REVIEW OF LITERATURE

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Measurement of pulmonary functions is of great value to the clinician in judging the degree of functional derangement, prognosis and therapeutic effect of drugs in many respiratory ailments.

Published literature on pulmonary ventilation in pregnancy begins with Wintrich (1854) who found no change in VC, but most of the work between then and the 1930's reported only measurements of vital capacity using primitive equipment (Alaily and Carrol, 1978).

Gupta (1972) in his editorial has given a brief account of history of pulmonary functions. He states that even in 17th century pulmonary physiology was misunderstood although some experiments in pulmonary physiology were undertaken before birth of Christ by Erisistratus and later by Galen (131-201 BC). Hippocrates (466 – 377 BC) first suggested that main purpose of breathing is to cool the heart. Vesalius (1514 – 1564) demonstrated the role of ventilation in maintenance of life. Lower (1631 – 1691) was the first to note the change in color of the oxygenated blood. Borelli (1679) was the one who first measured vital capacity or VC (at present defined as the full volume of air expired after a maximal inspiration). In 1831, Thackrah noticed that women and flax workers had a lower VC reading. Hutchinson (1846) noticed the correlation of height

and vital capacity. Strohl advocated measurement of the forced vital capacity (FVC) or forced expiratory volume (FEV) in 1919. Hermannsen proposed the measurement of the maximal voluntary ventilation (MVV) or maximal breathing capacity (MBC). The last procedure is rather exhausting to the patient. It varies with age, sex, height, temperature of surroundings, co-operation of the patient and a lot of other variable factors.

Recording of FVC, measured to time (timed vital capacity or TVC) is an important test, first described by Tiffeneau and Pinelli and elaborated later by Prowse and Gaensler (1965). Keith et al., 1982 reviewed that as early as 1904, Magnus – Levy noted an increase in minute ventilation of women during pregnancy. This observation was followed by reports from Hasselbach and Gammeltoft (1915) who observed the $PaCO_2$ was decreased in women not only during pregnancy but also during luteal phase of menstrual cycle when high level of serum progesterone is maintained.

STATIC LUNG VOLUMES, CAPACITIES & VENTILATION

RESPIRATORY RATE

Benjamin (1936) found respiratory rate (f) to be 16 and 18 while Cugell et al. (1953) gave it to be 15 and 16 during

nonpregnant state and at full term. Duncun (1962) reported f in pregnancy is accelerated and this combined with increase in TV results in 50% increase in MV (hyperventilation). Krunholtz et al. (1964) recorded a nonsignificant increase in f from 18 ± 6 in first trimester to 20 ± 6 in second trimester as mean and SD. Increase in f has been noticed during pregnancy (Bernard et al., 1967 and Burrow and Ferris, 1975). Bernes (1974) reported 10 % while Bonica (1974) documented 15% increase in f contributing to increase in RMV. Chhabra et al. (1988) found statistically significant rise of 4.1% excursion per minute in f from first trimester to third trimester, concluding f of pregnant women being more than nonpregnant women.

Role of progesterone in ventilatory control is suggested by finding of hyperventilation in human pregnancy and during menstrual cycle (Lucius et al., 1970). Cyril (1974) reports respiratory rate increase during pregnancy that may be due direct action of progesterone on respiratory centers. Weinberger et al. (1980) further confirms progesterone influence on total MV and its subcomponents TV and f as both increases. Keith et al. (1982) opined endogenous progesterone might induce increased respiration. Hosenpud et al. (1983) reported chronic progesterone administration produced hyperventilation and that estrogen facilitates this action of

progesterone. They had given the f (mean and SD) to be 96 ± 29, 109 ± 18 and 98 ± 20 in control, progesterone treated and estrogen and progesterone treated guinea pigs respectively.

Das and Jana (1991) noticed a rise of only 2% in f during luteal phase of menstrual cycle when progesterone level is high. Das (1998) in other study has also stated that hyperventilation during luteal phase was due to significant rise in TV without any appreciable change in f.

Puranik et al. (1994) recorded small significant increment in frequency of respiration with advancement of pregnancy. They gave average values of f as 11 ± 1.51, 13.73 ± 2.28, 15.74 ± 3.18 and 12 ± 1.22 in first, second, third trimester and postpartum respectively. All the obtained values were within normal range. Sahin et al. (1998) concluded that central and peripheral injection of acetycholine and epinephrine increase f and after vagotomy, effect of central and peripheral administration of both acetycholine and epinephrine on f was abolished. This finding showed that increase in f is mediated by vagal reflex. Increase in brain adrenergic receptors during pregnancy is associated with behavioral changes that can modify ventilation (Smiley & Finster, 1996). Luteal phase of menstrual cycle according to Tan et al., (1995) has also been reported to be associated with adrenoreceptor density.

Progesterone has an enhancing or facilitating effect on ß receptors (Raz et al., 1973).

Knuttgen and Emerson (1974) viewed hyperventilation during pregnancy due to increase in TV as no change was observed in frequency of breathing. Mean and SD values prepartum and postpartum given were 15.2 ± 1.5 and 15.6 ± 1.4 breaths/ min respectively. Alaily and Carrol (1978) stated the average f throughout pregnancy and postpartum to be 16 breaths/ min which was within normal limits but 9.85% (1.75 breaths/min) below the nonpregnant frequency, a difference that was statistically significant. Rees et al. (1990) postulated that f appeared not to be related to gestational age and the values during pregnancy were not different from those of postpartum.

According to Spatling et al. (1998) median f remained between 16 and 18 breaths / min at rest in nonpregnant as well as pregnant women. By 20 to 27 week of gestation median values were significantly lower than nonpregnant state and lasted till 32 week of gestation. Rasheed et al. (2000) gave the mean and SD of f in first, second and third trimester as 23.5 ± 4.2, 23.4 ± 1.95and 22.6 ± 1.05 respectively, an insignificant decrease.

TIDAL VOLUME

Plass and Oberst (1938) and Widlund (1945) found increase in TV at term as compared to nonpregnant state. Cugell et al. (1953) measured TV to be 487 ml and 678 ml in nonpregnant and at term respectively an increase of 191 ml or 30%. Increase in TV by 45% contributing to hyperventilation during pregnancy supports the clinical observation that a pregnant women breathe more deeply under basal condition than they do in nonpregnant state (Duncan, 1962). Bernard et al. (1967) has reported great increase in TV contributing to greater ventilation.

Pandya et al. (1972) have given 272.13, 284.37 and 288.73 ml as mean values for control, second and third trimester group respectively stating slight statistically non significant rise in TV during pregnancy. Bernes (1974) found a significant increase in TV from 500 ml to 700 ml, a rise of 40% that significantly contributes to increase in minute volume. A significant decrease in TV was observed from 0.65 L prepartum to 0.37 L postpartum (Knuttgen and Emerson, 1974). Burrow and Ferris (1975) also reported significant increase in TV. Rise in TV throughout gestation which reaches as much as 25 – 40% above nonpregnant level (Leontic, 1977). He has given the values of TV as 450 ml in nonpregnant and

600 ml at term. Alaily and Carrol (1978) mentioned that there was no obvious trend during pregnancy but at term the mean TV was 165 ml (28%) above that in non pregnant state and 67 ml (13.5%) in the late postpartum period. Both differences were statistically significant. They describe that TV increases in pregnancy as compared to nonpregnant state.

Increase of 38% in TV during pregnancy is reported by Artal (1986 a). According to Chhabra et al. (1988) mean TV increases gradually during pregnancy and the rise from first to third trimester is statistically significant. Mean and SD obtained for TV (ml) by them are 279 ± 48.5, 298.8 ± 45.2, 346.8 ± 53.7 and 374 ± 51.5 in nonpregnant state, first, second and third trimester respectively. They reported mean rise of 91.6 ml or 30.6% during pregnancy. Rees et al. (1990) gave baseline nonpregnant TV as 0.40 ± 0.01 L. This had risen to 0.55 ± 0.04 L at 8 to 11 weeks of gestation and to 0.60 ± 0.03 L. at 36 to39 weeks of gestation. Increase at term was more than 15% above the nonpregnant baseline.

Spatling et al. (1992) have got significant increase in median TV from 560 ml in early pregnancy, an increase of some 15% followed by further augmentation until term to 715 ml (27% higher than non pregnant value). Puranik et al. (1994) gave TV as 0.79 ± 0.16, 0.77 ± 0.28, 1.06 ± 0.27 and 0.74 ±

0.13 in first, second and third trimesters and postpartum respectively. Sahin et al. (1998) studied that peripheral and central administration of acetylcholine and epinephrine caused significant increase in TV. Increase in TV appears to be due to stimulation of peripheral chemoreceptors, lung receptors and change of airway caliber. Acetylcholine applied centrally or peripherally diminishes TV by muscarinic action and epinephrine produce excitatory effect on inspiratory neurons and hence increases TV. Vagal reflexes (Sahin et al., 1998) bring about respiratory response to peripheral stimulation of epinephrine, acetylcholine and atropine. Das (1998) stated hyperventilation during luteal phase significantly rises with increase in TV only without any appreciable change in respiratory rate.

Krunholtz et al. (1964) reported slight decrease in TV (ml) in last trimester. Mean values given by him are 660 ± 135 (first trimester) to 560 ± 210 (third trimester). Butler and Bonica (1975) also found a decrease in TV during pregnancy.

RESPIRATORY MINUTE VOLUME

Plass and Oberst, 1938 state that pregnant females have less carbon dioxide out put per alveolar breath. This was validated through progesterone administration that caused decrease in pCO_2 level within 24 hours and was significant

within 3 hours of administration. Cessation of progesterone brought pCO_2 back to normal in nonpregnant and puerperal women. Identical findings were found in pregnant state. The sensitivity of respiratory centers to the stimulus i.e. increased CO_2 or pCO_2 is more in pregnant state than normal nonpregnant state (Plass and Oberst, 1938). Similar were the findings of Doring et al. (1950) – that progesterone increased respiration and sensitivity to CO_2 and thought it acted directly on regulatory centers. Cugell et al. (1953) have found an increase of 3.07 or 40% in RMV from nonpregnant (7.27 lt.) to pregnant (10.34 lt.) state. Goodland et al. (1954) reported that progesterone level lowers pCO_2 during menstrual cycle and during pregnancy causing increase in RMV. Rubin et al. (1956) stated minute volume increases by 57% due to increase in TV and respiratory rate also slightly increases. Lyons and Antonio (1959) supported that progesterone does indeed affect the sensitivity of respiratory center in normal subjects and is probable active agent in pregnancy to produce the same alteration.

Engstrom (1960) has stated like progesterone thyroid hormone causes rise in body temperature and elevation of oxygen consumption and metabolism rate in pregnancy leading to hyperventilation. Duncun (1962) has stated increase O_2

consumption, decrease in respiratory volumes and increase in TV improves efficiency of ventilatory system during pregnancy. Hyperventilation occurs as the body attempts to compensate for reduction in the concentration of available base. There is 50% increase in minute ventilation (MV), due to increase in respiratory rate along with increase in TV. Bernes (1974) figures for minute ventilation is analogous to Duncun's that during pregnancy it is 50% more than nonpregnant state. This is attributed to the fact that TV increases by 40%, respiratory rate increases by 10% and that all changes start within first trimester of pregnancy. The pregnant women then breaths more deeply and more rapidly at rest than does a non pregnant women causing an increase in her alveolar ventilation these changes are brought probably due to direct action of progesterone in the central medullary respiratory centers. Changes in lung function appear to be related to following factors – progressive enlargement of uterus producing upward displacement of diaphragm; increase of progesterone and increase of blood volume and flow to meet increase requirement for fetus, placenta, uterus, breast tissue, respiratory and cardiac work. Knuttgen and Emerson (1974) state that pulmonary hyperventilation developed early in pregnancy and exists even at rest throughout pregnancy. This increase in ventilation was accomplished by increase in TV as

no change was observed in frequency. A significant decrease in TV from 0.65 L. prepartum to 0.37 L. postpartum was accompanied by a decrease in ventilation from 8.51 to 5.54 L./minute, pre to postpartum. Minute volume showed a constant increase during pregnancy.

Burrow and Ferris (1975) observed minute ventilation at rest increases significantly throughout pregnancy in proportion to increase in TV and represent the most significant change in lung function during pregnancy and that increase of minute ventilation is not associated with any significant change in respiratory rate. Animals treated with both estrogen and progesterone showed hyperventilatory responses more consistently than animals given progesterone alone and this response strongly correlates with serum progesterone concentration (Luci et al. 1975). They conclude that estrogen facilitates or modulates progesterone-induced hyperventilation. According to them one can speculate that estrogen effect on progesterone receptor synthesis such as was demonstrated in the uterus may be a possible cause of a hyperventilation. According to Pernoll et al. (1975) reports a change of 2.1 L./minute (9.52 – 7.41) in minute ventilation at 15 weeks exceeds by 50%, the average increase observed between 19 and 34 weeks.

Role of progesterone in ventilatory control is suggested by finding of hyperventilation in human pregnancy and during luteal phase of menstrual cycle (Lucius et al., 1970 and England and Farhi, 1976). In both instances serum progesterone concentration are substantially above control level. Additional evident to support this hypothesis is the finding of increase minute ventilation after exogenous progesterone administration (Lyons and Antonio, 1959 and Brodeur et al., 1986). Increase in minute ventilation is apparent during first trimester and at term and is between 48 to 57% above normal nonpregnant women. This change is result of a progressive rise in TV (40%) throughout gestation and slight increase in respiratory rate and an increase in alveolar ventilation at term of about 70% (Leontic, 1977).

Alaily and Carrol (1978) state that pregnancy was associated with progressive minute volume which at term (10.91 lt./min) was 1.74 lt./min (19%) above the nonpregnant mean (9.15 $\pm$ 2.71 lt./min) and 1.31 lt./min (12%) above the late postpartum period (9.70 $\pm$ 1.30 lt./min). Both changes were statistically significant. At term (10.91 lt./min) mean minute volume was 0.75 lt./min (7%) greater than early pregnancy (10.20 lt./min) measurement but the difference was not statistically significant. Marked increase in ventilation

(26%) is in relation to increase in body weight (20.8%) and surface area (8.5%). Skatrud et al. (1978) demonstrated appearance of medroxyprogesterone related products in plasma and cerebrospinal fluid in normal males receiving this compound coincident with the ventilatory response presumably progesterone and progesterone related material could cross blood brain barrier to exert the central effect. Zwillich et al. (1978) inferred increase in minute ventilation as well as an increased chemosensitivity to hypercapneoa and hypoxia in man after 32 hours of medroxyprogesterone acetate treatment.

As per Weinberger et al. (1980) progesterone exerts influence on total minute volume and its subcomponents TV and respiratory rate. Both respiratory minute volume and TV increase during pregnancy. De Swiet (1980 b) noted overall average increase from 7.5 lt./min in nonpregnant state to 10.5 lt./min in late pregnancy. Hyperventilation in nonpregnant state is observed in women during luteal phase of menstrual cycle when serum progesterone levels are increased. This and absence of hyperventilation in anaemic women support the possible role of progesterone (Schoene et al., 1981). Keith et al. (1982) in their study have mentioned decline in $PaCO_2$ (arterial CO_2 pressure) throughout pregnancy suggesting a gradual increase in respiration with gestational age. Significant

correlation of minute ventilation and $PaCO_2$ with serum progesterone level suggesting that endogenous progesterone may induce increased respiration.

Hosenpud et al. (1983) concluded that chronic progesterone administration produces hyperventilation in guinea pigs and that estrogen facilitates this action of progesterone. Hyperventilation was evident from reduction in pCO_2 and elevation in pH in pregnant guinea pigs as compared to controls. Consistent were the results of Brodeur et al. (1986) that increase ventilation in response to progestin is direct, hormone receptor mediated phenomenon. They proved this by giving exogenous synthetic progesterone – medroxyprogesterone acetate in combination with estradiol and concluded that estradiol induces progesterone receptor formation. Progesterone is thought to be ventilatory stimulant but its effectiveness in raising ventilation is variable in humans and other species.

Clapp et al. (1988) studied various cardiopulmonary and metabolic parameters during pregnancy and reported that they change by 7^{th} week. However, they followed a different pattern in that they rose abruptly during the initial seven weeks and then either plateaus or continued to increase over the ensuing eight weeks. Such changes were not observed in few

pregnancies that ended in unexpected abortion. They found minute volume (lt./min) to be 7.4 1 ± 0.24 before pregnancy while at 7th and 15th week of pregnancy it was 10.22 ± 0.27 and 9.52 ± 0.20 respectively with overall change of 2.11 ± 0.21 (28.5%). Heart rate and minute volume increase by 18% and 28% over initial 15 weeks. More than 80% of overall change observed at 15 weeks had occurred by 7th week with insignificant progression thereafter. It means respiratory minute volume is a chronic adaptive change that represents a new equilibrium between respiration and metabolic function in response to changes in the sensitivity of respiratory centers to CO_2 tension.

Hannhart et al. (1990) and Contreras et al. (1991) report that menstrual cycle and pregnancy both are associated with central ventilatory drive stating that there may be a decrease threshold to pCO_2 and hence an increase in peripheral chemoreceptor sensitivity. Rees et al. (1990) study in pregnancy have shown increase in MV i.e. due to progesterone induced increase in sensitivity of respiratory centers in brain to CO_2. The changes in MV during pregnancy reflected the changes in TV. The baseline nonpregnant MV was 6.6 ± 0.2 lt./min. This rose to 7.7 ± 0.6 lt./min. at 8 to 11 weeks of gestation. The increase in MV was 40% by term. This change

being achieved by an increase in TV rather than increase in respiratory frequency. The increase is related to the changes occurring in O_2 consumption, CO_2 production and CO_2 tension. It is probably associated with dyspnea during pregnancy. Das and Jana (1991) measured respiratory minute volume (lt./min.) as 8.63 $\pm$ 1.8 in luteal phase, 8.20 $\pm$1.7 in menstrual phase and 8.00 $\pm$ 1.8 in follicular phase of menstrual cycle. TV (6%) contributed more than respiratory rate (2%) to increase RMV.

Spatling et al. (1992) found 12% increase in ventilation per minute by 8 – 11 weeks of gestation. Further gradual increase until term was statistically significant by 22 – 23 weeks. Median level was 9.4 lt./min. in nonpregnant women to 12.6 lt./min. at 40 weeks gestation. They proposed that increase in RMV was not due to an increase in respiratory frequency but there must have been increased in TV. Increased ventilation is because of higher O_2 consumption due to pregnancy and hyperventilation needed to keep pCO_2 at lower pregnancy level. Ventilation increases but rate tends to decrease consequently TV increases and raises alveolar ventilation i.e. most characteristic feature of cardiopulmonary adaptation to pregnancy.

Persistent increment in hyperventilation has been observed in pregnancy by various authors in published

literature stating that pregnant women overbreathe. The rise in TV is at the expense of ERV, so fresh air inspired with each breath is much less diluted by the gas in the lung. This reduces the alveolar and arterial pCO2. $PaCO_2$ reduces from 38 to 32 mm Hg. The fetus using progesterone as manipulator resets the respiratory center to the new low level of CO_2 that is preserved so that it may itself enjoy a normal pCO_2 and still have a substantial gradient across the placenta to unload its CO_2. This maneuver satisfies the fetal needs of gas exchange and increases the margin of safety by protecting the fetus from high levels of CO_2; but it causes considerable inconvenience to mother. To maintain the plasma pH increased excretion of $NaHCO_3$ occurs. Thus the respiratory alkalosis is compensated. In this way hyperventilation in mother is beneficial to the fetus as better oxygenation of maternal blood is possible and it also facilitates feto-maternal gas exchange (Puranik et al., 1994). Leindorfer's suggested that increased lactic acid production might play a part in the control of respiration in pregnancy.

Progesterone exerts an influence on total MV and its sub components – TV and frequency. It has been advocated unanimously that the most important feature is a rising minute ventilation and TV during pregnancy. Increment in RMV as well

as TV was statistically very highly significant and the small increase in respiratory rate was statistically significant. Together with smooth muscle relaxation a direct effect of progesterone increasing the sensitivity of respiratory centers to CO_2 is probable cause of this rise. The altered thoracic configuration also contributes. Progesterone exert its influence by modifying the permeability of the chemoreceptors or directly stimulating central respiratory or hypothalamic neurons in contact with blood. Progesterone may increase facilitating stimuli from higher centers even though at high concentrations it has anaesthetic effect. Frequency of respiration though increased with advancement of pregnancy, all obtained values were within the normal range of frequency. Thus rise in RMV is mainly due to rise in TV and rise in TV is at expense of ERV concluded by Puranik et al. (1994). They have given values of RMV (lt./min.) as 7.91 $\pm$ 1.67, 9.73 $\pm$ 3.18, 16.07 $\pm$ 4.10 and 7.30 $\pm$ 1.55 in first, second, third trimester and postpartum. Plass and Oberst (1938) and Widlund (1945) found no change in RMV.

On searching number of studies in published literature decrease in minute ventilation during pregnancy is not yet reported till date.

EXPIRATORY RESERVE VOLUME

Cugell et al. (1953) found ERV decreased from 655 ml (nonpregnant state) to 555 ml (at term) a decrease of 100 ml or 15%. Rubin et al. (1956) also found a decrease in ERV and attributes this fact to decrease in VC during pregnancy. Duncan (1962) reported decrease in ERV by 100 ml in pregnant women of third trimester (600 ml) from nonpregnant state (700 ml). During late pregnancy there is 40% reduction in ERV as reported by Bernard (1967). Knuttgen and Emerson (1974) have reported significant decrease in ERV and FRC during pregnancy. A decrease of 0.19 liters (6% net decrease) with pre and postpartum ERV values being 1.02 $\pm$ 0.09 and 1.21 $\pm$ 0.08 respectively. Bernes (1974) has stated that ERV is reduced by 100 ml during pregnancy as diaphragm is displaced upward by about 4 cm. But range of movement during respiration is undiminished causing decrease in ERV. Butler and Bonica (1975) have given ERV to be 0.79 and 0.94 liters in pregnant and non pregnant state respectively and has rationalized that by fifth month the mechanical effects of the growing uterus begin to produce a progressive decrease in ERV 20% below nonpregnant state. Burrow and Ferris (1975) found progressive decrease in ERV during second half of pregnancy due to upward displacement of diaphragm.

Decrease in ERV of about 150 cc leads to decrease in FRC at term by 17 – 20 % more than nonpregnant female. This could be principally as a result of the elevation of diaphragm (Leontic, 1977) and decrease in TLC by 4% at term. Baldwin (1977) reports significant decrease by 17% in ERV during pregnancy. Mean and SD values of ERV in nonpregnant, first, second and third trimester subjects were reported to be 703.5 ± 204.5, 649.9 ± 196.9, 586.6 ± 191.6 and 482.8 ± 163.49 respectively by Chhabra et al. (1988). On an average statistically significant progressive fall obtained by them was 114.6 ml in ERV during pregnancy. Puranik et al. (1994) have reported decline in ERV and have attributed it to the reduction of power of expiratory muscles due to the stretching of abdominal wall with progress of pregnancy. They have given mean and SD values of ERV as 0.64 ± 0.11 (first trimester), 0.51 ± 0.19 (second trimester), 0.34 ± 0.16 (third trimester) and 0.75 ± 0.13 (postpartum).

Krunholtz et al. (1964) has given a nonsignificant rise of ERV (ml) from 1140 ± 430 to 1170 ± 285 in first and third trimester respectively. Pandya et al. (1972) have reported insignificant change in ERV but increase is seen from second to third trimester. They have given mean for ERV (ml) as

796.78, 686.62 and 730.32 in controls, second and third trimester subjects respectively.

INSPIRATORY RESERVE VOLUME

Krunholtz et al. (1964) found non significant change in IRV (ml) from 1550 ± 305 (first trimester) to 1670 ± 415 (third trimester). Bernes (1974) has reported increase in IRV by 100 ml balancing the reduction in ERV by 100 ml He reasons that circumference of thoracic cage increases by 10 cm. This is brought about by relaxation of ligamentous attachment of the ribs and increased mobility of the sternomanubrial joint; the subcostal angle widens from 70^0 to 100^0. These changes cause flaring of ribs causing increase in IRV. IRV reflects balance between lung and chest elasticity, muscie strength and thoracic mobility midposition and TV (Slonim and Hamilton, 1976). Leontic (1977) gave IRV values as 2050 ml in nonpregnant and at term showing no change in IRV. IRV shows some increase as pregnancy advances. However it is lower than values in control as stated by Pandya et al. (1972). They obtained 747.02 ml (control), 625,75 ml (second trimester) and 690.99 ml (third trimester) as mean values for IRV.

INSPIRATORY CAPACITY

Cugell et al. (1953) found an increase of 120 ml (5%) in inspiratory capacity from 2625 ml in nonpregnant state to 2745 ml at term. Duncun (1962) has reported increase in IC by 100 ml in pregnant women (2700 ml) as compare to nonpregnant women (2600 ml). Bernard et al. (1967) has stated an increase in IC by 200 ml or 5 % at term. Knuttgen and Emerson (1974) obtained 2.52 $\pm$ 0.10 (prepartum) and 2.14 $\pm$ 0.91 (postpartum) as mean and SD values for IC, an increase of 0.38 liter. They observed a significant decrease in IC postpartum along with decrease in VC as mentioned above, indicating that both capacities increased during the full course of pregnancy. Burrow and Ferris (1975) noticed modest increase in IC from second to third trimester i.e. in late pregnancy. This rise appears to compensate for decreased ERV so that TLC remains essentially unchanged. Corresponding increase in IC and IRV compensates volumetric loss of ER during pregnancy (Leontic, 1977), consequently VC remains unchanged. He gave IC values to be 2500 ml and 2650 ml in nonpregnant state and at term. Alaily and Carrol (1978) state that mean IC increased progressively throughout the pregnancy to 318 ml (10.7%) above the non pregnant mean. The increase in mean IC from early pregnancy to term was 225 ml (6.5%) and both

differences were statistically significant. The decline in mean IC from term to the late postpartum period was 396 ml (13%) a highly significant difference. Increase in IC is at expanse of decrease in expiratory capacity in pregnancy, fall in residual volume and functional residual capacity in pregnancy. Significant rise of IC is reported by Chhabra et al. (1988) during pregnancy. They gave mean and SD of IC as 1244.2 ± 397.7 in nonpregnant state and 1315.92 ± 188.4, 1485.36 ± 209.27and 1581.95 ± 209.27 respectively in all three trimesters. They reported mean rise of 374.88 ml. Puranik et al. (1994) gave 1.61 ± 0.22 (first trimester), 1.78 ± 0.36 (second trimester), 2.20 ± 0.36 (third trimester) and 1.61 ± 0.22 (postpartum) as mean and SD, showing an increase during pregnancy that can be due to altered thoracic configuration and to heightened sensitivity to the nervous stimuli required to produce muscular contraction.

Rubin et al. (1956) stated that IC did not differ significantly from its postpartum value. Krunholtz et al. (1964) as well found no change in IC (ml) of 2210 ± 380 in first trimester to 2230 ± 510 in third trimester. Baldwin (1977) has stated decrease in IC.

VITAL CAPACITY

Prowse and Gaensler (1965) have reviewed the numerous studies of VC since Wintrich study. One of the oldest work in pregnancy by Thomson and Cohen (1938) state almost 169 VC observations in 31 nonpregnant women at different gestational age. They state knowledge of the effect of pregnancy on VC is important and is useful in search for an early sign of heart failure in pregnant cardiac patient. They have studied VC in different postures and came to the conclusion that changes in VC in any posture was similar and hence they took VC in sitting position to discuss their findings. They found VC values to be within normal range for nonpregnant women. They obtained range of VC as 2150 cm^3 – 4190 cm^3 in pregnant women with average of 3345 cm^3. Whereas for normal non pregnant women range observed was 2530 – 4050 cm^3 with average of 3284 cm^3 they observed tendency for VC to increase in pregnancy and decrease after delivery. The average of vital capacities of entire group showed a progressive increase from 21^{st} to 24^{th} week being 3300 cm^3 reaching its highest value of 3455 cm^3 in 37^{th} to 40^{th} weeks. According to them the increase in VC during pregnancy parallels close to increase in subcostal angle value, as does the postpartum decrease. They have reported increase in

subcostal angle during pregnancy with postpartum decrease. The change in VC is associated with alteration in size and shape of chest rather than increase in body weight and surface area.

VC remains unchanged or increases slightly as per the study by Duncun (1962). Mean VC rose from 3260 ml in 21st week to 3450 ml in 40th week and dropped to 3150 ml 3 – 6 weeks after delivery (post partum). The upward displacement of diaphragm might be expected to decrease VC during pregnancy but such an effect fails to occur because of the increased circumference of the chest. If reduction is observed in VC then it is interpreted as pathological clinically. Krunholtz et al. (1964) has given mean and SD values of VC in first and third trimester as 3350 $\pm$ 735 ml and 3390 $\pm$ 645 ml, a less significant rise. Knuttgen and Emerson, 1974 have reported increase in VC and IC. They gave pre and postpartum value of VC as 3.53 $\pm$ 0.10 L. and 3.34 $\pm$ 0.10 L., a net 6% decrease and for IC as 2.52 $\pm$ 0.10 and 2.14 $\pm$ 0.09, a decrease of 0.38 L respectively. According to them an increase in VC can be explained by the more favorable condition under which muscles of expiration are acting due to stretch imposed by the increased abdominal volume. Butler and Bonica (1975) have given values of VC as 3.92 (nonpregnant) and 3.7 (third

trimester). Chhabra et al. 1988 found statistically significant progressive rise of 266.16 in VC. They obtained mean and SD of VC (ml) to be 1947.70 ± 216.6 (nonpregnant state), 1937.84 ± 239.87 (first trimester), 2052.28 ± 223.74 (second trimester) and 2071.48 ± 281.70 (third trimester).

Insignificant change in VC from 3.20 (nonpregnant state) to 3.14 (at term), a decrease of 1% was observed by Bernard (1967), suggesting that lung compliance be not greatly changed. VC is maintained by increase in IC. Preservation of VC also proves that inspite of higher end expiration portion of diaphragm; there can be no true restriction of diaphragm movement. Baldwin et al. (1977) reported no change in VC. Alaily & Carrol (1978) stated mean VC varied little during pregnancy and after delivery as VC was same in pregnant and nonpregnant woman. The mean value for the patients agreed well with the predicted value of 3.67 liters based on age and height according to nomogram of Cotes (1965).

Rubin et al. (1956) stated mean VC of 8 women during pregnancy was 2759 cc, significantly lower than the mean VC of 3054 cc obtained 7-14 weeks postpartum. Pandya et al. (1972) found VC being lower during pregnant than nonpregnant state. The gave VC as 1610 ml (second trimester) and 1678 ml (third trimester) during pregnancy and 1893.65 ml

during nonpregnant state. Sheikh et al. (1983) reported that VC is decreased because the decrease ERV is greater as compared to increase in TV during pregnancy (Pernoll et al. 1973). He states that changes in lung volumes and lung capacities were not dependent upon the patients' height, body weight and surface area of chest circumference. Puranik et al. (1994) study reports conflicting results of increase, decrease or no change in VC observations. They stated that such results could be due to the VC observations obtained from different subjects coming from different socioeconomic status at different periods of gestation and postpartum period. They had concluded insignificant decrease in VC from first trimester to third trimester while no change in nonpregnant and early pregnancy. They gave the values to be 2.53 $\pm$ 0.29 lt. (postpartum), 2.53 $\pm$ 0.12 lt. (first trimester), 2.51 $\pm$ 0.27 lt. (second trimester) and 2.49 $\pm$ 0.22 lt. (third trimester). The low results reported in their study are attributed to low socioeconomic status and poor nutrition of the subjects. The maintenance of VC according to them was due to in the increment in IC being compensated by the reduction in ERV.

MAXIMUM VOLUNTARY VENTILATION

Butler and Bonica (1975) have pointed an increase in MBC during pregnancy, which should otherwise decrease due

to mechanical alteration. They state decrease in pulmonary resistance due to relaxation of smooth muscle of tracheobronchial tree during pregnancy thus permitting enlargement of the respiratory lumen and increased freer flow of air, for given pressures hence normal or even increase maximum breathing capacity (MBC) during pregnancy. Datta et al. observed an increase in MVV in premenstrual syndrome. Progesterone causes rise in MVV in human females. In intact female rats it causes a fall of noradrenaline concentration in selected areas of brain (Chaudhuri et al., 1991 & Chaudhuri et al., 1992). They have reported MVV for controls before administration of progesterone as 103.13 ± 10.7 L./minute. They injected the drug on seventh day. MVV obtained on 14^{th} day was 110.73 ± 13.8 L./minute and on 21^{st} day it was 99.5 ± 14.1 L./minute. MVV rose after one week i.e. 14^{th} day in subjects taking progesterone on 7^{th} day onward, but after 21 days value of MVV became less than the controls. Progesterone causes increase in MVV and PEFR i.e. increase efficiency of respiratory system. Except the MVV all changes become less intensive with progress of time despite the continuance of progesterone (with MVV the response became biphasic). Rise in MVV and PEFR suggest an improvement of respiratory efficacy and this may be of some help during pregnancy (Chaudhuri et al., 1994).

No significant difference in pregnant and nonpregnant state was observed for MBC, though during pregnancy it was slightly more (Robin et al., 1956). According to Duncun (1962) value of finding MBC lies in the fact that success of its performance requires a normal VC, the absence of bronchial constriction and integrity of entire neuromuscular and skeletal respiratory apparatus. During normal pregnancy there is no significant variation in the ability of the patient to perform this test. He observed no significant change in MBC. Burrow and Ferris (1975) observed no significant change in MBC and FEV_1 during pregnancy. According to them, finding of normal MBC and FEV_1 suggest that there is no impairment of muscular efficiency or airway obstruction during normal pregnancy.

Krunholtz et al. (1964) observed insignificant decrease in MBC during pregnancy. They gave 94 $\pm$ 25 and 88 $\pm$ 36 as mean and SD of MBC in percent in first and third trimester respectively. Bernard et al. (1967) has stated decrease in MBC from 102 L./minute in nonpregnant state to 96 L./minute at term. Chhabra et al. (1988) reported MVV (L/min) to be lower in pregnant women than nonpregnant women from first to third trimesters though the change observed was less significant. The values given by them were 46.05 $\pm$ 6.23 in nonpregnant

women and 28.28 ± 5.51, 28.7 ± 5.68 and 30.60 ± 4.66 in 12 – 16, 24 –28 and 34 –36 weeks of pregnancy respectively.

FLOW PARAMETERS AND TIMED VITAL CAPACITY

FORCED EXPIRATORY VITAL CAPACITY

Rubin et al. (1956) found no significant difference in FEV_1, FEV_2 and FEV_3 between the results obtained during pregnancy compared with those found when the patients were not pregnant. They recorded decrease in FEV_1 from 80.3% in nonpregnant to 73.1% in pregnant state. Cameron et al. (1970) and Hytten and Leitch (1971) stated that FEV_1 remains constant or is not affected during pregnancy. Hytten and Leitch further state that rates of gas-flow both average and maximum during inspiration and expiration are little altered in pregnancy. Pressure required to achieve flow rate was less in pregnancy than was in nonpregnant subjects, airway resistance decreases and cross sectional area of airways increases due to relaxation of smooth muscles in airways by relaxin. Raz et al. (1973) stated progesterone increases ß adrenergic activity that cause bronchodilatation. Knuttgen and Emerson (1974) found insignificant change in TVC. FEV_1 (%) observed by them was 86.5 ± 2.00 and 89.3 ± 1.90 prepartum and postpartum. Butler and Bonica (1975) gave FEV_1 values to be 3.2 (at term)

to 3.3 (postpartum) liters suggesting a decrease in FEV_1 during pregnancy. Bernard (1967) and Baldwin (1977) reported insignificant change in FEV_1. Milne et al. (1977) measured FEV_1 and FVC on three separate occasions at 8 – 11, 12 – 23 and 24 – 36 weeks of gestational age using conventional water filled spirometer. He obtained FEV (lt.) as 3.1, 3.05 and 3.1 and FVC as 3.69, 3.67 and 3.75 showing no change in FEV_1 and insignificant increase in FVC, while ratio of FEV_1 / FVC (%) as 84, 82.9 and 82.5 respectively. Alaily and Carrol (1978) state that FEV_1 showed no statistically change during pregnancy or after delivery. The ratio of FEV_1 / VC was within normal limits in every case. The ratio averaged 82.3% during pregnancy and 83.6% postpartum and in nonpregnant state. No patient had value below 70%. Decrease in hemoglobin results to reduction in oxygen carrying capacity of blood especially in third trimester and causes tissue hypoxia and accumulation of intermediatry products of metabolism leading to exhaustion and respiratory effects become less powerful as reflected by decrease in expiratory flow rates (Singhal and Saxena, 1987)

Das et al. (1991) has given mean and SD values of nonsmokers during pregnancy for few parameters in first (7–13 weeks), second (14–26) weeks and third (27–40 weeks) trimester as such: FVC (L): – 3.90 $\pm$ 0.51, 3.89 $\pm$ 0.54 and 4.00

± 0.45; FEV_1 (L): – 3.34 ± 0.42, 3.33 ± 0.41 and 3.41 ± 0.34; FEV%: – 85.75 ± 4.09, 85.75 ± 4.54 and 85.47 ± 3.82; They indicate that all parameters are not affected by advancing pregnancy and P value for all parameters between trimesters is non significant. In another study, Das et al. (1998) obtained FVC as 3.9 ± 0.4 lt. and FEV_1 as 3.36 ± 0.39 lt. during pregnancy, a non significant change as compared to nonpregnant state.

Rao et al. (1991) noticed a rise in FVC (L) in progestational (2.76) phase as compared to follicular (2.71) phase while no change (2.43) in FEV_1 (L) in follicular and progestational phase. FVC (L) was found to be significantly higher in progesterogenic phase (2.24 ± 0.35) as compared to estrogenic phase (2.11 ± 0.32) of menstrual cycle while insignificant change in FEV_1 (L/sec) was observed in follicular (1.97 ± 0.39) and luteal (2.03 ± 0.35) phase (Rajesh et al., 2000). They also state that better results in lung functions and few of these are statistically higher in luteal phase as compared with follicular phase indicating possible role of progesterone causing ß adrenergic stimulation or sensitization.

Cugell et al. (1953) reported decrease in FEV_1 from 84% in nonpregnant to 82% at term. Colette et al. (1960) showed a steady decrease in forced expiratory volume throughout

pregnancy. Krunholtz et al. (1964) reported no significant change in FEV_1 and found FEV_1 as 85% in early pregnancy and 84% in late pregnancy. Schatz et al. (1990) accounted low maternal gestational FEV_1 during pregnancy and state that it is related to intrauterine growth. Mokapatti et al. (1991) recorded a significant decrease in FVC and FEV_1 in third trimester as compared to controls. Rao et al. (1991) observed a decrease in FEV_1 % from 89.9 (follicular phase) to 87.7 (progestational phase). FEV_1 % was seen to decrease significantly from 97.04 $\pm$ 4.00 in follicular phase to 94.37 $\pm$ 9.12 in luteal phase (Rajesh et al., 2000).

Puranik (1994) found mean and SD for FVC as 2.19 $\pm$ 0.25, 2.15 $\pm$ 0.28, 2.16 $\pm$ 0.27 and 2.20 $\pm$ 0.26 in first, second, third trimester and postpartum respectively, an insignificant reduction in FVC that may be due to restrictive effect of the enlarging uterus. They have also reported insignificant increase in FEV_1 and FEV_1 / FVC %. The mean and SD values for FEV_1 obtained by them are 2.00 $\pm$ 0.09 (first trimester), 2.07 $\pm$ 0.27 (second trimester), 2.10 $\pm$ 0.24 (third trimester) and 2.20 $\pm$ 0.22 (postpartum) while for FEV_1 / FVC % are 92.60 $\pm$ 5.01 (first trimester), 97.68 $\pm$ 3.53 (second trimester), 98.09 $\pm$ 3.26 (third trimester) and 99 10 $\pm$ 2.37 (postpartum).

FORCED INSPIRATORY VITAL CAPACITY

FIVC (L) as obtained by Rajesh et al. (2000) in luteal and follicular phase were 2.19 ± 0.35 and 2.04 ± 0.42 respectively showing a statistically significant increase.

MAXIMUM INSPIRATORY and EXPIRATORY FLOW RATE

Harris (1975) and Slonim and Hamilton (1976) have given an account of maximum inspiratory flow rate, maximum expiratory flow rate, their ratios and forced inspiratory vital capacity in pathological respiratory restrictive and obstructive conditions in their books but not during pregnancy.

Rubin et al. (1956) viewed insignificant changes in pregnant and nonpregnant subjects for maximal inspiratory and expiratory flow rates. Krunholtz et al. (1964) reported MEFR (lt./min) of 430 ± 70 in first trimester to 390 ± 125 in third trimester indicating insignificant change. Baldwin (1977) observed no significant change in MMF. Mokapatti et al. (1991) noticed a decrease in mid expiratory flow rate during first trimester. Das et al. (1991) studied effect of smoking on maternal airway function and has given mean and SD values of nonsmokers during pregnancy for some parameters in first (7–13 weeks), second (14–26) weeks and third (27–40 weeks) trimester as follows: $FEF_{.2-1.2}$ (L/sec): – 6 .52 ± 1.27, 6.70 ±

1.21 and 6.87 ± 1.16; $FEF_{.25-.75}$ (L/min): – 3.77 ± 0.71, 3.81 ± 0.72 and 3.90 ± 0.64. They computed statistically insignificant change in all parameters by advancing pregnancy. Das et al. again in 1998 gave values for $FEF_{.2-1.2}$ (L/sec) as 6.70 ± 1.22 and for $FEF_{.25-.75}$ (L/min) as 3.85 ± 0.69 during pregnancy. Datta et al. found no change in FVC, FEV_1, FEF_{25-75}% and FEV_1 / FEV.

Rao et al. (1991) recorded a rise in $FEF_{25-75\ \%}$ (L/sec) from 2.91 in follicular to 2.98 in progestational phase. Rao et al. (1991) and Rajesh et al. (2000) proposed the increase and decrease in flow rates as mentioned above due to increase progesterone level during progestational phase and a decrease in progesterone level during follicular phase.

Sparse literature on flow rates, their ratios and respiratory efficiency test is available. The research work carried out in flow rates as published is in pathological respiratory disorders. Insufficient literature is available on maximum inspiratory and expiratory flow rate parameters during pregnancy. Occasional mention of respiratory reserve – difference of MVV and RMV and breathing reserve ratio – percentage of RR to MVV (Bass, 1959) has been there in published literature during pregnancy. Cugell et al. (1953) reported decrease in BRR during pregnancy and Bernard et al.

(1967) stated breathing reserve was less than 90% during pregnancy sometimes still below as compared to control subjects. The published literature does not have any mention of respiratory efficiency tests as breath holding test, maximum expiratory effort (pressure) test and 40 mm Hg endurance test in pregnancy that is a physiological adaptive state.

Except the small number of studies referred above the researcher of present study has not come across any other published work of inspiratory and expiratory flow rates in pregnancy. In present study, first time an attempt has been made to find forced inspiratory vital capacity, maximum inspiratory flow rate, maximum expiratory flow rate, finding their ratios (to confirm the status of respiratory condition), respiratory reserve, breathing reserve ratio and respiratory efficiency tests during normal pregnancy.

A few of the very common routinely examined cardiocirculatory parameter hemoglobin, heart rate and blood pressure that affect pulmonary functions were incorporated. As these parameters were not the highlight of the study they are not reviewed in details and have been done so briefly in discussion.