Relationship between Maternal Meat Consumption during Pregnancy and Umbilical Cord Ferritin Concentration

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Research

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Abstract

Background

Nutrition during pregnancy impacts the health of the fetus and the newborn, with effects at the epigenetic level determining long-term neurological consequences. Iron requirements in pregnancy are estimated at 27 mg/day. The best absorbed heme iron is found in meat: beef, pork, poultry, and fish. The determination of ferritin in umbilical cord blood can be used to assess iron deposits reached during the fetal stage. Ferritin levels were associated with long-term effects on child development.

Methods

A descriptive, observational study with prospectively collected data was carried out during one-year period at the Department of Neonatology of the Pereira Rossell Hospital Center (CHPR) in Montevideo, Uruguay. A total of 188 patients met the inclusion criteria. Umbilical cord blood was drawn following a strict cord clamping after one minute of life. Ferritin was measured using the chemoimmunofluorescence method. A maternal nutritional survey was applied, using a qualitative-quantitative form measuring the frequency of consumption of iron source foods and approximated quantities consumed during the last trimester of pregnancy. This survey was focused on maternal consumption of beef as the major heminic iron source in Uruguay. The relationship between these variables was analysed.

Results

Latent iron deficiency (ferritin in the umbilical cord <100 ng / ml) was associated with less consumption of beef during pregnancy. Fisher p-value: 0.0133, OR: 3.71, 95% CI [1.25 - 11.05].

Conclusions

This study considers adequate evidence that low levels of total iron and meat consumption during pregnancy will determine an increased risk of latent iron deficiency and lower levels of ferritin in newborns, and therefore, greater risk of long-term adverse effects on myelination and neurocognitive development.

Introduction

The diet during pregnancy constitutes an environmental factor that has impact on the health of the fetus and the newborn. Eating habits during pregnancy will have consequences at the epigenetic level, determining long-term consequences on neurological development. (1) (2) During pregnancy, an adequate intake of energy, protein, minerals and vitamins must be achieved for which a daily consumption of fruits, vegetables and meats is essential.

Lack of information about an adequate diet in pregnancy, as well as the eating habits of families could have negative consequences on child development. (3) Data provided by the World Health Organization report that worldwide 30% of women between the ages of 15 and 49 suffer from anemia, which corresponds to 468 million. (4) Iron requirements in pregnancy are estimated at 27 mg/day. (5) To achieve this level of iron consumption, adequate nutritional advice, government policies aimed at fortifying food and supplemental iron intake are necessary. Iron is present in the mineral form as non-heme iron in vegetables and in the organic form known as heme iron in meats. Absorption of non-heme iron is lower than heme iron. The sources of heme iron are beef, pork, poultry, and fish. Eating meat and fish in portions greater than 50 g per day significantly increases the absorption of iron present in vegetables. (6)(7)

There are recommendations to reduce meat consumption (8) but these could have a negative impact on the intake of iron, vitamin B12 and zinc. (9) In the United Kingdom, total iron intake in 48% of girls aged between 11 to 18 and 27% of women aged between 19 to 64 years is inadequate. It was also observed that adults ingest a lower level than recommended zinc, selenium and vitamin D. These micronutrients are accessible when consuming red meat. (10) In the United Kingdom, women who consumed less than 40 g of red meat per day were at increased risk of zinc and vitamin D deficiency. (11)

Multiple studies related the level of umbilical cord ferritin with the levels of iron deposits reached during the fetal stage. The determination of ferritin in umbilical cord blood can be used to assess iron deposits in the body. Umbilical cord ferritin levels were associated with long-term effects on childhood development. (12) (13) The last trimester of pregnancy is a critical time for iron deposition, and therefore, premature newborns have lower levels of ferritin in the umbilical cord. Cord ferritin values are inversely related to gestational age. (14) The lack of standard ranges of normality and abnormality to describe iron status from ferritin umbilical cord levels for healthy term infants is still a weakness. The cut-off level of umbilical cord ferritin level to define Latent Iron Deficiency (LID) is taken to be under 100ng/ml. (15)

Uruguay is a country that produces high quality red meat, which is accessible to the population. In addition, it is the country with the greatest consumption of beef per capita in the world, but there are no studies to date investigating the level of meat consumption during pregnancy and its relationship with the iron capital of the fetus.

The aim of the study was to assess the relationship between umbilical cord ferritin and meat consumption during pregnancy.

Methodology

A descriptive, observational study with prospective acquisition of cases was carried out over a period of one year at the Department of Neonatology of the Pereira Rossell Hospital Center (CHPR), in Montevideo, Uruguay. The CHPR obstetric/perinatal department is the most important in the country, assisting around 6000 births per year from the low-income population (6279 births were registered in 2018. Data provided by the Perinatal Computer System, Uruguay). The project was carried out in the following stages: a) Pilot Study: 15 patients were included during a week-period, this phase of the study allowed the verification of all processes, procedure adjustments and training of the team. b) Execution: it involved the inclusion of study samples with measurement of umbilical cord ferritin at birth, the application of the nutritional survey to mothers and the posterior data analysis.

The inclusion of patients was performed according to a checklist system designed to verify the absence of exclusion criteria. during this process and verified the strict match of the inclusion criteria before and after labor. The study was approved by the CHPR’s ethics committee. All patients gave their written informed consent.

Participants

The study included term and healthy newborns, with a gestational age equal to or greater than 37 weeks’, from families established addresse in the metropolitan area of Montevideo, who were born in CHPR’s obstetrics/perinatal department during the one-year study period. The exclusion criteria was: newborns born before 37 weeks gestation, severe small for gestational age (less than Percentile 3 of the Fenton charts), major congenital malformations, neonatal depression at birth, risk of specific/nonspecific connatal infection, multiple pregnancy infants, children born to mothers who received iron intravenously, mothers with problematic consumption of psychoactive substances for recreational use, mothers with insulin-requiring diabetes and those newborns who had an early clamping of the umbilical cord, before the first minute of life.

A total of 220 newborns fulfilled the inclusion criterio, 14 did not give their informed consent therefore were directly excluded. In relation to umbilical cord ferritin samples: 2 were not processed, 4 were considered as outliers since results went outside from the lower or upper limits described in the literature. The nutritional survey was applied to 206 mothers, of whom 12 were discarded, considering that the answers offered unreal data in relation to the quantitative variables. Finally, a bivariate analysis of 188 patients with the corresponding variables was possible (Figure 1.)

Regarding the hemogram samples: 23 were not processed due to the inadequate state of the sample and 167 were processed.

Because there are no studies to date investigating the association between beef consumption during pregnancy and ferritin levels at birth, we cannot report information on the proportion of maternal exposure to consumption of beef in the cohort or the OR value to calculate the sample size. In the present study, we use an empirical sample size.

Data Collection

Through a face-to-face interview with the patients, data was collected on the demographic characteristics. Information on the maternal baseline health history (reproductive history, pathological history, lifestyle, exposure to toxic substances, complications during pregnancy, and others) aa well as neonatal relevant data were obtained from medical records. In addition, a family socioeconomic assessment was carried out through a direct interview with the newborns' parents.

Laboratory analysis

Succeeding a strict cord clamping following one minute of life, umbilical cord blood was drawn, and hemogram and ferritin tests were performed. All samples were collected by trained health personnel. The umbilical cord blood was collected in a heparinized tube to perform the hemogram and a dry tube for the measurement of ferritin. These samples were transferred to the CHPR's on-call laboratory, where they were stored for a period of less than 24 hours, refrigerated at 4–8ºC, until they were processed. Hemograms were processed in DXH800 hematological quantifier and ferritin was measured by the Cobas 6000 automated equipment, which uses the chemoimmunofluorescence method. All samples were processed following the same protocol. Samples with result values out of the minimun or maximun described values, were processed a second time with the same laboratorial techniques and the results were the same, so they were excluded as outlier data.

Nutritional Interview

A maternal nutritional survey was applied, using a qualitative-quantitative form of frequency of consumption of iron source foods and an approximation of the portions consumed during the last 3 months of pregnancy. The first part of the form collected quantitative information about heme iron sources from animal origin (beef, organ meats, chicken, fish, and pork), non-heme iron sources from vegetable origin (chard and spinach, legumes) and iron fortified foods (products made from iron-fortified wheat flour and iron-fortified dairy products). For a most reliable data collection collection of data, a photographic atlas Visual atlas Guide of food portions and weights (ILSI Argentina, 2018) was used to estimate the weights and volumes of food, preparations and beverages. Mothers' consumption of pharmacological iron supplement was also explored qualitatively in two groups with good and poor adherence. The total grams of food consumed daily were obtained from the frequency of consumption form and from these the total iron of the diet was calculated, determining both the heme and non-heme fraction. The focus of the results is highlighted in the analysis of beef consumption, since this is the highest consumed in the uruguayan population, consolidating itself as the main source of heme iron. The responses to this survey depended on the mothers' recall ability and estimation of proportions.Twelve extraordinary quantitative responses were identified, so the interview with the mothers was therefore repeated and given that the responses on the second opportunity did not vary, it was decided to exclude those responses from the analysis.

Data Analysis

It was started by controlling the quality of the data collected, it was analyzed through an exploratory analysis of its consistency, outliers were identified, they were confirmed or were excluded when performing a second analysis of the data sources. For continuous variables, normality was tested graphically and using the Shapiro-Wilk test. When the hypothesis of normality was rejected, the data were presented with the median, interquartile range (IIQ: 25–75)), and range with minimums and maximums (Mn-Mx). Qualitative variables were presented as absolute frequency and percentages. The association between the considered exposure factors and the ferritin levels lower or higher than 100ng / ml was tested by means of a bivariate analysis. The Chi-square independence test or Fisher's exact test for the categorical variables and the Test were used. Wilcoxon-Mann-Whitney waws used for continuous variables. Risk was estimated using OR and their respective 95% CI confidence intervals. A significance level of 5% was considered. The adjustment of a logistic regression model that considers the variables that in the bivariate analysis had a p value <0.20 that allows explaining and predicting cord ferritin levels below or above 100 ng/ml was explored.

Statistical analysis was performed with the R program (R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.)

Results

Characteristics of the study population

The demographic characteristics, maternal and neonatal health records data, and iron consumption are summarized in Table 1. Additionally the "p" value of the Fisher Test for each variable is presented in the last column of the same table in relation to Newborn umbilical cord ferritin levels under 100 ng/ml or over 100ng/ml, given that umbilical cord ferritin levels below 100 ng/ml are considered diagnostic values for Latent Iron Deficiency (LID). The study population belongs homogeneously to a group of low- income society strata. Over 70% of mothers are categorized in the age group of over 25 years and under 35 years, no significant relationship (p = 0.595) was found between maternal age and LID. The identification of race/ethnicity of the mother evaluated by skin tone could not establish an association with the LID. Only 10% of the maternal population had access to an educational level of more than 12 years of schooling, and this variable found no association with LID (p: 0.7713). Moreover, records the status of anemia or non-anemia in the third trimester of pregnancy is presented in Table 1, defined by the levels of hemoglobin (Hb) <13 gd / dL and hematocrit (Hto) <33%, only 12.7% of the population was classified into an anemic status; this variable did not demonstrate a statistically significant relationship with the LID (p: 0.2521). The 81.3% of mothers had one or more complications during pregnancy, most of them were urinary tract infections or genital infections, and 15.4% of mothers presented gestational diabetes as a complication in pregnancy (gestacional diabetes is defined as a measure of blood glucose > 92mg/dL) this complication was not associated with LID (p: 0.2411). The dietary characteristics in relation to iron consumption during the third trimester of pregnancy, showed that 99.5% of the mothers had a total iron consumption under than the recommended 27mg/day of total iron during pregnancy (data obtained from estimation of content of iron from foods reported by the mother, during the third trimester of pregnancy, in the diet (heme iron and non-heme iron). Regarding the consumption of iron supplement during pregnancy 81.3% reported receiving the pharmacological supplement adequately (daily supplementation was defined as “adequate” because this is an iron supplementation administration strategy that strengthens maternal adherence) despite high adherence to pharmacological treatment, an association with LID was not established (p: 0.08). The quantitative of parental controls was also not associated with LID (p: 0.6682), in fact, 91% of the population had a well-controlled pregnancy defined as a number of five or more prenatal checkups.

Concerning newborns’ characteristics Table 1. sex of the patients did not showed a significant association between the female sex (51.1%) of the population or the male sex (49.9%) of the population and the DLH (p: 0.5409). From the total of participants, 89.4% had a gestational age (GA) > 37 weeks and with respect to the relationship between weight and GA the 88.3% classified as Adequate for Gestational Age (AGE), none of them were associated with LID. Anemia at birth after measurement of hemoglobin in the umbilical cord <13g/dL occurred in 4.8% of the newborn population, this variable was not significantly associated with LID umbilical cord ferritin values (p: 1.0).

Table 2. shows the variables grouped in the variables in the median, quartiles, minimum and maximum values, in addition to the “n” value for each category. Among the maternal variables are: hemoglobin values in the third trimester of pregnancy (n: 175), beef consumption, total iron consumption and heme and non-heme iron differentiation from 188 mothers whose responses to the nutritional survey were validated, excluding outliers and unreliable responses for providing extraordinary consumption quantities. The median value for Maternal Hemoglobin in the last trimestre of pregnancy this variable was 11.9g/dL; for maternal beef it was 61.8 gr/day (35.8gr/day - 238.1gr/day). And among the variables of the neonates, the hemoglogin (Hb) (n: 167) and umbilical cord ferritin (n: 188) are grouped, the “n” of both variables is given by the number of samples processed that fulfilled with the quality requirements, outliers were also excluded.

Table 3. presents the association between beef consumption (grams per day) and latent iron deficiency (LID) defined as a level of cord ferritin <100ng/ml. When the maternal consumption of 100gr/day was used as a reference, the risk of LID increased by a proportion of three times the risk among the newborns from mothers with a consumption <100gr/day Fisher’s test p-value: 0.0133 (95% CI 1.25- 11.05) the OR was significantly associated was 3.71.

Table 4. reflects the independence between the maternal variables of beef consumption and adequate pharmacological iron supplementation, there is no evidence to reject independence. Fisher’s test p-value: 0.1747.

Table 1. General characteristics of the population and in categories according to levels of ferritin in the umbilical cord.

Variable	"n"	(%)	LID, Ferritin (< 100ng/ml)	No LID, Ferritin (>100ng/ml)	*p Value*
Total Participants: Maternal Data	188	100	42 (22.3)	146 (77.6)	
Maternal age (years)					0.595
< 20	36	19.1	6 (16.7)	30 (83.3)	
>=20 y <35	138	73.4	32 (23.2)	106 (76.8)	
>=35	14	7.4	4 (28.6)	10 (71.4)	
Race / Ethnicity					
White	135	71.8	30 (22.2)	105 (77.8)	
Mixed	50	26.6	11 (22)	39 (78)	
Black	3	1.6	1 (33.3)	2 (66.7)	
Maternal Educational Level					0.7713
< 12 years	169	89.9	37 (21.9)	131 (78.1)	
>12 years	19	10.1	5 (26.3)	14 (73.7)	
Third trimester maternal anemia*n: 166					0.2521
Anemia	21	12.7	2 (9.5)	19 (90.5)	
No anemia	145	87.3	33 (22.8)	112 (77.2)	
Total iron consumption (mg/day)					
< 27mg/day	187	99.5	42 (22.5)	145 (77.5)	
>27mg/day	1	0.5	0 (0)	1 (100)	
Adequate Iron Supplement					0.08
Yes	134	88.3	25 (18.7)	109 (81.3)	

No	54	28.7	17 (31.5)	37 (68.5)	
Number of pregnancy controls					0.6682
1 a 5	17	9.0	5 (29.4)	12 (70.6)	
More than 5	171	91.0	37 (21.6)	134 (78.4)	
Total Participants: Newborn Data	188	100	43 (22)	155 (78)	
Sex					0.5409
Female	96	51.1	22 (22.3)	74 (77.7)	
Male	92	48.9	20 (21)	72 (79)	
Gestacional Age (GA)					0.1613
37 weeks	20	10.6	7 (35)	13 (65)	
More than 37 weeks	168	89.4	35 (20.8)	133 (79.2)	
Relationship weight at birth / (GA)					
Small for GA	15	8.0	5 (33.3)	10 (66.7)	
Adequate for GA	166	88.3	34 (20.5)	132 (79.5)	
Big for GA	7	3.7	3 (42.9)	4 (57.1)	
Anemia at birth (umbilical cord Hb)					1.0000
Anemia (<13 g/dl)	8	4.8	1 (12.5)	7 (87.5)	
No anemia (>=13 g/dl)	159	95.2	35 (22.0)	124 (78.0)	

Table 2. Grouping of Variables

Variables	Minimum	First quartile	Median	Third quartine	Maximum	"n"
Maternal Variables: Third trimester maternal hemoglobin	8.8	11.4	**11.9**	12.5	16.2	175
Maternal beef consumption (gr per day)	0	35.8	**61.8**	97.7	238.1	188
Total iron (mg/day)	1.6	5.9	**9.2**	13.4	34.7	188
Heminic iron (mg/day)	0.1	0.7	**1.0**	1.6	5.2	188
Non heminic iron (mg/day)	1.3	5.1	**8.2**	11.9	29.6	188
Newborn Data: Umbilical cord hemoglobin (g/dL)	11.2	14.1	**15.2**	16.25	19.2	167
Umbilical cord ferritin (ng/ml)	24	111.8	**163**	225	478	188

Table 3. Relationship between maternal beef consumption and latent deficit levels of ferritin

Variable	“n”	(%)	LID - Ferritin (<100ng/ml)	Non LID – Ferritin (>= 100ng/ml)	P Value
Total	188	100	42	146	
Beef consumption (grams per day)			22%	78%	0.0133
Less than 100gr/day	143	76.1%	38 (26.6)	105 (73.4)	
100 gr/day or more	45	23.9%	4 (8.9)	41 (91.1)	
Fisher valor-p: **0,0133;** OR**: 3.71;** IC al 95%: **[1,25 - 11,05)**					

Table 4. Independence between beef consumption and pharmacological iron supplementation

Variable	“n”	(%)	Adequate iron supplementation	Inadequate iron supplementation	p Value
Total	188	100	134	54	
Beef consumption (grams per day)			88.3%	28.7%	0.851
Less than 100gr/day	143	76.1	101 (70.6)	42 (29.4)	
100 gr/day or more	45	23.9	4 (8.9)	12 (26.7)	

Discussion

In this study, we describe the positive association between the maternal meat consumption during the third trimester of pregnancy and the values of ferritin in the umbilical cord of the newborn. In general, we observed that maternal consumption of meat (beef) under than 100gr/day increased the risk of a latent iron deficiency (LID) (ferritin <100ng/ml). Currently to our knowledge, there are no studies to date that have evaluated this association. In our study, based on a sample of 188 patients (mothers/newborns), we found a risk of LID approximately three times greater in the children of mothers whose beef consumption is <100gr/day. Iron and ferritin levels in the fetus depend directly on the maternal contribution and therefore on its deposits. When the maternal iron supply is insufficient, the fetus prioritizes its use for hemoglobin synthesis for its subsistence, leaving behind the development of the central nervous system. Therefore, processes of neuronal development, synthesis of neurotransmitters, the myelin and glia cells production are affected. Alterations that occur in neurogenesis, mediated by the deficit of ferritin during embryonic and fetal life will determine permanent consequences on neurocognitive development from birth and throughout life (16) (17). Serum ferritin levels are directly related to iron deposits (18) (19). Multiple studies related the level of umbilical cord ferritin with the levels of iron deposition reached during the fetal stage. The determination of ferritin in umbilical cord blood can be used to assess iron deposits in the body (16)(17) (20). To our knowledge, this study is the first to asses the association between consumption of beef during the third trimester of pregnancy and the level of umbilical cord ferritin in newborns. We found that there was no relationship between regular supplemental iron intake with the level of ferritin in the umbilical cord. Iron intake levels during pregnancy are not only achieved by dietary intake that is why supplemental iron intake is required to decrease the incidence of maternal anemia, 88.3% of the participants had an adequate adherence to pharmacological supplementation of iron and this variable seems to be independent of beef consumption (21) (22). Ferritin levels are associated with better white matter myelination results at the central nervous system level (23). On the other hand, iron deficiency determines disruption in myelination of the axons and development of the auditory nerve (24) (25). Ferritin levels in the umbilical cord are higher than in other life stages, and are associated with iron deposits at birth (20). Latent iron deficiency is defined by low ferritin levels without the presence of anemia and is associated with developmental disturbances (26)(27). Multiple studies demonstrated deleterious effects of latent iron deficiency on long-term development (13)(28). The deleterious effects of iron deficiency described in animal studies have been validated in humans. There is growing evidence associating iron deficiency in early childhood with worse motor, cognitive, social and affective patterns that can persist into adulthood even after supplementation (29) (30). One of this study strengths is that it is a first-of-its-kind poblational study with cuantification of maternal beef consumption, other iron containing foods, and pharmacological supplementation of iron, following strict conversion standards, minimizing the chance that the results might be altered by any confounder factors and allowing us investigate the relationship between maternal consumption of beef and levels of umbilical cord ferritin, with the adjustment of possible interference factors. One of the strategies to decrease the ferritin deficiency is the timing of the umbilical cord clamping. Early clamping of the umbilical cord is associated with impaired white matter myelination in the central nervous system at four months of age. These adverse results are mediated by low ferritin levels. (30) (31). Our study controlled this confounder by performing a timely clamping of the umbilical cord and the early clamping of the umbilical cord was considerared as exclusion criteria. In addition, there was carried out a strict control of the quality umbilical cord blood samples and its processing, through obtaining the sample by trained health personnel for this function, using the same quality control system and processing technique. Regarding to the nutritional survey, the information collected about the maternal diet consumption specifies the frequency of the consumption of food iron sources and their weight estimation. Therefore, we used nutrient-based adjustment procedures in this study. However, this study also has several limitations. An intrinsic limitation of the study is the memory bias. In order to control this bias, we determined whether there was a significative difference in the distribution of maternal consumption of meat compared to the average of average consumption described for the Uruguayan population (268,2grams perday in 2018 - National Survey). Distribution of beef consumption between LID cases and cases without LID is similar, which suggests the memory recall bias in this study is low. As well as these, to further minimize recall bias, participants were interviewed in delivery rooms before the start of labor or after the immediate postpartum period. And the interviewers helped confirm the study period, the third trimester of pregnancy, using the date of the last menstrual period, if it was reliable or from the date of delivery retrospectively according to the gestational age of the newborn. Moreover, sample size for some subgroups defined by other maternal and neonatal characteristics was small, limiting our capability to detect statistical differences or associations. Another limitation can be that attributable to the questionnaire strategy of obtaining most of the qualitative data of the study. We did not measure with a blood laboratory test the maternal iron deficiency in the third trimester of pregnancy. Finally, we consider that the results of this study cannot be generalized to the general country population, given that our study population comes from a low income strata that does not represents diet or other eating habits in the population of medium or high income level, who one can presume, has a diet at least more varied.

Conclusions

This study cannot recommend which is the daily beef consumption related to an adequate level of ferritin in the umbilical cord, However, it sheds light on the fact that lower levels of total iron intake and beef meat consumption during pregnancy will determine an increased risk for presenting latent iron deficiency and lower levels of ferritin in cord blood, with the possible effects throughout life on myelination, neurocognitive development and worse performance throughout life.

Abbreviations

CHPR: Hospital Center Pereira Rossell

INAC: Instituto Nacional de Carnes / National Institute of Meats

LID: Latent Iron Defficiency

Hb: Hemoglobin

Hto: Hematocrit

GA: Gestacional Age

Declarations

• *Ethics approval and consent to participate*

This study was approved by the Ethics Committee of the Pereira Rossell Hospital Center. All participants provided written informed consent.

• *Consent for publication*

Not applicable

• *Availability of data and materials*

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

• *Competing interests*

The authors declare not to have any conflicts. Álvarez Caldeyro Barcia Fundation did not participate in the design of the study neither in the interpretation of the data.

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• *Authors' contributions*

MMoraes designed the study. MMoraes, FCastedo, THerrera, CVazFerreira, EArocena, AGirona and FCeriani developted the study; AGirona and FCeriani designed the nutritional survey, organized nutritional data collection and its processing. VColistro and FCavalleri analyzed the data, contributed to the acquisition and cleaning of data. FCastedo established the population selection and umbilical sample collection system and drafted the manuscript; NFares verified systematically the quality of the umbilical cord samples processing. MMoraes, THerrera and CVazFerreira contributed to the revision of the manuscript. All authors read and approved the final manuscript.

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References

1. Georgieff MK. Iron assessment to protect the developing brain. Am J Clin Nutr [Internet]. 2017 Dec 1 [cited 2020 Apr 8];106(Supplement 6):1588S–1593S. Available from: http://ajcn.nutrition.org/lookup/doi/10.3945/ajcn.117.155846
2. Walker SP, Wachs TD, Meeks Gardner J, Lozoff B, Wasserman GA, Pollitt E, et al. Child development: risk factors for adverse outcomes in developing countries. Vol. 369, Lancet. 2007. p. 145–57.
3. Cusick SE, Georgieff MK. The Role of Nutrition in Brain Development: The Golden Opportunity of the "First 1000 Days." J Pediatr [Internet]. 2016 Aug 1 [cited 2020 Apr 8];175:16–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27266965
4. Salud Y Bienestar De La Población S LA. IMPACTO DEL CRECIMIENTO Y DESARROLLO TEMPRANO PERSPECTIVAS Y REFLEXIONES DESDE EL CONO SUR.
5. Front Matter | Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc | The National Academies Press [Internet]. [cited 2020 Apr 8]. Available from: https://www.nap.edu/read/10026/chapter/1
6. Baech SB, Hansen M, Bukhave K, Jensen M, Sørensen SS, Kristensen L, et al. Nonheme-iron absorption from a phytate-rich meal is increased by the addition of small amounts of pork meat. Am

J Clin Nutr [Internet]. 2003 Jan [cited 2020 Apr 8];77(1):173–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12499338

7. Navas-Carretero S, Pérez-Granados AM, Sarriá B, Vaquero MP, Carbajal A, Pedrosa MM, et al. Oily Fish Increases Iron Bioavailability of a Phytate Rich Meal in Young Iron Deficient Women. J Am Coll Nutr. 2008 Feb 1;27(1):96–101.
8. Red meat and the risk of bowel cancer - NHS [Internet]. [cited 2020 Apr 8]. Available from: https://www.nhs.uk/live-well/eat-well/red-meat-and-the-risk-of-bowel-cancer/
9. SACN: Iron and Health. [(accessed on 18 July 2017)]; Available online: [Internet]. 2010 [cited 2020 Apr 8]. Available from: www.sacn.gov.uk
10. Bates B., Cox L., Nicholson S., Page P., Prentice A., Steer T. SG. National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013—2013/2014) [Internet]. 2016 [cited 2020 Apr 8]. Available from: www.facebook.com/PublicHealthEngland
11. Derbyshire E. Associations between red meat intakes and the micronutrient intake and status of UK females: A secondary analysis of the UK national diet and nutrition survey. Nutrients [Internet]. 2017 Jul 18 [cited 2020 Apr 8];9(7). Available from: http://www.ncbi.nlm.nih.gov/pubmed/28718824
12. Amin SB, Orlando M, Eddins A, MacDonald M, Monczynski C, Wang H. In Utero Iron Status and Auditory Neural Maturation in Premature Infants as Evaluated by Auditory Brainstem Response. J Pediatr. 2010 Mar;156(3):377–81.
13. Tamura T, Goldenberg RL, Hou J, Johnston KE, Cliver SP, Ramey SL, et al. Cord serum ferritin concentrations and mental and psychomotor development of children at five years of age. J Pediatr [Internet]. 2002 Feb [cited 2020 Apr 8];140(2):165–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11865266
14. Lorenz L, Peter A, Poets CF, Franz AR. A review of cord blood concentrations of iron status parameters to define reference ranges for preterm infants [Internet]. Vol. 104, Neonatology. S. Karger AG; 2013 [cited 2020 Apr 8]. p. 194–202. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23989077
15. Anker SD, Comin Colet J, Filippatos G, Willenheimer R, Dickstein K, Drexler H, et al. Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency. N Engl J Med [Internet]. 2009 Dec 17 [cited 2020 May 19];361(25):2436–48. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa0908355
16. Alwan N, Hamamy H. Maternal Iron Status in Pregnancy and Long-Term Health Outcomes in the Offspring. J Pediatr Genet [Internet]. 2015 Jul 31 [cited 2020 Apr 8];04(02):111–23. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27617121
17. Delaney KM, Guillet R, Fleming RE, Ru Y, Pressman EK, Vermeylen F, et al. Umbilical Cord Serum Ferritin Concentration is Inversely Associated with Umbilical Cord Hemoglobin in Neonates Born to Adolescents Carrying Singletons and Women Carrying Multiples. J Nutr [Internet]. 2019 [cited 2020 Apr 8];149(3):406–15. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30770543

18. OMS. Concentraciones de ferritina para evaluar el estado de nutrición en hierro en las poblaciones. Sist Inf Nutr sobre Vitaminas y Minerales [Internet]. 2011 [cited 2020 Apr 8]. p. 1–5. Available from: https://www.who.int/vmnis/indicators/serum_ferritin_es.pdf
19. M. W. Indicators of the iron status of populations: ferritin.
20. Siddappa AM, Rao R, Long JD, Widness JA, Georgieff MK. The assessment of newborn iron stores at birth: A review of the literature and standards for ferritin concentrations [Internet]. Vol. 92, Neonatology. 2007 [cited 2020 Apr 8]. p. 73–82. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17361090
21. Del Riego MG. Nutrición y Embarazo. [Internet]. Vol. 41, Revista Peruana de Ginecología y Obstetricia. 1995 [cited 2020 Apr 8]. Available from: http://www.msal.gob.ar/images/stories/bes/graficos/0000000315cnt-a11-nutricion-y-embarazo.pdf
22. Health Organization Regional Office for Europe W. Good Maternal Nutrition The best start in life [Internet]. 2016 [cited 2020 Apr 8]. Available from: http://www.euro.who.int/pubrequest
23. Georgieff MK. Iron assessment to protect the developing brain. In: American Journal of Clinical Nutrition [Internet]. Oxford University Press; 2017 [cited 2020 Apr 8]. p. 1588S–1593S. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29070550
24. Lee DL, Strathmann FG, Gelein R, Walton J, Mayer-Pröschel M. Iron deficiency disrupts axon maturation of the developing auditory nerve. J Neurosci [Internet]. 2012 Apr 4 [cited 2020 Apr 8];32(14):5010–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22492056
25. Todorich B, Pasquini JM, Garcia CI, Paez PM, Connor JR. Oligodendrocytes and myelination: The role of iron [Internet]. Vol. 57, GLIA. 2009 [cited 2020 Apr 8]. p. 467–78. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18837051
26. Choudhury V, Amin SB, Agarwal A, Srivastava L, Soni A, Saluja S. Latent iron deficiency at birth influences auditory neural maturation in late preterm and term infants. Am J Clin Nutr [Internet]. 2015 Nov 1 [cited 2020 Apr 8];102(5):1030–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26310540
27. Amin SB, Orlando M, Wang H. Latent iron deficiency in utero is associated with abnormal auditory neural myelination in ≥35 weeks gestational age infants. J Pediatr [Internet]. 2013 Nov [cited 2020 Apr 8];163(5):1267–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23932211
28. Lozoff B, Georgieff MK. Iron Deficiency and Brain Development [Internet]. Vol. 13, Seminars in Pediatric Neurology. 2006 [cited 2020 Apr 8]. p. 158–65. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17101454
29. Grantham-McGregor S, Ani C. A Review of Studies on the Effect of Iron Deficiency on Cognitive Development in Children. J Nutr. 2001 Feb 1;131(2):649S–668S.
30. Congdon EL, Westerlund A, Algarin CR, Peirano PD, Gregas M, Lozoff B, et al. Iron deficiency in infancy is associated with altered neural correlates of recognition memory at 10 years. J Pediatr. 2012 Jun;160(6):1027–33.

31. Mercer JS, Erickson-Owens DA, Deoni SCL, Dean DC, Collins J, Parker AB, et al. Effects of Delayed Cord Clamping on 4-Month Ferritin Levels, Brain Myelin Content, and Neurodevelopment: A Randomized Controlled Trial. J Pediatr. 2018 Dec 1;203:266–272.e2.

Figures

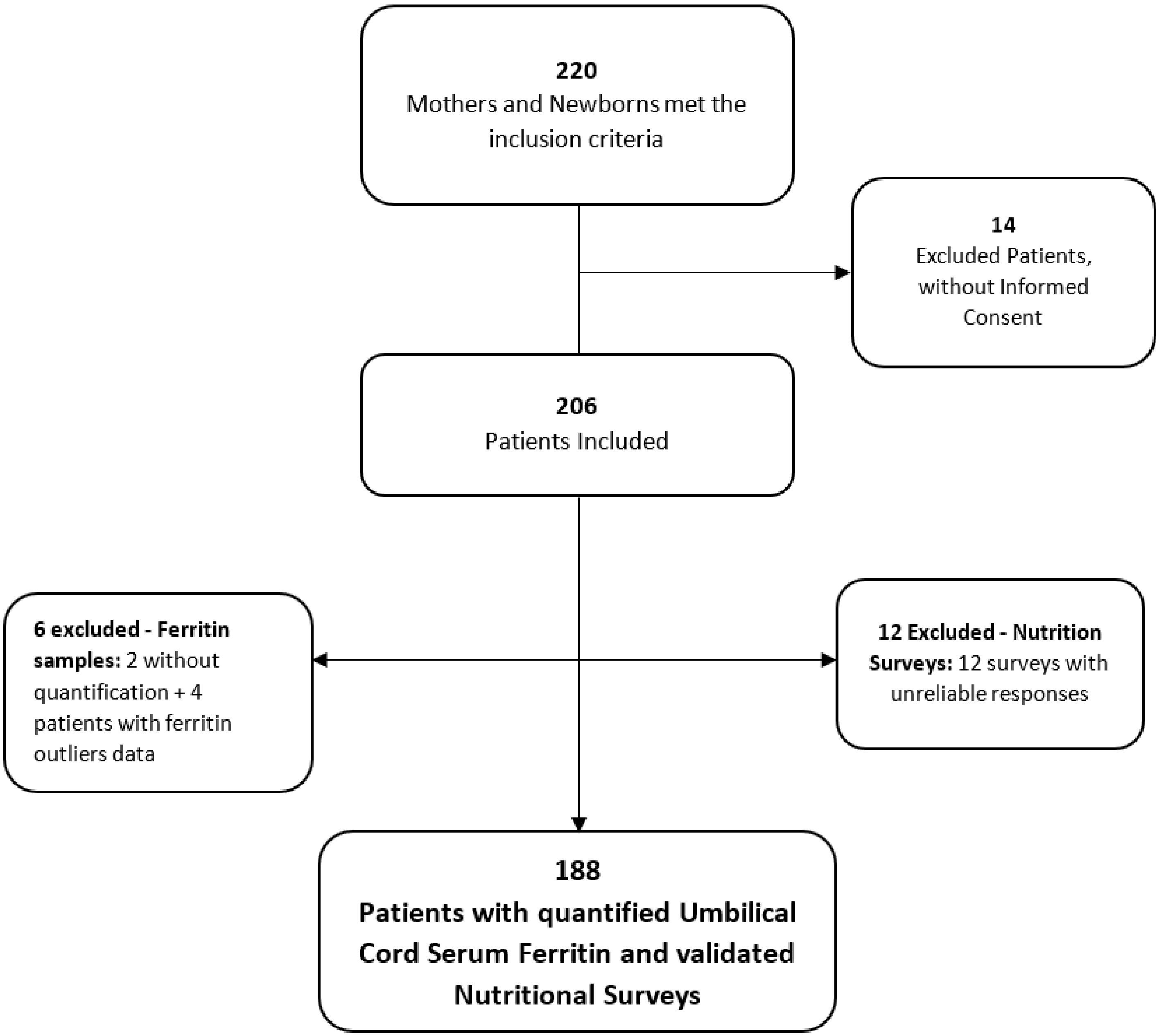

Figure 1

Study Population

Supplementary Files

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- STROBEchecklistMeatConsumptionandFerritin.docx