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Original Article

A Cross-sectional Study of Resting Cardio-respiratory and Metabolic Changes in Pregnant Women

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Abstract. [Purpose] We examined cardiorespiratory and metabolic changes across the 1st (G1), 2nd (G2) and 3rd (G3) trimesters in pregnant women. [Subjects and Methods] Forty-two healthy, active, non-smoking, pregnant women participated in this study. They were divided into G1, G2 and G3 groups depending on their mean gestational ages at the time of testing which were 10.5 ±2.9, 19.2 ±3.4, and 33.3 ±2.4 weeks of gestation, respectively. Cardio-respiratory and metabolic variables, VO_2 (oxygen consumption), VCO_2 (carbon dioxide production), and VE (minute ventilation), were measured using indirect calorimetry (IC, gas analyser) to estimate ventilatory equivalents of oxygen (VE/VO_2) and carbon dioxide (VE/VCO_2), RER (respiratory exchange ratio) and REE (resting energy expenditure). [Results] Women in the late pregnancy period had higher resting VCO_2 and RER, whereas the VE/VCO_2 ratio was significantly lower than in G1 and in G2. Even though the values of VO_2 and REE increased throughout the course of pregnancy, no significant differences were found. [Conclusion] In pregnant women, resting cardiorespiratory and metabolic variables continuously changed throughout the 3 trimesters. Changes in VE/VCO_2 and RER indicate shifting metabolic energy substrates. In addition, changes in cardiorespiratory variables, in parallel with gas exchange, indicate a better gas exchange process.
Key words: Resting cardiorespiratory, Metabolic, Trimester pregnancy

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INTRODUCTION

Women in Southeast Asia are characterized by small body size, and usually gain less weight during pregnancy than larger Caucasian[1)]. Lower resting minute ventilation (VE), oxygen consumption (VO_2), and carbon dioxide production (VCO_2) have been reported for healthy Thai women than for western women[2)]. Adaptation to pregnancy in humans involves major anatomical, physiological and metabolic changes to compensate for nutritional and metabolic demands throughout the 3 trimesters. The most evident change in the physical appearance of a mother's body during pregnancy is the consequential weight gain which depends on the individual[3)]. Cardiorespiratory alterations take place in the early stages of pregnancy resulting in an increase in tidal volume (VT) which remarkably affects minute ventilation (VE) throughout pregnancy. The enlargement of the uterus occurs later in gestation, and increases the pressure on the diaphragm causing an increase in resting VO_2, and an increase in the energy required for breathing[4)]. In the initial stage of pregnancy, maternal metabolism changes to anabolic metabolism accumulating a greater proportion of nutrients, as evidenced by an accumulation of fat stores. During the final stage of pregnancy period, when fetal growth is rapid, maternal metabolism switches to catabolic metabolism which enhances transfer of nutrients across the placenta[5)]. Very few studies have attempted to estimate energy expenditures in pregnant Thai women, and interestingly, none have investigated all 3 trimesters. Considering that maternal anthropometry differs across populations and physiological adaptations occur during the 3 trimesters, the present study aimed to examine cardiorespiratory and metabolic changes across the 1st (G1), 2nd (G2) and 3rd (G3) trimesters in pregnant women.

SUBJECTS AND METHODS

This investigation was a cross-sectional study of 42 healthy pregnant women, attending the Maternal Fetal Medicine Unit, Thammasat University Hospital. They were screened by an obstetrician who was also one of the investigators. All subjects were non-smokers, and were not taking long-term medication, or habitually abusing alcohol or

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Table 1. General physical characteristics of Thai pregnant women (n=42)

	Pregnant		
	G1 (n=14)	G2 (n=14)	G3 (n=14)
Ages (yrs)	27.7±5.8	26.9±5.1	24.0±5.2
Height (m)	1.59±0.04	1.59±0.06	1.57±0.05
Weight (kg)	57.6±7.8	61.4±11.6	66.6±7.4[a]
Body Mass Index (BMI, $kg.m^{-2}$)	22.7±3.4	24.1±3.6	26.7±4.2[a]
Gestation (weeks)	10.5±2.9	19.2±3.4	33.3±3.1

All values are presented as means ± SD; [a], Significantly different from G1 ($p<0.05$)
G1: Trimester 1; G2: Trimester 2 and G3: Trimester 3

drugs, and they were normoglycemic, euthyroid, and non-anemic. Gestational age was confirmed via the gynecological report of the last menstrual period, or by ultrasound. The first, second and third trimesters of pregnancy were classified using gestational age as follows: the first group extended from conception through week 14 of pregnancy (G1); the second group from weeks 14 through 28 (G2), and the third group from weeks 28 through 36 (G3). Both interview and physical activity questionnaire revealed that subjects of this study had sedentary lifestyles. This study was approved by both Thammasat University Hospital and Mahidol University Ethics Committee. Experimental protocols and testing procedures were clearly explained to the subjects prior to them providing their informed consent. To prevent risk during measurements, our study was conducted under the direct supervision of an obstetrician, who was also one of the investigators. Physical characteristics including height (H), body-weight (BW) and blood pressure (BP) were obtained at the enrollment. Body mass index (BMI, $kg.m^{-2}$) was calculated thereafter[6]. Cardiorespiratory and metabolic changes were measured using a telemetric indirect calorimetry method (Oxycon, USA) for variables including heart rate (HR), minute ventilation (VE), breathing frequency (BF), tidal volume (VT), oxygen consumption (VO_2), carbon dioxide production (VCO_2), ventilatory equivalents of oxygen (VE/VO_2) and carbon dioxide (VE/VCO_2), the respiratory exchange ratio (RER), and resting energy expenditure (REE). Before each evaluation, the metabolic cart was calibrated using 95% O_2 and 5% CO_2. All subjects were admitted to the hospital at 0700 after a 12-h overnight fast. They were instructed to avoid any intense physical activity with appropriate work/rest period during the 24 h before measurement. After 30 min of resting in a sitting position, metabolic profiles were measured continuously for 35 min. After subjects had had adequate acclimation, data were recorded as the average of every minute of quiet breathing. Subjects were instructed to avoid hyperventilation, fidgeting, or falling asleep during the test. REE was calculated using Weir's equation[7], without urinary urea nitrogen level. Data for general physical characteristics are reported as the mean ±SD. Data for resting cardiovascular and metabolic variables are reported as the mean ±SEM. The statistical differences among the three groups were analyzed using ANOVA followed by *post hoc* analysis with Tukey's test. The results were considered significant when $p<0.05$.

RESULTS

Mean gestational age at the time of testing was 10.5± 2.9 weeks in G1, 19.2 ±3.4 weeks in G2, and 33.3± 3.1 weeks in G3. The non-anemic status of the women was confirmed by routine tests for hemoglobin (Hb) and hematocrit (Hct) levels. All women were followed with routine, standard prenatal care at Thammasat University Hospital. As shown in Table 1, G1, G2 and G3 were matched for age and body height. Maternal weight and BMI increased with advancing gestation and were significantly greater in G3 than in G1 ($p< 0.05$). The results of BP, HR, VE, BF and VT in G1, G2 and G3 are reported in Table 2. Only HR in G3 was significantly higher than in G1 ($p< 0.05$). No significant difference in any other cardiorespiratory variable was detected. At rest, VO_2, VE and VT showed modest increases with advancing gestation but no significant differences were found among the groups. Significant differences in VCO_2, VE/VCO_2 and RER were found (Table 2), with G3 showing statistically higher values of VCO_2 and VE/VCO_2 than G1 ($p< 0.05$) and G2 ($p< 0.05$). RER was significantly higher in G3 than in G1 ($p< 0.05$). Despite REE being higher in G3, there were no significant differences in REE among the groups.

DISCUSSION

To our knowledge, this is the first study to determine cardiorespiratory and metabolic adaptations across 3 trimesters in pregnant women. Several types of evidence have shown that the smaller size of Southeast Asian women is related to their lower weight gain during pregnancy than Caucasian women[1]. Our study showed that the average value of BMI in the 1st trimester of pregnant women is 22.7 $kg.m^{-2}$. This is consistent with Liabsuetrakul T et al.[8], who studied 485 pregnant women, aged between 13–46 years with a gestational age of < 14 weeks, and reported their average value of BMI was about 22.4 $kg.m^{-2}$. In contrast, more than 50% of pregnant women in the United States have a BMI greater than 25.13 $kg.m^{-2}$ [9]. In comparison, Vietnamese women have a maternal body size [height (154±4.8 cm), BW (56±2.9 kg) and BMI (20.3±1.2 $kg.m^{-2}$] which is similar to that of pregnant Thai women during the 1st gestational stage[1]. As shown in our results, the maternal weight and BMI of pregnant Thai women continuously increased with a remarkable peak in the last trimester, indicating our subjects were well-nourished. These results therefore need to be interpreted with caution. Even though the changes

Table 2. Resting cardiorespiratory and metabolic changes of Thai pregnant women

Variables	Pregnant		
	G1	G2	G3
Cardiorespiratory variables			
BP (Systolic, mmHg)	106.9±2.43	105.1±2.48	106.0±3.24
(Diastolic, mmHg)	68.3±1.68	65.0±1.49	69.6±1.86
Heart rate (HR, bpm)	81.3±2.1	84.2±2.8	90.7±2.0 [a]
Minute ventilation (VE, L/min)	10.4±0.64	10.47±0.50	11.30±0.66
Breathing frequency (BF, breaths/min)	19.50±0.51	20.19±0.73	18.36±0.83
Tidal volume (VT, L)	0.57±0.03	0.57±0.02	0.60±0.02
Metabolic variables			
Oxygen consumption (VO_2, ml/min)	253.9±13.56	262.3±11.94	298.2±15.38
Carbon dioxide production (VCO_2, ml/min)	205.1±13.97	226.4±11.32	268.3±13.62[a, b]
VE/VO_2	38.71±0.99	40.84±0.95	38.81±0.88
VE/VCO_2	48.56±1.62	47.59±1.43	43.05±0.63 [a, b]
Respiratory exchange ratio (RER)	0.79±0.03	0.86±0.03	0.91±0.12 [b]
Resting energy expenditure (REE, kcal/day)	1861±103.49	1815.6±84.62	2081.8±108.07

All values are presented as means ± SEM; [a], Significantly different from G1 ($p<0.05$); [b], Significantly different from G2 ($p<0.05$)
G1: Trimester 1; G2: Trimester 2 and G3: Trimester 3

seem to be typical maternal anthropometric characteristics of Southeast Asian women, the nutritional and socioeconomic status of pregnancy should also be considered for Thai women.

The average values of resting HR, VE, VO_2 and VCO_2 in the 1st trimester of pregnancy were within the normal ranges of Thai women of this age range[2]. With advancing gestation, the present study found progressive changes: HR increased 6 beat per min. (bpm) in the 1st trimester, and 9 and 15 bpm in the 2nd and 3rd trimesters; VE increased 60%, 33% and 83% in the 1st, 2nd and 3rd trimesters; VO_2 increased 19%, 15% and 34% in the 1st, 2nd and 3rd trimesters; and VCO_2 increased 7% in the 1st and 2nd trimesters and 28% in the 3rd trimester. These findings are in agreement with reports in the literature on the physiological adaptations of the mother to the developing embryo[10]. The heart must work harder during pregnancy in order to pump more blood to the uterus. This was reflected in the rise in heart rate of around 6 bpm in the 1st trimester, with a further 20% increase during the 2nd and 3rd trimesters, for a rise of around 15 bpm by the end of pregnancy[4, 10]. Our study confirms the results of previous studies that pregnancy-induced increases in VE are greater than those typically observed for the metabolic rates of VO_2 and VCO_2[11]. Our results differ from those of a previous study with regard to changes in VE/VO_2 and VE/VCO_2 values[12]. We found that the value of VE/VO_2 did not change, whereas the VE/VCO_2 value in late gestation was significantly lower than in the first two trimesters of gestation. Since the VE/VCO_2 ratio represents the responsiveness of ventilation to changing CO_2 concentrations and the lung's efficiency in removing CO_2 from the body, the lower VE/VCO_2 ratio may reflect a better gas exchange efficiency[13]. However, further investigations with larger sample sizes are required to confirm this result.

RER is the ratio between VO_2 and VCO_2 and is used as an indicator of the energy substrate being metabolized within the body. Our data show that the value of RER gradually increased from 0.8 in the 1st trimester to 0.86 in the 2nd trimester and 0.91 in the 3rd trimester. Most previous studies have reported an increase in RER in pregnant women, indicating higher rates of net carbohydrate utilization[5]. Our results confirm the evidence of increasing RER of pregnant women, towards greater carbohydrate utilization, as gestation progresses. This indicates that carbohydrate and fat are the main energy supply during the 1st trimester, whereas a higher contribution comes from carbohydrate during the last trimester. The magnitude of the increase in REE during pregnancy varies considerably among women. Although several studies have reported energy expenditure increases during pregnancy, our data show only a moderate increase during the final trimester. The small increase in REE could be due to either low energy reserves or low BMI before pregnancy a characteristic of Southeastern Asian women. However, various biological or behavioral factors may also mediate or modify resting energy expenditure which is influenced by height, weight, age, nutritional status and body composition[1].

In pregnant women, resting cardiorespiratory and metabolic variables continuously changed throughout the 3 trimesters. Changes in VE/VCO_2 and RER indicate shifts in metabolic energy substrate. In addition, changes in cardiorespiratory variables, in parallel with gas exchange, indicate a better gas exchange process. We suggest further studies are needed to determine the effects of daily physical activity or exercise on cardiorespiratory and metabolic changes during the three phases of pregnancy.

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