

SUMMARY OF THE THESIS ENTITLED
PERINATAL OUTCOME IN RELATION WITH
MATERNAL AIRWAY FUNCTION ABNORMALITY



Submitted to
The Maharaja Sayajirao University of Baroda
for the degree of

DOCTOR OF PHILOSOPHY
(MEDICAL – PHYSIOLOGY)

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Summary

Pregnancy alters the maternal lung functions and may influence the maternal history of common pulmonary disorders. During normal pregnancy FRC decreases by 20% at term as a combined result of a decreased ERV and a lesser decrease in RV. The flow rates remain normal, whereas specific conductance may remain normal or may even get increased, probably due to the bronchodilatory effect of progesterone. Also pregnancy is associated with significant hyperventilation that is in excess of the observed increase in O_2 consumption and is postulated to be a result of the increased progesterone which acts as a respiratory center stimulant. This hyperventilation results in a decreased P_{aCO_2} but blood pH is maintained in a slightly alkalotic range by renal compensation. As a result of the decrease in P_{aCO_2} and hence P_{ACO_2} , alveolar P_{O_2} increases and P_{aO_2} therefore also increases. However, an abnormally high (A-a) P_{O_2} near term, presumably related to airway closure, partially offsets the increase in P_{O_2} expected for hyperventilation.

The patient with underlying pulmonary disease who become pregnant not only experience the effects of normal mechanical and biochemical events, but may also find the natural course of her pulmonary disease altered. Both obstructive and restrictive pulmonary diseases in pregnancy are associated with varying degree of ventilatory impairment and maternal arterial hypoxemia. Obstructive pulmonary diseases or factors related to maternal habit or environmental/exposure causing small airway (≤ 2 mm) obstruction are associated with substantial reduction in arterial oxygen saturation causing maternal hypoxemia.

During pregnancy, the fetus and its vital organ system grow and mature in a carefully organized interrelated sequence. Adequate maternal oxygenation and efficiency of the uteroplacental unit are one

of the major determinants of the fetal growth. The uteroplacental insufficiency associated with obstructive maternal airway function is related to an asymmetrical type of IUGR, where the birth weight is adversely affected. Ultrasound examination aids in prenatal detection of IUGR.

Although a good number of studies concerning maternal respiratory functions are available in normal pregnant women, paucity in data of the respiratory diseases is encountered. Maternal S_aO_2 determination to assess maternal hypoxemia, in case of airways obstruction, is seldom conducted. The correlation of maternal hypoxemia to fetal growth is hardly sought out. Based on this fact the present study was taken up to examine the effect of maternal small airway functions, in the subjects who were clinically stable but in asymptomatic state, on their arterial hemoglobin oxygen saturation during pregnancy, more particularly during the third trimester, when FRC is also abnormally decreased. The study also focuses on perinatal outcome, especially on neonatal birth weight related to maternal respiratory changes.

Pregnant women attending the antenatal clinical of obstetric and gynecology at SSGH, Baroda were recruited in the study. They were grouped as normal healthy nonsmoking pregnant subjects (group I-P: n=93) and those with a past history of respiratory illness, present history of active smoking (≥ 5 bidis or cigarettes/day for more than three years) or passive smoke exposure of > 2 hours/day at workplace or at home (group II-P: n=57). The same subjects in their postpartum were grouped as group I-PP and group II-PP. All the subjects belonged to lower socioeconomic class.

FVC determination in all subjects was carried out on an expirograph in standing posture. SpO_2 was determined using a portable Datex-Ohmeda pulse oximeter in sitting posture. Per abdomen

ultrasound examination was performed on Phillips, Sono Diagnost 100 instrument with a B mode key and 3.5 MHz curved array probe.

The statistical outcomes were measured for both groups as mean \pm SD, the difference in their means were calculated using unpaired "t" test, the results were considered significant at $P < 0.05$.

The mean age, height and weight recorded in the subjects of both groups were similar and comparable. The physiological parameters in both the groups were similar and correspond to the normal variations expected in pregnancy. Several cross sectional and longitudinal studies involving all the three trimesters of pregnancy have reported their airway function to be unaltered throughout pregnancy. Considering this fact, the forced spirometry was conducted only once during the course of pregnancy that is the third trimester while their postpartum values were considered as their control values (non-pregnant data). The mean gestational age calculated was 32 weeks for both groups.

The airway functions when compared in subjects during pregnancy to their postpartum findings in both groups have shown no significant mean difference though a little higher value in each parameter is noted. The preservation of large airway function in pregnancy may be related to the opposing effects of hypocapnia and increased β adrenergic activity induced by progesterone and the small airway function remain unaltered probably due to the smooth muscle relaxant effect and higher β adrenergic activity both attributed to progesterone. It seems likely that the constancy of large and small airways function in pregnancy is a balance between factors tending to increase and those tending to decrease airways resistance.

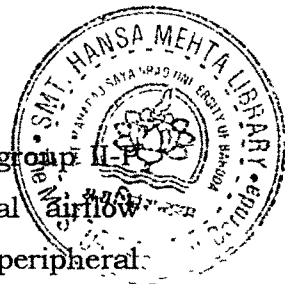
The objective of the current study involves the assessment of maternal airways function in group I-P and group II-P. The mean FVC

recorded were 2.11 in group I-P and 2.01 liters in group II-P, the latter showing little lower value that was statistically insignificant ($P>0.1$). This insignificant change may be related to narrowing or closure of small airways (because 20% of FVC is related to these structures) or loss of elastic recoil pressure of the lungs probably due to some underlying etiology as group II-P is associated with airways obstruction.

The mean FEV_1 and $FEV_{1\%}$ were 1.93 and 1.41 liters and 90.03% and 69.67% in group I-P and group II-P respectively. The statistically mean difference in FEV_1 and $FEV_{1\%}$ between the two groups were found to be significantly and abnormally lower in group II-P ($P<0.001$). These findings suggest an overall airway obstruction, although bronchoconstriction, compliance or elastic recoil was actually not measured. A significant reduction in FEV_1 reflects small airway change in addition to large airway changes.

The mean $FEF_{0.2-1.2}$ obtained were 2.59 and 1.53 and $V_{\max 25\%}$ were 1.40 and 0.89 in group I-P and group II-P respectively. The mean difference calculated statistically of both the parameters were seen to be significantly lower ($P<0.001$) in group II-P. These parameters reflect the large airway resistance or a decrease in effort, as much of these flows are effort dependent. Since the subjects were made to give in their maximal effort the latter view can be ruled out but a decrease in expiratory muscle power amongst subjects of this group cannot be entirely ruled out.

$FEF_{25-75\%}$, $FEF_{75-85\%}$, $V_{\max 50\%}$ and $V_{\max 75\%}$ in lt/sec are independent of effort and are important to detect small airway patency, particularly of airways with a diameter ≤ 2 mm. The mean values observed were as follows: $FEF_{25-75\%}$: 2.24 and 1.29; $V_{\max 50\%}$: 2.42 and 1.43; $FEF_{75-85\%}$: 1.10 and 0.72 and $V_{\max 75\%}$: 2.96 and 1.79 in group I-P and group II-P respectively. These flow rates values on



statistical analysis were found to be significantly lower in group II-PP (P<0.001). These parameters are sensitive to peripheral airflow obstruction and such significantly reduced values indicate peripheral obstruction and an increased resistance to flow.

The lung function conducted in postpartum showed non significant mean difference in FVC (X=2.11 in group I-PP, X=2.00 liters in group II-PP). A lower mean FVC is observed when compared with group I and group II pregnant women. Thus in postpartum too, the narrowing or the closure of small airways and probably loss of elastic recoil could be the attributable cause. The mean FEV₁ (lit) was 1.83 and 1.42 and the mean FEV_{1%} was 86.7 and 70.6 in group I-PP and group II-PP respectively. The mean difference calculated statistically in postpartum was found to be significantly and abnormally lower in group II-PP. the same were the findings in pregnant group, thus indicating overall airway obstruction.

Mean values (lit/sec) for both postpartum groups on statistical analysis showed significant decrease (P<0.001) in group II-PP for FEF_{0.2-1.2} (2.49 and 1.62) and V_{max25%} (2.73 and 1.85) suggesting reduced large airway functions.

Obtained mean values of small airways flow rates (lit/sec) are as follows for group I-PP and group II-PP. FEF_{25-75%}: 1.97 and 1.35; V_{max 50%}: 2.14 and 1.44; FEF_{75-85%}: 0.93 and 0.75; V_{max 75%}: 1.15 and 0.89 where the significantly lower values were found in group II-PP (P<0.001) suggesting significant reduction in small airways flow rates. These postpartum findings of lung function confirms the existence of airway obstruction prior to pregnancy and that the bronchodilation brought about by increased level of progesterone in pregnancy, specially near term, may not be sufficient to overcome the deleterious effects in airways function of group II subjects.

As the FRC is reduced by about 20% at term the oxygen reserve in lungs of pregnant women gets diminished rendering them incapable of withstanding periods of apnea and clinically this may be responsible for arterial de-saturation. The maternal respiration may be compromised in the presence of airway diseases, specifically of smaller airways. There is a possibility of small airways with low flow rates that may be occluded even during the tidal breathing. Alveoli served by these occluded airways would be poorly ventilated yet perfused and may be responsible for the development of maternal hypoxemia due to ventilation-perfusion mismatch. There are reports stating that pregnant women with hypoxemia may experience impairment of uterine blood flow and oxygen transfer from mother to fetus, as this level is flow limited and thus may have far reaching effect on fetal outcomes. This despite of the remarkable reserve of pulmonary function in normal pregnant women, pregnancy can tip the balance towards deterioration when underlying lung disease is present. Thus, the pregnant women with respiratory diseases pose a special challenge.

In an attempt to assess maternal hypoxemia pulse oximetry, a safe and noninvasive technique of monitoring arterial hemoglobin oxygen saturation (SpO_2) was used both during pregnancy (32 weeks) and postpartum (6-8 weeks). The mean SpO_2 was recorded 98.89 in group I-P and 97.92 in group II-P. Though the mean values in both the groups were within the normal range, the values of group II-PP lies in the lower limits of normal range and the difference statistically showed significantly lower SpO_2 in group II-PP ($P < 0.001$). This lower value is suggestive of maternal hypoxemia most likely to ventilation-perfusion mismatch. Since the SpO_2 determination was conduction in the wakefulness state of subjects, a higher reduction in SpO_2 during sleep needs to be considered as both sleep and supine posture are

associated with development of maternal hypoxemia, especially in the last trimester.

The mean SpO₂ (%) postpartum was 97.08 in group I-PP and 95.98 group II-PP. The difference of mean evaluated statistically was found to be significantly lower below normal limits in group II-PP. Here again the ventilation-perfusion mismatch might be the likely cause. Also the lower SpO₂ values seen in both groups in postpartum suggests that probably the bronchodilatory effect produced by progesterone might have improved the lung functions and thus maternal oxygenation in subjects during pregnancy while due to marked reduction in levels of progesterone associated with postpartum and lactation might have caused lower SpO₂.

Obstetric ultrasonography was performed in all the subjects to assess the fetal growth and development. The morphometric parameter measured and studied were BPD, HC, FL, AC and ratios as HC/AC, BPD/FL and FL/AC were calculated while EFW was determined using the biometric parameter and the ratios.

The mean (cm) of measured BPD and HC were 8.06 and 7.91 and 29.59 and 29.35 in group I and group II respectively. The mean difference calculated between both groups was not found to be statistically significant ($P>0.1$). These parameters give the head size and thus the brain growth, the measure of which is found to be normal in the present study.

The mean (cm) of measured AC was 26.76 and 25.97 and FL was 6.09 and 6.02 in group I and group II respectively. The mean difference calculated between the groups was not found to be statistically significant ($P>0.1$). The normal AC indicates fetal trunk size and soft tissue development is normal, while normal FL indicates the normal linear growth of the fetuses.

The mean of the ratios calculated were BPD/FL as 1.31 and 1.30 and HC/AC as 1.11 and 1.14 and FL/AC as 23.11 and 23.42 in group I and group II respectively. The difference of mean calculated statistically in each were not found to be significant indicating that growth of the fetuses was proportionate and corresponding to normal growth pattern observed in the subjects of mean 32 weeks of gestation.

Currently the most frequently used parameter to screen and identify IUGR is the estimated fetal weight. In the present study the EFW (gm) obtained were 1808.97 and 1683.33 in group I and group II respectively. The mean difference calculated between them though not significant showed a lower mean birth weight in group II. This finding probably indicated the commencement of asymmetrical IUGR. Asymmetrical IUGR is believed to occur in late gestation (>32wks). This fetal growth phase is commonly referred to as the phase of cellular hypertrophy and is characterized by a rapid increase in cell size and it is in this phase in which most fetal fat deposition is thought to occur and thus the growth lag occurring in this phase results in low birth weight.

The neonatal data showed a mean CC (cm) as 32 and 31.75, neonatal height or length (cm) as 47.90 and 47.70, HC (cm) as 33.93 and 33.75 of group I and group II respectively. The mean difference calculated statistically was not found to be significantly differing ($P>0.1$). These findings correspond to normal expected values documented in standard Indian books.

The mean neonatal birth weight (gm) noted were 2643.97 and 2319.29 of group I and group II respectively. The PI was found to be 2.4 and 2.13 in group I and group II respectively. The significantly mean low birth weight ($P<0.001$) noted in face of a normal neonatal length is held responsible for the significantly reduced ($P<0.001$) PI in

neonates delivered by group II as compared to group I. Asymmetrical IUGR is associated with the HC and length being relatively normal for the gestational age, but with a reduced weight/length ratio and PI (< 2.2). Thus the PI findings along with other neonatal findings of the present study indicates that the lower mean birth weight observed in neonates delivered by group II subjects is a resultant of asymmetrical IUGR which is commonly associated with maternal uteroplacental insufficiency.

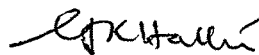
Thus the data obtained in the present study confirms the association of lower maternal airway function and oxygen saturation with lower birth weight and a decreased PI suggest a asymmetrical type of growth retardation.

CONCLUSION

Pregnancy is associated with significant anatomic and functional changes in respiration influenced by mechanical, endocrinal and metabolic factors. The increased requirements of the mother and the fetus for O₂ during pregnancy would be most efficiently served by smooth transport and exchange of gases through the maternal respiratory system. Several adaptive physiological changes occurring during normal pregnancy preserves airway function. Any maternal disease or factor adversely affecting the airway function causes maternal hypoxemia mainly due to ventilation perfusion mismatch which in turn causes fetal growth retardation due to uteroplacental insufficiency as fetal oxygenation and thus its growth depends on it. IUGR due to uteroplacental insufficiency usually ensues in the late phase of gestation during which the cellular hypoplasia and most of the fat deposition is believed to occur. Hence, the fetal vital organs like brain, heart, kidneys and lungs are spared while the birth weight is adversely affected, this type of growth retardation is termed as asymmetrical (type II) IUGR. Thus, pregnant women with underlying obstructive airways function abnormalities are found to deliver low birth weight baby. These infants have a better prognosis with a good intrapartum surveillance and are usually associated with a catch-up growth later in childhood.



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27-9-04

