ORIGINAL ARTICLE

Analysis of Pulmonary Function and Serum Progesterone Level during Pregnancy: A Cross-sectional Study

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Abstract

Aim and objective: Pregnancy is often accompanied by physiological variations, especially variations in the respiratory function. However, there is insufficient information regarding the association of hormonal changes and pulmonary function tests in different trimesters of pregnancy. Hence This was aimed to assess the effects of progesterone levels on the lung function of pregnant women.

Materials and methods: A total of 150 pregnant women comprising 50 women in each of the 3 trimesters of pregnancy were recruited for this study to compare the lung function variations across the trimesters. Both dynamic and static pulmonary function tests were measured. Serum progesterone and blood hemoglobin levels were also estimated. Data was analyzed using ANOVA and Kruskal–Wallis test. Tukey's HSD and Dunn's test were used as *post hoc* tests. $p < 0.05$ was considered as statistically significant.

Results: Variations in the lung functions were observed across all the trimesters of pregnancy. Among the dynamic lung function tests, peak expiratory flow rate (PEFR, $p = 0.0043$) and forced expiratory flow (FEF, $p = 0.0151$) were significant in the first trimester. PEFR ($p = 0.0047$) and FEF ($p = 0.016$) were significant in the second trimester. Among the static lung function tests, maximum voluntary ventilation ($p = 0.0003$) was a significant variable in the second trimester. Progesterone levels were significant in all the 3 trimesters of pregnancy ($p < 0.0001$) and were associated with increased gestational age. In contrast, hemoglobin levels were insignificant throughout pregnancy ($p = 0.8548$).

Conclusion: The progesterone levels did not have any significant association with the pulmonary function test during gestation.

Clinical significance: The chronic respiratory diseases ranked third most cause and in order to evaluate any respiratory ailment during pregnancy, an accurate knowledge of the physiological changes in pulmonary functions during normal pregnancy is necessary.

Keywords: Female, Maximum voluntary ventilation, Peak expiratory flow rate, Pregnancy trimesters, Progesterone.

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Introduction

Pregnancy marks numerous alterations in the physiological, biochemical, and anatomical profiles. The major anatomical changes associated with thorax during pregnancy are expansion of circumference of lower thorax, upward movement of diaphragm, and 50% increase in costal angle.[1–3] Alteration in thoracic cage, respiratory drive, and airway affects pulmonary function. Biochemical variations are increased in prostaglandins, estrogen, progesterone, cyclic nucleotide, and corticosteroids that accompany pregnancy. Hormone-induced changes in elastance of the connective tissue and smooth muscle tone may result in mechanical modulation of the respiratory system.[4] An upward movement of the diaphragm in the later stages of pregnancy is an indication of the pressure developed by the uterus on the abdomen, mitigating negative intrapleural pressure and hyperventilation with a decrease in the partial pressure of carbon dioxide.[5,6] Transverse diameter of the chest increases due to the expanded subcostal angle that resists the effect of expanding the uterus and the upward movement of diaphragm to provide change in the pulmonary function as required for the pregnancy.[7] In the Western part of the globe, parity and smoking are associated with the lung function of pregnant women, which is evaluated by a spirometer.[8] The birth weight of newborn is affected by a decrease in the forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC.[4]

The pulmonary function test (PFT) provides information about the different types of pulmonary diseases, lung capacities, pre- and post-treatment differences, and severity of the disease. Computerized spirometry has an advantage over manual spirometer, as it presents with general information about the patients and spirogram (graphical representation of volume-time curve).[9]

Some studies state that the dynamic lung function, specifically FVC, decreases with the duration of pregnancy, whereas another study states that increase in FVC was observed after 14–16 weeks of pregnancy and remain persistent until postpartum.[4,10,11] Spirometry outcomes such as FVC, FEV_1, and peak expiratory flow (PEF) remain unaltered during pregnancy. Other studies have reported that decrease in PEF was associated with increasing pregnancy duration, high altitude, and maternal positioning. However, there is a dearth of studies on the respiratory changes and its association

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with hormonal changes during pregnancy.[6,12] A well-planned study design and appropriate statistical methods are important to study the physiological variations in pregnancy. Longitudinal studies illustrate individual variations with regard to the pregnancy duration.[11] The present study was conducted with an objective to assess the association between PFT and progesterone level during the trimesters of pregnant women attending a tertiary-care hospital in Belagavi, Karnataka, India.

Materials and Methods

This cross-sectional study recruited 150 pregnant women visiting the outpatient Department of Obstetrics and Gynecology of a tertiary-care hospital. The study was conducted between October 2018 and July 2019 after obtaining approval from the Institutional Ethics Committee and an informed consent from all the study participants prior to the commencement of the study. Pregnancy had been confirmed for all the subjects by a well-qualified gynecologist prior to the recruitment.

Healthy pregnant women willing to participate were included in the study. The health status of the pregnant women was determined by a thorough clinical examination. Subjects with acute respiratory infections in the previous 3 months; chronic respiratory infection including asthma; history or clinical signs of cardiovascular diseases, diabetes mellitus, hypertension, tobacco consumption, alcohol intake, endocrine disorders, obesity; and severe anemia were excluded from the study.

The study subjects were interviewed for demographic data, personal history, and diet pattern in comprehensive detail, and the data were recorded in a structured *pro forma*.

The pregnant women (n = 150) were allocated into three different groups of 50 women each, representing 3 trimesters, respectively. For clinical examination, systolic and diastolic blood pressures, pulse rate, pulse pressure, and respiratory rate were recorded. Progesterone and hemoglobin levels were estimated. Crown-rump length chart finding suggests that all the study participants had singleton pregnancy. Each group of participants underwent dynamic and static PFTs for each specified trimester.

Static and dynamic PFTs were measured with computerized spirometer MEDSPIROR, and it was standardized and calibrated by the manufacturing company. Dynamic lung functions, such as FVC, FEV_1, peak expiratory flow rate (PEFR), and forced expiratory flow (FEF), and static lung functions, such as tidal volume (TV), inspiratory reserve volume (IRV), inspiratory capacity (IC), and maximum voluntary ventilation (MVV), were measured.[13,14]

Under the supervision of observer from pulmonary medicine, a trial run was carried out to familiarize and accommodate participants to the procedure. Subjects were instructed to perform deep and rapid expiration through the mouthpiece of the spirometer followed by deep inspiration. The FEV_1, FVC, PEFR, and FEF were recorded at the mid portion of the FVC.

For progesterone level estimation in the pregnant women, blood was collected in a plane bulb and centrifuged at 300×g for 10 minutes. The progesterone level was assessed by commercial ARCHITECT progesterone kit (Abbott, Ireland) and was processed following the manufacturer's instructions.[15]

Data analysis was performed using R i386.3.5.1 and Microsoft Excel. Continuous data were presented in the form of mean ± SD, and the categorical variables were represented by the frequency table. Continuous variables (demographic data, anthropometric data, and dynamic and static PFTs) from the three trimesters were compared using analysis of variance (ANOVA)/Kruskal–Wallis test. Tukey's HSD and Dunn's test were used as *post hoc* tests. p value <0.05 was considered as statistically significant.

Results

The study consisted of 150 pregnant women who were recruited to analyze the dynamic and static lung functions which were compared between the trimesters. The mean age and height of the pregnant women during the three consecutive trimesters were comparable in all the groups, and an increase in the mean weight was observed from the first to the third trimester (Table 1).

ANOVA was used for comparison across the trimesters, and body mass index (BMI) (p value = 0.0106), and body surface area (BSA) (p value = 0.0179) were significantly different between the trimesters. Clinical examination revealed that the pulse rate (p value = 0.43164), systolic (p value = 0.050) and diastolic (p value = 0.2519) blood pressure, and pulse pressure (p value = 0.6275) had no significant difference, whereas the respiratory rate (p value = 0.0296) was significantly influential during the progression of the trimesters according to the Kruskal–Wallis test. By Tukey's HSD test, the mean BMI of the subjects in the second (p value = 0.0387) and third trimesters (p value = 0.0158) was significantly different from the first trimester. Moreover, the mean of BSA of the subjects in the third trimester (p value = 0.0130) was significantly different from that in the first trimester. Furthermore, the distribution of the respiratory rate in the second trimester (p value = 0.0166) was significantly different from that in the first trimester (Table 1).

The mean of different tests of dynamic PFT are as follows: FVC in first trimester was 2.15 ± 0.55 L, in second trimester 2.09 ± 0.40 L, and 2.12 ± 0.52 L in third trimester. FEV_1 was 1.93 ± 0.52 L in first trimester, 1.78 ± 0.37 L in second trimester, and 1.82 ± 0.39 L in third trimester. PEFR was recorded as 3.77 ± 2.08 L, 2.77 ± 0.89 L, and 3.12 ± 1.34 L in first, second, and third trimesters, respectively. FEF (L/s) (25–75) was reported as 2.88 ± 1.31 L/s, 2.88 ± 1.31 L/s, and 2.52 ± 1.10 L/s in first, second, and third trimesters, respectively.

Upon controlling BMI, PEFR (p = 0.0047) and FEF (p = 0.0160) were significant in second trimester. Upon controlling the dynamic lung function, PEFR (p = 0.0043) and FEF (p = 0.0151) were recorded to be significant in first trimester. After controlling BMI in first trimester, FVC mean ± standard deviation (SD) was 2.15 ± 0.55 L, residual standard deviation (RSD) was 35.98 L, FEV_1 mean ± SD was 1.93 ± 0.52 L, and RSD was 28.31 L, PEFR mean ± SD was 3.77 ± 2.08 L/s and RSD was 363.69 L/s and FEF (25–75) mean ± SD was 2.88 ± 1.31 L/s and RSD was 189.52 L/s. In second trimester FVC mean ± SD was 2.09 ± 0.40 L, RSD was 35.89 L, degree of freedom (Df) was two, and p value was 0.8263. FEV_1 mean ± SD was 1.78 ± 0.37 L, RSD was 27.73 L, Df was 2, and p value was 0.2161; PEFR mean ± SD was 2.77 ± 0.89 L/s, RSD was 337.74 L/s, Df was two and p value was 0.0047[b] and FEF (25–75) Mean ± SD was 2.24 ± 0.84 L/s, RSD was 179.01 L/s, Df was 2, and p value 0.0160[b]. In third trimester FVC Mean ± SD was 2.12 ± 0.52 L, Df was 3, RSD was 34.03 L, and p value was 0.0530. FEV_1 Mean ± SD was 1.82 ± 0.39 L, Df was 3, RSD was 26.92 L, and p value was 0.2324, PEFR Mean ± SD was 3.12 ± 1.34 L/s, Df was 3, RSD was 336.08 L/s, and p value was 0.8698. FEF (25–75) Mean ± SD was 2.52 ± 1.10 L/s, Df was 3, RSD was 177.88 L/s, and p value was 0.8220.

When dynamic lung function was compared to trimesters, FVC mean ± SD was 2.15 ± 0.55 L, Df was 2, sum of squares (SS) was 0.090, and p value was 0.8314; FEV_1 mean ± SD was 1.93 ± 0.52 L, Df was 2, SS was 0.5788, and p value was 0.219; PEFR mean ± SD was 3.77

Table 1: Baseline characteristics of the cohort and comparison of anthropometric parameters across the groups

		Trimesters			
Demographic factors		*I (mean ± standard deviation)*	*II (mean ± standard deviation)*	*III (mean ± standard deviation)*	*p value*
Age (years)		23.34 ± 2.85	23.48 ± 3.2	23.2 ± 2.6	
Gestational height (cm)		151.4 ± 5.72	150.34 ± 6.66	151.52 ± 6.43	
Gestational weight (kg)		49.94 ± 9.47	53.6 ± 9.56	55.8 ± 9.42	
Body mass index (kg/m^2)		21.94 ± 4.11	24.08 ± 4.84	24.36 ± 3.98	0.0106[b]
Body surface area (m^2)		1.44 ± 0.14	1.49 ± 0.15	1.53 ± 0.14	0.0179
Pulse rate (pulse/minute)		83 ± 9.49	83.44 ± 9.79	85.32 ± 9.14	0.4314
Systolic blood pressure (mm Hg)		110.16 ± 7.64	113.48 ± 6.75	112.32 ± 7.83	0.0500[a]
Diastolic blood pressure (mm Hg)		69.60 ± 6.96	71.64 ± 6.12	71.28 ± 7.36	0.2519[a]
Pulse pressure (mm Hg)		40.56 ± 6.10	42.24 ± 8.35	41.44 ± 8.11	0.6275[a]
Respiratory rate (cycles/minute)		17.74 ± 2.66	16.44 ± 2.43	17.40 ± 2.26	0.0296[a,b]
Body mass index (kg/m^2)	I		0.0387	0.0158	
	II		–	0.9409	
Body surface area (m^2)	I		0.2570	0.0130	
	II			0.4031	
Respiratory rate (breaths/min)	I		0.0166	0.8127	
	II			0.0802	

[a]Kruskal–Wallis test
[b]$p < 0.05$ is statistically significant

± 2.08 L/s, Df was 2, SS was 25.94, and *p* value was 0.0043[b]; and FEF (25–75) mean ± SD was 2.88 ± 1.31 L/s, Df was 2, SS was 10.51, and *p* value was 0.0151[b] in first trimester. In second trimester, FVC mean ± SD was 2.09 ± 0.40 L, Df was 147, and SS was 35.89; FEV_1 mean ± SD was 1.78 ± 0.37 L, Df was 147, and SS was 27.73; PEFR mean ± SD was 2.77 ± 0.89 L/s, Df was 147, and SS was 337.74; and FEF (25–75) mean ± SD was 2.24 ± 0.84 L/s, Df was 147, and SS was 179.01. In third trimester, FVC mean ± SD was 2.12 ± 0.52 L, FEV_1 mean ± SD was 1.82 ± 0.39 L, PEFR mean ± SD was 3.12 ± 1.34 L/s, and FEF (25–75) mean ± SD was 2.52 ± 1.10 L/s. Here 'b' indicates *p* value < 0.05 which was statistically significant.

Static PFTs were compared to the trimester, and the maximum voluntary ventilation (MVV) were significant (*p* value = 0.0003) in the second trimester (Table 2).

Progesterone and hemoglobin levels were compared in the third trimester, and it was found that only progesterone level was significant (*p* value <0.001) (Table 3).

Chi-square test yielded an insignificant association between anemia and the 3 trimesters of pregnancy. In the first, second, and third trimesters, 24%, 22%, and 24% of the pregnant women were mildly anemic, respectively.

None of the PFTs were significant with changes in progesterone levels during pregnancy. FVC (Rho = −0.0100, *p* value = 0.9033), FEV_1 (Rho = −0.0684, *p* value = 0.4054), FEV% (Rho = −0.0604, *p* value = 0.463), PEFR (Rho = −0.0565, *p* value = 0.4925), and FEF (25–75) (Rho = −0.0473, *p* value = 0.5651). In static LFTs, TV (Rho = −0.0506, *p* value = 0.321), IRV (Rho = −0.0506, *p* value = 0.5383), IC (Rho = −0.0379, *p* value = 0.645), and MVV (Rho = 0.0759, *p* value = 0.3557) were insignificant.

The association of the dynamic LFTs with the progesterone levels was insignificant. Among the static LFTs, IRV (*p* value = 0.0144) was significantly associated with the progesterone level in third trimester (Table 4).

Discussion

Numerous physiological changes accompanied by hormonal changes are apparent during pregnancy, and one such physiological modulation is observed about the respiratory system. This study aimed to assess the influence of progesterone level on the pulmonary function among pregnant women in all the trimesters. It was observed that BMI, BSA, diastolic blood pressure, pulse pressure, MVV, respiratory rate, and progesterone levels were significant factors and should be constantly monitored throughout the progression of pregnancy. The study compared dynamic LFTs of pregnant women across the three trimesters, and it was observed that PEFR and FEF were significant in the first trimester. However, after controlling the BMI, PEFR was significant in the second trimester.

PFTs are influenced by parity. In this study, FVC and FEV_1 test scores were consistent with Gupta et al.'s findings but were lower than those observed in Pastro et al. study.[5,16] Gupta et al.'s study which was also conducted on Indian pregnant women reported that the decreased FVC and FEV_1 could possibly be influenced by parity more than the habit of smoking. However, influence of lifestyle cannot be ruled out.[5,16] This study observed lower values of PEFR and FEF than those reported by Pastro et al. (PEFR = 6.179 ± 1.113 L/s for 1st trimester and 6.042 ± 0.964 L/s for 2nd trimester and FEF = 3.409 ± 0.887 L/s for 1st trimester and 3.390 ± 0.773 L/s for 2nd trimester), and by Gupta et al. (case group PEFR = 3.9 ± 1.09 L/s).[5,16] In the third trimester of pregnancy, the intra-abdominal pressure increases due to the gravid uterus, which restricts the movement of diaphragm and increases the intrathoracic pressure.[6,10] This could probably lower the efficacy of lung functioning during pregnancy.

During the eighth week of pregnancy, minute ventilation in pregnant women is increased by 36–50% in comparison to nonpregnant women to meet the oxygen demand by the fetus. This is achieved by increase in progesterone secretion, which stimulates

Table 2: Correlation between lung function tests and trimester

		Trimester			
	Tests	*I (mean ± SD)*	*II (mean ± SD)*	*III (mean ± SD)*	*ANOVA results*
Dynamic lung functions	FVC (L)	2.15 ± 0.55	2.10 ± 0.40	2.12 ± 0.52	F (2,147) = 0.18 p = 0.8314
	FEV_1 (L)	1.93 ± 0.52	1.78 ± 0.37	1.82 ± 0.39	F (2,147) = 1.53 p = 0.219
	PEFR (L/s)	3.77 ± 1.08	2.77 ± 0.89	3.12 ± 1.34	F(2,147) = 5.65 p = 0.0043[b]
	FEF (25–75) (L/s)	2.88 ± 1.31	2.24 ± 0.84	2.52 ± 1.10	F(2,147) = 4.32 p = 0.0151[b]
Static lung functions	TV (L)	0.63 ± 0.41	0.78 ± 0.46	0.67 ± 0.41	F(2,147) = 1.81 p = 0.1674
	IRV (L)	0.80 ± 0.49	0.64 ± 0.36	0.73 ± 0.39	F(2,147) = 1.80 p = 0.1692
	IC (L)	1.47 ± 0.53	1.43 ± 0.43	1.44 ± 0.43	F(2,147) = 0.13 p = 0.8775
	MVV (L)	36.67 ± 19.57	44.23 ± 14.75	40.56 ± 17.77	F(2,147) = 0.18 p = 0.8314

TV, tidal volume; IRV, inspiratory reserve volume; IC, inspiratory capacity; MVV, maximum voluntary ventilation; PEFR, peak expiratory flow rate; FEF, forced expiratory flow; FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity
[b]$p < 0.05$ Statistically significant

Table 3: Comparison of progesterone and hemoglobin levels across the three trimesters

Factor	*Trimester*	*Mean ± standard deviation*	*Median [range]*	*p value[(1)]*	*Trimester*	*Pairwise comparison p value[(2)] (Bonferroni)* I	*II*
Comparison of progesterone across the trimester							
Progesterone (ng/mL)	I	34.25 ± 13.07	33.75 [6.95,60]	<0.0001[b]	II	<0.0001[b]	–
	II	55.02 ± 7.25	60 [34.54,60]		III	<0.0001[b]	<0.0188[b]
	III	59.21 ± 3.11	60 [40.14,60]				
Comparison of hemoglobin across the trimesters							
Hemoglobin (g%)	I	11.13 ± 1.31					
	II	10.99 ± 1.15		0.8548			
	III	11.08 ± 1.35					

[b]$p < 0.05$ Statistically significant
[(1)]Gives the overall p value
[(2)]Indicates p value of post hoc test i.e, pairwise comparison

Table 4: Correlation between lung function tests and progesterone level in three different trimesters

		I		II		III	
Lung function tests	*Tests*	*r[b]*	*p value*	*rho*	*p value*	*rho*	*p value*
Dynamic lung function tests	FVC	0.2220	0.1213	−0.0662	0.648	−0.0153	0.9159
	FEV	0.1741	0.2265	−0.003	0.9808	−0.0569	0.6946
	PEFR	0.2065	0.1501	0.0060	0.9671	0.0504	0.7283
	FEF	0.1659	0.2495	0.0643	0.6574	0.0643	0.6576
Static lung function tests	TV	0.2242	0.1175	−0.0357	0.8057	−0.0808	0.5771
	IRV	−0.0660	0.6485	−0.1161	0.4222	0.34	0.0144[a]
	IC	0.0352	0.8081	−0.0804	0.5787	0.0178	0.9026
	MVV	0.1122	0.438	0.0762	0.5989	−0.0964	0.5054

PEFR, peak expiratory flow rate, FEF, forced expiratory flow; FEV_1: forced expiratory volume in the first second; FVC, forced vital capacity; TV, tidal volume; IRV, inspiratory reserve volume; IC, inspiratory capacity; MVV, maximum voluntary ventilation
[a]Indicates significance i.e., p value < 0.05 considered as significant
[b]$p < 0.05$ statistically significant
'ç' Pearson correlation

the respiratory centers. The increase in ventilation is accomplished by an increase in the TV to 700 mL without altering the respiratory rate. Vital capacity is increased by 100–200 mL and in late pregnancy, IRV increases by 300 mL; expiratory reserve volume decreases from 1,300 mL to 100 mL; and residual volume (RV) decreases from 1,500 to 1,200 mL.[17] As pregnancy advances, the abdominal volume increases and proportionately reduces the strength of expiratory muscles, including the diaphragm. An increase in the secretion of progesterone increases the sensitivity toward carbon dioxide at the respiratory center, which alters the thoracic configuration and restricts the expansion of smooth muscles. This could justify the increase in the TV.[8] This study observed that TV was higher than that reported in the previous studies, and MVV was lower than that observed in Gupta et al.'s study.[6,8,15] Additionally, IC was lower in Puranik et al.'s study, (range from 1.61 ± 0.22 L to 2.29 ± 0.29 L from first to ninth month) and consistent with our study (1.47 L, 1.3 L, and 1.43 L in first, second, and third trimesters, respectively).[18,19] This study observed IRV value is slightly lower than the our previous study (0.78 L in first trimester, 0.75 in second trimester, and 0.92 L in third trimester).[19]

Our study evaluated the progesterone levels in addition to the lung function among pregnant women. However, this study could not find any correlation as established by the previous studies. In our study, the hemoglobin level was lower than that in Gupta et al.'s study (13.10 ± 0.93 g%)[16] and was inconsistent throughout pregnancy due to the increased plasma volume.[20]

This study had its share of limitations. The influence of parity on the lung function was not evaluated. Additionally, there were three groups of pregnant women, and each group was assigned to only one trimester for the evaluation of PFT. Future studies are recommended for assessing the respiratory characteristics through all the stages of gestation among the same subjects to obtain more robust results.

Conclusion

The variables of PFTs and progesterone levels varied across the trimesters of pregnancy. However, the pulmonary function and progesterone levels were not correlated and thus mandate monitoring. Future longitudinal studies are needed to be conducted to assess the correlation of lung function with parity and hormonal changes among pregnant women.

Clinical Significance

According to the study conducted in 2017 and published in *Lancet*, there were about 9·7 million deaths and 486 million DALYs (Disability Adjusted Life Years) in India. DALY rates in rural areas were at least twice those of urban areas for perinatal and nutritional conditions, chronic respiratory diseases, diarrhea, and fever of unknown origin. The top 15 conditions that accounted for the most DALYs were mostly those causing mortality (ischemic heart disease, perinatal conditions, chronic respiratory diseases, diarrhea, respiratory infections, cancer, stroke, road traffic accidents, and tuberculosis). The chronic respiratory diseases ranked third most cause, and in order to evaluate any respiratory ailment during pregnancy, an accurate knowledge of the physiological changes in pulmonary functions during normal pregnancy is necessary. It was therefore the study undertaken, and the findings of normal pulmonary functions were studied and their relation with the hormonal levels were assessed which helps to differentiate the normal physiological changes occurring from the pathological changes.

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