and obesity risk for all influential factors using two models. Model 1 contained all fourteen food frequency measures. To adjust for demographic and SES, seven additional covariates had been adjusted. Three maternal covariates were residence (rural *v.* urban), age at enrollment and education (< 9 years, 9–12 years *v.* more than 12 years); and four neonatal covariates were first birth (yes/no), race (Tibetan *v.* Han) and sex (male *v.* female). We used stepwise logistic regression to perform feature selection. As an alternative, model 2 was constructed by removing the most influential variable 'fruit consumption' in model 1 to avoid overshadowing the effects of other factors.

In addition to conventional methods, classification and regression trees (CART) was used as a classification tool to examine the potential hierarchal and nested relationships among the variables in our study[33]. CART is a popular classification tool widely used in the field of machine learning[33]. To begin the CART analysis, simple random sampling without replacement was used to split the sample into 80 % sized train samples and 20 % validation samples. Using CART, we were able to partition our data sequentially by selecting splitting variables (nodes) based on the Gini index which measures the degree of purity of class distribution at a given node. The CART algorithm searches for the splitting variable with the lowest Gini impurity at each step and keeps splitting the subsets until it cannot reduce impurity. The tree-like structure produced by CART enabled us to investigate the hierarchical and nested relationships among the variables, advancing regression analysis. However, the CART algorithm has its disadvantages, such as susceptibility to overfitting, particularly when dealing with complex datasets. To address this and potential collinearity issues, we utilised the Random Forest SHapley Additive Explanation (SHAP) decomposition for result validation. Sensitivity and specificity are employed to evaluate and compare the predictive performance of both logistic regression and CART.

All statistical analyses were completed using software R version 4·1·3. The R functions glm() was used for logistic regression, rpart() was used for CART and randomForest() was used for random forest analysis.

Results

Demographic and lifestyle characteristics

As shown in Table 1, most mothers were aged 25–34 years with a mean (SD) of 28·8(5·0) years. Of the sample, 682 (56·3 %) were from rural areas and 530 (43·7 %) were from urban areas and 794 (66·7 %) with a middle (9-year) or higher levels of education. Table 1 also presents the characteristics of the offspring. Of these newborns, 496 (40·5 %) were Tibetan and 730 (59·5 %) were Han, 621 (50·7 %) were males and 604 (49·3 %) were females

https://doi.org/10.1017/S0007114524002009 Published online by Cambridge University Press

Table 1. Characteristics of the study participants, including the mothers and neonates (*n* 1226)

	Total			Tibetan			Han			
Character	*N*	Mean or %	SD	*N*	Mean or %	SD	*N*	Mean or %	SD	*P*
Total sample	1226	100 %		496	40·5 %		730	59·5 %		**< 0·001**
Mothers										
Age at enrollment										
< 25 years	208	17·0		130	26·2		78	10·7		**< 0·001**
25–29 years	543	44·3		200	40·3		343	47·0		
30–34 years	323	26·3		103	20·8		220	30·1		
35+ years	152	12·4		63	12·7		89	12·2		
Mean (SD)	1226	28·8	5·0	496	28·1	5·6	730	29·3	4·5	**< 0·001**
Pre-pregnancy BMI (kg/m^2)										
Mean (SD)	1226	21·0·	3·1	496	21·1·	3·1	730	21·0·	3·2	0·580
Residence*										
Rural	682	56·3		357	72·7		325	45·1		**< 0·001**
Urban	530	43·7		134	27·3		396	54·9		
Years of education*										
< 9 years	396	33·3		275	57·1		121	17·1		**< 0·001**
9–12 years	342	28·7		76	15·8		266	37·6		
12+ years	452	38·0		131	27·2		321	45·3		
Neonates										
Sex										
Male	622	50·7		253	51·1		369	50·5		0·810
Female	604	49·3		242	48·9		362	49·5		
Gestational age										
< 37	90	7·3		34	6·9		56	7·7		0·591
≥37	1136	92·7		462	93·2		674	92·3		
First birth*										
Yes	628	51·3		198	40·1		430	58·9		**< 0·001**
No	596	48·7		296	59·9		300	41·1		
Apgar score at 1 min*										
< 3	8	0·6		1	0·2		7	1·0		**0·027**
3–7	30	2·5		18	3·7		12	1·6		
8+	1180	96·9		470	96·1		710	97·4		
Birth weight (g)										
< 2500 g	115	9·4		43	8·7		72	9·9		0·206
2500–4000 g	1063	86·7		428	86·3		635	87·0		
> 4000 g	48	3·9		25	5·0		23	3·1		
Mean (SD)	1226	3151·2	525·8	496	3185·3	535·5	730	3128·0	518·2	0·061
Birth height (cm)										
Mean (SD)	1226	50·4	3·5	496	50·4	3·5	730	50·3	3·4	0·666
Head circumference (cm)*										
Mean (SD)	1212	32·3	2·7	491	32·9	2·9	721	31·9	2·4	**< 0·001**
Ponderal index (PI)										
Mean (SD)	1226	24·7	3·3	496	25·0	4·3	730	24·4	2·5	**0·009**
High PI (PI > 90 percentile)										
Yes	66	5·4		45	9·1		21	2·9		**< 0·001**
No	1160	96·6		451	90·9		709	97·1		

PI, ponderal index.
* Means these variables contain missing data. Methods: Pearson's χ^2 tests or students' *t*-test.

with a mean birthweight of 3151·2 (SD 525·8) g. Of the total neonates, 66 (5·4 % with 95 % CI of 4·2–6·8 %) were classified as having obesity.

Food frequencies

Table 2 presents the frequencies of all fourteen foods consumed during pregnancy, overall and stratified by maternal ethnicity. The results suggest a general healthy dietary practice, such as high frequencies of consuming vegetables (92·3 % daily), fruits (77·1 % daily), dairy products (56·9 % daily) and low frequencies of consuming prepared foods such as pickles. Additionally, the reported food frequencies reflected the traditional cultures and the impact of economic growth. For example, 77·1 % of the mothers reported consuming fruits on a daily basis; 52·9 % reported consuming red meats (such as beef) on a daily basis and significantly more Tibetan mothers than Han mothers (44·2 % *v.* 12·2 %) consumed Samba daily.

Results from logistic regression

In model 1 with all twenty-one variables analysed using logistic regression to control for both maternal and neonatal covariates, results indicate that of the fourteen food items, only consuming fruits was associated with reduced risk of obesity with OR (95 % CI) = 0·61 (0·43, 0·87). With stepwise logistic regression, only one variable was associated with reduced risk of obesity, consuming fruits (OR (95 % CI) = 0·61 (0·44, 0·84)). Likewise, in model 2 with logistic regression after removing of the variable fruit consumption (determined by the CART in model 1), only

Table 2. Maternal dietary practice during pregnancy as measured using the food frequency*, overall and by ethnic group (n 1226)

	Total		Tibetan		Han		
Self-reported food frequency	*N*	%	*N*	%	*N*	%	*P*
Total sample	1226	100 %	496	40·5 %	730	59·5 %	
Refined carbohydrates (rice and noodle)							
Less than monthly (0)	10	0·8 %	6	1·2 %	4	0·6 %	0·405
Monthly (1)	12	1·0 %	6	1·2 %	6	0·8 %	
Weekly (2)	64	5·2 %	29	5·9 %	35	4·8 %	
Daily (3)	1140	93·0 %	455	91·7 %	685	93·8 %	
Multigrain and roots							
Less than monthly (0)	80	6·5 %	43	8·7 %	37	5·1 %	**0·006**
Monthly (1)	122	10·0 %	54	10·9 %	68	9·3 %	
Weekly (2)	740	60·3 %	304	61·3 %	436	59·7 %	
Daily (3)	284	23·2 %	95	19·1 %	189	25·9 %	
Samba and butter (Tibetan food)							
Less than monthly (0)	780	63·6 %	213	42·9 %	567	77·7 %	< **0·001**
Monthly (1)	51	4·2 %	13	2·6 %	38	5·2 %	
Weekly (2)	87	7·1 %	51	10·3 %	36	4·9 %	
Daily (3)	308	25·1 %	219	44·2 %	89	12·2 %	
Vegetables							
Less than monthly (0)	3	0·2 %	2	0·4 %	1	0·1 %	< **0·001**
Monthly (1)	9	0·7 %	9	1·8 %	0	0·0 %	
Weekly (2)	83	6·8 %	51	10·3 %	32	4·4 %	
Daily (3)	1131	92·3 %	434	87·5 %	697	95·5 %	
Fruits							
Less than monthly (0)	26	2·1 %	18	3·6 %	8	1·1 %	< **0·001**
Monthly (1)	110	9·0 %	100	20·2 %	10	1·4 %	
Weekly (2)	145	11·8 %	89	17·9 %	56	7·7 %	
Daily (3)	945	77·1 %	289	58·3 %	656	89·8 %	
Red meats							
Less than monthly (0)	68	5·6 %	19	3·8 %	49	6·7 %	< **0·001**
Monthly (1)	124	10·1 %	38	7·7 %	86	11·8 %	
Weekly (2)	385	31·4 %	125	25·2 %	260	35·6 %	
Daily (3)	649	52·9 %	314	63·3 %	335	45·9 %	
Poultry							
Less than monthly (0)	416	33·9 %	272	54·8 %	144	19·7 %	< **0·001**
Monthly (1)	384	31·3 %	114	23·0 %	270	37·0 %	
Weekly (2)	377	30·8 %	100	20·2 %	277	38·0 %	
Daily (3)	49	4·0 %	10	2·0 %	39	5·3 %	
Fish and sea food							
Less than monthly (0)	478	39·0 %	295	59·5 %	183	25·1 %	< **0·001**
Monthly (1)	409	33·4 %	114	23·0 %	295	40·4 %	
Weekly (2)	308	25·1 %	82	16·5 %	226	31·0 %	
Daily (3)	31	2·5 %	5	1·0 %	26	3·5 %	
Eggs							
Less than monthly (0)	242	19·8 %	139	28·0 %	103	14·1 %	< **0·001**
Monthly (1)	173	14·1 %	100	20·2 %	73	10·0 %	
Weekly (2)	405	33·0 %	138	27·8 %	267	36·6 %	
Daily (3)	406	33·1 %	119	24·0 %	287	39·3 %	
Dairy products							
Less than monthly (0)	76	6·2 %	38	7·6 %	38	5·2 %	**0·001**
Monthly (1)	85	6·9 %	44	8·9 %	41	5·6 %	
Weekly (2)	367	30·0 %	165	33·3 %	202	27·7 %	
Daily (3)	698	56·9 %	249	50·2 %	449	61·5 %	
Beans and related products							
Less than monthly (0)	402	32·8 %	220	44·4 %	182	25·0 %	< **0·001**
Monthly (1)	307	25·1 %	123	24·8 %	184	25·2 %	
Weekly (2)	432	35·2 %	131	26·4 %	301	41·2 %	
Daily (3)	85	6·9 %	22	4·4 %	63	8·6 %	
Pickles and other processed foods							
Less than monthly (0)	860	70·1 %	371	74·8 %	489	67·0 %	**0·027**
Monthly (1)	271	22·1 %	90	18·1 %	181	24·8 %	
Weekly (2)	84	6·9 %	31	6·3 %	53	7·3 %	
Daily (3)	11	0·9 %	4	0·8 %	7	0·9 %	
Soda and sugar beverages							
Less than monthly (0)	757	61·7 %	265	53·4 %	496	67·4 %	< **0·001**
Monthly (1)	320	26·1 %	157	31·7 %	163	22·3 %	
Weekly (2)	133	10·9 %	68	13·7 %	65	8·9 %	
Daily (3)	16	1·3 %	6	1·2 %	10	1·4 %	

Table 2. (*Continued*)

Self-reported food frequency	Total N	Total %	Tibetan N	Tibetan %	Han N	Han %	P
Snacks							
Less than monthly (0)	472	38·5 %	210	42·4 %	262	35·9 %	**0·002**
Monthly (1)	493	40·2 %	202	40·7 %	291	39·9 %	
Weekly (2)	229	18·7 %	79	15·9 %	150	20·5 %	
Daily (3)	32	2·6 %	5	1·0 %	27	3·7 %	

* Means the food frequency was measured using the Chinese FFQ – Tibet Plateau version (CFFQ-TP).
Methods: Pearson's χ^2 test or Fisher's exact test.

Table 3. Multivariable logistic regression‡ of maternal dietary practice and neonatal obesity (PI > 90 %)

Food consumed during pregnancy (frequency†)	Model 1* OR	Model 1* 95 % CI	Model 1* P	Model 2* OR	Model 2* 95 % CI	Model 2* P
Fruits	0·61	0·43, 0·87	**0·006**	n/a	n/a	n/a
Samba and butter (Tibetan food)	1·12	0·83, 1·51	0·455	1·22	0·91, 1·62	0·180
Eggs	0·81	0·61, 1·07	0·136	0·76	0·58, 0·99	**0·040**
Poultry	0·89	0·57, 1·39	0·621	0·84	0·54, 1·31	0·448
Beans and related products	0·99	0·70, 1·39	0·965	0·98	0·70, 1·37	0·904
Fish and sea food	1·37	0·85, 2·18	0·184	1·37	0·85, 2·18	0·186
Dairy products	0·89	0·68, 1·19	0·425	0·86	0·66, 1·14	0·276
Vegetables	1·13	0·63, 2·23	0·705	0·91	0·52, 1·77	0·765
Soda and sugar beverages	1·12	0·78, 1·59	0·531	1·08	0·75, 1·54	0·656
Multigrain and roots	0·96	0·69, 1·34	0·781	0·93	0·68, 1·30	0·658
Pickles and other processed foods	1·04	0·66, 1·57	0·860	1·01	0·63, 1·53	0·972
Red meats	0·84	0·62, 1·18	0·298	0·86	0·63, 1·20	0·370
Snacks	1·03	0·72, 1·47	0·858	1·01	0·71, 1·44	0·948
Rice and noodle (refined carbohydrates)	1·27	0·70, 2·93	0·498	1·30	0·70, 3·02	0·470

* Means model 1 contained twenty-one variables, including fourteen food frequency measures and seven covariates. Four maternal covariates were residence (rural *v.* urban), age at enrollment and education (< 9 years, 9–12 years *v.* more than 12 years) and pre-pregnancy BMI; and three neonatal covariates were first birth (yes/no), race (Tibetan *v.* Han) and sex (male *v.* female). Model 2 was built based on model 1 with the removal of 'fruit consumption', a most influential variable in model 1.
† Means food frequency measures: 0 = less than monthly, 1 = monthly, 2 = weekly and 3 = daily.
‡ Means significant predictors from stepwise logistic regression (not shown in the table): model 1: fruits with OR (95 % CI) = 0.61 (0.44, 0.84) and years of maternal education with OR = 0.88 (0.79, 0.98); model 2: eggs with OR = 0.72 (0.57, 0.92) and years of maternal education with OR = 0.86 (0.77, 0.97).

one of the remaining thirteen food items was associated with obesity, consuming eggs (OR (95 % CI) = 0·76 (0·58, 0·99)) (Table 3). Additionally, with stepwise logistic regression, consuming eggs (OR = 0·72 (0·57, 0·92)) was significantly associated with a reduced risk of obesity. Furthermore, interaction analyses revealed a significant interaction between ethnic groups and pre-pregnancy BMI (p interaction value is 0·037 in model 1 and 0·046 in model 2) (online Supplement Fig. 2).

We also detect the association between PI and fourteen food items, as presented in the online Supplement Table 1. In model 1, consuming fruit (β = –0·43 (–0·77, –1·27)) was negatively associated with PI, and consuming samba (β = 0·21 (0·01, 0·63)) was positively associated with PI. Likewise, in model 2 only consuming samba (β = 0·26 (0·06,0·77)) was positively associated with PI.

Result from classification and regression trees

In model 1 with all twenty-one variables with CART, the resulting OR (95 % CI) indicates the following two food items were associated with reduced odds for obesity, including consuming fruit weekly or more frequently (0·20 (0·12, 0·35), consuming eggs monthly or more frequently (0·22 (0·06, 0·65), respectively (Fig. 1). However, the mother's age and pre-pregnancy BMI were not associated with the risk of obesity.

In model 2 with the most influential diet of fruit consumption was removed, the following factors were significantly associated with the risk of obesity (Fig. 2(b)). Receiving more than middle school years of education by mothers was associated with reduced risk (OR (95 % CI) = 0·22 (0·13, 0·37)), and consuming samba daily (OR = 2·58 (1·09, 7·10)) was associated with increased risk. The CART demonstrates superior sensitivity (0·818 *v.* 0·617) and specificity (0·953 *v.* 0·738) when compared with traditional logistic models, providing it with a notable advantage in terms of prediction accuracy.

Result from random forest

Figure 2 presents a SHAP summary plot that succinctly displays the importance of all 21 variables, the magnitude of their impact (i.e., the effect size) and the direction of a specific feature's association with neonatal obesity. As shown in Fig. 2(a), the SHAP value and the contribution of all 21 variables are represented in the beeswarm figure. Variables are ordered based on their importance. The higher positive SHAP value of a variable indicated more likelihood to the occurrence of neonatal obesity. The red colour dots signify higher predictor values, and

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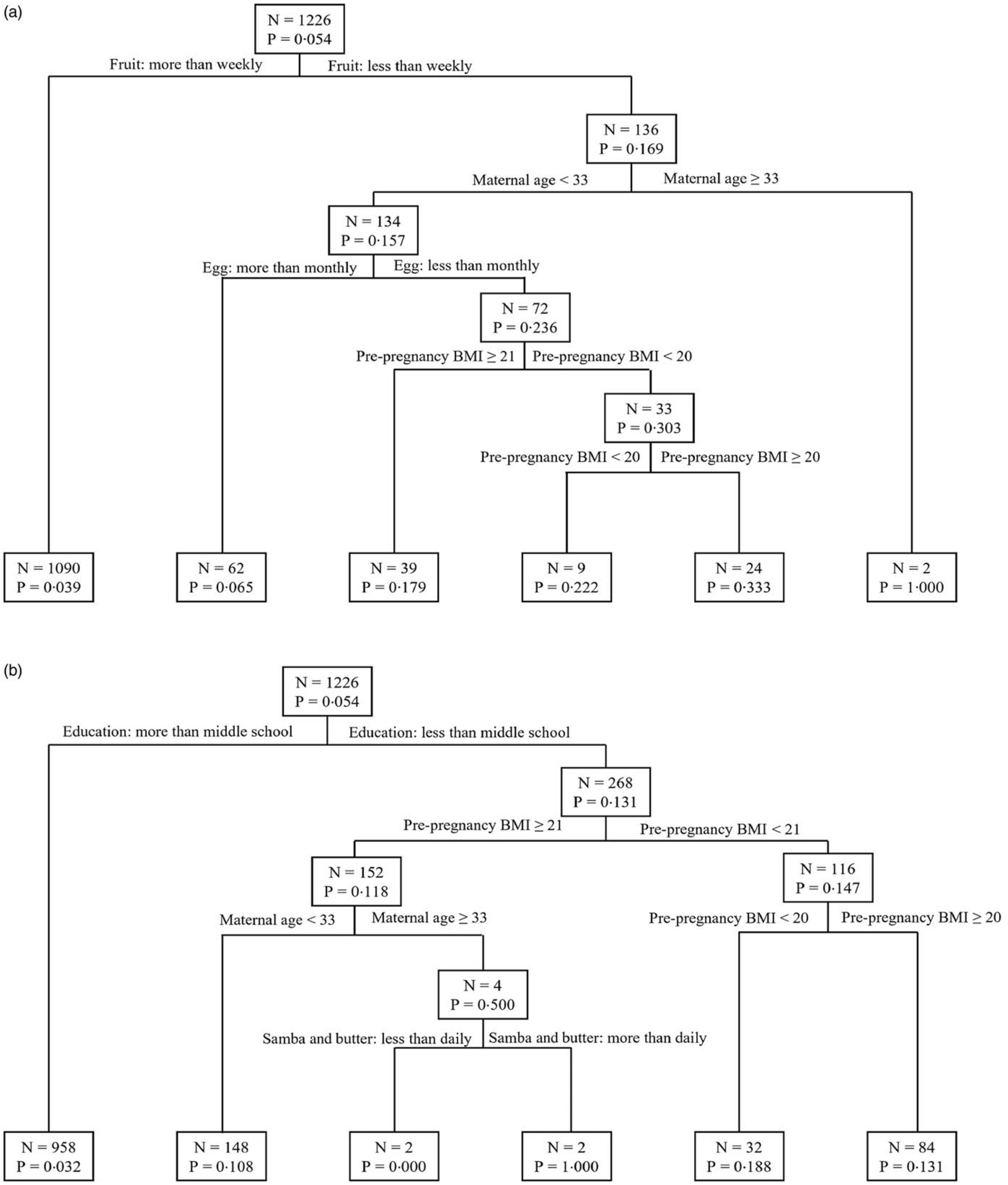

Fig. 1. Machine learning method CART determined hierarchical and nested relationship of dietary and other factors with neonatal obesity: (a) Decision tree of model 1 for neonatal obesity with 21 independent variables. Model 1 contained fourteen food frequency measures (less than monthly, monthly, weekly and daily) and seven covariates. Four maternal covariates were: residence (rural *v.* urban), age at enrollment, education (< 9 years, 9–12 years *v.* more than 12 years) and pre-pregnancy BMI; and three neonatal covariates were first birth (yes/no), race (Tibetan *v.* Han) and sex (male *v.* female); (b) decision tree of model 2 with fruits removed from model 1. Model 2 was built based on model 1 with the removal of 'fruit consumption', a most influential variable in model 1. P means the proportion of neonatal obesity. CART, classification and regression trees.

https://doi.org/10.1017/S0007114524002009 Published online by Cambridge University Press

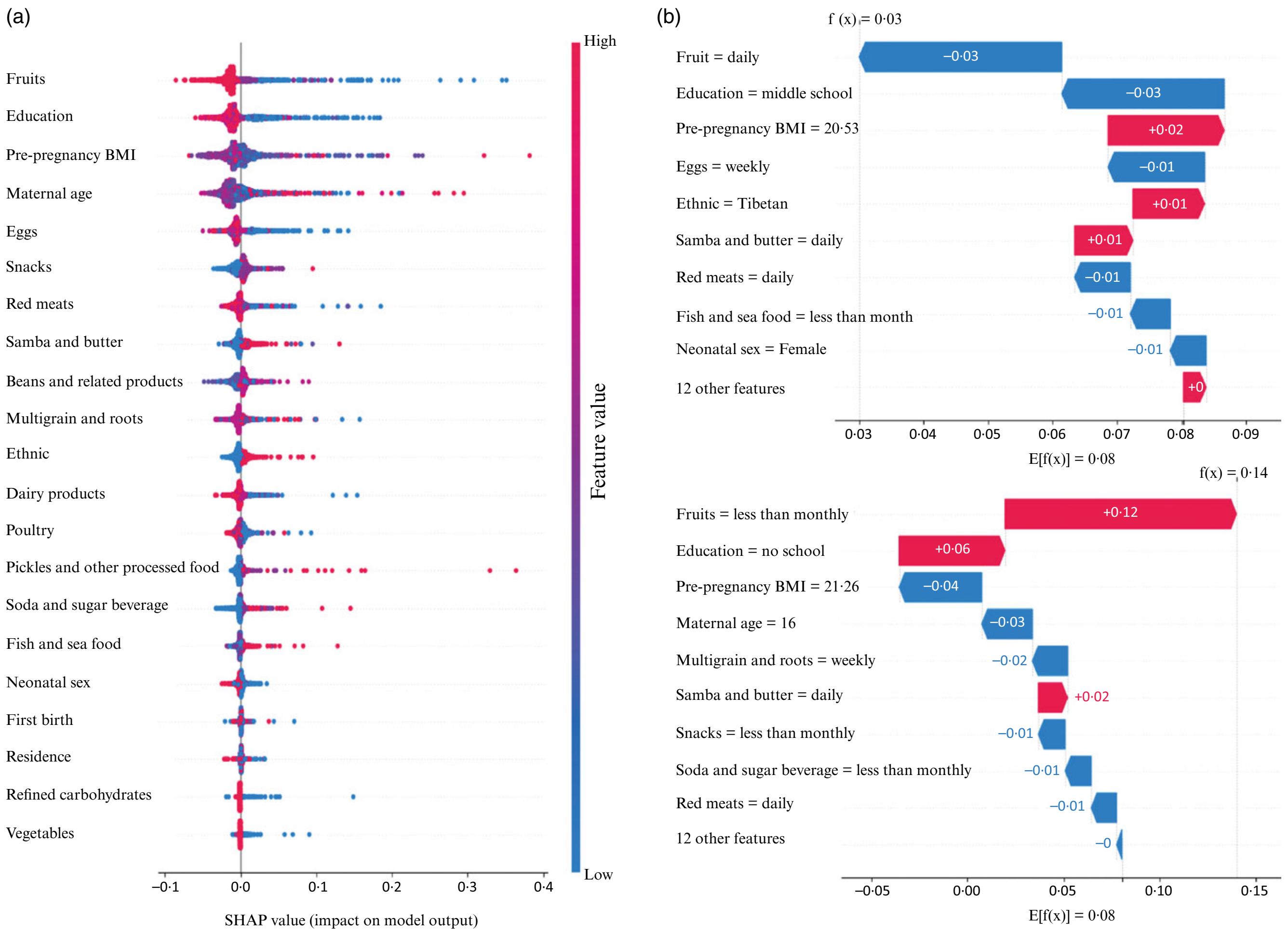

Fig. 2. Random forest method determined the relationship of dietary and other factors with neonatal obesity: (a) Explainability and interpretability of the SHAP framework for twenty-one independent variables. (b) The SHAP framework for individual predictions. The model contained fourteen food frequency measures (less than monthly, monthly, weekly and daily) and seven covariates. Four maternal covariates were residence (rural *v.* urban), age at enrollment, education (< 9 years, 9–12 years *v.* more than 12 years) and pre-pregnancy BMI; and three neonatal covariates were first birth (yes/no), race (Tibetan *v.* Han) and sex (male *v.* female). SHAP, Random Forest SHapley Additive Explanation.

the blue colour dots signify lower predictor values. Fruit is the most important variable and was associated with reduced odds of obesity. The education level of mothers was associated with reduced odds of obesity. Samba and butter (Tibetan food) was associated with increased odds of obesity. Figure 2(b) shows the SHAP framework for individual predictions. The red colour bar represents the positive effect on neonatal obesity, while the blue colour bar represents the opposite. For example, consuming fruit less than a month (SHAP value = 0·12) and mother with no education (SHAP value = 0·06) are positively associated with neonatal obesity; however, consuming fruit daily (SHAP value = –0·03) and mother with primary education (SHAP value = –0·03) are negatively associated with neonatal obesity.

Discussion

In this large cohort study of mother–neonate dyads, we are the first to detect the high prevalence of obesity among neonates in the Tibet Plateau area, and its associated maternal dietary and other influential factors during pregnancy. We are also the first to innovatively employ CART and random forest, a machine learning method to gain insights into the complex hierarchical nested relationship among all predictor variables, thus offering a new approach to enhance statistical causal inference. Findings from this study are promising and provide timely data much needed for the development of life-course interventions for obesity control by starting actions during pregnancy.

High prevalence of obesity in neonates as a health threat

In this study, we first detected that 5·4 % (95 % CI: 4·2–6·8 %) of neonates have obesity at birth. The prevalence of macrosomia in China was 7·35 % in 2013, which was higher than that reported in Mexico[34,35]. This finding is of significant concern, particularly when considering the long-term health implications for these infants. A cross-sectional survey conducted in China from 2015 to 2018 reported a prevalence of large gestational age at 9·9 %, which is comparable to the prevalence reported in the USA, a high-income country, in 2011[36,37]. Although there is a lack of prevalence data identified by PI in China and other countries in the world for comparison, the observed obesity prevalence from

https://doi.org/10.1017/S0007114524002009 Published online by Cambridge University Press

https://doi.org/10.1017/S0007114524002009 Published online by Cambridge University Press

our study underscores the urgency for further research in other areas of China. Tibet Plateau areas are the least developed area that only experienced rapid growth in recent years. We believe that the obesity rate of neonates could be much higher in other areas, presenting a great health threat to China[38,39]. Population statistics indicated a total of 10·6 million newborns per year in China[40]. Applying the prevalence rate of 5·4 % as a conservative estimate, there would be at least 572 400 (ranging from 445 200 to 1 088 000) new babies who will have obesity at birth.

Following the life-course perspective, we recommend that effective control of the obesity epidemic must start from the fetus[41,42]. Development of obesity during pregnancy has long been linked to obesity and a series of health consequences in adolescence and adulthood, including metabolic syndrome and CVD[3–5]. There is a rapid increase in overweight and obesity among youth and adults in China[1,2]. One reason for the increase could be in part attributable to the high obesity rate among neonates. This impact will continue if no action is taken.

Dietary factors and the risk of obesity in neonates

First, our results from bivariate, multivariable logistic regression, CART and random forest all indicated that fruit consumption during pregnancy was associated with a substantial reduction in the obesity risk for neonates. Further, this protective effect persisted after controlling for a group of key covariates, including maternal education. For example, according to model 1 with CART, consuming fruits at least once a week was associated with a 4·4 times reduction (OR = 0·202) in the obesity risk in neonates. Studies supporting our research include one cohort study among Chinese in northeast China that reported a negative association between healthy diets of mothers and BMI in infants[12]; another cohort study among Koreans reported a protective relationship between fruit consumption and fetal growth but did not examine its relationship with risk of obesity[43].

Second, results from CART indicated that consuming more eggs were associated with a reduced risk of obesity. Poor nutrition with low birth weight has been well documented[44–47]. Our study detected the impact of good nutrition in reducing the risk of obesity in neonates, this is consistent with reported studies in Tas-mania, Australia[48].

Third, this study revealed that some traditional Tibetan dietary products, although practiced only by a few women, were associated with an increased risk of obesity in neonates. For example, if a less educated mother (< 9 years of education) consumed samba on a weekly basis or more, her newborns would be 2·58 more times likely to be obese. The high energy provided by the large amount of added butter and sugar in samba due to recent economic growth may explain the association. Although there might be reductions in consuming traditional Tibetan food in the Tibet Plateau region, the impact of traditional food on the obesity risk cannot be ignored.

Fruits, dairy products and eggs were once consumed often only by mothers in a few high-income families in the Tibet Plateau area because of the poor economic status and the difficulties in accessibility. Recently, supplies of these products have been increased greatly along with economic growth. To reduce obesity risk in neonates, intervention programs should encourage pregnant women to consume these obesity-reduction foods for healthy babies.

Maternal education as a protective factor for obesity in neonates

Another important finding of this study is the negative association between maternal education and risk of obesity in neonates. Mothers with middle school or more education were associated with a 4·5 times decrease in the risk. This finding suggests the importance of enhancing maternal education in the Tibet Plateau area for obesity control in neonates and maternal health. Low levels of maternal education are reported to be associated with low birth weight and high infant mortality[49,50]. Our study is the first to detect that low maternal education is a risk factor for obesity in neonates.

The relationship between maternal education and obesity in neonates remains unclear, and a lot of research studies are needed. An Australian study found no association between maternal education level and birth outcomes, whereas pre-pregnancy BMI did exhibit an influence[51]. This contradicts our findings, possibly due to the unique characteristics of our study population. In our research, we noted an impact of maternal education on neonatal obesity, potentially influenced by significant disparities in education levels between Han and Tibetan populations (Tibetan: 57·1 % with less than 9 years of education, compared with Han: 17·1 %). Additionally, there exists an interaction between pre-pregnancy BMI and ethnicity, which to some extent influenced our analysis outcomes. Moreover, our population generally exhibits lower pre-pregnancy BMI (mean: 21·0). Most prior studies have predominantly focused on maternal obesity leading to neonatal obesity, which may not apply to our population[52]. Therefore, it is imperative to conduct further research to explore whether mothers with more education may not adhere to the norm of having a ‘large baby’, less likely to consume traditional foods, such as samba, and pay more attention to a healthy diet. Additional studies are needed to examine this important factor and potential mechanisms underlying the relationship between maternal education and obesity risk in neonates. Despite many unknowns, room to improve maternal education is enormous in the Tibet Plateau area where more than 57 % of Tibetan mothers have received education less than 9 years even today. In addition to the quality of life, enhancing maternal education will be an intervention to reduce neonatal obesity in a short term and population obesity in the long term for residents in Tibet Plateau areas.

Limitations

Several limitations need to be addressed. First, we conducted the study in the Tibet Plateau areas with rather limited technologies and resources despite recent growth in economy. Although we devoted much effort to combatting a number of challenges and barriers in completing the planned research, still a small number of participants were lost to follow-up. Of those who completed the follow-up, a small portion did not provide complete data. Second, we assessed dietary practice during pregnancy through self-recall. Despite wide use of the method in research, we have to admit that recall bias cannot be ruled out. Also, most mothers were recruited close to term. Dietary patterns across gestation may have changed close to term, which may not be captured in the current study. Lastly, although CART is a powerful tool to detect hierarchical nested relationships, but this machine learning method is data driving in nature, thus can best be used as a complementary approach to many conventional statistical methods such as logistic regression and Poisson regression.

Conclusions

In conclusion, obesity in neonates is prevalent in the study population. Promoting a healthy diet during pregnancy including increasing the intake of fruits and reducing the intake of traditional Tibetan food and strengthening maternal education could be part of the life-course strategies for obesity control in this area.

Acknowledgements

We would like to express our sincere gratitude to the Professor Chen Xinguang. It is with great sadness that we acknowledge Professor Chen's passing away. His significant contributions to this paper, unwavering pursuit of academic excellence and strong commitment to nurturing young scholars will continue to profoundly influence us. We are deeply grateful for his invaluable contributions to this work and his lasting impact on the academic community. We thank Guolian Qi, Min He, Jinxue Wang and Runhua Li from Qinghai University and all of the medical care personnel in the obstetrics department of Qinghai Red Cross Hospital and Nangqian People's Hospital for their help and support of this study.

The study was funded by the National Science Foundation of China (grant number 81860579) and Natural Science Foundation in Qinghai (grant number 2019-ZJ-932Q). This work was also partly supported by the Danone Nutrition Center (grant number DIC 2018–08) and the Medical College of Qinghai University (foundation grant number 2019-kyt-02).

W. P., X. C. and Y. W.: designed the research. W. P., J. Z., X. W. and L. W.: investigation and resources. X. T., X. C., B. Z., M. Z. S. and W. P.: writing – original draft preparation. B. Z. and X. T.: formal analysis. X. T., R. X. and W. J.: literature search. X. T., B. Z., H. X., B. Z., X. S., Y. X., Y. W. and W. P.: writing – review and editing. All authors have read and agreed to the published version of the manuscript.

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics approval was granted by the Ethics Committee of the Medical College at Qinghai University, Qinghai Province, China (Approval No: 2018–36). Informed consent was obtained from all subjects involved in the study.

The data used in this study can be obtained by contacting the corresponding author.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114524002009

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