SUPPLEMENTARY MATERIALS

Establishing a Multifaceted Comprehensive Maternity Cohort Facilitates Understanding of How Environmental Exposures Impact Perinatal Health

Cohort Profile: Zhejiang Environmental and Birth Health Research Alliance (ZEBRA) Maternity Cohort

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Supplementary Contents

Content S1 | Detailed Reasons for Choosing Zhejiang Province as Pilot Site

Zhejiang Province, located in the Yangtze River Delta region on the east coast of China, spans 105,500 square kilometers (longitude 118°01'–123°10' E, latitude 27°02'–31°11' N). The province lies within the Humid Subtropical Climate Zone, characterized by significant monsoon alternation, moderate annual temperature, four distinct seasons, abundant sunshine, and rainfall. However, environmental problems, particularly air pollution, persist in Zhejiang Province. Despite effective reduction campaigns on several criteria air pollutants (i.e. PM_{10}, sulfur dioxide, nitrogen dioxide, and carbon monoxide) in recent years,[1] the excess rates of $PM_{2.5}$ and ozone (O_3) remain relatively high, at 6.8% and 4.9%, respectively, with peak O_3 concentrations reaching 60–80 ppb.[2] Such high O_3 pollution poses population health hazards[3] and warrants future environmental epidemiological studies in Zhejiang Province.

The selection of Zhejiang as a priority province for the pioneering study of the large maternity cohort is justified by several reasons. Firstly, clinical treatment and primary care must take precedence over data-driven empirical studies, in keeping with the principle of humanism. In cases of limited resources, hospitals, medical schools, and medical research institutes must prioritize the prevention of maternal and neonatal deaths. While China has achieved significant reductions in maternal mortality rates through years of medical staff efforts, significant heterogeneity persists in the geographical distribution of mortality rates. Regions with low maternal mortality rates are concentrated in the east and southeast of China. In Zhejiang, the maternal and infant mortality rates were controlled within 7/100,000 and 5‰, respectively, maintaining the lowest levels in China. However, in southwest China, such as Yunnan, the maternal mortality rate was four times higher than that in Zhejiang Province in 2012. Therefore, for areas with high maternal mortality, the focus of medicine is still on the care of pregnant women and newborns. When the mortality rate is reduced to the forefront level globally, research based on data will be carried out.

Secondly, Zhejiang's critical role in the economic development of China also justifies its selection. In 2020, Zhejiang's GDP reached 936.7 billion US dollars, accounting for 6.4% of the nation-level total GDP and ranking fourth among all provinces. Zhejiang's economy even surpassed that of the Netherlands (909.1 billion US dollars), which ranks 17th worldwide. This flourishing economy also promotes the popularization of digital medicine, which provides a solid foundation for epidemiological studies, such as the ZEBRA Maternity Cohort and the Zhejiang Birth Cohort (ZBC).

Thirdly, geographical coverage and population representativeness were considered in the selection process. Beijing, Shanghai, and Zhejiang are the provincial regions with the lowest maternal and infant mortality rates in China, with the first two regions being municipalities directly under the Central Government. Beijing and Shanghai have attracted individuals with the highest education and economic status in China, with territorial areas of 16,411 and 6,340 square kilometers, respectively, which is far less than that of Zhejiang Province (101,800 square kilometers). Hence, Zhejiang Province is the ideal location to carry out digital maternal health public health research based on the current situation in China. The ZEBRA study also promises to share clinical experience and research findings with other regions of the country and even the world through the China Cohort Consortium (CCC), with the radiation driving less-developed regions to achieve geographical health justice.

Content S2 | Cohort Follow-up Design

The postpartum follow-up of the ZEBRA maternal cohort is an important aspect of the study, which continues until six months after delivery. The follow-up mainly includes the following procedures:

(1) Within three days after delivery, the mothers undergo a set of fundamental physical examinations. These may include, but are not limited to, a blood routine test (which is decided independently by the obstetrician based on the condition of the pregnant woman), blood pressure measurement, and cardiac function evaluation. If the pregnant woman has pregnancy complications, targeted blood tests may be conducted.
(2) We recommend that mothers undergo a hospital follow-up in the sixth week after delivery, which includes an assessment of weight recovery, blood pressure, and uterine involution. If the pregnant woman has pregnancy complications, targeted blood tests may be conducted.
(3) We advise the mothers to report any abnormal health conditions within six months after delivery to the hospital by telephone. If the hospital has not received any such report, it will conduct a unified telephone follow-up in the sixth month, including an assessment of the mother's blood pressure, weight, and breastfeeding. If the mother is healthy, the cohort follow-up ends, and the participants exit the cohort. However, if the mother has abnormal conditions or shows any signs of abnormal health, we will add a case-by-case follow-up for further clinical observation according to the situation.

The follow-up of neonates in the ZEBRA maternal cohort is conducted until six months after birth, and it mainly includes:

(1) Documentation of birth weight and Apgar score at birth.
(2) Clinical observation of jaundice, respiration, and feeding status within three days of birth.
(3) Evaluation of weight and height development at 42 days after birth and recording of other health abnormalities.
(4) It is recommended that the mother report any abnormal health conditions of the neonate by telephone within six months after birth. If the hospital where the mother gave birth has not received any report, a unified telephone follow-up will be conducted in the sixth month to gather information.

Content S3 | Questionnaire-based Lifestyle and Behavioral Pattern Collection

In the upcoming stage of data collection for ZEBRA Maternity Cohort participants, we will focus on including but not limited to the following list of lifestyle and behavioral characteristics:

Dietary habits, primarily referring to the intake quantity and frequency of different types of foods, including vegetables, fruits, nuts, poultry, red meat, seafood, vitamins and nutritional supplements, dairy products, coffee, as well as sugar and salt.

Smoking habits, including active and second-hand smoking, and currently under exposure, or with exposure history.

Sleep patterns, including bedtime, wake-up time, self-rated sleep quality, and habits of napping or siesta.

Screen exposure, including the frequency of screen exposure, types of screens exposed to (smartphones, tablets, desktop computers, laptops, etc.), and the purposes of screen exposure (work, study, entertainment, etc.).

Pre-pregnancy physical activity, mainly referring to the intensity and frequency of different types of exercises, including running, racket sports (e.g. tennis, table-tennis, badminton), cycling, swimming, dancing, extreme sports (e.g. rock climbing, scuba diving), etc.

Therapies, mainly including the frequency of massage therapy and psychological counseling.

Artistic activities, mainly including the intensity and frequency of painting, calligraphing, playing musical instrument, singing, dancing, etc.

Mental conditions, including mild to moderate levels of anxiety and depression (considering the privacy protection of the cohort participants, severe mental disorders, such as bipolar disorder, are not included in the items to be collected by self-report.

Behavioral changes for climate adaptation, referring to behavioral adjustments to extreme heat, extreme cold weather, and high outdoor air pollution. This primarily includes the use of air conditioners, central heating system, and air purifiers, as well as changes in means of transportation.

Content S4 | Overview of Published Studies Based on ZEBRA Maternity Cohort

Previous research conducted by ZEBRA primarily involves microscale laboratory experiments, as well as data-driven macroscale population-based epidemiological studies. For the purposes of this summary, we have selected publications that are of significant clinical or public health importance.

Uterine rupture risk factor identification

We identified 19 cases of uterine rupture among pregnant women who had not previously undergone caesarean section between 1992 and 2017. We collected demographic and sociological characteristics, clinical features, and details on the location and extent of the rupture (i.e. complete or incomplete), as well as pregnancy complications and childbirth risk factors (e.g. prolonged labor, dystocia, induced labor, use of oxytocin, etc.). We found that a history of curettage and multiple pregnancy were associated with complete uterine rupture, which was more likely to occur in the fundus of the uterus and at a smaller gestational age, leading to adverse pregnancy outcomes. Compared to neonates with complete uterine rupture, those with incomplete uterine rupture exhibited higher Apgar scores and lower perinatal mortality.[4] While findings from these rare cases may be used for clinical guidance, the limited sample size restricts generalization, highlighting the need for more cases from the ZEBRA maternity cohort in the future to support these findings.

Neonatal organic pollutant exposure

Currently, research into the pregnancy exposure characteristics and transplacental metastasis of isoforms of per- and polyfluoroalkyl compounds (PFASs) is limited. Such evidence not only advances our comprehension of the mechanism of transplacental transfer of PFASs, but also provides guidance for controlling the production process associated with particular PFASs to lessen occupational and daily exposure. To enhance our understanding of the transplacental and breastfeeding transfer of PFASs, and provide data that supports neonatal health risk assessment, we gathered mother-child paired maternal serum, cord serum, breast milk, or placenta samples from three Chinese cities—Hangzhou, Wuhan, and Mianyang—to capture geographical variability for the determination of various PFAS species' concentrations. The mean concentration of ΣPFAS in maternal serum followed the order of Mianyang (4.44 ng/mL) < Wuhan (9.88 ng/mL) < Hangzhou (19.72 ng/mL).[5] Perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), and 6:2 chlorinated polyfluorinated ether sulfonates (6:2 Cl-PFESA) were the most prevalent PFASs found in serum.[6,7] Linear and branched PFOS and PFOA can be effectively transferred across the placenta, with exposure levels ranked in the order of maternal serum > cord serum > placenta.[8,9] Moreover, we have critically summarized the current knowledge on the inner exposure status and mother-to-infant transfer characteristics of PFASs, drawing on hundreds of studies published from 2000 to date, in order to better comprehend this field.[10,11]

In addition, we collected paired serum and cerebrospinal fluid samples from 49 and 22 neonates, respectively, to determine the concentrations of PFASs in these biological samples. Our findings showed positive concentrations of PFASs in the cerebrospinal fluid, leading us to conclude that both PFASs and emerging PFAS substitutes have the ability to penetrate the developing blood-cerebrospinal fluid barrier (BCSFB), thus posing a potential risk to the healthy development of newborns.[12]

Mother-to-child intergenerational transmission

In order to investigate the potential transmission of Hepatitis B Virus (HBV) from mother to infant, we obtained placental tissues from three groups of women: 30 healthy pregnant women who were not infected with HBV ($HBV^{-/-}$), 30 HBV-positive women who did not infect their neonates ($HBV^{+/-}$), and 30 HBV-positive women who did infect their neonates ($HBV^{+/+}$). Additionally, peripheral blood samples were collected from the femoral vein of six $HBV^{+/+}$ and six $HBV^{+/-}$ neonates. Serum protein expression profiles of HBV were analyzed by proteomics, and the expression of proteins related to intrauterine HBV transmission was further confirmed through immunohistochemistry and PCR techniques in both serum samples and placental tissues. After screening and identifying 35 differential proteins, we found that high expression levels of S100-family proteins and exocytosis mediated by the AnxA2-S100A10 complex were associated with intrauterine HBV transmission through the placenta.[13,14]

The intergenerational effects of maternal antibiotic abuse on mother-child health have been a subject of concern among public health researchers, given the evidence of potential hazards to the healthy growth and development of children. Notably, the damage to gut bacteria is a significant outcome of antibiotic exposure.[15] In light of this, we collected breast milk and fecal samples from 25 mothers in 2020, among which 9 received no antibiotic treatment, 13 received cefuroxime (CXM) treatment, and 3 received cefuroxime-cefoxitin (CXM-CFX) combined treatment. At a 6-month postpartum follow-up, we collected fecal samples

from five infants whose mothers had undergone antibiotic treatments. We analyzed the microbiota in both breast milk and fecal samples to investigate the undesirable effects of antibiotics on the microbiota. Furthermore, we compared the relative abundance of antibiotic resistance genes (ARGs) in the infant gut microbiota to investigate their transfer. While antibiotic treatments had no influence on the microbiota of breast milk, they did disturb the gut microbiota in neonates. The abundance of ARGs in the infant gut microbiota showed a declining trend in the antibiotic-treated groups but significantly increased after 6 months of recovery.[16]

Gestational effects from severe diseases

Gestational trophoblastic neoplasia (GTN) is a specific tumor that affects pregnant women, originating from the malignant transformation of trophoblastic cells in placental villi during pregnancy. Chemotherapy has been recognized as an effective method to treat GTN, although concerns have been raised regarding its potential impact on pregnancy outcomes. In order to investigate this potential effect, we recruited 319 pregnant patients diagnosed with low-risk GTN in 2018 from the ZEBRA cohort. The patients were divided into two groups according to the occurrence of severe myelosuppression. We found that the occurrence of severe myelosuppression did not have an impact on the chemotherapy effect of methotrexate or the pregnancy outcomes.[17]

Gestational diabetes mellitus (GDM) is a crucial issue that has an impact on pregnancy outcomes and the long-term health of pregnant women. To investigate the feasibility of an early clinical diagnosis of GDM, we recruited all pregnant women diagnosed with GDM from the ZEBRA maternity cohort in 2019 and randomly selected healthy pregnant women with normal glucose tolerance as the control group. We used qRT-PCR to detect the expression level of the gene miR-520h in serum samples and analyzed the association between fasting blood glucose (FBG) level and miR-520h expression. Our results revealed that the expression level of miR-520h was up-regulated in the serum of GDM patients. We concluded that miR-520h could serve as a potential biomarker for the earlier-stage diagnosis of GDM.[18]

ZEBRA has directed attention towards understanding the pathological progression of endometrial carcinoma (EC). To this end, we obtained endometrial samples from 345 ZEBRA participants between 2006 and 2013, consisting of 55 normal endometrium (NE), 27 atypical hyperplasia (AH), and 263 Type-I EC. Immunohistochemical staining was performed to investigate the correlation between the expression of the TWIST1 chromosome and survival, as well as clinicopathological characteristics. Our findings indicate that TWIST1 expression gradually increased from NE to AH, implying that heightened TWIST1 expression is a significant indicator of the progression from hyperplasia to AH and eventually malignant tumor. Furthermore, we observed that high TWIST1 expression in Type-I EC patients suggested an increased invasive ability and a greater risk of distant metastasis of the tumor.[19]

Supplementary Tables

Table S1. Provincial distribution of ZEBRA Maternity Cohort participants.
Provinces with no participants are not displayed in the table.

Province	Participants
North China	
Beijing	169
Tianjin	32
Hebei	47
Shanxi	36
Inner Mongolia	18
Northeast China	
Liaoning	12
Jilin	8
Heilongjiang	2
East China	
Shanghai	1,179
Jiangsu	2,026
Zhejiang	100,648
Anhui	6,502
Fujian	725
Jiangxi	4,299
Shandong	681
Central China	
Henan	1,216
Hubei	228
Hunan	472
Guangdong	132
Guangxi	45
Hainan	20
Southwest China	
Chongqing	67
Sichuan	55
Guizhou	9
Yunnan	46
Northwest China	
Shaanxi	12
Gansu	2
Ningxia	1

Table S2. Full list of cases and prevalence of pre-pregnancy diseases and histories of surgeries.

Items are listed in descending sequence of prevalence.

Disease history	Cases (Prevalence, %)
Anemia	20,084 (16.9%)
Assisted reproduction	8,194 (6.9%)
Uterine leiomyomas	7,393 (6.2%)
Carrier of hepatitis B virus	6,645 (5.6%)
History of hepatitis B infection	5,129 (4.3%)
Mesosalpinx cyst	2,975 (2.5%)
Streptococcus carrier	2,813 (2.4%)
Thrombophilia	2,139 (1.8%)
Ovarian cyst	2,107 (1.8%)
Liver abnormality	2,070 (1.7%)
Immune system diseases	1,950 (1.6%)
Cervical incompetence	1,413 (1.2%)
Hematopathy	1,142 (1.0%)
Hashimoto thyroiditis	1,049 (0.9%)
Placenta implantation (accreta/increta/percreta)	1,023 (0.9%)
Antiphospholipid syndrome	974 (0.8%)
History of cervical surgery	968 (0.8%)
Mycoplasma infection	933 (0.8%)
Cholecystolithiasis and cholecystitis	881 (0.7%)
Endometriosis	790 (0.7%)
History of malignant neoplasm of thyroid gland	692 (0.6%)
Thrombocytopenia	690 (0.6%)
Candida vaginitis	680 (0.6%)
Septate uterus	648 (0.5%)
Membranitis	622 (0.5%)
Vaginitis	589 (0.5%)
Cardiac arrhythmia	538 (0.5%)
History of hypothyroidism	510 (0.4%)
Abnormal umbilical arterial flow	484 (0.4%)
Single umbilical cord artery	468 (0.4%)
Pelvic inflammation	466 (0.4%)
Uterine rupture	459 (0.4%)
History of syphilis	434 (0.4%)
Cervical polyps	428 (0.4%)
Adenomyosis	428 (0.4%)

Disease history	Cases (Prevalence, %)
Thalassemia	416 (0.4%)
Hyperthyroidism	403 (0.3%)
Polycystic ovary syndrome	403 (0.3%)
History of thyroid surgery	403 (0.3%)
Total thyroidectomy associate	355 (0.3%)
History of gallbladder disease	355 (0.3%)
Congenital uterine malformation	351 (0.3%)
History of intrahepatic cholestasis of pregnancy (ICP)	313 (0.3%)
Cervical conization and LEEP	303 (0.3%)
Nephropathy and nephritis	291 (0.2%)
History of hypertension	277 (0.2%)
Subtotal thyroidectomy	250 (0.2%)
Non-gestational diabetes mellitus	242 (0.2%)
Cardiac insufficiency	233 (0.2%)
History of Hashimoto's thyroiditis	228 (0.2%)
Amniotic fluid pollution	201 (0.2%)
History of Preeclampsia	182 (0.2%)
Depression	180 (0.2%)
Congenital heart disease	174 (0.1%)
Bacterial vaginitis	165 (0.1%)
Urolithiasis	159 (0.1%)
Didelphic uterus	159 (0.1%)
Ankylosing spondylitis	157 (0.1%)
Intrauterine death	141 (0.1%)
Hellp's syndrome	140 (0.1%)
Antiphospholipid syndrome	125 (0.1%)
Total thyroidectomy	105 (0.1%)
Epilepsy	92 (0.1%)
Mental or behavioral disorders	87 (0.1%)
Hepatitis E	83 (0.1%)
Fatty liver	72 (0.1%)
Systemic lupus erythematosus	69 (0.1%)
Thyroid nodule	64 (0.1%)
Hepatic hemangiomas	58 (0.05%)
Pulmonary arterial hypertension	35 (0.03%)

Table S3. Full list of statistics on obstetric-relevant diagnostic indicators.

Obstetric-relevant indicators	Mean (SD) or Count (%)
Gravidity	2.1 (1.2)
Parity	1.5 (0.6)
Abortion(s) or miscarriage(s)	
0	69,065 (58.2%)
1 to 2	44,282 (37.3%)
3 to 5	5,173 (4.4%)
above 5	169 (0.1%)
Live birth(s)	
0	66,803 (56.3%)
1	48,994 (41.3%)
2	2,707 (2.3%)
3 or above	186 (0.2%)
Spontaneous singleton delivery	62,818 (52.9%)
Caesarean singleton delivery	51,506 (43.4%)
Stillbirth	1,605 (1.4%)
Gestational age (*in days*)	271 (18)
Preterm birth	12,386 (10.4%)
Singleton preterm birth	11,385 (9.6%)
Twins or multiplets	4,926 (4.2%)
Spontaneous preterm birth	6,738 (5.7%)
Singleton spontaneous preterm birth	5,332 (4.5%)
Singleton medical-indicated preterm birth	6,053 (5.1%)
Menarche age (years)	13.9 (1.4)
Gestational weight gain (kg)	13.5 (6.0)
Gestational diabetes mellitus	22,393 (18.9%)
Gestational hypertension	2,465 (2.1%)
Pre-eclampsia	6,553 (5.5%)
Severe pre-eclampsia	4,342 (3.7%)
Single-symptom intrahepatic cholestasis of pregnancy (ICP)	2,872 (2.4%)
Multi-symptomatic ICP	724 (0.6%)
Birth weight, singleton (g)	3,195 (580)
Low birth weight infants, singleton	8,365 (7.0%)
Apgar score, singleton, 1 min	9.7 (1.3)
Apgar score, singleton, 5 min	9.9 (0.5)

Obstetric-relevant indicators	Mean (SD) or Count (%)
Neonatal sex, singleton	
Male	61,322 (51.7%)
Female	57,289 (48.3%)
First-degree obstetric lacerations	30,493 (25.7%)
Second-degree obstetric lacerations	131 (0.1%)
Third-degree obstetric lacerations	86 (0.1%)
Intrauterine fetal distress	27,057 (22.8%)
Premature rupture of membranes	25,160 (21.2%)
Caesarean scar	24,587 (20.7%)
Postpartum anemia	21,787 (18.4%)
Precipitate labor	8,962 (7.6%)
Battledore placenta	8,921 (7.5%)
Oligohydramnios	8,559 (7.2%)
Macrosomia	7,712 (6.5%)
Breech presentation	7,133 (6.0%)
Postpartum hemorrhage	6,163 (5.2%)
Intrauterine infection during pregnancy	5,337 (4.5%)
Meconium-stained amniotic fluid	4,744 (4.0%)
Intrahepatic cholestasis of pregnancy	4,188 (3.5%)
Adherent placentas at delivery	3,719 (3.1%)
Placenta previa	3,121 (2.6%)
Placental abruption	2,988 (2.5%)
Fetal growth restriction	2,447 (2.1%)
Polyhydramnios	2,212 (1.9%)
Fetal malformation	1,431 (1.2%)
Vaginal birth after caesarean	984 (0.8%)
Hypothyroidism in pregnancy	401 (0.3%)
Fetal chromosome abnormalities	316 (0.3%)
Twin pregnancies with single fetal demise	266 (0.2%)
Multifetal pregnancy reduction	253 (0.2%)
Threatened uterine rupture	243 (0.2%)
Fetal arrhythmia	230 (0.2%)

Table S4. Full list of biochemical indices at parturient period and oral glucose tolerance test (OGTT) in second trimester, 24–28th gestational week.

Sample size: parturient period, N=118,689; second trimester, N=63,887.

Biochemical indices	Ref. range	Parturient period	Second trimester
Fasting plasma glucose (mmol/L)	≤5.1	-	4.9 (1.2)
OGTT 1-h plasma glucose (mmol/L)	≤10	-	7.5 (2.1)
OGTT 2-h plasma glucose (mmol/L)	≤8.5	-	7.3 (1.6)
White blood cell count ($\times 10^9$/L)	3.5–9.5	10.7 (3.4)	9.6 (2.2)
Hemoglobin (g/L)	115–150	115.1 (13.8)	114.7 (8.9)
Platelet ($\times 10^9$/L)	125–350	187.0 (49.1)	209.9 (49.2)
Neutrophils (%)	40.0–75.0	77.4 (6.9)	74.9 (4.8)
Lymphocytes (%)	20.0–50.0	15.4 (5.9)	17.9 (4.2)
Monocytes (%)	3.0–10.0	6.5 (1.7)	6.0 (1.3)
Eosinophils (%)	0.4–8.0	0.6 (0.6)	1.0 (0.9)
Basophils (%)	≤1.0	0.2 (0.1)	0.3 (0.2)
Hematocrits (%)	35.0–45.0	34.6 (34.7)	34.3 (2.5)
Serum protein, total (g/L)	65–85	59.3 (6.1)	64.1 (3.6)
Albumin (g/L)	40–55	33.1 (3.4)	36.4 (2.2)
Alanine aminotransferase (U/L)	7–40	15.2 (24.7)	17.7 (17.4)
Aspartate aminotransferase (U/L)	13–35	21.7 (18.3)	18.7 (11.1)
Bilirubin, total (μmol/L)	≤23.0	8.3 (4.0)	6.9 (2.7)
Bilirubin, conjugated (μmol/L)	≤4.0	2.6 (1.6)	2.2 (1.0)
Bilirubin, unconjugated (μmol/L)	≤19.0	5.8 (3.0)	4.7 (2.1)
Bile acids, total (μmol/L)	0–13	4.5 (6.7)	2.3 (3.0)
Lactate dehydrogenase (U/L)	120–250	208.6 (66.7)	157.8 (29.9)
Alkaline phosphatase (U/L)	35–100	155.6 (65.1)	62.9 (20.0)
5'-Nucleotidase (U/L)	≤10	4.9 (17.1)	4.8 (2.0)
Adenosine deaminase (U/L)	≤20	6.6 (1.8)	5.9 (1.2)
Gamma-glutamyl transpeptidase (U/L)	120–250	12.6 (11.9)	12.2 (8.6)
α-hydroxybutyrate dehydrogenase (U/L)	90–180	153.2 (38.2)	117.6 (26.9)
Creatine Kinase (U/L)	40–200	124.8 (167.1)	38.4 (21.2)
Creatinine (μmol/L)	41–73	52.6 (11.4)	51.5 (10.6)
Urea nitrogen (mmol/L)	2.6–7.5	3.1 (1.0)	2.8 (0.7)
Uric acid (μmol/L)	155–357	315.1 (76.2)	237.4 (49.3)
Triglycerides (mmol/L)	0.56–1.70	3.20 (1.60)	2.40 (0.90)
Cholesterol, total (mmol/L)	2.84–5.69	6.10 (1.30)	6.10 (1.10)
HDL-cholesterol (mmol/L)	1.03–1.55	1.70 (0.40)	1.90 (0.40)
LDL-cholesterol (mmol/L)	1.55–3.36	3.20 (1.00)	3.10 (0.90)
Potassium (mmol/L)	3.5–5.3	3.9 (0.3)	4.0 (0.3)
Sodium (mmol/L)	137.0–147.0	137.4 (2.2)	137.7 (1.8)
Chlorine (mmol/L)	99.0–110.0	105.1 (2.1)	103.8 (2.1)
Calcium, total (mmol/L)	2.11–2.52	2.20 (0.10)	2.20 (0.10)
Magnesium (mmol/L)	0.75–1.02	0.80 (0.10)	0.80 (0.20)
Phosphate (mmol/L)	0.85–1.51	1.20 (0.20)	1.20 (0.20)
Total iron binding capacity (μmol/L)	7.8–32.2	14.7 (8.3)	17.3 (10.7)
Hypersensitive C-reactive protein (mg/L)	≤5.0	17.7 (24.7)	5.2 (6.5)
Prealbumin (g/L)	180–350	203.4 (40.9)	221.6 (30.2)
Transferrin (μmol/L)	2.00–3.60	3.6 (0.7)	3.6 (0.7)
Glycosylated albumin (%)	10.8–17.1	11.6 (1.3)	12.1 (0.9)
Homocysteine (μmol/L)	5–15	7.9 (2.4)	6.8 (2.1)
Plasma glucose (mmol/L)	≤5.1	0.3 (1.5)	1.5 (2.9)
Cholylglycine (μg/dL)	≤270	232.5 (270.3)	148.2 (134.5)
Prothrombin time (sec)	11.8–13.9	12.6 (0.7)	12.6 (0.5)
International normalized ratio	0.89–1.90	0.98 (0.07)	0.98 (0.05)
Partial thromboplastin time, activated (sec)	29.7–41.8	33.2 (3.0)	31.8 (2.3)
Thrombin time (sec)	15.0–18.0	15.1 (1.0)	14.9 (0.7)
Fibrinogen (g/L)	1.90–3.80	4.6 (0.8)	4.3 (0.7)
Urine specific gravity	1.003–1.030	1.014 (0.007)	1.014 (0.007)
Proteinuria			
- (Negative)	-	113,724 (95.8%)	63,600 (99.6%)
+	-	3,328 (2.8%)	206 (0.3%)
++	-	1,226 (1.0%)	51 (0.1%)
+++	-	411 (0.3%)	30 (0.05%)

Biochemical indices	Ref. range	Parturient period	Second trimester
Microscopic hematuria			
-	-	60,404 (50.9%)	60,577 (94.8%)
+	-	6,865 (5.8%)	1,966 (3.1%)
++	-	9,143 (7.7%)	799 (1.3%)
+++	-	42,278 (35.6%)	545 (0.9%)
Glycosuria			
-	-	111,848 (94.2%)	60,397 (94.5%)
+	-	2,545 (2.1%)	1,267 (2.0%)
++	-	2,810 (2.4%)	1,362 (2.1%)
+++	-	1,365 (1.1%)	828 (1.3%)
++++	-	122 (0.1%)	21 (0.1%)
Urine bilirubin			
-	-	117,884 (99.3%)	63,747 (99.8%)
+	-	707 (0.6%)	106 (0.2%)
++	-	63 (0.1%)	26 (0.04%)
+++	-	34 (0.03%)	6 (0.01%)
Urine leucocyte			
-	-	85,636 (72.2%)	39,018 (61.1%)
+	-	11,060 (9.3%)	11,769 (18.4%)
++	-	8,947 (7.5%)	5,392 (8.4%)
+++	-	13,047 (11.0%)	7,708 (12.1%)
Protein excretion, 24-hr (g)	<0.15	1.10 (2.30)	0.10 (0.10)

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