



Article Baseline Complete Blood Count and Chemistry Panel Profile from the Japan Environment and Children's Study (JECS)

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Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). Abstract: Background: The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study of environmental factors affecting children's health and development. We summarize the complete blood count and chemistry panel statistical data from pregnant women enrolled in JECS. Methods: Statistical data of up to 58,056 mother's sample in their first (gestational age ≤ 13 weeks) and second trimester (22–27 weeks) were calculated. Results: Mean (SD) values in the first trimester were: white blood cell count, 7866 (1906)/µL; red blood cell count, 417 (33) 10⁴/µL; hemoglobin, 12.4 (1.0) g/dL; hematocrit, 37.1 (2.6)%; mean corpuscular volume, 89.2 (4.7) fL; mean corpuscular hemoglobin, 29.8 (1.9) pg; mean corpuscular hemoglobin concentration, 33.3 (0.9)%; platelet count, 24.8 (5.2) 10⁴/µL; HbA1c, 5.26 (0.26)%; total cholesterol, 181 (28) mg/dL; low density lipoprotein cholesterol, 95 (23) mg/dL; high density lipoprotein cholesterol, 73 (13) mg/dL; free cholesterol, 41 (7) mg/dL; triglycerides, 109 (47) mg/dL; total protein, 6.9 (0.4) g/dL; and albumin, 4.1 (0.2) g/dL. Mean values (SD) in the second trimester were: total cholesterol, 246 (38) mg/dL; free cholesterol, 61 (9) mg/dL; triglycerides, 183 (70) mg/dL; total protein, 6.5 (0.4) g/dL; and albumin, 3.6 (0.2) g/dL. Conclusions: These data will be useful for future JECS studies.

Keywords: birth cohort; epidemiology; blood cell count; chemistry

1. Introduction

The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study launched in January 2011 to evaluate the effects of chemical exposure during the fetal stage and in early childhood on children's health and development [1]. Recruitment of women in early pregnancy was conducted from launch until March 2014, during which a total of 103,099 pregnancies were registered [2]. Based on selected maternal and infant characteristics in the first year of recruitment, the JECS cohort is representative of the general Japanese population [3]. Details of the JECS concept and design have been published elsewhere [1,2].

JECS examines the effects of exposure to a wide range of environmental factors [1] using questionnaires [3–7], chemical analysis of bio-specimens [8–11], environmental measurements [12,13], and atmospheric simulation based on monitoring of ambient air quality. Previous studies in JECS have reported various profile data on chemical analyses of bio-specimens, including the allergic profiles of mothers and fathers [8], metabolic status in

pregnant women [9], concentrations of metallic elements in pregnant women [10], and urinary cotinine in pregnant women [11].

To our knowledge, no previous study has reported the complete blood count and chemistry panel data of a large sample of pregnant women in Japan. Further, there are no standard blood data values. In this descriptive study, we summarized the complete blood count and chemistry panel data of 58,056 mothers in their first and second trimesters with singleton pregnancies and live births. To examine regional differences in complete blood count and chemistry panel data in Japan, we also summarized the values for six regions. We hope that the complete blood count and chemistry panel data provided in this study will facilitate the establishment of standard values for Japanese pregnant women. The data from this study will also be useful for future studies in JECS that aim to examine the effect of maternal biochemistry on children's health and development.

2. Materials and Methods

2.1. Study Participants

JECS is funded by Japan's Ministry of the Environment. The ultimate goal of JECS is "to identify environmental factors that affect children's health and development in order to help decision-makers design better chemical risk management strategies" [1]. JECS involves collaborations between the Program Office (National Institute for Environmental Studies), the Medical Support Center (National Centre for Child Health and Development), and 15 Regional Centers (Hokkaido, Miyagi, Fukushima, Chiba, Kanagawa, Koshin, Toyama, Aichi, Kyoto, Osaka, Hyogo, Tottori, Kochi, Fukuoka, and South Kyushu/Okinawa) [2]. A total of 103,099 pregnancies were recruited and registered at the 15 Regional Centers across Japan via Co-operating health care providers and/or local government offices between 2011 and 2014. We previously reported that the number of live births registered in JECS accounted for approximately 45% of total live births within the study area [2]. The JECS protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and the Ethics Committees of all participating institutions. JECS was conducted in accordance with the Helsinki Declaration and other nationally valid regulations and guidelines. Written informed consent was obtained from all participants.

2.2. Assessment during Pregnancy

Complete Blood Count and Chemistry Panel

Non-fasting maternal blood samples were collected by medical staff when the pregnant women visited co-operating health care providers during periods named in JECS as MT1 (gestational age 12–16 weeks) and/or MT2 (gestational age 22–28 weeks), respectively. Volumes of 32 mL at MT1 and 33 mL at MT2 of whole blood samples were collected into 5 tubes. The following biomarkers were assayed by a contract clinical laboratory (SRL, Inc., a commercial laboratory in Tokyo, Japan): white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count (PLT), HbA1c, total cholesterol (T-Cho), low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), free cholesterol (F-Cho), triglycerides (TG), total protein (TP), and albumin (Alb).

The methods used to measure the biomarkers were as follows: WBC, flow cytometry with semiconductor laser (SYSMEX XE-2100); RBC and PLT, hydrodynamic focusing DC detection (SYSMEX XE-2100); Hb, SLS-Hemoglobin Method (SYSMEX XE-2100); Ht, RBC pulse height detection (SYSMEX XE-2100); MCV, MCH, and MCHC, calculated using RBC, Hb, and Ht values (SYSMEX XE-2100); HbA1c, high-performance liquid chromatography (ADAMS-A1c HA-8160); T-Cho and F-Cho, enzymatic method (HITACHI 7700 SERIES); LDL-C, accelerator selective detergent (HITACHI 7700 SERIES); HDL-C, liquid selective detergent (HITACHI 7700 SERIES); TG, enzymatic method using glycerol phosphate oxi-

dase (HITACHI 7700 SERIES); TP, biuret (HITACHI 7700 SERIES); and Alb, bromocresol green (HITACHI 7700 SERIES).

HbA1c was calculated using reference values from the National Glycohemoglobin Standardization Program or Japan Diabetes Society. For HbA1c values calculated using reference values from the Japan Diabetes Society, the following formula was used: Calculated HbA1c = $1.02 \times$ HbA1c (Japan Diabetes Society) + 0.25 [9,14].

WBC, RBC, Hb, Ht, MCV, MCH, MCHC, PLT, HbA1c, LDL-C, and HDL-C were measured only at MT1.

Questionnaires

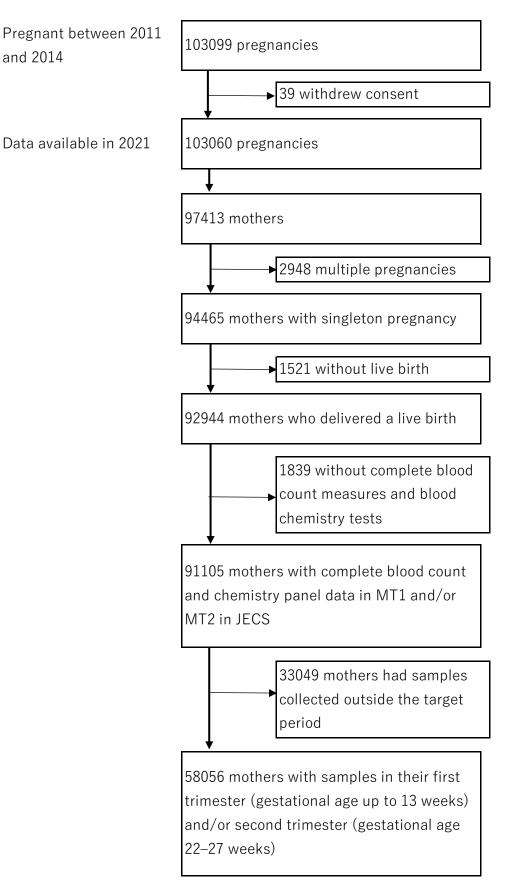
Self-administered questionnaires were completed by the pregnant women during MT1 and MT2. Self-administered questionnaires covered demographic factors, medical and obstetric history, physical and mental health, lifestyle, occupation, environmental exposure at home and in the workplace, housing conditions, and socioeconomic status [2]. In this study, we extracted data on the following baseline demographic and health characteristics: age, marital status, educational attainment, household income, occupation [15], smoking habit [16], alcohol consumption [16], height, weight, body mass index (BMI), and parity.

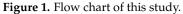
Height, pre-pregnancy weight, and parity were transcribed from medical records before and at birth and from self-administered questionnaires at MT1. Educational attainment and household income were assessed at MT2 only, while the remaining variables were assessed at MT1 and/or MT2.

2.3. Statistical Analysis

The present study used the jecs-ta-20190930 dataset, released in October 2019, and modified in June 2021. To be eligible for the study, pregnant women had to have undergone a complete blood count and chemistry panel in the first and/or second trimester and had to have a singleton pregnancy and live birth. Among 103,099 pregnancies, the study excluded women who withdrew consent (n = 39). A total of 103,060 pregnancies were identified among 97,413 mothers. We further excluded those with multiple pregnancies (n = 2948), without live birth (n = 1521), and without complete blood count and chemistry panel data (n = 1839). Among the 91,105 pregnant women with complete blood count and chemistry panel data in MT1 and/or MT2, we used the 58,056 samples collected in the first trimester (gestational age up to 13 weeks in MT1: n = 23,709) and/or second trimester (gestational age 22–27 weeks in MT2: n = 49,857) based on the definition used in clinical settings and previous research. Finally, data for this study were obtained from 58,056 mothers with complete blood count and chemistry panel data in the first trimester and previous research. Finally, data for this study were obtained from 58,056 mothers with complete blood count and chemistry panel data in the first trimester and previous research. Finally, data for this study were obtained from 58,056 mothers with complete blood count and chemistry panel data in the first trimester and/or second trimester, singleton pregnancy, and live birth (Figure 1).

First, we summarized a wide range of maternal baseline demographic and health characteristics in the first trimester and/or second trimester. Second, we summarized complete blood count and chemistry panel data in the first trimester and second trimester. These variables were reported as mean (standard deviation: SD) and 10, 25, 50, 75, and 95 percentiles. Third, we summarized complete blood count and chemistry panel data collected in the first trimester for 6 regions in Japan: Hokkaido and Tohoku (Hokkaido, Miyagi, Fukushima), Kanto (Chiba, Kanagawa), Chubu (Koshin, Toyama, Aichi), Kinki (Kyoto, Osaka, Hyogo), Chugoku and Shikoku (Tottori, Kochi), and Kyushu (Fukuoka, and South Kyushu = Okinawa). All descriptive statistics were conducted using SAS version 9.4.





3. Results

Female participants in JECS in their first trimester with singleton pregnancies and live births had a mean (SD) age of 30.9 (4.5) years. About 95.7% were married, and 29.7% were homemakers, while 22.0% were professional or engineering workers. In terms of lifestyle habits, 59.7% were never smokers, and 35.3% were never alcohol drinkers. Mean BMI was 21.2 (3.3) kg/m², and 44.7% were primiparas. Among women in their second trimester, 65.0% had graduated from college, junior college, university, or graduate school, and 34.7% and 33.2% had a household income of 2 to <4 million Japanese yen and 4 to <6 million Japanese yen, respectively (Table 1).

Table 1. Baseline demographic and health characteristics of pregnant women in their first and/or second trimester.

Variable	First Trimester (Gestational Age Up to 13 Weeks) <i>n</i> = 23,709	Second Trimester (Gestational Age 22–27 Weeks) <i>n</i> = 49,857		
Age (years)	30.9 (4.5)	31.7 (5.0)		
Marital status (%)				
Married	95.7	-		
Unmarried	3.6	-		
Divorced/widowed	0.8	-		
Educational attainment (%)				
Junior high school	-	4.8		
High school/technical college	-	30.2		
College/junior college/university/graduate school	-	65.0		
Household income (%)				
<2 million Japanese yen/year	-	5.8		
2 to <4 million Japanese yen/year	-	34.7		
4 to <6 million Japanese yen/year	-	33.2		
6 to <8 million Japanese yen/year	-	15.9		
8 to <10 million Japanese yen/year	-	6.4		
\geq 10 million Japanese yen/year	-	4.1		
Occupation (%)				
Administrative and managerial work	0.6	-		
Professional and engineering work	22.8	-		
Clerical work	17.0	-		
Sales work	5.7	-		
Service work	14.5	-		
Security work	0.3	-		
Agriculture, forestry and fishery work	0.5	-		
Manufacturing process work	2.6	-		
Transport and machine operation workers/Construction and mining work	0.3	-		
Carrying, cleaning, packaging, and related work	0.6	-		
Homemaker	29.7	-		
Other (students, inoccupation, workers not classifiable by occupation)	5.5	-		

Variable	First Trimester (Gestational Age Up to 13 Weeks) <i>n</i> = 23,709	Second Trimester (Gestational Age 22–27 Weeks) <i>n</i> = 49,857		
Smoking habit (%)				
Never smoker	59.7	58.7		
Past smoker	36.0	36.8		
Current smoker	4.3	4.5		
Alcohol consumption (%)				
Never drinker	35.3	33.8		
Past drinker	54.9	63.4		
Current drinker	9.8	2.8		
Height (cm)	158.3 (5.3)	-		
Weight (kg)	53.0 (8.8)	-		
BMI (kg/m ²)	21.2 (3.3)	-		
Parity (%)	45.6	-		
0	44.7			
1	37.7			
≥2	17.6			

Table 1. Cont.

Data indicate mean (standard deviation) or %. "-" indicates data were not collected.

Table 2 shows the women's complete blood count and chemistry panel profile in the first and second trimester. The mean (SD) values in the first trimester were as follows: WBC, 7866 (1906)/ μ L; RBC, 417 (33) 10⁴/ μ L; Hb, 12.4 (1.0) g/dL; Ht, 37.1 (2.6)%; MCV, 89.2 (4.7) fL; MCH, 29.8 (1.9) pg; MCHC, 33.3 (0.9)%; PLT, 24.8 (5.2) 10⁴/ μ L; HbA1c, 5.26 (0.26)%; T-Cho, 181 (28) mg/dL; LDL-C, 95 (23) mg/dL; HDL-C, 73 (13) mg/dL; F-Cho, 41 (7) mg/dL; TG, 109 (47) mg/dL; TP, 6.9 (0.4) g/dL; and Alb, 4.1 (0.2) g/dL. The mean (SD) values in the second trimester were as follows: T-Cho, 246 (38) mg/dL; F-Cho, 61 (9) mg/dL; TG, 183 (70) mg/dL; TP, 6.5 (0.4) g/dL, and Alb, 3.6 (0.2) g/dL.

When the data were stratified by six regions in Japan (Table 3), the regional difference was a maximum of 5.0% for TG and 4.2% for RBC compared with all participants. PLT, Alb, HDL-C, and TP showed a maximum regional difference of 2.6%, 1.5%, 1.2% and 1.2%, respectively, compared with all participants. The remaining complete blood count and chemistry panel variables showed a regional difference of less than 1%.

Variable	(G	Second Trimester (Gestational Age 22–27 Weeks) $n = 49,857$										
	Mean (SD)	10%	25%	50%	75%	90%	Mean (SD)	10%	25%	50%	75%	90%
White blood cell count (/µL)	7866 (1906)	5600	6600	7800	9000	10,300	-	-	-	-	-	-
Red blood cell count ($10^4/\mu$ L)	417 (33)	375	395	417	439	459	-	-	-	-	-	-
Hemoglobin (g/dL)	12.4 (1.0)	11.2	11.8	12.4	13.0	13.6	-	-	-	-	-	-
Hematocrit (%)	37.1 (2.6)	33.8	35.4	37.1	38.9	40.4	-	-	-	-	-	-
Mean corpuscular volume (fL)	89.2 (4.7)	84.0	87.0	89.6	92.1	94.3	-	-	-	-	-	-
Mean corpuscular hemoglobin (pg)	29.8 (1.9)	27.7	29.0	30.0	30.9	31.7	-	-	-	-	-	-
Mean corpuscular hemoglobin concentration (%)	33.3 (0.9)	32.3	32.9	33.4	33.9	34.4	-	-	-	-	-	-
Platelet count (10 ⁴ /µL)	24.8 (5.2)	18.7	21.3	24.4	27.9	31.4	-	-	-	-	-	-
HbA1c (%)	5.26 (0.26)	4.94	5.1	5.25	5.4	5.55	-	-	-	-	-	-
Total cholesterol (mg/dL)	181 (28)	147	161	179	198	217	246 (38)	200	220	244	269	295
Low density lipoprotein cholesterol (mg/dL)	95 (23)	68	79	93	108	124	-	-	-	-	-	-
High density lipoprotein cholesterol (mg/dL)	73 (13)	57	64	72	81	90	-	-	-	-	-	-
Free cholesterol (mg/dL)	41 (7)	33	37	41	45	50	61 (9)	50	55	61	67	73
Triglycerides (mg/dL)	109 (47)	62	77	99	129	167	183 (70)	111	135	169	213	267
Total protein (g/dL)	6.9 (0.4)	6.4	6.6	6.9	7.1	7.4	6.5 (0.4)	6.0	6.2	6.5	6.7	6.9
Albumin (g/dL)	4.1 (0.2)	3.8	3.9	4.0	4.2	4.4	3.6 (0.2)	3.4	3.5	3.6	3.8	3.9

 Table 2. Baseline complete blood count and chemistry panel profile of pregnant women in their first and/or second trimester.

"-" indicates data were not collected.

Variable		Region in Japan											
	Hokkaido and Tohoku n = 5422			Kanto n = 2163		Chubu n = 5283		Kinki <i>n</i> = 5521		Chugoku and Shikoku n = 1245		Kyushu n = 4075	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
White blood cell count (/ μ L)	7833 (1926)	7700 (6500, 9000)	8088 (1830)	7900 (6800, 9200)	7737 (1888)	7600 (6500, 8900)	8028 (1928)	7900 (6700, 9200)	7536 (1932)	7500 (6400, 8700)	7841 (1873)	7700 (6600, 9000)	
Red blood cell count ($10^4 / \mu L$)	418 (34)	417 (395, 439)	418 (33.14)	419 (397, 441)	419 (32.53)	418 (397, 440)	416 (32)	416 (394, 437)	411 (33)	411 (389, 431)	417 (33)	416 (395, 438)	
Hemoglobin (g/dL)	12.4 (1.0)	12.4 (11.8, 13.1)	12.5 (1.0)	12.5 (11.9, 13.1)	12.4 (1.0)	12.4 (11.9, 13.0)	12.3 (1.0)	12.4 (11.7, 13.0)	12.3 (0.9)	12.3 (11.7, 12.9)	12.4 (1.0)	12.4 (11.8, 13.0)	
Hematocrit (%)	37.0 (2.7)	37.0 (35.3, 38.8)	37.4 (2.6)	37.4 (35.8, 39.2)	37.3 (2.6)	37.3 (35.6, 39.1)	37.1 (2.6)	37.1 (35.4, 38.8)	36.8 (2.6)	36.8 (35.1, 38.5)	37.1 (2.6)	37.0 (35.4, 38.9)	
Mean corpuscular volume (fL)	88.8 (4.6)	89.2 (86.7, 91.6)	89.5 (4.3)	89.9 (87.4, 92.2)	89.3 (4.6)	89.7 (87.1, 92.2)	89.3 (4.8)	89.8 (87.1, 92.3)	89.8 (4.3)	90.0 (87.8, 92.5)	89.2 (4.7)	89.7 (86.9, 92.0)	
Mean corpuscular hemoglobin (pg)	29.8 (1.9)	30.0 (29.0, 30.9)	29.8 (1.8)	30.0 (29.1, 30.8)	29.8 (1.9)	30.0 (29.0, 30.9)	29.7 (2.0)	30.0 (29.0, 30.9)	30.0 (1. 8)	30.3 (29.2, 31.2)	29.7 (2.0)	30.0 (29.0, 30.9)	
Mean corpuscular hemoglobin concentration (%)	33.5 (0.9)	33.5 (33.0, 34.1)	33.3 (0.9)	33.3 (32.8, 33.9)	33.3 (0.9)	33.4 (32.8, 33.9)	33.2 (1.0)	33.3 (32.7, 33.8)	33.4 (0.9)	33.4 (33.0, 34.0)	33.3 (0.9)	33.4 (32.8, 33.9)	
Platelet count (10 ⁴ / µL)	25.0 (5.2)	24.6 (21.5, 28.1)	25.1 (5.1)	24.8 (21.6, 28.1)	24.4 (5.2)	24.0 (20.9, 27.5)	25.0 (5.1)	24.6 (21.5, 28.1)	24.2 (4.9)	23.8 (20.8, 27.3)	24.9 (5.2)	24.6 (21.3, 28.0)	
HbA1c (%)	5.26 (0.28)	5.25 (5.10, 5.40)	5.26 (0.25)	5.25 (5.10, 5.40)	5.27 (0.26)	5.25 (5.10, 5.45)	5.25 (0.25)	5.25 (5.10, 5.40)	5.24 (0.24)	5.25 (5.10, 5.40)	5.26 (0.27)	5.25 (5.10, 5.40)	
Total cholesterol (mg/dL)	180 (29)	178 (160, 197)	182(29)	180 (162, 199)	180 (28)	178 (160, 197)	182 (29)	180 (162, 199)	181 (26)	179 (163, 198)	179 (28)	177 (160, 196)	
Low density lipoprotein cholesterol (mg/dL)	95 (24)	93 (79, 109)	95 (24)	93 (79, 110)	94 (23)	92 (78, 108)	96 (23)	94 (80, 109)	95 (22)	93 (80, 109)	94 (23)	91 (78, 108)	
High density lipoprotein cholesterol (mg/dL)	72 (13)	71 (63, 80)	74 (13)	73 (65, 82)	73 (13)	72 (64, 81)	74 (13)	73 (65, 82)	73 (13)	72 (65, 81)	72 (13)	72 (63, 80)	
Free cholesterol (mg/dL)	41 (7)	41 (36, 45)	41 (7)	41 (37, 46)	41 (7)	41 (36, 45)	42 (7)	41 (37, 46)	42 (6)	41 (37, 46)	41 (7)	41 (37, 45)	
Triglycerides (mg/dL)	107 (47)	98 (76, 127)	109 (48)	100 (77, 131)	108 (46)	98 (76, 128)	110 (48)	100 (77, 131)	115 (47)	104 (82, 135)	110 (46)	100 (78, 131)	
Total protein (g/dL)	6.9 (0.4)	6.9 (6.6, 7.1)	6.9 (0.4)	6.9 (6.6, 7.1)	6.9 (0.4)	6.9 (6.7, 7.2)	6.9 (0.4)	6.9 (6.6, 7.2)	6.8 (0.4)	6.8 (6.6, 7.1)	6.9 (0.4)	6.9 (6.6, 7.1)	
Albumin (g/dL)	4.1 (0.3)	4.0 (3.9, 4.2)	4.1 (0.3)	4.0 (3.9, 4.2)	4.1 (0.2)	4.1 (3.9, 4.2)	4.1 (0.2)	4.1 (3.9, 4.2)	4.0 (0.2)	4.0 (3.8, 4.1)	4.0 (0.2)	4.0 (3.9, 4.2)	

Table 3. Baseline complete blood count and chemistry panel profile of pregnant women in their first trimester by region in Japan.

Data indicate mean (standard deviation) and median (IQR).

4. Discussion

In this descriptive study, we confirmed a wide range of maternal baseline demographic and health characteristics for female participants and summarized the mean values of parameters of a complete blood count and chemistry panel conducted during the first trimester and second trimester in pregnant women in JECS, who are regarded as being representative of the general Japanese population [3]. We also examined regional differences in these variables in Japan.

Although there are currently no standardized complete blood count and chemistry panel data for pregnant women in Japan, the Japan Society of Obstetrics and Gynecology has published a guideline for the first trimester (gestational age up to 13 weeks) [17] for several complete blood count measures. According to this guideline, the present JECS data showed that 97.6%, 97.1%, and 98.6% of pregnant women were in the normal range for WBC (<12,000/µL), Hb (\geq 10.5 g/dL), and PLT (\geq 15 × 10⁴/µL), respectively [17]. The Japan Society of Laboratory Medicine has published reference ranges for laboratory test parameters for the Japanese population [18]. The mean values for WBC, RBC, Hb, Ht, MCV, MCH, MCHC, PLT, HbA1c, T-Cho, LDL-C, HDL-C, TG, TP, and Alb for women in their first trimester in this study fell within these reference ranges [18]. We also confirmed that the present data were consistent with those reported in previous studies in JECS [9,19,20].

The mean values for T-Cho, F-Cho, and TG increased between the first trimester and second trimester in this study. A recent study reported that an increase in cholesterol levels is observed during pregnancy and that it is considered a normal adaptive response to the development of the fetus [21]. Maternal cholesterol increases throughout gestation by 50–70% [22], particularly in the second and third trimesters [23]. T-Cho increases up to 39% and TG up to 138% in the third trimester [24]. Although accumulated evidence shows that cholesterol levels are increased during late gestation, the present study revealed that T-Cho, F-Cho, and TG rose 36%, 49%, and 68% between the first and second trimester, respectively. In general, maternal serum Alb levels fall as pregnancy progresses [18], especially during late gestation [25]. The present study showed that Alb decreased by 12% between the first and second trimester, suggesting that Alb levels may begin to gradually decline in early pregnancy.

Stratified analysis of complete blood count and chemistry panel data by region in Japan showed there was a maximum regional difference of 5.0%. While we speculate that differences in regional cultural lifestyle such as dietary habits within Japan may explain the variability in complete blood count and chemistry panel data, the precise reason is unclear. Additional studies that consider regional characteristics may be needed to establish standard values for complete blood count and chemistry panel parameters for pregnant women. Moreover, future studies in JECS using these variables should consider regional differences when examining the effect of maternal biochemistry on child health and development. Based on the results for a wide range of maternal baseline demographic and health characteristics, future studies that have similar characteristics to this study also should consider regional differences.

5. Conclusions

This descriptive study summarized the mean values of parameters of a complete blood count and chemistry panel conducted during the first trimester and second trimester in pregnant women in JECS. These data will be useful for future studies in JECS that aim to examine the effect of maternal biochemistry on child health and development. Author Contributions: Conceptualization, Y.T., S.Y. and S.F.N.; data curation, Y.T., S.F.N., T.M., T.I., M.I.-S., Y.K. and M.T.; formal analysis, Y.T., S.Y., and T.M.; funding acquisition, S.Y., S.F.N. and M.K.; investigation, S.Y., S.F.N., M.S., T.I., M.I.-S. and M.K.; methodology, S.Y., S.F.N., T.M., M.I.-S., Y.K., M.T. and M.K.; project administration, S.Y., S.F.N., M.K. and the Japan Environment and Children's Study Group; resources, Y.T., S.Y., S.F.N., M.S., T.M., T.I., Y.K. and M.T.; Software, Y.T.; supervision, S.Y., S.F.N. and M.K.; validation, Y.T.; writing—original draft, Y.T.; writing—review and editing, Y.T., S.Y., S.F.N., M.S., T.M., M.K. and the Japan Environment and Children's Study Group. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The JECS protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and the Ethics Committees of all participating institutions (approval code: 100910001 and approval date: 10 September 2010). JECS is being conducted in accordance with the Helsinki Declaration and other nationally valid regulations and guidelines.

Informed Consent Statement: Written informed consent was obtained from all participants.

Data Availability Statement: Data are unsuitable for public deposition due to ethical restrictions and the legal framework of Japan. It is prohibited by the Act on the Protection of Personal Information (Act No. 57 of 30 May 2003, amendment on 9 September 2015) to publicly deposit the data containing personal information. Ethical Guidelines for Medical and Health Research Involving Human Subjects enforced by the Japan Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare also restrict the open sharing of the epidemiologic data. All inquiries about access to data should be sent to: jecs-en@nies.go.jp. The person responsible for handling enquiries sent to this e-mail address is Shoji F. Nakayama, JECS Programme Office, National Institute for Environmental Studies.

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References

- Kawamoto, T.; Nitta, H.; Murata, K.; Toda, E.; Tsukamoto, N.; Hasegawa, M.; Yamagata, Z.; Kayama, F.; Kishi, R.; Ohya, Y.; et al. Rationale and study design of the Japan environment and children's study (JECS). *BMC Public Health* 2014, 14, 25. [CrossRef] [PubMed]
- Michikawa, T.; Nitta, H.; Nakayama, S.F.; Yamazaki, S.; Isobe, T.; Tamura, K.; Suda, E.; Ono, M.; Yonemoto, J.; Iwai-Shimada, M.; et al. Baseline Profile of Participants in the Japan Environment and Children's Study (JECS). *J. Epidemiol.* 2018, 28, 99–104. [CrossRef] [PubMed]
- Michikawa, T.; Nitta, H.; Nakayama, S.F.; Ono, M.; Yonemoto, J.; Tamura, K.; Suda, E.; Ito, H.; Takeuchi, A.; Kawamoto, T.; et al. The Japan Environment and Children's Study (JECS): A Preliminary Report on Selected Characteristics of Approximately 10,000 Pregnant Women Recruited During the First Year of the Study. J. Epidemiol. 2015, 25, 452–458. [CrossRef] [PubMed]

- Iwai-Shimada, M.; Nakayama, S.F.; Isobe, T.; Michikawa, T.; Yamazaki, S.; Nitta, H.; Takeuchi, A.; Kobayashi, Y.; Tamura, K.; Suda, E.; et al. Questionnaire results on exposure characteristics of pregnant women participating in the Japan Environment and Children Study (JECS). *Environ. Health Prev. Med.* 2018, 23, 45. [CrossRef]
- Konishi, M.; Tomotaki, A.; Yamamoto-Hanada, K.; Mezawa, H.; Ayabe, T.; Ishitsuka, K.; Saito, M.; Saito, H.; Ohya, Y.; The Japan Environment and Children's Study Group. Sleep status varies by age among Japanese women during preconception and pregnancy in a nationwide birth cohort study [the Japan Environment and Children's Study (JECS)]. *Sleep Biol. Rhythms* 2019, 17, 161–172. [CrossRef]
- Yang, L.; Yamamoto-Hanada, K.; Ishitsuka, K.; Ayabe, T.; Mezawa, H.; Konishi, M.; Shoda, T.; Sago, H.; Saito, H.; Ohya, Y.; et al. Medical and surgical complications in pregnancy and obstetric labour complications in the Japan Environment and Children's Study (JECS) cohort: A birth cohort study. J. Obstet. Gynaecol. 2020, 40, 918–924. [CrossRef]
- Ishitsuka, K.; Sasaki, S.; Yamamoto-Hanada, K.; Mezawa, H.; Konishi, M.; Ohya, Y.; Japan Environment and Children's Study Group. Changes in Dietary Intake in Pregnant Women from Periconception to Pregnancy in the Japan Environment and Children's Study: A Nationwide Japanese Birth Cohort Study. *Matern. Child Health J.* 2020, 24, 389–400. [CrossRef]
- Yamamoto-Hanada, K.; Yang, L.; Ishitsuka, K.; Ayabe, T.; Mezawa, H.; Konishi, M.; Shoda, T.; Matsumoto, K.; Saito, H.; Ohya, Y.; et al. Allergic profiles of mothers and fathers in the Japan Environment and Children's Study (JECS): A nationwide birth cohort study. *World Allergy Organ. J.* 2017, 10, 24. [CrossRef]
- Sasaki, H.; Arata, N.; Tomotaki, A.; Yamamoto-Hanada, K.; Mezawa, H.; Konishi, M.; Ishitsuka, K.; Saito-Abe, M.; Sato, M.; Nishizato, M.; et al. Time course of metabolic status in pregnant women: The Japan Environment and Children's Study. J. Diabetes Investig. 2020, 11, 1318–1325. [CrossRef]
- Nakayama, S.F.; Iwai-Shimada, M.; Oguri, T.; Isobe, T.; Takeuchi, A.; Kobayashi, Y.; Michikawa, T.; Yamazaki, S.; Nitta, H.; Kawamoto, T.; et al. Blood mercury, lead, cadmium, manganese and selenium levels in pregnant women and their determinants: The Japan Environment and Children's Study (JECS). J. Expo. Sci. Environ. Epidemiol. 2019, 29, 633–647. [CrossRef]
- Nishihama, Y.; Nakayama, S.F.; Tabuchi, T.; Isobe, T.; Jung, C.-R.; Iwai-Shimada, M.; Kobayashi, Y.; Michikawa, T.; Sekiyama, M.; Taniguchi, Y.; et al. Determination of Urinary Cotinine Cut-Off Concentrations for Pregnant Women in the Japan Environment and Children's Study (JECS). *Int. J. Environ. Res. Public Health.* 2020, 17, 5537. [CrossRef] [PubMed]
- 12. Nishihama, Y.; Jung, C.-R.; Nakayama, S.F.; Tamura, K.; Isobe, T.; Michikawa, T.; Iwai-Shimada, M.; Kobayashi, Y.; Sekiyama, M.; Taniguchi, Y.; et al. Indoor air quality of 5000 households and its determinants. Part A: Particulate matter (PM2.5 and PM10–2.5) concentrations in the Japan Environment and Children's Study. *Environ. Res.* **2021**, *198*, 111196. [CrossRef] [PubMed]
- Jung, C.-R.; Nishihama, Y.; Nakayama, S.F.; Tamura, K.; Isobe, T.; Michikawa, T.; Iwai-Shimada, M.; Kobayashi, Y.; Sekiyama, M.; Taniguchi, Y.; et al. Indoor air quality of 5000 households and its determinants. Part B: Volatile organic compounds and inorganic gaseous pollutants in the Japan Environment and Children's Study. *Environ. Res.* 2021, 197, 111135. [CrossRef] [PubMed]
- Kaneko, K.; Ito, Y.; Ebara, T.; Kato, S.; Matsuki, T.; Tamada, H.; Sato, H.; Saitoh, S.; Sugiura-Ogasawara, M.; Yamazaki, S.; et al. Association of Maternal Total Cholesterol With SGA or LGA Birth at Term: The Japan Environment and Children's Study. J. Clin. Endocrinol. Metab. 2021, 107, e118–e129. [CrossRef] [PubMed]
- 15. Ministry of Internal Affairs and Communications. Japan Standard Occupational Classification. Available online: https://www.soumu.go.jp/english/dgpp_ss/seido/shokgyou/index09.htm (accessed on 7 February 2022).
- Yokoyama, Y.; Takachi, R.; Ishihara, J.; Ishii, Y.; Sasazuki, S.; Sawada, N.; Shinozawa, Y.; Tanaka, J.; Kato, E.; Kitamura, K.; et al. Validity of Short and Long Self-Administered Food Frequency Questionnaires in Ranking Dietary Intake in Middle-Aged and Elderly Japanese in the Japan Public Health Center-Based Prospective Study for the Next Generation (JPHC-NEXT) Protocol Area. J. Epidemiol. 2016, 26, 420–432. [CrossRef]
- 17. Japan Society of Obstetrics and Gynecology. Available online: https://www.jsog.or.jp/activity/pdf/gl_sanka_2020.pdf (accessed on 7 February 2022).
- Maher, J.E.; Goldenberg, R.L.; Tamura, T.; Cliver, S.P.; Hoffman, H.J.; Davis, R.O.; Boots, L. Albumin levels in pregnancy: A hypothesis–decreased levels of albumin are related to increased levels of alpha-fetoprotein. *Early Hum. Dev.* 1993, 34, 209–215. [CrossRef]
- Iwama, N.; Sugiyama, T.; Metoki, H.; Saito, M.; Hoshiai, T.; Watanabe, Z.; Tanaka, K.; Sasaki, S.; Sakurai, K.; Ishikuro, M.; et al. Associations between glycosylated hemoglobin level at less than 24 weeks of gestation and adverse pregnancy outcomes in Japan: The Japan Environment and Children's Study (JECS). *Diabetes Res. Clin. Pract.* 2020, 169, 108377. [CrossRef]
- Mitsuda, N.; Naw Awn, J.-P.; Eitoku, M.; Maeda, N.; Fujieda, M.; Suganuma, N.; Japan Environment and Children's Study (JECS) Group. Association between maternal hemoglobin concentration and placental weight to birthweight ratio: The Japan Environment and Children's Study (JECS). *Placenta* 2020, 101, 132–138. [CrossRef]
- Jayalekshmi, V.S.; Ramachandran, S. Maternal cholesterol levels during gestation: Boon or bane for the offspring? Mol. Cell. Biochem. 2021, 476, 401–416. [CrossRef]
- Gunderson, E.P.; Quesenberry, C.P., Jr.; Ning, X.; Jacobs, D.R., Jr.; Gross, M.; Goff, D.C., Jr.; Pletcher, M.J.; Lewis, C.E. Lactation Duration and Midlife Atherosclerosis. *Obstet. Gynecol.* 2015, 126, 381–390. [CrossRef]
- Bartels, Ä.; O'Donoghue, K. Cholesterol in pregnancy: A review of knowns and unknowns. *Obstet. Med.* 2011, 4, 147–151. [CrossRef] [PubMed]

- 24. Butte, N.F. Carbohydrate and lipid metabolism in pregnancy: Normal compared with gestational diabetes mellitus. *Am. J. Clin. Nutr.* **2000**, *71*, 1256s–1261s. [CrossRef] [PubMed]
- 25. Agbecha, A.; Yisa, E.N. Serum Albumin Level in Second and Third Trimester Pregnancies in Makurdi, Nigeria. *Saudi J. Biomed. Res.* **2018**, *3*, 175–180.