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"TIMING, DEPTH AND DRIVE OF VENTILATION DURING PREGNANCY: INDIAN RURAL PERSPECTIVE"

Physiology

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ABSTRACT

Normal pregnant women (N=300) were studied for SVC maneuver during all three trimesters. Respiratory frequency (Rf), tidal volume (TV), minute ventilation (VE), Inspiratory (Ti) and expiratory time (Te), duty cycle (Ti/Ttot) and inspiratory flow (TV/Ti) were studied longitudinally during pregnancy in different trimesters. Apparently healthy 100 nonpregnant women matched with age and socioeconomic status were studied as control. Ventilation increases initially and remains constant throughout the pregnancy. This increment in VE during pregnancy is due to gradual and significant increase in TV (ANOVA <0.05), because Rf was unaltered throughout the pregnancy. Inspiratory time (Ti), flow (TV/Ti) and duty cycle found to be significantly higher in pregnant women when compare to nonpregnant control. Progesterone may effective centrally as respiratory drive maintained at high level throughout pregnancy. Progesterone may not effective locally at the level of respiratory apparatus because earlier study in same population suggest no changes in FVC manoeuvre.

KEYWORDS:

Inspiratory flow, Duty cycle, SVC manoeuvre

Introduction:
At a first glance, resting breathing pattern appears to be an oscillatory event approximating a sinusoidal function, of which the amplitude is tidal volume (VT) and the period is the total breath duration (Ttot). The combination of hormonal changes, teleological alterations and mechanical effects may alter the lung functions during pregnancy and influence the natural history of associated pulmonary disorders. Understanding of these changes is critical in distinguishing the common dyspnea that occurs during normal pregnancy from associated clinical states, anticipating disease worsening in pregnancy and the peripartum period in compromised women.[1,2] Unlike western world this aspect of Indian female is still remain untouched and no reference values has been reported for Indian rural pregnant female for pulmonary parameters.

Hormonal changes during pregnancy affect the upper respiratory tract and airways.[3] Progesterone, as in literature reported, is known to increase the ventilatory capacity, but centrally or locally is still remain unsolved.4-5 Studies on lung functions during pregnancy are extensive but the findings are controversial and inconsistent, so the conclusive changes are not yet reported. Moreover literature is lacking studies which analyzed the timing and depth component in pregnancy. This study was aimed to assess timing, depth and drive of ventilation in normal human pregnancy.

Material and methods:
Study population: Pregnant women attending antenatal clinic of Dhiraj General Hospital, Vadodara city. Nonpregnant women matched with age and socioeconomic status studied as control.

Sample size: Random sampling was used. Total 400 female participants were studied. Group 1 comprised pregnant group included 300 pregnant women, 100 in each trimester serially and vertically both. Determination of different trimester was based on last menstrual phase (LMP) reported by clinician. Group 2 was control group included 100 apparently healthy nonpregnant women.

Ethics: This study was complied with the ethical committee guidelines of SVIEC (EC No. SVIEC/ON/MEDI/PhD/1202) and the procedures followed were in accord with the ethical standards of Sumandeep Vidyapeeth.

Inclusion criteria's: Age group: 20-40 years, Gestational age: 4th to 40th weeks, primipara or multipara, Singleton pregnancy.

Exclusion criteria's: Respiratory tract infection, acute/active asthma, unsatisfactory training with instrument

After informed consent and information about the study, participants were invited to the respiratory laboratory and given 15 min rest. SVC maneuver was performed with the help of digital spirometer SpiroWin + (Genesis medical systems Pvt ltd, Made in India). Vital capacity, (VC) respiratory frequency (Rf), tidal volume (TV), minute ventilation (VE), Inspiratory (Ti) and expiratory time (Te), duty cycle (Ti/Ttot) and inspiratory flow (TV/Ti) were measured. All participants were investigated for at least thrice (as per the ATS guidelines).

Statistical analysis: ANOVA used for within group variation analysis during each trimester of pregnancy and unpaired student's t-test was used for between group variations of pregnant and control group. The α error for a significant t-test was set at the 5% level.

Results &Observation:
Table-I: Anthropometric parameters and Gestational age in nonpregnant control and during all three trimesters of pregnancy

Parameters	I trimester (N=100)	II trimester (N=100)	III trimester (N=100)	Control (N=100)
Age (Yrs)	23.03±2.45	22.32±2.5	22.73±2.6	26.4±4.41
Weight (Kg)	46±7.3	48.3±6.52	50.7±6.5	47.9±7.13
Height (mt)	1.56±.05	1.56±.05	1.53±.06	1.54±.05
Gestational age (wks)	10.37±2.69	19.45±3.5	38.9±2.68	-

The trimester variations are insignificant for all parameters except TV and Ti (ANOVA, $p>0.05$) as shown in Table-II. Significant increase was found for TV (0.491±0.14 vs 0.734±0.26, $p<0.01$) and decrease was found for ERV (0.460±0.2 vs 0.387±0.2, $p<0.05$) when non pregnant group (N=100) compared with pregnant group (N=300), while SVC, IRV altered insignificantly. Changes are significant when overall comparing pregnant group (N=300) with non pregnant group (N=100) for ventilation (14.66±5.5 in pregnant group vs 10.73±3.69 in nonpregnant group), while Rf remains within physiological limit.

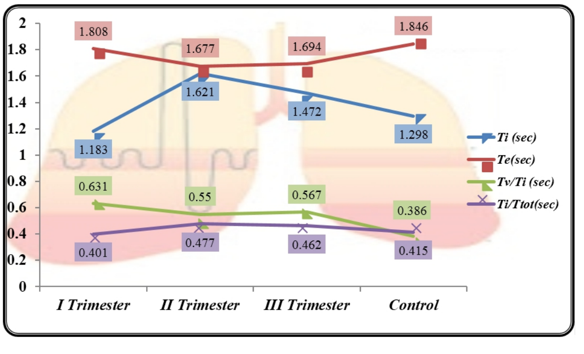
Changes are significant for inspiratory time (1.458±0.62 vs 1.298±0.26, $p<0.05$), inspiratory flow (0.580±0.28 vs 0.386±0.25, $p>0.001$) and duty cycle (0.452±0.07 vs 0.415±0.07, $p>0.05$) when comparing pregnant group (N=300) with nonpregnant control group (N=100).

Table-II: Timing, Depth and Drive of Ventilation in nonpregnant control and during all three trimesters of pregnancy

Variables		I Trimester N=100	II Trimester N=100	III Trimester N=100	Control N=100	Statistics (ANOVA)
SVC (Ltr)	M	2.004	1.993	1.985	1.885	P>0.05,NS
	SD	0.55	0.49	0.53	0.39	
ERV (Ltr)	M	0.384	0.392	0.390	0.460	P>0.05,NS
	SD	0.24	0.21	0.23	0.20	
IRV (Ltr)	M	1.020	1.087	1.095	1.078	P>0.05,NS
	SD	0.45	1.13	0.50	0.34	
TV (Ltr)	M	0.672	0.739	0.737	0.491	P<0.05,S
	SD	0.25	0.24	0.28	0.14	
VE (Ltr)	M	13.54	14.219	13.89	10.73	P>0.05,NS
	SD	4.8	7.09	5.86	3.68	
Rf (/min)	M	19.89	20.99	20.59	21.28	P>0.05,NS
	SD	5.9	5.6	6.57	2.27	
Ti (sec)	M	1.183	1.621	1.472	1.298	P<0.05,S
	SD	0.49	0.69	0.58	0.26	
Te (sec)	M	1.808	1.677	1.694	1.846	P>0.05,NS
	SD	0.78	0.68	0.63	0.39	
TV/Ti (sec)	M	0.631	0.550	0.567	0.386	P>0.05,NS
	SD	0.28	0.27	0.31	0.258	
Ti/Ttot (sec)	M	0.401	0.477	0.462	0.415	P>0.05,NS
	SD	0.06	0.08	0.06	0.08	

S-Significant, NS=Nonsignificant, N- Number of subjects

Graph I: Inspiratory time (Ti), Expiratory Time (Te), Inspiratory Flow (TV/Ti) and Duty cycle (Ti/Ttot) of nonpregnant (control) group and pregnant women in three different trimesters



Discussion:

Unlike earlier author found ERV, VC and IRV as unaltered during three trimesters of pregnancy.[6,7,8] Unaltered changes found for ERV, VC and IRV during pregnancy can be explained by the mechanism that the shortening of the thorax by growing fetus is compensated by an increase in other dimensions as transverse diameters, coastal angle and lower thoracic perimeters. Significant difference between nonpreg nant and pregnant group for ERV (0.460±0.20 vs 0.387±0.20 respectively, $p<0.05$) can be justified by the less effort and cooperation put by the pregnant group for the measurement or comparatively poor nutritional status during gestation. The low results of VC in both groups may be because of the low socio-economic status of the subjects as most of the subjects were from rural areas and lower socioeconomic strata. Present study showed an unaltered IRV in pregnancy as compared to control. In contrast to present study, Phatak and Kurhade showed an increase in the IRV and IC during pregnancy due to mechanical changes in thoracic cage thus increasing its volume.[9]

Our study found the gradual increase in TV during pregnancy, which is in concordance with earlier studies by by Artal et al (2006) and Kolarzyk et al [10,11] Study carried out by Heidemann, stated that increased Rf lead to the fall in $PaCO_2$ level of 4.1kPa (31mmHg) by the end of the first trimester. Moreover secondary to progesterone mediated hypersensitivity to CO_2 increase alveolar and minute ventilation during pregnancy which is a result of increased RR and TV both.[12]

Author presumes that together with the smooth muscle relaxation; a direct effect of progesterone increasing the sensitivity of respiratory centre to carbon dioxide is the probable cause of the rise in TV in present study which is also stated by other studies.[13,14] Altered thoracic configuration is also considered to be one of the contributor as reported by Novey et al.[15] Progesterone may also exert its influence by modifying the permeability of the chemoreceptor cells or directly stimulating central respiratory or hypothalamic neurons in contact with blood.[16]

Recently published study by Anita Teli et al (2014), is in contrast to present study, found decrease in TV from 1st trimester to 3rd trimester as compared to control with maximum decrease in 2nd trimester with gradual increase in RR. The significant increase in RR considered to be due to sensitization of respiratory center due to progesterone and compensated by a decrease in TV ultimately maintaining the constant MV even during all trimesters of pregnancy.[17]

In this study minute ventilation was about 39% more in pregnant group than control (14.66±5.5 vs 10.73±3.68 respectively, $p<0.001$), although the different time course data for this increment is reported in various studies, as some reported at the end of II trimester while most studies reported at the end of the III trimester.[15,18,19] Increased ventilation is secondary to increase in TV because Rf, though increased with advancement of pregnancy; all the obtained values were within the normal range of frequency.

Inspiratory and expiratory time with variables inspiratory flow (VT/Ti) and duty cycle (Ti/Ttot) have been interpreted as drive and timing components of ventilation which may be independently controlled. Our study also demonstrated that mean inspiratory flow (VT/Ti) remains unaltered in all trimesters, but when compare to nonpregnant, it is significantly higher in pregnant group ($p>0.001$), indicative of an augmented ventilatory drive. Moreover, specified by Das et al, where again we find increased progesterone level from menstrual to luteal phase with increased inspiratory flow favors our results.[19] The hyperventilation during pregnancy has been attributed to the effect of progesterone on ventilatory drive. The mechanism through which progesterone acts is centrally, as shown in various studies for unaltered FVC maneuver.[20,21] Contreas study further confirms our results, where they measure p0.1 the index of inspiration drive, which is independent of mechanical properties.[7]

Studies have reported that progesterone increases the ventilatory performance in healthy individuals and in patients with COPD.[22] In addition, studies on postmenopausal women with respiratory insufficiency or partial upper airway obstruction have confirmed the effectiveness of medroxyprogestrone in restoring the patency of their upper airway and respiratory control mechanism.[23] Progesteron improves ventilatory performance in adult trauma patients during partial support mechanical ventilation[24] and Medoxy-progesteron has been administered to stimulate an increased respiratory drive in Pick wickian syndrome.[25]

Thus author depicted that although the pregnant woman, causing restrictive changes in the respiratory apparatus, has apparent handicap; Physiological and hormonal changes compensate for them causing no discomfort to the pregnant woman. Hyperventilation in pregnant female made better oxygenation possible for mother and it also facilitates feto-maternal gas exchange.

Conclusion: Increased diaphragmatic excursion and preserved respiratory muscle strength are important adaptations, given the increase in tidal volume and minute ventilation that accompanies pregnancy. In conclusion, our findings in healthy subjects demonstrate that hyperventilation during pregnancy is associated with an augmented ventilatory drive without any alteration in pulmonary mechanics. Extensive studies on larger population with hormonal assay need to be done.

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