INTRODUCTION

Preterm labour is more common in smokers, teenagers, drug abusers, women with bacterial vaginosis, multiple pregnancy, hypertensive, and women who have previously delivered preterm ***(Johnston et al., 2000***).

It often takes several days or even weeks to establish full enteral feeds in preterm**,** especially extremely low birth weight neonates**.** Feeding intolerance is a common problem for preterm infants that frequently results in dependence on prolonged parenteral nutrition ***(Gomez et al., 2003)***.

It is common practice to check the gastric residuals before each feeding in very low birth weight infants. The gastric residual volume is regarded as an objective parameter for intestinal tolerance of feeding. Gastric residuals are benign and relate to immature gastro-intestinal motility ***(Shaul et al., 2000)***.

Amylin is a novel 37 amino acid peptide hormone that is co-secreted with insulin from the pancreas in response to food intake ***(Kairamkonda et al., 2005)***. It has been shown to have both vasodilator ***(Hall et al., 1999)*** and anti-inflammatory properties ***(Clementi et al., 1995)***. It shares 50% homology with calcitonin gene related peptide, which is recognised to be raised in acute inflammatory states such as trauma **(*Onuoha et al., 1999);*** sepsis and hypotensive shock ***(Kairamkonda et al., 2005)***.

As a potent inhibitor of gastric emptying, amylin plays an important role in the control of carbohydrate absorption. This is in keeping with the physiological action of amylin, as it is 15–20 times more potent than other known inhibitors of gastric motility ***(Young et al., 1997)***.

Amylin has been shown to be raised in rat intestinal ischaemic injury ***(Phillips et al., 2001)*** and raised in infants of diabetic mothers ***(Kairamkonda et al., 2005)***.

AIM OF THE WORK

This study is designed to evaluate the serum amylin level in preterm babies with feeding intolerance and to correlate it with different clinical variables.

PREMATURITY

Introduction:

Preterm birth is a major challenge in perinatal health care. Most perinatal deaths occur in preterm infants, and preterm birth is an important risk factor for neurological impairment, including cerebral palsy. Providing care for preterm infants, who may spend several months in hospital, has increasing cost implications for health services ***(Tucker & Mc Guire, 2005)***.

Prematurity is the leading cause of neonatal mortality and a major cause of pediatric morbidity and disability, associated with up to one half of all pediatric neurodevelopmental disorders ***(Gray et al., 2004).*** Furthermore, preterm birth and low birth weight (LBW) may also be associated with lifelong chronic conditions, such as hypertension and dyslipidemia ***(Russell et al., 2007).***

Definitions:

Preterm birth is the delivery of a baby before 37 completed weeks of gestation. Even in developed countries, there is often uncertainty and incomplete recording of estimates of gestation ***(Tucker & Mc Guire, 2005)***. The categories for birth weight are: Low birth weight (<2500 g), very low birth weight (<1500 g) extremely low birth weight (<1000 g) ***(Cockburn, 2000)***.

Only about two thirds of low birth weight infants are preterm. Term infants may be of low birth weight because they are small for gestational age. These infants are usually defined as below the 10th centile of the index population's distribution of birth weights by gestation that is, in the lowest 10% of birth weights ***(Tucker & Mc Guire, 2005)***.

Incidence:

The global incidence of LBW is around 17%, although estimates vary from 19% in the developing countries to 5% to 10% of all births in developed countries ***(Valero et al., 2004)***. The percentage of babies born preterm in the United Strates has risen slowly over the past two decades. In the year 2000, preterm (< 37 weeks of gestation) births accounted for 11.6 % of all births, and births of infants before 28 weeks of gestation for just below 1% ***(Martin et al., 2005)***.

Maternal undernutrition and chronic infection in pregnancy are the main factors that cause intrauterine growth restriction. Although the technical advances in the care of preterm infants have improved outcomes in developed countries with well resourced care services, they have not influenced neonatal morbidity and mortality in countries that lack basic midwifery and obstetric care. In these developing countries, the priorities are to reduce infection associated with delivery, identify and manage pregnancies of women who are at risk, and provide basic neonatal resuscitation ***(Tucker & Mc Guire, 2005)***.

The estimated percentage of low birth weight varies from 5-10% for Egypt. In an early study in Alexandria, the incidence of low birth weight was found to be 10.8% ***(Mansour et al., 2002).***

Mortality & Morbidity of LBW:

Low birth weight is one of the major determinants of neonatal survival as well as post-neonatal morbidity. The post-neonatal physical, neurological and mental handicaps are known to be significantly higher ***(Steplewski et al., 1998)***.

Compared with term births, infant mortality rates are 15-fold and 75-fold higher for those who are born preterm and very preterm (<32 weeks), respectively. Approximately 10% of all newborns are admitted to NICUs, many because of prematurity ***(Schwartz et al., 2000)***.

There was a significant reduction in mortality in LBW babies after training of medical and nursing staff, Reduction in overall Perinatal Mortality Rate (PMR) & Neonatal Mortality Rate (NMR) was also due to decrease in mortality in LBW babies ***(Mufti et al., 2006)***. Compared to normal weight infants, LBW is positively associated with infant mortality and negatively associated with normative childhood cognitive and physical development ***(Kitsntas et al., 2006)***. In 1997, in England and Wales, 50.3% of all neonatal deaths were due to immaturity ***(Johnston et al., 2000)***.

Low birthweight (LBW) is highly associated with death during infancy, and countries with the highest LBW rates also have the highest infant mortality rates ***(Kramer et al., 2005)***. Birth weight remains an important factor affecting infant and child mortality ***(Chhabra et al., 2004)***.

Morbidity and Mortality of Low-Birth-Weight Infants in Egypt:

In a study assessed the morbidity and mortality of low-birth-weight (LBW) infants during the first 3 months. It was found that admission to neonatal intensive care unit and mortality was more frequent in LBW (31.6%, 2.0%) than normal birth weight (NBW) infants (2.0%, 0.2%). They also had increased risk of neonatal jaundice at 1 month, and increased risk of mortality ***(Mansour et al., 2005)***.

Etiology:

The underlying physiology and molecular biology of preterm labour is complex and not yet fully understood ***(Bocking et al., 1998)***. The causes are also diverse and multifactorial. Preterm labour is more common in smokers, teenagers, drug abusers, women with bacterial vaginosis, multiple pregnancy, and women who have previously delivered preterm. Some of these observations would suggest that low grade cervical infection may contribute to preterm labour ***(Johnston et al., 2000).***

Most preterm births follow spontaneous, unexplained preterm labour, or spontaneous preterm prelabour rupture of the amniotic membranes. The most important factors that contribute to spontaneous preterm delivery are a history of preterm birth and poor socioeconomic background of the mother. Interaction of the many factors that contribute to the association of preterm birth with socioeconomic status is complex ***(Tucker & Mc Guire, 2005)***.

Mothers who smoke cigarettes are twice as likely as non-smoking mothers to deliver before 32 weeks of gestation. Cigarette smoking is recognized to be among the most prevalent, preventable causes of adverse pregnancy outcomes. Smoking is strongly related to placental abruption, reduced birth weight, and infant mortality ***(Cnattingius et al., 2004)***.

Evidence suggests that a low prepregnancy weight is associated with an increased risk of preterm birth. In the Preterm Prediction Study, a low prepregnancy body mass index (BMI) was strongly associated with an increased risk of preterm birth ***(Mercer, 2003)***.

Folate has been studied mostly in relation to birth defects, but several studies have related increased folate levels to the risk of preterm birth. There are plausible biological

pathways by which folate levels could influence preterm birth ***(Scholl and Johnson, 2000)***.

There was some suggestion that intercourse in the presence of certain infections; namely, Trichomonas vaginalis and Mycoplasma hominis, might increase risk for preterm birth ***(Cauci et al., 2002)***.

Multifetal pregnancy increases the risk of preterm delivery. About one quarter of preterm births occur in multiple pregnancies. Half of all twins and most triplets are born preterm. The incidence of multiple pregnancies in developed countries has increased over the past 20-30 years. This rise is mainly because of the increased use of assisted reproduction techniques, such as drugs that induce ovulation and invitro fertilization. Singleton pregnancies that follow assisted reproduction are at a considerable increased risk of preterm delivery, probably because of factors such as cervical trauma, the higher incidence of uterine problems, and possibly because of the increased risk of infection ***(Tucker & Mc Guire, 2005)***.

About 15-25% of preterm infants are delivered because of maternal or fetal complications of pregnancy. The principal causes are hypertensive disorders of pregnancy and severe intrauterine growth restriction, which is often associated with hypertensive disorders Risk factors for preterm delivery are summarized in table (1) ***(Tucker & Mc Guire, 2005).***

Cost of Hospitalization for Preterm and LBW Infants in USA:

Hospital costs decrease with increasing birth weight and gestational age, with the smallest and earliest infants having the highest costs and longest length of stay ***(St John et al., 2000)***.

Mean hospital costs for preterm/LBW infants who weighed <2500 g and had specific complications were 4 to 7 times higher than those for infants without these complications. One fourth of stays studied had 1 or more of the following complications: RDS, BPD, IVH, and NEC. Costs for these 4 conditions totaled $3.1 billion. Among these preterm/LBW infants, the single costliest complication in terms of average cost per discharge was BPD, with an average cost of $116000, reported in 4.4% of cases. The most common complication was RDS, reported in 23.3%. Average cost for stays with RDS was $56800, compared with $10700 for infants without RDS. IVH was reported in 4.2% and NEC in 1.4% of all preterm/LBW infants who weighed <2500 g. These infants had high hospital costs: $76000 for IVH and $100000 for NEC. Use of mechanical ventilation was identified among 27.3% of preterm/LBW infants who weighed <2500 g, with costs averaging $55100 ***(Russell et al., 2007).***

Table (1): Overview of Risk Factors for Preterm Delivery ***(Kliegman, 2006)*****:**

Demographic
* Race (black)
* Present low socioeconomic status
* Socioeconomic status of infant's grandparents

Prepregnancy
* Low weight for height
* Short stature
* Chronic medical illness
* Poor nutrition
* Low maternal weight at mother's birth
* Previous preterm babies
* Uterine or cervical anomalies
* Parity (none or more than five)

Pregnancy
* Multiple gestation
* Birth order
* Anemia
* Elevated hemoglobin concentration
* Fetal disease
* Preeclampsia and hypertension
* Infections
* Placental problems
* Premature rupture of membranes
* Heavy physical work
* Altitude
* Renal disease
* Assisted reproductive technology

Behavioral
* Low educational status
* Smoking
* No care or inadequate prenatal care
* Poor weight gain during pregnancy
* Alcohol abuse
* Illicit and prescription drugs
* Short interpregnancy interval (less than 6 months)
* Age (less than 16 or over 35 years)
* Unmarried
* Stress (physical and psychological)

Assessment of Gestational Age & Maturity:

I. Obstetric information:

a) Date of last menstrual period: The expected date of delivery can be quickly calculated by Mc Donald's rule; add 7 days & subtract 3 months ***(Chen et al., 1997)***.

b) Date of first recorded fetal activity (quickening) it is first felt at approximately 16-18 weeks ***(Lee, 2008)***.

c) Date of first recorded fetal heart sounds: these are first detected at approximately 10 - 12 weeks by ultrasonic Doppler & at about 20 weeks by fetoscope ***(Selbing, 1995)***.

d) Ultrasonic examination during pregnancy: ultrasonographic estimate is based upon crown rump length whose measurement can provide an estimate of the gestational age accurate to within 3-5 days at the period of 7-12 weeks of gestation. Biparietal diameter can help in estimating the gestational age between 20 & 30 weeks of gestation ***(Chevenak et al., 1998)***.

II. Assessment of lung maturity:

1) Lecithin-sphingomyelin (L-S) ratio, Lecithin, a saturated phosphatidylcholine, can be measured specifically in amniotic fluid and is a principal active component of surfactant. Sphingomyelin is a phospholipid found predominantly in body tissues other than the lungs. The L-S

ratio compares levels of lecithin, which increase in late gestation, with levels of sphingomyelin, which remain constant. The L-S ratio is usually 1: 1 by 31 – 32 weeks' gestation and 2: 1 by 35 weeks' gestation. The following are guidelines to L-S ratios.

* L-S ≥ 2:1: Lungs are mature (98% accuracy).
* L-S = 1.5 – 1.9:1. 50% of infants will experience RDS.
* L-S < 1.5:1. 73% on infants will experience RDS

(Boehm, 2001)

2) **Phosphatidlglycerol**. It appears in amniotic fluid at 35 weeks and levels increase at 37–40 weeks. This substance is a useful marker for lung maturation late in pregnancy ***(Wilson, 2000)***.

3) **TDX fetal lung maturity (TDx FLM).** This test measures the relative concentrations of surfactant and albumin (millgrams of surfactant per gram of albumin) in amniotic fluid. Results are interpreted in the following ways:

*30 – 70 mg/dl: The infant is at risk for immature lungs.

*> 70 mg/g: The likelihood of RDS is small

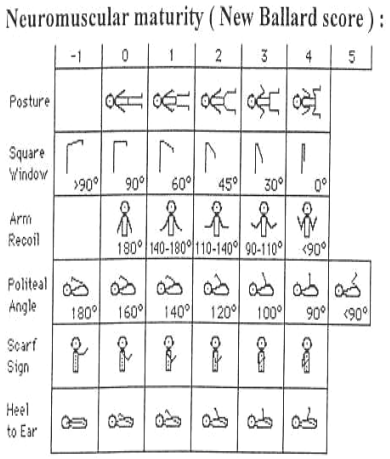
(Russell et al., 1999)

III. Clinical estimation of gestational age:

Several clinical methods have been described to assess gestational age in the neonate, based on external physical

characteristics & neuromuscular evaluation Dubowitz scoring system is based on eleven physical & ten neurological criteria. There may be an error of 1-2 weeks but trained & experienced physician can closely estimate gestational age. Neurological status is not easily evaluated & can change in relation to the state of the infant (quiet sleep, crying, etc...) if there is CNS depression due to drugs or asphyxia or if the infant is critically ill ***(Ballard et al., 1991)***. Therefore, **Ballard et al., (1991)** had modified Dubowitz scoring system eliminating head lag & ventral suspension resulting in a simplified method that includes six parameters of neuromuscular maturation & six physical characteristics. Each receives an individual score; gestational age is determined from the sum of these scores. ***(Stoll et al., 2007)***.

Table (2): New Ballard score for physical assessment of gestational age ***(Ballard et al., 1991)***.



Score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Figure (1): Dubowitz – Ballard scoring system for neuromuscular assessment of gestational age ***(Ballard et al., 1991).***

	-1	0	1	2	3	4	5
Skin	Sticky, friable, transparent	Gelatinous red, translucent	Smooth, pink, visible veins	Superficial peeling and/or rash, few veins	Cracking, pale areas, rare veins	Parchment, deep cracking, no vessels	Leathery, cracked wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald area	Mostly bald	
Plantar	Heel-toe 40-50 mm: -1 < 40 mm: -2	> 50mm, no crease	Faint red marks	Anterior transverse crease only	Creases Anterior 2/3	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1-2 mm bud	Raised areola, 3-4mm bud	Full areola, 5-10mm bud	
Eye-Ear	Lids fused Loosely: -1 Tightly: -2	Lids open: pinna flat; stays folded	Slightly curved pinna, soft slow recoil	Well curved pinna soft but ready recoil	Formed & firm, instant recoil	Thick cartilage, car stiff	
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitals (female)	Clitoris prominent, labia flat	Clitoris prominent, small labia minora	Clitoris prominent enlarging minora	Majora & minora equally prominent	Majora large, minora small	Majora over clitoris & minora	