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Institute of Postgraduate
Childhood Studies (Med. Dep.)

Study of Some Minerals in Cord Blood of Infants of Diabetic and Non Diabetic Mothers.

Thesis
Submitted in Fulfillment of Ph.D. Degree in
Medical Childhood Studies

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بسم الله الرحمن الرحيم

الله لا إله إلا هو الحي القيوم لا تأخذه سنة ولا
نوم له ما في السماوات وما في الأرض من ذا
الذي يشفع عنده إلا بإذنه يعلم ما بين أيديهم
وما خلفهم ولا يحيطون بشيء من علمه إلا بما شاء
وسع كرسيه السماوات والأرض ولا يئوده
حفظهما وهو العلي العظيم

صدق الله العظيم

آية ٢٥٤ من سورة البقرة

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ABBREVIATIONS

ADP	:	Adenosine diphosphate.
BPIs	:	Brachial plexus injuries.
Ca	:	Calcium.
cAMP	:	Cyclic adenosine monophosphate.
CS	:	Cesarean section.
Cu	:	Copper.
DM	:	Diabetes mellitus.
DNA	:	Deoxyribonucleic acid.
ECF	:	Extracellular fluid.
GD	:	Gestational diabetes
GDM	:	Gestational diabetes mellitus.
HbA_{1c}	:	Glycosylated hemoglobin fraction C.
IDDM	:	Insulin dependent diabetes mellitus.
IDMs	:	Infant of diabetic mothers.
L/S	:	Lecithin / sphingomyelin ratio.
Mg	:	Magnesium.
NMDA	:	N-methyle -D- aspartate.
P	:	Phosphorus.
PTH	:	Parathyroid hormone.
RDS	:	Respiratory distress syndrome.
SPC	:	Saturated phosphatidl choline.
VD	:	Vaginal delivery.
Zn	:	Zinc.

Introduction And Aim of The work

INTRODUCTION AND AIM OF THE WORK

Introduction:

Infants of diabetic mothers (IDMs) have many problems, tending to be large and plump with puffy plethoric facies. They are liable for birth injuries, developing respiratory distress syndrome, asphyxia, congenital anomalies, jaundice and certain metabolic disorders such as hypoglycemia, hypocalcemia and hypomagnesemia *(Kliegman and Behrman, 1992).*

Disorders in mineral element nutrition and metabolism in embryos are potentially mutagenic and teratogenic and may lead to abortion or a wide variety of malformations. Similarly, mineral element disorders later in fetal life may produce growth retardation *(Doyle et al., 1989).* Other effects may be latent and be expressed much later in life in the form of neurological and psychological disorders, carcinogenesis, atherogenesis, and even teratogenesis in the subsequent generation *(Perlman, 1984).*

Diabetes mellitus with pregnancy have interrelated effects that can cause both physiological and pathological disturbances in maternal concentrations of macro-and microelements and may lead to fetal variations *(Mimouni et al., 1987).*

Disturbances in metabolism of minerals, particularly essential trace elements in diabetic mothers could cause fetal malformations *(Wibell et al., 1985)*.

Aim of The Work:

This work aimed to study serum concentrations of total calcium (Ca), magnesium (Mg), phosphorus (P), Copper (Cu), and Zinc (Zn) levels in cord blood of infants of diabetic mothers compared to that of healthy infants of non diabetic mothers and to search for possible relationships between gestational age and growth variables (birth weight, length, and head circumference) and the concentrations of these minerals.

Hypothesis :

The controlled diabetic mothers have favorable effects on their infants' growth and minerals concentrations than the non controlled diabetic mothers.

Review of Literature

I. Diabetes Mellitus And Pregnancy

The deleterious effects of maternal diabetes mellitus (DM) on development and outcome of the fetus and newborn have long been recognized, and the opportunity to improve this outcome has been one of the first challenges to be met by a co-ordinate perinatal-neonatal approach to management *(Ballard, 1991).*

Before the discovery of insulin in 1921, pregnancy in the diabetic woman was uncommon and was accompanied by high maternal and fetal mortality rates. Though improved understanding of the pathophysiology of diabetes in pregnancy as well as implementation of care programs emphasizing normalization of maternal glucose levels, fetal and neonatal mortality rates have been reduced from approximately 65% before the discovery of insulin to 2%-5% at the present time. If optimal care is delivered to the diabetic woman, the perinatal mortality rate, excluding that due to congenital malformation, is nearly equivalent to that observed in normal pregnancies *(Landon, 1992).*

Incidence:

The incidence of insulin - dependent diabetes mellitus (IDDM) is estimated at 0.1 to 0.5 percent of all pregnancies in the united state, with an additional 3 to 12 percent of woman experiencing transient biochemical

abnormalities that produce gestational diabetes mellitus (GDM) *(Ballard, 1991).*

Normal pregnancy:

The maternal glucose - insulin balance that occurs during normal pregnancy favors hyperglycemia because, despite some degree of hyperinsulinism secondry to islet cell hyperplasia, pregnancy is apparently associated with insulin resistance. This resistance is thought to be related to changes in other maternal hormones, such as human placental lactogen, progesterone, cortisol, and possibly prolactin *(Gabbe, 1985).* In addition, disposal of glucose after carbohydrate intake appears to be impaired, causing somewhat higher maternal glucose level. Glucagon is suppressed by glucose during pregnancy, and secretory responses of glycogen to amino acids are not increased above non pregnancy level, lipid metabolism is also altered with more glucose being converted to triglyceride in pregnant, compared with non - pregnant women. The effect of this process is to conserve calories and enhance fat deposition *(Ballard, 1991).*

Maternal metabolism and the pathophysiology of diabetes in pregnancy:

During pregnancy, maternal metabolism adjusted to provide adequate nutrition for both the mother and the growing feto-placental unit. Pregnant women needs more insulin to maintain normal carbohydrate meta-

bolism. If she is unable to produce more insulin to meet the demand, she may become diabetic with the resultant changes in carbohydrate metabolism which in turn, affects lipid metabolism. The level of glucose in the women's blood is a measure of her ability to respond to this challenge of pregnancy, this level is reflected in the fetal blood glucose level. Insulin does not cross the placental barrier, so that excess production of insulin by the mother or the fetus remains with the producer *(Brudenell and Doddridge, 1989).*

The general insulin resistance of pregnancy makes hyperglycemia in women with true DM very difficult to control, particularly after the first trimester. It is not unusual for a diabetic woman's insulin requirement to increase up to three-folds during pregnancy. In addition, hepatic keton production increases during pregnancy, therefore, the development of ketoacidosis may be more rapid and occurs at relatively low blood glucose levels *(Becerra et al., 1990).*

It is most important that diabetic women be well

Women with DM are also more likely to develop hypoglycemia which is due to increased placental fetal utilization of glucose and limitation of hepatic gluconeogenesis due to relative lack of alanine, a major substrate. In hypoglycemia the risk is primarly to the mother, since the fetus appears to be protected at the mother's expense *(Menon and Sperling, 1988).*

Classification of diabetes in pregnancy:

More than 40 years ago, Priscillia White noted that the patient's age at the onset of diabetes, the duration of the disease and the presence of vasculopathy significantly influenced perinatal outcome. Her pioneering work led to a classification system that has been widely applied to pregnant women with diabetes. The White's classification, along with identification of vascular complications facilitates this evaluation *(Hare, 1989).*

Gestational Diabetes:

Gestational diabetes is defined as diabetes that is discovered during pregnancy *(Magee et al., 1993).*

Several possibilities are explained. By far the most common possibility is the unmasking of incipient type II diabetes by the metabolic demands of the pregnancy which outstrip the pregnant woman's β cell secretory reserve. An ever-increasing secretion of insulin is needed to conduct the maternal metabolic symphony. Once the woman delivers, her hormone levels rapidly revert to normal and diabetes disappears *(Hare, 1994).*

Table (1): White's classification of maternal diabetes (revised).

Gestational diabetes (GD):	Diabetes not known to be present before pregnancy. Abnormal glucose tolerance test in pregnancy.
GD diet:	Euglycemia maintained by diet alone
GD insulin:	Diet alone insufficient; insulin required
Class A:	Chemical diabetes; glucose intolerance prior to pregnancy; treated by diet alone; rarely seen. Prediabetes; history of large babies more than 4 Kg or unexplained stillbirths after 28 weeks.
Class B:	Insulin-dependent; onset after 20 years of age, duration less than 10 years.
Class C:	C_1: Onset at 10 to 19 years of age. C_2: Duration 10 to 19 years.
Class D:	D_1: Onset before 10 years of age. D_2: Duration 20 years. D_3: Calcification of vessels of the leg (macro vascular disease). D_4: Benign retinopathy (micro-vascular disease). D_5: Hypertension (not pre-eclampsia).
Class F:	Nephropathy with over 500 mg per day of proteinuria.
Class R:	Proliferative retinopathy or vitreous hemorrhage.
Class RF:	Criteria for both classes R and F Coexist.
Class G:	Many reproductive failures.
Class H:	Clinical evidence of arteriosclerotic heart disease.
Class T:	Prior renal transplantation.

Note: All classes below A require insulin. Classes R, F, RF, H and T have no criteria for age of onset or duration of disease but usually occur in long term diabetes (Hare, 1989).

Approximately 3 to 12% of previously non-diabetic pregnant women develop some glucose intolerance during the second half of gestation. The mechanism of this is not fully understood, these women have about a 50% chance of developing type II diabetes during middle age *(Ballard, 1991).*

Some women have undiagnosed type II diabetes before pregnancy. Because the diabetes is discovered during pregnancy, these women are considered to have GD, but their diabetes will persist post-partum. In fact, the failure of GD to disappear during the puerperium suggests that it was present before pregnancy *(Hare, 1994).*

Before type I diabetes becomes clinically overt, there is a period of active autoimmunity and, in the late stages, very subtle defects in β-cell secretion. The defect may not be identified except by intravenous glucose tolerance testing. However, if pregnancy is superimposed at this point, mild diabetes may develop. It may also disappear after delivery but is likely to reappear in months or years rather than decades because of the shorter natural history of the development of type I diabetes *(Eisenbarth, 1986).*

Gestational diabetes is typically asymptomatic, and the diagnosis must be sought actively. The American Diabetes Association suggests that all women be screened between gestational weeks 24 and 28. This screening is

accomplished by giving 50 gm of glucose orally at any time of day, fasting is not necessary. One hour later, the plasma glucose level should not exceed 140 mg/dL. If it is higher, a 3-hour glucose tolerance test must be performed to confirm the diagnosis. Pregnant women are challenged with 100 g of glucose for this test *(Freinkel, 1985).*

The diagnosis is established if any two values during the glucose tolerance test exceed the upper limit of normal.

Table (2): Glucose tolerance tests during pregnancy.

Time	**Upper limits of normal for plasma glucose levels (mg/dL)**
Fasting	105
After glucose challenge*	
1hr.	190
2hr.	165
3hr.	145

* Oral glucose load of 100 g.

(Hare, 1994)

Once the diagnosis is made, the initial treatment is dietary (GD diet), with insulin therapy added if dietary measures fail to normalize the glucose levels (GD insulin) *(Metzger et al., 1990).*

Class A: Identified women whose diabetes, whether gestational or pregestational, is treated by diet alone.

Class B: Includes women who have had diabetes for less than 10 years and were 20 years or older at its onset.

Class C: Comprises both women with onset of diabetes before age 20 (C_1) and those with 10 to 20 years of uncomplicated diabetes (C_2).

Class D: Is a transitional class that includes not only women with diabetes onset before age 10 (D_1) or of more than 20 years' duration (D_2) but also those with background calcification of vessels of the leg (D_3), retinopathy (D_4) and hypertension (D_5).

Class F: Indicates nephropathy, defined as proteinuria of more than 500 mg/day. Thus the diagnosis of pre-eclampsia must be entertained. Prematurity and low birth weight were common in infants of women in this class.

Class R: Which identifies women with proliferative retinopathy, includes those with neovascularization with or without vitreous hemorrhage.

Class FR: Includes women with combined nephropathy and proliferative retinopathy.

Class G: That of adverse obstetrical history unrelated to vascular disease.

Class H: Includes women with coronary artery disease.

Class T: Which includes women with prior renal transplantation, is really a variant of class F.
(Hare, 1994).

Maternal - fetal problems:

Women with poor diabetic control in pregnancy have a significantly increased incidence of spontaneous abortions, which is not increased in early pregnancy in well-controlled diabetic as compared with non-diabetic pregnancies *(Sutherland and Pritchard, 1986).*

In the third trimester, a major problem is sudden unexpected fetal death, which is sometime associated with keto-acidosis, pre-eclampsia, or maternal vascular disease of the decidua and myometrium, but many are unexplained, the incidence of this problem has decreased during the past 10 years with the use of tests of fetal well being, but it still occurs occasionally. The most difficult maternal, fetal and neonatal problems occur in women with renal, cardiac, or retinal diseases. However, the risk of complication is minimal in gestational diabetes, although macrosomia and neonatal hypoglycemia are sometimes seen *(Hare, 1989).*

Renal disease with diabetic pregnancy necessitates early delivery, while cardiac disease is associated with maternal death, and retinopathy may progress during pregnancy. In diabetic women with vascular disease, there is an increased risk of in-utero growth retardation, which is associated with a small infarcted placenta,

decreased utero-placental perfusion, increased incidence of fetal distress, and in-utero fetal death. In addition, hypertension in pregnancy is the largest cause of premature delivery and thus of respiratory distress syndrome (RDS) *(Landon and Gabbe, 1991).*

Detection of diabetes mellitus in pregnancy:

Many perinatologists have recommended that, if possible, women should be routinely screened for diabetes during pregnancy, but all agree that women who have any of the risk factors of being overweight, previous delivery of a macrosomic or stillborn infant, malformed infant or family history of diabetes as well as all women over 25 years of age should be screened *(Ballard, 1991).*

It is therefore recommended that all pregnant women be screened for GDM with a 50 gm oral glucose load followed by a glucose determination one hour later *(Cousins et al., 1991).* If they have GDM or class A diabetes, they should be managed by diet to keep their fasting plasma glucose level below 105 mg/dL and their postprandial plasma glucose level below 120 mg/dL. If these goals are not reached by dietary therapy, then insulin should be used. This will require home monitoring of capillary blood glucose, urine glucose, and acetone levels several times a day along with multiple daily injections of insulin. Hemoglobin A_1 (HbA_1) is measured to assess control over a longer period of time.

Also fetal ultrasonography at 18 weeks must be done to rule out anomalies and to confirm the duration of pregnancy *(Cloherty and Stark, 1991).*

Amniocentesis is performed at 38 weeks for measurement of lecithin / sphingomyelin (L/S) ratio and saturated phosphatidylcholine (SPC) level, unless there are fetal or maternal reasons to deliver earlier *(Cloherty and Stark, 1991).*

The route of delivery for the diabetic patient remains controversial, delivery by cesarean section (C S) is usually favored when fetal distress has been suggested by antepartum heart rate monitoring, an elective delivery is scheduled if, at 37 to 38 weeks of gestation, the fetus has a mature lung profile and is at significant risk for intrauterine death because of the mother's poor metabolic control, or if there is a history of stillbirth. Elective CS now reserved for cases in which the cervix can not be ripened with prostaglandin gel or when fetal macrosomia is suspected. Although there are clear limitations to the accuracy of sonographic estimation of fetal weight, cesarean delivery is favored if the fetus is believed to weigh greater than 4000 gm. In well controlled patients without vascular disease and an unfavorable cervix, intervention is often delayed. Despite this approach, the CS rate for women with classes B to R diabetes remains as high as 50% *(Landon, 1992).*

CS may reduce the risk to the fetus of perinatal asphyxia and birth trauma, but it is not without cost. However there is no doubt that CS increases the risk of respiratory distress from wet lung syndrome and in those babies less than 37 weeks of gestation from hyaline membran disease and this may represent a significant increase in risk to the baby's survival in a group of babies already at high risk from RDS because of biochemical lung immaturity *(Mountain, 1991).*

II. The Infants Of Diabetic Mothers

Physiology Of Insulin In Neonates And Its Control.

A) Insulin biosynthesis:

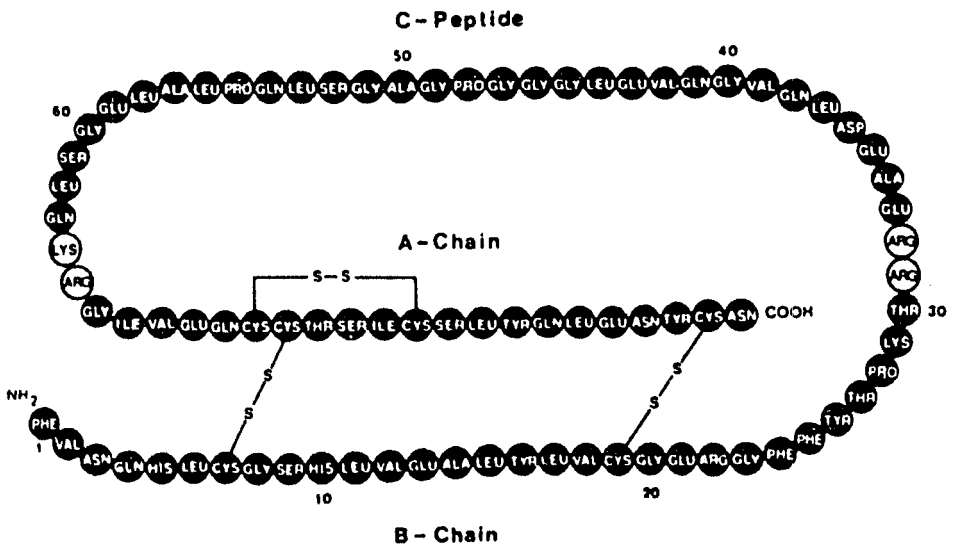
During intrauterine life the pancreatic islets or islets of Langerhans develop from the parenchymatous pancreatic tissue in the 3rd month of fetal life and are scattered throughout the gland. Insulin secretion begins at approximately the 5th month. Since the fetal insulin level is independent from the maternal insulin level, it is unlikely that insulin crosses the placenta *(Sadler, 1993).*

Insulin is a polypeptide containing 2 chains of amino acids linked by disulfide bridges. It is synthesized in the endoplasmic reticulum of the β cells, it is then transported to the Golgi-apparatus, where it is packaged in membrane-bound granules. These granules move to the cell wall and fuse with its membrane, expelling the insulin to the exterior by exocytosis.

The gene for insulin is located on the short arm of chromosome 11 in human. Preproinsulin has a 23 amino acid signal peptide, removed as it enters the endoplasmic reticulum. The remainder of the molecule is then folded, and the disulfide bounds are formed to make proinsulin. The peptide segment connecting the A and B chains is normally detached in the granules

before secretion. The polypeptide that remains in addition to insulin after the connection is severed is called the connecting peptide (C peptide) *(Ganong, 1993).*

Fig. (1): Insulin structure



(Sperling, 1990).

B) Control of insulin secretion:

Insulin secretion is governed by the interaction of nutrients, hormones and the autonomic nervous system. Glucose, as well as certain other sugars that are metabolized by islets, stimulate insulin release. There is evidence that the β cells membrane contains a specific receptors for glucose that trigger insulin release independently of glucose utilization, cAMP is involved

in stimulating insulin release. Also, calcium ions plays a role in the contractile forces that propel insulin to the cell surface. Other ions, including potassium and magnesium, are involved in insulin secretion. In addition, amino acids, free fatty acids and ketone-bodies also stimulate insulin release *(Sperling, 1990).*

Insulin responses to oral glucose administration are always greater than responses to intravenous glucose administration. This had led to the concept that gut factors modulate insulin secretion. Of these, gastrointestinal polypeptide hormone plays a major role. Somatotropin release-inhibiting factor, produced in the delta cells of islets, inhibits insulin and glucagon release. Pancreatic and gut glucagon also stimulate insulin release *(Felig et al., 1976).*

Growth hormone is involved in insulin synthesis and storage. Similarly, glucocorticoids and estrogens evoke greater insulin secretion *(Sperling, 1990).*

Insulin secretion is constantly modulated by the autonomic nervous system. The parasympathetic arm, via the vagus, directly stimulates insulin release. The sympathetic arm depends on whether α-or β adrenergic receptors are activated. Activation of β_2 receptors stimulates insulin secretion by a process that involves cAMP generation. Conversely, activation of α adrenergic receptors blunts insulin secretion *(Woods and Porte, 1974).*

Table (3): Factors affecting insulin secretion.

Stimulators	Inhibitors
Glucose	Somatostatin
Mannose	2-Deoxyglucose
Amino acids (leucine, arginine, others)	Mannoheptulose
Intestinal hormones (GIP, gastrin, secretin, CCK, glucagon, others?)	α-Adrenergic stimulators (norepinephrine, epinephrine)
β-Keto acids	β-Adrenergic blockers (propranolol)
Acetylcholine	Galanin
Glucagon	Diazoxide
Cyclic AMP and various cyclic AMP-generating substances	Thiazide diuretics
β-Adrenergic stimulators	K^+ depletion
Theophylline	Phenytoin
Sulfonylureas	Alloxan
	Microtubule inhibitors
	Insulin

(Ganong, 1993).

Table (4): Effects of insulin on various tissues.

Adipose tissue:

1. Increased glucose entry.
2. Increased fatty acid synthesis.
3. Increased glycerol phosphate synthesis.
4. Increased triglyceride deposition.
5. Activation of lipoprotein lipase.
6. Inhibition of hormone-sensitive lipase.
7. Increased K^+ uptake.

Muscle:

1. Increased glucose entry.
2. Increased glycogen synthesis.
3. Increased amino acid uptake.
4. Increased protein synthesis in ribosomes.
5. Decreased protein catabolism.
6. Decreased release of gluconeogenic amino acids.
7. Increased ketone uptake.
8. Increased K^+ uptake.

Liver:

1. Decreased ketogenesis.
2. Increased protein synthesis.
3. Increased lipid synthesis.
4. Decreased glucose output due to decreased gluconeogenesis and increased glycogen synthesis.

General:

1. Increased cell growth.

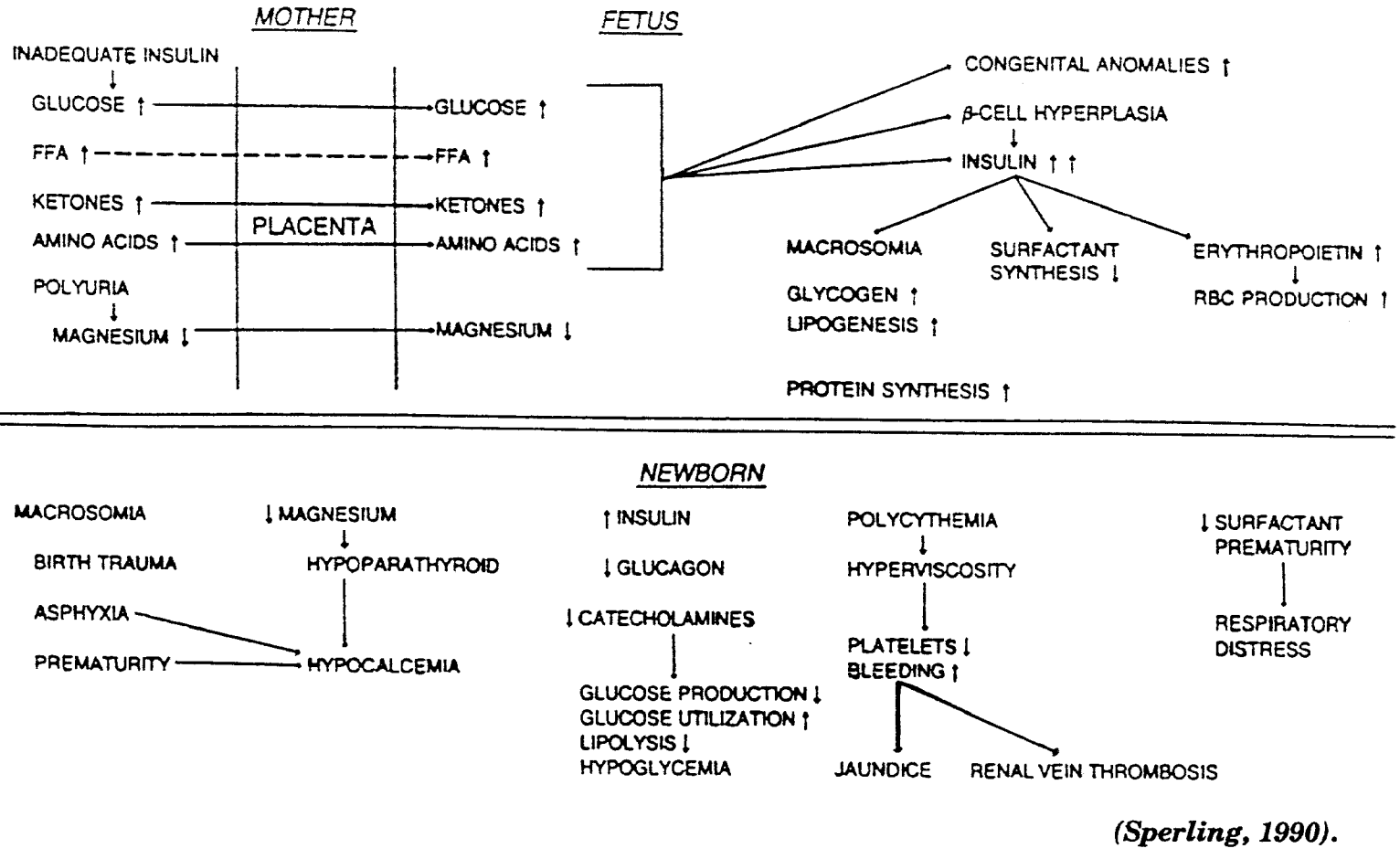
(Ganong, 1995).

Pathophysiology of the infants of diabetic mothers:

The probable pathogenic sequence of maternal hyperglycemia is that it causes fetal hyperglycemia and the fetal pancreatic response leads to hyperinsulinemia, fetal hyperinsulinemia and hyperglycemia then cause increased hepatic glucose uptake and glycogen synthesis, accelerated lipogenesis, and augmented protein synthesis. The related pathogenic findings are hypertrophy and hyperplasia of the pancreatic islets with a disproportionate increase in the number of β cells, increased weight of the placenta and infant organs except for the brain; myocardial hypertrophy; increased amount of cytoplasm in liver cells; and extramedullary hematopoiesis *(Kliegman, 1996)*.

Hyperinsulinism produces fetal acidosis, which may result in an increased rate of stillbirth. Also hyperinsulinemia promotes macrosomia, impairs surfactant synthesis, and directly stimulates erythropoietin formation. In addition to the neonatal hypoglycemia and hypocalcemia, the polyuria consequent to maternal hyperglycemia may deplete maternal and hence fetal magnesium stores *(Sperling, 1990)*.

Fig. (2): Pathophysiology of development of abnormalities in the fetus and infant of the diabetic mother.



(Sperling, 1990).

Clinical picture (appearance):

IDMs tend to be large and plump as a result of increased body fat and enlarged viscera, with puffy blethoric facies. These infants may however, also be of normal or low birth weight, particularly if they are delivered before term or if there is associated maternal vascular disease. Also they tend to be jumpy, tremulous, and hyperexcitable during the first 3 days of life, although hypotonia, lethargy and poor suckling may occur. Early appearance of these signs is more likely to be related to hypoglycemia, and later appearance is related to hypocalcemia. Perinatal asphyxia or hyperbilirubinemia may produce similar signs. Rarely, hypomagnesemia may be associated with hypocalcemia *(Kliegman, 1996).*

Specific Complications With Infants Of Diabetic Mothers:

Table (5): Problems of the infant of diabetic mothers.

Maternal	Neonatal
Ketoacidosis	Macrosomia and birth trauma
Hypoglycemia	Birth asphyxia.
Pre-eclampsia	Prematurity.
Polyhydramnios	Respiratory distress syndrome
Retinopathy.	Transient tachypnea of newborn
	Hypoglycemia
	Hypocalcemia
	Polycythemia
	Hyperbilirubinemia
	Congenital malformations
	Cardiac septal hypertrophy
	Small left colon syndrome
	Renal vien thrombosis.
	Intrauterine fetal deaths.

(Kliegman, 1990).

1- Macrosomia

Definition:

Macrosomia is defined as a birth weight over the 90th percentile using a population specific growth curve *(Langer et al., 1989)* or birth weight more than 2 SD above the mean weight for gestational age *(Menon et al., 1990)*. Recently, defined as an absolute birth weight greater than 4 Kg *(Hare, 1994)*.

The IDM is classically macrosomic and the birth of a macrosomic infant of more than 4.500 g at term suggests that, the mother is prediabetic eventhough abnormal glucose tolerance may not have been documented before or during pregnancy *(Black, 1991)*.

Incidence:

It had been recorded as high as 50% of pregnancies complicated by GDM and 40% of pregnancies in IDDM *(Miller and Spellacy, 1985)*.

The following factors were hypothesized to predispose to macrosomia:

1. Increased maternal weight gain during gestation.
2. Increase number of birth until infant No. 3.
3. White race.
4. Increased maternal age.
5. Poor glycemic control from the 20th week of gestation and an increased insulin requirement *(Berk et al., 1989)*.

Pathophysiology:

The Pedersen hypothesis (1977) is now generally accepted. It was suggested that maternal and hence fetal hyperglycemia results in fetal hyperinsulinism secondary to hypertrophy of fetal pancreatic islet cells and subsequently macrosomia. It is known that β-cell hyperplasia starts to develop sometime between the 16th and 34th week of gestation. So it is, therefore, likely that during the first half of pregnancy the fetus of a diabetic mother is only exposed to hyperglycemia but not to hyperinsulinemia and macrosomia probably does not start to develop prior to approximately 30 weeks of gestation. Insulin is considered to have dual role in fetal growth; in early pregnancy it brings about the growth and development of the cells, in late pregnancy insulin is secreted in response to fetal glucose levels and it stimulates lying down of fat *(Berk et al., 1989).*

In a study done by *Menon et al. (1990)* they found that considerable amount of insulin are transferred as insulin antibody complex from mother to fetus during pregnancy in some women with IDDM receiving animal insulin. The extent of transfer correlated with the maternal concentration of anti-insulin antibody. The correlation between macrosomia and the concentrations of animal insulin in cord serum indicated that the transferred insulin had biologic activity.

The IDMs (especially those with poorly controlled insulin dependent diabetes or gestational diabetes) have

selective organomegaly that involves the liver, adrenal gland, heart and muscles but not the brain and the kidneys *(Schwartz, 1990).*

Macrosomia Is Associated With The Following Problems:

A) Asphyxia:

Several mechanisms had been suggested. Maternal diabetes may produce alteration in red blood cell oxygen release and placental blood flow. This change, which may be most marked in patients recovering from diabetic ketoacidosis, results in increasing hemoglobin oxygen affinity, and therefore reduced red cell oxygen delivery at the tissue level *(Madsen, 1986).*

Hyperinsulinemia in the fetus of diabetic mother may increase fetal metabolic rate and oxygen requirements in the face of several factors such as hyperglycemia, ketoacidosis, pre-eclampsia, maternal vasculopathy which can reduce placental blood flow and fetal oxygenation *(London and Gabbe, 1991).*

The significant association between both maternal and fetal glucose concentration and the degree of fetal acidemia suggests that the later may be the consequence of increased metabolic role, which is the result of fetal hyperglycemia *(Salvesen et al., 1992).*

IDMs are more prone to intrauterine hypoxia during pregnancy and therefore more prone to develop

fetal distress in labor, thus fetal heart monitoring with a scalp electrode during labor is mandatory with or without measuring the scalp pH. The decision to proceed to CS with early signs of fetal distress is perhaps more readily taken, specially with a macrosomic fetus, because adifficult forceps produces a very depressed baby at birth with shoulder dystocia as well as intra-uterine hypoxia *(Mountain, 1991).*

B) Birth trauma:

Because of macrosomia, birth injuries are much more common in IDMs. Fracture clavicles, Erb's palsy and other bracial plexus injuries (BPIs), fracture humerus, cephalhematoma and excessive bruising have all been reported to be more common in IDMs born vaginally *(Mountain, 1991).*

The commonest cause of birth trauma is shoulder dystocia, this can cause fractured clavicles, and more important BPIs, which have the potential of causing permanent disability. The incidence of shoulder dystocia was found to be 1 in 100 births. Although most Erb's palsies recover completely within 6 to 8 weeks, the risk of permanent disability was reported to range from 22 to 44% depending on the severity of the initial injury and duration of follow up *(Benedetti, 1987).*

Hypocalcemia, hypomagnesemia, hyperbilirabinemia, polycythemia and cardiomegaly also affect macrosomic infants *(Neiger, 1992)* (discussed later).

Tight maternal serum glucose control during weeks 20 to 30 of gestation can decrease the incidence of fetal macrosomia, however, good glycemic control during the third trimester may not have similar effect *(Langer et al., 1989).*

Moreover, 30% of infants whose mother's diabetes has been fairly controlled fall above the 90th percentile in weight for gestational age *(Schwatz, 1990).*

2. Intrauterine growth retardation

Incidence:

Poor intrauterine growth can be seen in 3% to 7% of non diabetic pregnancies and up to 20% of diabetic pregnancies. Similar rates of these infants have been observed among offsprings of GDM and IDDM *(Langer et al., 1989).*

Abnormalities in cell replication and reduction in the cells number results in a pattern of impaired fetal growth that is early in onset and symmetrical in distribution. Not surprisingly, chronic hypertensive and diabetic women with documented vascular disease are at great risk for the delivery of growth retarded infant *(Cordero and London, 1993).*

3. Hypoglycemia

Definition:

Hypoglycemia is defined as a blood glucose level under 30 mg/dL in any infant, regardless of gestational age and whether associated with symptoms or not *(Cloherty and Epstein, 1991).*

Incidence:

About 75% of IDMs and 25% of infant of mothers with gestational diabetes develop hypoglycemia but only a small percentage of these infants become symptomatic *(Kliegman, 1996).*

The onset is frequently within 1 to 2 hours of age. Because it is not unusual to observe a single low blood glucose value, the diagnosis of hypoglycemia should be based on two consecuative low values taken no more than 30 minutes a part *(Cowett, 1992).*

Mechanism:

At birth the clamping of umbilical cord would interrupt the continous supply of glucose while the infant is still in hyperinsulinemic status, thus leads to fall of serum glucose level. The degree of hypoglycemia may be influenced by at least two factors:

1. Maternal glucose control during the latter half of pregnancy.
2. Maternal glycemic control during labor and delivery *(Cordero and Landon, 1993).*

Premature infants born to mothers with vascular disease are at increased risk for hypoglycemia because their foreshortened intrauterine existence precludes sufficient hepatic glycogen storage *(Ogata, 1986).*

Limited data also suggest that IDMs may have a diminished counter-regulatory responses of glucagon and catecholamines thus leading to hypoglycemia *(Bloom and Johnston, 1972).*

IDMs are unable to respond to hypoglycemia by releasing glucagon from alpha-cells of the pancreas and in addition they are relatively glucagon resistant, requiring ten times the usual amount of glucagon to cause glycogen release and degradation to glucose, as a result IDMs have numerous amount of glycogen laid down approximately in every tissue particularly liver, spleen, skeletal muscles but it is unavailable to compensate for the rapid fall in glucose during the first few hours of life *(Mountain, 1991).*

Aggravating factors for hypoglycemia:

1. Polycythemia, it may cause hypoglycemia by increasing number of red blood cells directly absorbing glucose from the serum *(Downey and Cloherty, 1991).*
2. Decreased secretion and peripheral action of glucagon.
3. Administration of a large doses of intravenous glucose to diabetic mothers during labor as well as in

cases of placental insufficiency syndrome *(Hay and Sparks, 1985).*

Signs and Symptoms:

The clinical features of infants with hypoglycemia are relatively non specific and range from jitterness, tremors, lethargy, apnea, tachypnea, respiratory distress, cyanosis, pallor, hypotonia, hypothermia, and poor feeding to repeated convulsions *(Geffner, 1990).*

These signs may be absent or apparent only with careful observation, most of IDMs are asymptomatic with very low plasma glucose levels. This may be due to initial brain stores of glycogen *(Edward et al., 1986).*

Diagnosis:

Blood glucose level is measured at birth and at 1, 2, 3, 6, 12, 24 and 48 hours. It is measured more often if the infant is symptomatic, if the infant has a low blood glucose level, and to see the response to therapy. Chemostrip B-G is used for screening and laboratory for confirmation *(Cloherty and Epstein, 1991).*

It is best to maintain plasma glucose above 40 mg/dL *(Korones and Bada Elizey, 1993).*

Treatment:

a) Asymptomatic infants with normal blood glucose levels:

- Well IDMs are fed by bottle or gavage with dextrose 10% (5 ml/kg body weight) at or before 1 hour of age.
- Infant less than 2 kg should not be given oral feeding; they should have parenteral dextrose starting in the first hour of life.
- larger infants can be fed hourly for 3 or 4 feeding until the blood glucose determinations are stable. The feeding can then be given every 2 hours and later every 3 hours.
- If the infant feeds successfully by 12 hours of age and the blood sugar level is normal, 20 cal per 30ml of formula should be given, with extra dexstrose added as needed.
- If by 2 hours of age the blood glucose level is low (under 30 mg/dL) despite feeding, or if feeding are not tolerated, parenteral treatment is indicated.

b) Symptomatic infants, infants with a low blood glucose level after an enteral feed, or infants less than 2 kg in weight:

- The basic element in treatment is IV glucose administration.
- If the infant is in distress, 0.5 to 1 gm glucose/kg body weight is given by an IV push of 2 to 4

ml/kg 25% dextrose in water (D/W) at a rate of 1mL/minute. This is followed by a continuous infusion of dextrose at a rate of 4 to 8 mg/kg/minute. Another method is to give 2ml/kg of 10% dextrose over 2 to 3 minutes, followed by a maintenance drip of 6 to 8 mg of glucose/kg/minute.

c) Asymptomatic infant with low blood glucose level:

An initial infusion of 5 to 10 ml 10% D/W at 1mL/min is followed by continuous infusion of glucose at 4 to 8 mg/kg/min.

d) In resistant cases (unresponsiveness to treatment or persistence over 48 hours) other causes should be searched for (e.g., infection, islet cell tumor).

(Cloherty and Epstein, 1991)

- Hydrocortisone 5 to 10 mg/kg/day in two divided doses IM or IV may be effective if hypoglycemia persists inspite of a glucose load of 12mg/kg/min *(Korones and Bada-Ellizey, 1993).*
- Glucagon 0.1 mg/kg IM (maximum 1.0 mg) may be given in infants with good glycogen stores to mobilize glucose in an emergency until IV dextrose is restored *(Downey and Cloherty, 1991).*

Conditions Associated With Neonatal Hypoglycemia

A) Hyperinsulinism:

- Infant of diabetic mother.
- Erythroblastosis.
- Beckwith-Wiedemann syndrome.
- Islet cell adenoma or nesidoblastosis.

B) Decreased glucose production:

- Prematurity.
- Intrauterine growth retardation.
- Starvation.

C) Defects in carbohydrate metabolism:

- Glycogen storage disease.
- Galactosemia.
- Fructose intolerance.

D) Other causes:

- Polycythemia.
- Sepsis.
- Hypothermia.
- Hypothalamic or hypopituitary disorders.

(Geffner, 1990 & Downey and Cloherty, 1991).

4. Hematologic problems

A) Polycythemia:

Definition:

In the neonatal period polycythemia is defined as a hematocrit > 65%, and the reported incidence in IDMs is 16 to 34% *(Goorin, 1991).*

Pathogenesis:

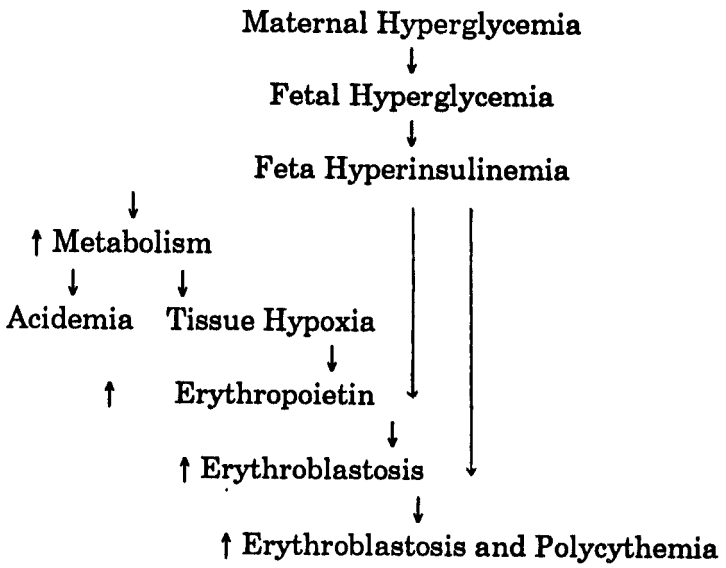
Maternal hyperglycemia causes fetal hyperglycemia and hyperinsulinism. Insulin may stimulates erythropoiesis either through a direct effect on the marrow or indirectly through increased metabolic rate, tissue hypoxia and consequent erythropoietin release. Also, it may be due to reduced oxygen delivery secondary to elevated HbA_1c in both maternal and fetal serum *(Shannon et al., 1986).*

Neonatal polycythemia in IDMs has been speculated to contribute to hypoglycemia, hypocalcemia, hypomagnesemia and hyperbilirubinemia. It correlates with third trimester maternal glycemic control. Neonatal hematocrit is correlated with the materal glycosylated hemoglobin level at delivery. Improved maternal glycemic control during late gestation may decrease the incidence of neonatal polycythemia *(Green, 1992).*

Neonatal polycythemia and its subsequent hyperviscosity may be associated with cardiopulmonary failure, decreased renal function, renal vien thrombosis,

necrotizing enterocolitis and central nervous system damage *(Black, 1991).*

Fig. (3): Suggested mechanism for fetal erythroblastosis, and polycythemia in pregnancies complicated by maternal diabetes mellitus



(Salvesen et al., 1993).

Symptoms:

Most of infants with polycythemia are asymptomatic. Clinical findings include feeding problems, plethora, jitterness, hypotonia, respiratory symptoms such as tachypnea, cardiac symptoms including cyanosis, murmurs and congestive heart failure, lethargy hypoglycemia, poor suckling, convulsions, increased incidence of jaundice, cerebral infarcts and testicular infarcts. Measurement of blood viscosity should be done if available because some infants with hematocrit less

than 65% will have hyperviscous blood *(Cloherty and Epstein, 1991).*

Treatment:

Symtomatic infants should have a partial exchange transfusion. Asymptomatic infants with a peripheral venous hematocrit between 60 and 70% can usually be managed by pushing fluids *(Goorin, 1991).*

B) Thrombocytopenia:

Stuart et al. (1979) noticed that mild fetal thrombocytopenia occurs in IDMs that was in relation to maternal HbA_{1c} level but not with maternal or fetal blood glucose concentration (at time of cordocentesis).

Au-Green et al. (1995) found that IDMs have hematologic indices consistent with increased fetal erythropoiesis, presumably in response to chronic intra-uterine hypoxemia. In addition, they found that increased erythropoiesis would be accompanied by interrelated changes in thrombopoiesis and would correlate with maternal glycemic control during pregnancy. They concluded that in IDMs, increased erythropoiesis is accompanied by decreased platelet counts. These data are consistent with the theory of an erythropoietin induced shift of fetal multipotent stem cell differentiation toward erythropoiesis at the expense of thrombopoiesis.

C) Thrombophilia:

IDMs have tendency to thrombophilia, this is explained by hyperviscosity syndrome due to polycythemia as well as exaggerated platelet aggregation which may be partly explained by increased serum level of adenosine diphosphate (ADP) secondary to polycythemia. Thrombophilia manifests itself in the form of renal or adrenal vien thrombosis the former will lead to unilateral or bilateral flank masses and hematuria while the latter may lead to acute suprarenal failure if the condition is bilateral *(Perrine et al., 1985).*

The combination of fetal polycythemia and increased platelet aggregation could often be an explanation for the increased incidence of intravascular thrombosis in IDMs *(Salvesen et al., 1992).*

5. Hyperbilirubinemia

Definition:

Hyperbilirubinemia (bilirubin >15 mg/dL) is seen with increased frequency in IDMs. Bilirubin levels over 16 mg/dL were seen in 19% of IDMs *(Cloherty and Epstein, 1991).*

Incidence:

The incidence of neonatal jaundice was up to 53% of pregnancies with IDDM and 38% of pregnancies with GDM *(Widness et al., 1985).*

Etiology:

The polycythemia in IDMs leads to excessive hemolysis with exaggerated neonatal jaundice which is further aggravated by immaturity of liver, asphyxia, prematurity, hypoglycemia, constipation and birth trauma *(Perrine, 1985).*

There may be decreased red blood cell life span because of less deformable red cell membranes, possibly related to glycosylation of the cell membrane. This mild hemolysis is compensated for but may result in increased bilirubin production *(Stevenson, 1986).*

Higher concentrations of breast milk β-glucuronidase in diabetic mothers may be an additional important cause leading to hyperbilirubinemia in the breast fed IDMs by enhancing the amount of bilirubin in the entero-hepatic circulation *(Sirota et al., 1992).*

The use of oxytocin in labor may be associated with neonatal hyperbilirubinemia *(Cloherty and Epstein, 1991).*

Hypoglycemia may also decrease uridyl diphosphoglucuronic acid, the substrate for bilirubin conjugation leading to hyperbilirubinemia *(Stevenson, 1986).*

The increased gestational age of IDMs at delivery has contributed to the decreased incidence of hyperbilirubinemia. A careful check on the level of bilirubin in the IDMs is clearly necessary and phototherapy or rarely exchange transfusion is carried out as required *(Brudenell and Doddridge, 1989).*

6. Respiratory Problems

A) Respiratory distress syndrome:

Incidence:

With changes in the management of pregnant diabetics resulting in longer gestations and more vaginal deliveries, the incidence of RDS in IDMs has fallen from 28% in 1950-1960 to 8% in 1975-1976, to 5.7% in 1983-1984. Since the major difference in the incidence of RDS between diabetics and non diabetics is in infants before 37 weeks of gestation. The longer gestations allowed by better utero surveillance and more accurate prediction of pulmonary maturity have had a marked influence on the reduction of RDS in IDMs *(Cloherty and Epstein, 1991).*

Etiology:

Although insulin is an important growth factor for the lung, yet it causes delay of lung maturity. This is mediated by inhibition of the stimulatory effect of corticosteroid on lung maturity via occupation of the hormone-binding receptors. Insulin also causes delay in the appearance of lamellar bodies, thus it leads to delay of maturation and secretion of surfactant *(Smith, 1984).*

Surfactant synthesis:

Cortisol acts on pulmonary fibroblasts to induce synthesis of fibroblast-pneumocyte factor, which then

acts on type II cells to stimulate phospholipid synthesis *(Post and Barsoumian, 1986).*

Surfactant synthesis takes place in type II pneumocytes. The process of surfactant formation is governed by many factors including hormonal influences. The cytoplasm of type II pneumocytes contains hormone-binding receptors. Corticosteroids bind to these receptors forming hormone-receptor complexes which are then transferred to the inside of the nucleus, these complexes act upon the DNA coding for a specific type of mRNA which codes for synthesis of enzymes needed for synthesis of phosphatidylcholine, the main lipid component of surfactant. After that phosphatidylcholine and other components needed for surfactant synthesis are transferred to the inside of lamellar bodies "secondary granules" present inside type II pneumocytes. Inside these bodies mature surfactant is formed and then secreted to outside of the cells *(King, 1985).*

Surfactant appears in the amniotic fluid between 28 and 32 weeks, but mature levels of it are present after 35 weeks *(Floros et al., 1985).*

The cardinal signs of RDS include tachypnea, expiratory grunting, nasal flaring, and costal retractions due to decreased lung compliance resulting from surfactant deficiency which has been reported to occur more frequently in IDMs *(Siri et al., 1990).*

Surfactant assessment:

If the L/S ratio is greater than 3.5 and the SPC concentration is greater than 1000μg/dL, the risk of RDS is very low. The presence of phosphatidylglycerol (a marker of complete surfactant maturation) in amniotic fluid may be particularly helpful in the IDMs *(Torday and Richardson, 1991).*

The fluorescence polarization assay for amniotic fluid surfactant has been proposed as a faster and more precise alternative to determining L/S ratio. This procedure is based on the change in fluorescence polarization produced by the association of different fluorescent molecules with surfactant, it provides an indirect estimation of surfactant concentration. Though technically simple, rapid and precise, the diagnostic power of this remains in question *(Thomas et al., 1994).*

The rate of pulmonary maturation in diabetic pregnancies is related to the adequacy of glucose control which will allow maturation to proceed at the same rate as in non diabetic pregnancies *(Piper and Wolfe, 1993).*

B) Transient tachypnea of the newborn (TTN):

Many IDMs develop tachypnea during the first 5 days of life. Transient tachypnea of the newborn is the primary cause. TTN occasionally called RDS type II and usually follows cesarean delivery *(Robert, 1996).*

TTN is probably caused by incomplete evacuation of fetal lung fluid in infants born at or near term *(Korones and Bada-Elizey, 1993).*

Clinical picture:

TTN may be characterized only by the early onset of tachypnea, somtimes with retractions, or expiratory grunting, and occasionally cyanosis that is relieved by minimal oxygen. Patients usually recover rapidly within 3 days *(Robert, 1996).*

C) Meconium aspiration:

Acute or chronic hypoxia, and acidosis were suggested to result in the passage of meconium inutero. Gasping by the fetus or newlyborn infant can then cause aspiration of amniotic fluid contaminated by meconium. This theory may explain the mechanism of occurrence of meconium aspiration in IDMs who are at great risk of asphyxia *(Korones and Bada Elizey, 1993).*

Clinical manifestations:

Thick meconium is aspirated into the lung resulting in small air way obstruction that may produce respiratory distress within the first hours with tachypnea, retractions, grunting and cyanosis in severly affected infants. Partial obstruction of some airways may lead to pneumothorax or pneumomediastinum, or both *(Yoder, 1994).*

D) Others causes:

Metabolic disturbances, hyperviscosity syndrome, cardiac anomalies, hypothermia, neonatal pneumonia and airway malformations may also lead to tachypnea as well as respiratory distress. Cerebral oedema or hemorrhage, traumatic phrenic nerve palsy and diaphragmatic hernia should be considered in the differential diagnosis *(Cloherty and Epstein, 1991).*

The degree of respiratory support is determined by the severity of the disease. Treatment of respiratory distress varies from application of oxygen in a hood up to intermittent mechanical ventilation *(Korones and Bada-Elizey, 1933).*

7. Congenital Anomalies

Incidence:

Congenital malformations have emerged as the most important cause of perinatal loss in pregnancies complicated by IDDM. At present it account for 30% to 50% of perinatal mortality *(Damm and Pedersen, 1989).*

Cousins (1991) noticed these malformations in 7.5-12.9% of IDMs and this rate is 7-10 times more greater than the rate among infants of non diabetic mothers.

In general, the incidence in world wide studies of offsprings of IDDM has ranged from 6%-9% *(Green, 1993).*

Gestational diabetes, on the other hand, does not seem to be associated with an increased incidence of birth defects *(Becerra et al., 1990).*

Pathophysiology:

It was suggested that, anomalies might arise from inhibition of glycolysis, the key energy producing process during embryogenesis *(Freinkel et al., 1984).*

Miodovnik et al. (1988) in a prospective study, demonstrated a significant correlation between HbA_{1c} in early pregnancy and congenital anomalies. Maternal hyperglycemia has been proposed by most investigators as the primary metabolic factor responsible for abnormal

embryogenesis, but hyperketonemia and hypoglycemia have also been suggested *(Horton, 1983).*

Goldman et al. (1986) had suggested that the mechanism responsible for the increased incidence of neural tube defects in embryo cultures in hyperglycemic medium may involve a functional deficiency of arachidonic acid, since supplementation with arachidonic acid or myo-inositol will reduce the frequency of neural tube defects in this experimental model.

It was demonstrated that the hyperglycemia induced alterations in neural tube closure include disordered cells, decreased mitoses, and increased differentation and cell processes, changes indicative of premature maturation *(Pinter and Reece, 1986).*

It is however clear that a genetic predisposition to birth defects in IDMs is also considered important *(Rosenn and Tsang, 1991).*

Table (6): Malformation associated with maternal diabetes and their estimated risk ratio.

Malformation	Risk ratio
Sacral dysgenesis	200-600
Situs inversus	84
Ureter duplex	23
Renal agenesis	6
Cardiac anomalies	4
Anencephaly	3
Holoprosencephaly	40-400

(Mills, 1987).

Skeletal Anomalies:

The congenital defect thought to be the most characteristic of diabetic embryopathy is sacral agenesis or caudal dysplasia, an anomaly found 200 to 400 times more often in offsprings of diabetic women *(Landon and Gabbe, 1991).*

Central Nervous System Anomalies:

Central nervous system malformations, particularly anencephaly, open spina bifida, holoprosencephaly and possibly meningomyelocele, hydrocephaly and microcephaly are increased tenfold in IDMs *(Kousseff et al., 1991).*

Cardiac Anomalies:

Incidence:

The incidence of congenital heart defects are increased five times in IDMs. Cardiomegaly is common (30%) and heart failure occurs in 5-10% of IDMs *(Kliegman, 1996).*

Transient hypertrophic subaortic stenosis resulting from ventricular septal hypertrophy is an important cause of congestive heart failure in IDMs without congenital heart disease *(Wolther et al., 1985).*

Pathophysiology:

As a consequence of fetal insulin stimulation, an increase in myocardial nuclei, cell number, and fiber occur leading to septal hypertrophy with decreased left ventricular function, and left ventricular outflow

obstruction. Fortunately, this condition generally spontaneously resolves in 8 to 12 weeks *(Cordero and Landon, 1993).*

In a study carried out by *Cooper et al. (1992),* infants were assessed for hypoglycemia, macrosomia and septal thickening by echocardiography. They found that 31% of infants whom had septal hypertrophy, were heavier and had heigher cord blood C-peptide level and lower serum glucose levels than unaffected infants. Maternal HbA_{1c} levels were higher during the 3rd trimester in mothers of affected infants. These data supports a possible relationship between 3rd trimester maternal hyperglycemia and neonatal septal hypertrophy, macrosomia and hypoglycemia.

Clinical features:

Cardiorespiratory distress may be evident at birth and usually appears within the first week of life. Finding may include cardiomegaly, cyanosis, tachycardia, tachypnea, pulmonary oedema, hepatomegaly or peripheral oedema in addition to systolic ejection murmur *(Wolther et al., 1985).*

Most of the symptomatic infants need only supportive care, such as intravenous administration of maintenance fluids, ventilatory support, and correction of hypoglycemia, hypocalcemia and polycythemia. If intervention is necessary, propranolol appears to be the

drug of choice, whereas digitalis and other inotropic drugs are contraindicated unless myocardial dysfunction can be demonstrated by echocardiography *(Wolther et al., 1985).*

Other cardiac malformations include transposition of great vessels, patent ductus arteriousus, situs inversus, single ventricle, hypoplastic left ventricle, co-arcitation of oarta and ventricular and atrial septal defects *(Landon and Gabbe, 1991 & Lavin et al., 1983).*

Renal System Anomalies:

It includes renal agenesis, hypoplastic kidney, polycystic kidneys and double ureters. Hypospadias may also be seen *(Miller et al., 1981).*

Renal vein thrombosis may occur inutero or postpartum. Diagnosis may be made by ultrasound examination. Postnatal presentation may be as hematuria, flank mass, hypertension or embolic phenomena *(Cloherty and Epstein, 1991).*

Moreover, some cases of Di George anomaly with bilateral renal agenesis associated with hemivertebrae were discribed in infant of IDDM *(Novak and Robinson, 1994).*

Gastrointestinal Tract Anomalies:

Small left colon syndrome; it presents as generalized abdominal distension because of inability to pass meconium which is obtained by passage of a rectal

catheter. An enema performed with gastrograffin will make the diagnosis and often results in evacuation of the colon. This syndrome is transient and it is due to immaturity of ganglion cells in the intermyenteric plexus. It usually resolves after treatment with half-normal saline enemas (5ml/kg) and glycerine suppositories *(Cloherty and Epstein, 1991).*

In addition, tracheoesophageal fistula, bowel atresia and imperforate anus can be seen in IDMs *(Mills et al., 1988).*

Also, hypoglossia, hypodactylia associated with complete jejunal atresia was reported in an IDM. A common pathogenesis for these malformations could be a vascular disruptive mechanism within utero or arterial thrombosis *(David et al., 1992).*

Prevention Of Congenital Malformations

1. Preconceptional counselling:

Anomalies of the cardiac, renal, and central nervous system arise during the first 7 weeks of gestation, a time when it is most unusual for patient to seek prenatal care. Therefore, the management and counselling of women with diabetes in the reproductive age group should begin prior to conception. Diabetic clinics, physicians and obstetricians seeing non diabetic women should take the opportunity to press this point *(Landon and Gabbe, 1991).*

HbA_{1c} levels are of considerable value during pregnancy and form a logical part of pre-pregnancy counselling. The level of HbA_{1c} in the first trimester identifies those diabetic pregnancies most likely to be associated with congenital malformations. Levels of HbA_{1c} above normal during the latter part of pregnancy indicate that greater attention needs to be given to the patient's diabetic control and may give a worning of developing macrosomia. The post partum HbA_{1c} level may be of value as a screen for unrecognized gestational diabetes where there has been macrosomia or unexplained late intrauterine fetal death *(Brudenell and Doddridge, 1989).*

2. Strict metabolic control:

Begun before conception and continued during the first weeks of gestation can apparently lower significantly the incidence of congenital malformations among IDMs *(Goldman et al., 1991).*

8. Poor feeding

It is a major problem in these infants which is sometime related to prematurity, respiratory distress, or other problems. However, it is often present in the absence of other problems.

It was found in 17% of class B to D IDMs and in 31% of class F IDMs. Infant born to class F diabetic mothers are often premature. There was no difference in the incidence of poor feeding in large for gestational age infants versus appropriate for gestational age and no relation to polyhydramnios. Poor feeding is a major reason for prolongation of hospital stay and parent infant separation *(Cloherty and Epstein, 1991).*

9. Hypocalcemia

Definition:

Neonatal hypocalcemia is defined as total serum calcium values lower than 6mg/dL (3mEq/L) or ionized calcium levels below 2 mg/dL (1mEq/L) *(Cordero and Landon, 1993).*

Incidence:

IDMs have a 25 to 50% incidence of hypocalcemia during the first 24 to 48 hours. It may persists for several days *(Rubin, 1991).*

Etiology:

Although the cause for the high incidence of this complication is unclear it is well recognized that it relates to the severity of maternal diabetes, perinatal distress, birth asphyxia and the presence of prematurity *(Rosenn and Tsang, 1991).*

Hypocalcemia in IDMs is related to hypoparathyroid status produced by hypomagnesemia, the later occurs due to excess loss of magnesium as a result of maternal polyuria. Also, endogenous hyperphosphatemia from increased tissue glycogen break down as well as delayed calcium intake because of illness, contribute to hypocalcemia in IDMs *(Scott, 1984).*

Hypocalcemia may be caused by delay in the usual postnatal rise of parathyroid hormone (PTH), in

addition to vitamin D antagonism at the intestine from elevated cortisol and hyperphosphatemia from tissue catabolism *(Schedewie and Fisher, 1980).*

The macrosomia associated with IDMs also may increase neonatal calcium demands, producing a more profound and prolonged hypocalcemia *(David et al., 1993).*

Moreover, neonatal hypomagnesemia seems to impair PTH secretion and also blunt end organ response all of which lead to hypocalcemia *(Cordero and Landon, 1983).*

Clinical features:

Symptoms of hypocalcemia are similar to those of hypoglycemia except that they occur between 24 and 36 hours of postnatal age. Hypocalcemia in "well" IDMs resolves spontaneously *(Scott, 1984).*

Infant who are sick for any reason ; prematurity, asphyxia, infection, respiratory distress or IDMs with symptoms of lethargy, jitterness or seizures, should have their serum calcium measured. If the infant has symptoms that co-exist with a low calcium level, has an illness that will delay onset of Ca-regulation, or is unable to feed, treatment with calcium may be necessary *(David et al., 1983).*

Treatment:

If the serum Ca level drops to 6.5mg/dL or less, we recommend beginning a continuous Ca infusion with the goal of producing a sustained increase in serum Ca level (7 to 8mg/dL).

A convenient starting dose is 45mg/kg/day (5ml/kg/day) of Ca gluconate 10%. In hypocalcemic crisis with seizures, apnea, or tetany, serum Ca level is usually less than 5.0mg/dL. Emergency Ca therapy consists of 1 to 2 mL of Ca gluconate 10%/kg (9 to 18mg of elemental Ca/kg) by IV infusion over 5 minutes:

(1) Monitor heart rate and infusion site.
(2) Repeat dose in 10 min. if there is no clinical response.
(3) Following the initial dose (s), maintenance Ca should be given parenterally or orally.

Symptomatic hypocalcemia unresponsive to Ca therapy may be due to hypomagnesemia *(Rubin, 1991).*

10. Long Term Complications

Long-range complications claimed to be associated with diabetic pregnancies are disorders of ponderal growth in childhood, neuropsychological deficits, and an increased tendency to develop DM at birth. 50% of IDMs have body weight above the 90th percentile, but at the end of the first year, this difference is no longer noticeable. Accelerated weight gain reoccur at about 5 years and by eighth year of life; half of IDMs exceed

again the 90th percentile for body weight. This childhood obesity correlated with maternal pregnant weight and amniotic fluid insulin levels *(Silverman et al., 1991).*

It seems that IDMs of IDDM whould have an increased incidence of DM and that infants born to gestational diabetic women would be at great risk as well. Some authors reported a 20-fold greater incidence of DM among offspring of IDDM mothers than in offspring of non diabetic mothers *(Petersen et al., 1988 & Persson and Gentz, 1984).*

In a recent study it was summarized that, if the diabetes is well controlled begining early in the first trimester, intellectual function in the offspring, at least through age 3 years, will on average, be normal. Achieving diabetes control in the first trimester does not however, remove the liability for congenital malformations, which carry their own burden of impaired intellectual function at least through age 2 years and probably longer. Physical growth of the children of diabetic mothers in terms of weight, length, and head circumference is associated with intellectual function regardless of when maternal diabetes control is achieved but a reduced mean head circumference is seen in those offspring whose mother's poor control was documented through the second trimester *(Sells et al., 1994).*

III. Some Minerals And Its Relation To IDMs.

Definition and classifications:

An element is considered essential when a deficient intake produces an impairment of function and restoration with physiological amounts of only that element prevent or alleviates the impairment *(Milne, 1994).*

Minerals are required for both physiologic and biochemical functions. Minerals may be divided arbitrarily into 2 groups:

1. Macrominerals, which are required in amounts greater than 100mg/day. This includes 7 essential elements which are: calcium, magnesium, phosphorus, sodium, potassium, sulfur and chloride.
2. Microminerals (trace elements) which are required in amount less than 100mg/day *(Mayes, 1993).*

These are elements that occur in living tissues in small amounts. They are constituents of metalloenzyme complexes and are cofactors in numerous metabolic process *(Crouch and Rubin, 1991).*

Essential microminerals or trace elements include: Copper, zinc, iron, iodine, fluorine, cobalt, arsenic, chromium, manganese, molybdenum, nickle, selenium, silicon and vanadium *(Ganong, 1993).*

Mineral contents of the fetus:

The ash content of the fetus is about 3% of the body weight at birth. It increases contiuously through childhood, adult ash content is 4.35% of body weight. For each gram of protein retained, 0.3 gm of mineral matter is deposited. The principal cations are calcium, magnesium, potassium and sodium, the comparable anions are phosphorus, sulfur and chloride. Iron, iodine and cobalt appear in important organic complexes.

The trace elements flourine, copper, zinc, chromium, and manganese have known metabolic roles; selenium, silicon, boron, nickel, aluminum, arsenic, bromine, molybdenum and strontium are present in the diet and in the body *(Barness, 1992).*

Calcium (Ca)

Importance and metabolism:

The fetus acquires 80% of the eventual total Ca in the last trimester of pregnancy, therefore a preterm baby needs to acquire 23gm of Ca between 28 weeks gestation and term. The in-utero accretion rate is thus 130mg/kg/day in the last trimester. A typical 28 weeks gestation baby at term has a total body Ca which is one-third less than that of a newly born term baby *(Horsman et al., 1989).*

Ninety-nine percent of the body's Ca is in bone; in the extracellular fluid 40% of Ca is bound to albumin, of the non-albumin-bound Ca almost all is ionized: neuromuscular transmission depends upon this form of Ca, which is now possible to be measured directly. Ionized Ca falls as the pH rises and alkalotic tetany is a real danger when hyperventilation is used *(Rennie, 1992).*

Calcium balance:

The homeostatic control of Ca is achieved by variation in intake and excretion, in absorption from gastrointestinal tract and in the formation of bone. Control occurs under the influence of calcitonin, parathormone and the active metabolites of vitamin D. Preterm infants are able to synthesize vitamin D and to convert it to the active form of 1, 25 dihydroxyvitamin D. Parathormone conserves Ca by acting on the gut to

increase Ca-binding protein in the duodenum and jejunum, and by altering absorption by the kidney. Parathormone levels are detectable after 48 hours of postnatal life and increase Ca excretion in the urine *(Rennie, 1992).*

At birth the cord blood Ca exceeds the maternal Ca value but correlates with it. There is a postnatal fall in Ca level, the cessation of the maternal calcium infusion giving rise to a surge of calcitonin secretion. Ionized Ca levels rise with increasing gestational age *(Tsang et al., 1979).*

Hormonal regulation of calcium homeostasis:

Regulation of serum and extracellular fluid (ECF) ionized Ca concentration within a narrow range is critical for blood coagulation, neuromuscular excitability, cell membrane integrity and function, and cellular enzymatic and secretory activity. The principal calcitropic, or calcium regulating, hormones are parathyroid hormone and 1,25 dihydroxy vitamin D [1, 25 $(OH)_2D_3$] *(Rubin, 1991).*

1. PTH:

When ECF ionized Ca level declines, parathyroid cells secrete PTH; which mobilizes Ca from bone, increases Ca reabsorption in the renal tubule and stimulates renal production of $1,25(OH)_2D_3$. PTH also mobilizes phosphate from bone and produces significant phosphaturia. Therefore, PTH secretion causes the

serum Ca level to rise and the serum phosphorus level to be maintained or fall. Newborns in the first 2 days of life may exhibit decreased renal responsiveness to PTH.

2. 1,25(OH)$_2$D$_3$ (calcitriol):

Inactive vitamin D is synthesized in skin exposed to sunlight and is ingested in the diet. The liver then synthesizes 25(OH)D$_3$ and the kidney synthesizes the biologically active hormone, 1,25(OH)$_2$D$_3$ which increases the intestinal Ca absorption and mobilizes Ca and phosphorus from bone.

3. Calcitonin:

It is secreted by the thyroid C-cells, inhibits bone resorption and has an antihypercalcemic effect.

(Rubin, 1991).

Calcium and pregnancy:

Data on the effect of maternal DM on placental unidirectional materno-fetal flux of Ca and Mg suggested that, untreated maternal DM reduces fetal Ca and Mg accretion by an effect on the expression of placental transport components involved in materno-fetal transfer of these cations *(Husain et al., 1994).*

It was found that strict management of diabetes in pregnancy was associated with a reduction in the rate of neonatal hypocalcemia *(Demarini et al., 1994).*

Hypocalcemia in IDMs:

Discussed before.

Magnesium (Mg)

Importance and metabolism:

Magnesium is principally an intracellular ion. It is important in the central nervous system: neuronal damage has recently been shown to be related to Ca influx occuring because of activation of a particular type of glutamate receptors, the N-methyl-D-aspartate (NMDA). Mg is a natural NMDA receptor blocker, and as such may help to limit the damage in conditions such as birth asphyxia and convulsions. Mg shortage may allow uninhibited stimulation of glutamate NMDA receptors with glutamate and hence cause fits. If Mg deficiency is associated with a low serum Ca it may prevent any benefit from Ca replacement until both ions are corrected *(Goldman and Finkbeiner, 1988).*

It is important in energy production and cell membrance function. It also has important roles in regulation of mitochondrial function and in protein and deoxyribonucleic acid (DNA) synthesis *(Mimouni and Tsang, 1987).*

Total body Mg amounts to approximately 22 mEq/kg in the infant, sixty percent of body Mg is in bone, most of the remaining 40% is intracellular, more than 50% is in muscle and much of the remainder in liver. Extracellular Mg levels account for only 1% of body Mg *(Robson, 1992).*

Normal serum Mg levels in neonates range between 1.6 to 2.8mg/dL. Roughly 35% of total serum Mg is bound to serum proteins. Fetal Mg levels are higher than maternal levels because of active transport across the placenta *(Anast, 1991).* Intrauterine accretion rate for Mg is approximately 3 to 4mg/kg/day *(Crouch and Rubin, 1991).*

Following birth, there is a rise in serum Mg levels, except in infants receiving caw's milk formulas with an inherent high phosphate load *(Anast, 1991).* An early postnatal drop from high fetal values of serum Mg is commonly observed and is most prominent in prematures *(Avery and Fletcher, 1987).*

Body Mg content rises rapidly in the third trimester so that preterm infants are born with low reserves. In preterms Mg absorption in the first week is about 50% and is largely independent of vitamin D *(Lucas, 1992).*

Mg absorption occurs throughout the entire gastrointestinal tract mainly in small intestine and does not appear to vary with either gestational age or postnatal age *(Byrne, 1991).*

Mg homeostasis:

It is intimately related to calcium and PTH homeostasis *(Koo and Tsang, 1987).*

Serum Mg concentration is mainly regulated by the kidney. In normal conditions 95% to 97% of filtered Mg is reabsorbed. An increase in serum Mg leads to decreased reabsorption, whereas in Mg deficiency states or in a low Mg diet, urinary excretion almost disappear. Other factors that increase urinary Mg include hypercalcemia and phosphate depletion. PTH increases serum Mg concentration by increased Mg mobilization from bone, increased intestinal Mg absorption, and decreased renal Mg excretion. However, chronic Mg deficiency reduces PTH secretion, most likely through altering Ca-sensitive, Mg-dependent adenylate cyclase involved in PTH secretion. Excessive vitamin D may lead to hypomagnesemia, possibly secondary to increased intestinal calcium absorption, which results in competition for Mg absorption. Calcitonin may decrease serum Mg concentrations *(Mimouni and Tsang, 1987).*

Magnesium and pregnancy:

In a study to investigate a possible ionic basis linking pregnancy and gestational diabetes it was found that, compared with non pregnant controls, total and ionized Mg were significantly lower in both normal pregnant and gestational diabetic women. Moreover, gestational diabetic women had significantly lower intracellular free Mg value compared with non pregnant and normal pregnant women. These results supported the presence of Mg depletion in pregnancy

itself and to a great extent in gestational diabetes *(Bardicef et al., 1995).*

The interrelationships between Mg and carbohydrate metabolism have regained considerable interest over the last few years. Insulin secretion requires Mg, experimental Mg deficiency reduces the tissue sensitivity to insulin. Subclinical Mg deficiency is common in diabetes. Some studies suggested that Mg deficiency may play a role in spontaneous abortion of diabetic women, in fetal malformations and in the pathogenesis of neonatal hypocalcemia of the IDMs *(Lefebvre et al., 1994).*

Hypomagnesemia in IDMs:

Definition:

Hypomagnesemia occurs when serum Mg level falls below 1.6mg/dL, although clinical signs usually do not develop until serum Mg levels falls below 1.2mg/dL *(Minouni and Tsang, 1987).*

In poorly controlled maternal diabetes, serum, amniotic fluid and fetal and neonatal Mg levels are low *(Cordero and Landon, 1993).*

It results from decreased placental supply of Mg to the fetus due to maternal hypomagnesemia resulting from decreased intake and urinary Mg loss. Data from the rat suggested that, the bulk of materno-fetal placental Mg transfer occurs via a transcellular route

utilising a Na/Mg exchanger and that materno-fetal flux of Mg is reduced in the presence of maternal DM *(Husain and Sibley, 1993).*

Hypomagnesemia gives the same clinical features as hypocalcemia and hypoglycemia and so, it should be considered, whenever there is failure of response to parenteral glucose and Ca in symptomatic cases *(Landon and Gabbe, 1988).*

Treatment:

Correct severe hypomagnesemia (≤ 1.2mg/dL) with 0.1 to 0.2mL of 50% magnesium sulphate/kg IV or IM. When administering IV; infuse slowly and monitor heart rate; IM administration may cause local tissue necrosis. The dose may be repeated every 6 to 12 hours *(Rubin, 1991).*

Maintenance Mg therapy consists of oral administration of magnesium sulphate 50% 100mg, or 0.2mg/kg/day. If there is significant malabsorption, the dose may be increased two to five-fold *(Rubin, 1991).*

Phosphorus (P)

Importance and metabolism:

Phosphorus is a major constituent of bone, with about 85% of body stores present in hydroxyapatite. The remainder is important as a component of energy-containing compounds such as adenosine triphosphate *(Carey et al., 1985).*

In the fetus, the accumulation of P during the last trimester of pregnancy is about 10g, which represents accretion rate of 65-70mg/kg/day *(Lapillonne et al., 1994).*

It is impossible to achieve this with current intravenous or enteral feeding regimens without exceeding the solubility product with Ca. Very low-birth weight infants fed on breast milk develop a low serum P, hypophosphaturia, hypercalciuria. In addition to the contribution which, inadequate mineralization of the ribs can make to respiratory distress, low serum P causes muscle hypotonia and has been associated with difficulty in weaning from artificial ventilation *(Carey et al., 1985).*

Phosphate is better absorbed than Ca, with 90% absorption being the norm. 1,25-dihydroxy vitamin D is necessary for absorption. Human milk contains only 0.4mmol/L of P and therefore needs to be supplemented for preterm babies: current recommendations suggest supplementing to 1.6mmol per 100 kilocalories. When

used together with a Ca supplement the aim is to minimize osteopenia of prematurity and to prevent frank rickets *(Rennie, 1992).*

Normally all the phosphate present in serum is filtered by the glomerulus. 95% is then reabsorbed, the tubular maximum being set by parathormone: If levels of parathormone rise the tubular maximum for phosphate falls and more is excreted. The urine can be phosphate-free even in preterm babies unlike for Ca. Serum P should be maintained close to 1.5mmol/L *(Rowe et al., 1984).*

Prevention Or Reduction Of Calcium And Phosphorus Deficiency:

1. The use of Ca and P enriched preterm formulas result in considerable reduction in bone disease.
2. If human milk is used, it should be supplemented, at least with P. Addition of buffered phosphate solution sufficient to increase the P concentration from 15mg per 100ml to around 30mg per 100ml will improve P status and increase Ca retention. Addition of both Ca and P to milk is feasible, but if both minerals are added together they precipitate. The correct technique is to add the P first which allows it to enter milk fat globules and then Ca *(Salle et al., 1986).*

Zinc (Zn)

Importance and Metabolism:

Zn is present in and indispensable to all forms of life. It is essential for the normal growth of human beings, and Zn proteins have been shown to be involved in the transcription and translation of the genetic material. Zn deficiency has been incriminated in infertility, abortions, malformations, intrauterine growth retardation, prematurity, perinatal death and abnormal deliveries with dystocia and placental ablation *(Jameson, 1993).*

Zn is essential to the function of a number of enzymes as a cofactor or as part of metalloenzymes. such enzymes include alkaline phosphatase, carbonic unhydrase, and superoxide dismutase. Zn is particularly important in the metabolism of amino acids, RNA and DNA polymerase *(Lucas, 1992).*

Even though fetal needs for Zn are highest in late pregnancy, Zn is critically important in very early pregnancy organogenesis *(Hambidge et al., 1983).*

The overall concentration of Zn is 38mg/kg body weight in the term neonate. At the 50th centile for weight in-utero, Zn accumulates at a rate of 249μg and 675μg daily at 26 and 36 weeks' gestation, respectively. Although the Zn content of the heart, kidney and brain is constant throughout gestation, the content in muscle

increases from 110 to 160μg/gm dry weight at 20 to 40 weeks' gestational age, respectively. In neonate, the liver contains 25% of the total body Zn and the skeleton contains about 40% compared with 10% and 25%, respectively, in these tissues in the adult *(Aggett, 1994).*

Zinc is absorbed throughout the small intestine and possibly in the large bowel, although it is most efficient in the proximal gut. Zn absorption is increased by most proteins, aminoacids and possibly lactose, and it is reduced by complexing with phytate, phosphate, calcium and magnesium *(Cousins, 1985).*

Absorption rates for Zn are better with human milk than with cow's milk formulas. Iron and copper may interfere with Zn absorption. Zn absorption is regulated in the intestinal cell by metallothionein, which binds absorbed Zn which is transported in the blood bound to albumin (60-70%) and alpha 2 macroglobulin (30-40%), with a small amount associated with transferrine and free amino acids. Normal serum Zn concentrations are between 76-222μg/dL, then Zn levels often decline postnatally *(D'Harlingue, 1991).*

Zinc and pregnancy:

Zn appears to be conserved in early pregnancy by a decrease in urinary excretion, compared with non pregnant controls *(Hambidge et al., 1983).*

Increase in urinary Zn excretion late in pregnancy are consistent with increased losses of Ca, water soluble

vitamins, and other substances through increased glomerular filtration rate. Increased absorption and possible release of bone and muscle Zn may meet the fetal Zn needs during the last trimester *(King and Weininger, 1989).*

Risk groups for developing Zn deficiency include abnormal renal excretion, as in diabetes with insufficient metabolic control. These data are compatible with the presence of a Zn deficiency syndrome in pregnancy which includes increased maternal morbidity, abnormal taste sensations, abnormally short or prolonged gestation, atonic bleeding and increased risk to the fetus such as malformations, growth retardation, prematurity and perinatal death. Zn therapy has reduced the frequencies of these abnormalities in low Zn groups *(Jameson, 1993).*

Trace element like Zn prevents hyperinsulinemia, partly because of their own insulin activity particularly during periods of illness and stress. Zn forms complex with metallothionein in β cells that provides protection against free oxygen radicals, which become active during immune responses triggered by bacteria and viruses, for instance. In addition, Zn is the only non-toxic trace element in the body that regulates concentration dependent immune responses on many levels. Avoiding deficiencies of trace elements will enable the reduction of the incidence of diabetes *(Sprietsma and Schuitemaker, 1994).*

Zinc deficiency:

Zink deficiency has been described in preterm and term infants. Among reported cases, males predominated and most infants presented at around 3 months of age.

The pathogenesis of Zn deficiency in breast-fed infants includes a preceding period of parenteral nutrition, impaired or immature intestinal absorption and homeostasis of Zn, increased requirements imposed by rapid growth and inadequate intake from their mother's milk *(Aggett, 1994).*

These infants develop a syndrome very similar to acrodermatitis enteropathica with growth arrest, irritability, anorexia, alopecia, diarrhea, vesiculopustular lesion of hands and feet, plus the characteristic perioral, facial and perineal dermatitis; plasma Zn levels are usually <35μg/100ml. Infants respond rapidly to oral Zn sulphate providing 1.0-3.5mg Zn per day *(Lucas, 1992).*

The classic picture of Zn deficiency is acrodermatitis enteropathica. It is an autosomal recessive disorder, usually presents at the time of weaning from breast feeding. The skin manifestations dominate the clinical picture. Severe involvement leads to alopecia and loss of nails. Other symptoms include growth failure, pale bulky stool, impaired immune response and malabsorption of carbohydrates and fats. Infant with

acrodermatitis enteropathica should receive Zn sulphate a dose of 1-2mg/kg/day of elemental Zn *(D'Harlingue, 1991).*

Newborn with sepsis, due to increased requirement is also at risk for developing Zn deficiency *(Hubbell, 1991).*

Intractable diaper rash in a full term or preterm breast-fed infant or in a patient with prolonged diarrhea may be due to zinc deficiency. A theraputic trial of Zn (1mg of elemental Zn/kg/day) in a patient with high index of suspicion of Zn deficiency is a reasonable and safe approach *(Khoshoo et al., 1992).*

Zn deficiency in infancy commonly presents with growth failure, retarded bone age, decreased wound healing, hepatosplenomegaly, decreased growth hormone and failure or weak adrenocortical responses. In older individuals it results in sexual infantilism *(Avery and Fletcher, 1987).*

Requirements:

The Zn requirement for full term infant is based on the Zn content of human milk *(Khoshoo et al., 1992).*

In human breast milk the Zn content (μmol/L) falls from 176±72 in colostrum to 71.9±18.3, 44.3±10.7 and 7.6±4.6 at 6 days, 1 month and 7 months respectively *(Casey et al., 1989).*

Parenteral Zn requirement are much lower than oral requirements due to lower fecal losses in infants who are not being fed enterally. Term newborn may require only 150-175μg/kg/day Zn in the first month of life. The parenteral Zn requirements for older infants are between 30 and 100μg/kg/day unless there are gastrointestinal fluid losses. Moreover, parenteral Zn requirements are much higher in premature infants than in the term newborn. It was found that a parenteral Zn intake of more than 438μg/kg/day is necessary to achieve Zn retention rates comparable to those in-utero in premature infants *(Green et al., 1988).*

Copper (Cu)

Importance and metabolism:

Copper is incorporated into a number of metallo-enzymes. Cytosolic superoxidase dismutase scavenges superoxide ions, thus protecting against oxygen toxicity. Ceruloplasmin, which binds much of the Cu in blood, has ferroxidase activity. It oxidizes ferrous iron released from tissues to ferric iron, which is then transported to bone marrow and other sites. Other Cu containing enzymes participate in collagen, dopamine, and melanin synthesis. The intrauterine accretion rate of Cu in the third trimester is calculated to be 51μg/kg/day *(D'Harlingue, 1991).*

Most of this Cu is stored in the fetal liver, of which concentration increases up to 200μg/gm of dry weight, which is 10 to 20-fold greater than adult levels. The fetal liver stores the Cu bound to metallothionein, which probably protects the fetal liver from Cu toxicity these high fetal hepatic stores of Cu then act as a reservoir for postnatal needs *(D'Harlingue, 1991).*

Cu absorption in the small intestine is reduced by excessive intakes of ascorbic acid, iron, and Zn. Cu is transported in the blood bound to ceruloplasmin, albumin, low molecular proteins, and amino acids. It's excreted primarily in the biliary tract, which explaines the accumulation of Cu in cholestatic disorders.

Urinary excretion of Cu is low (2 to 6μg/kg/day) in both enterally and parenterally fed infants *(Zlotkin and Buchaman, 1983).*

Serum Cu levels are much lower in term (32±21μg/dL) and premature infants (26±17μg/dL) at birth as compared with those of adults (101±20μg/dL). There is a postnatal maturational change in Cu level, which appears to be somewhat independent of Cu intake. Cu level slowly rises to adult values over several months. This phenomenon probably represents developmental maturation of the hepatic synthesis of ceruloplasmin, because the immunoreactive apoceruloplasmin concentration is lower in cord blood than in the adult circulation *(Salmenpera et al., 1986).*

Deficiency:

Because of the large stores of Cu available in liver at birth, Cu deficiency appears in term infants at around 6 months of age, and in preterms at about 3 months. The effectiveness of the hepatic Cu stores depend on its initial size and the rate at which it is redistributed peripherally and repleted with dietary Cu. Cu deficiency is predisposed by preterm delivery, total parenteral nutrition with inadequate Cu supplements, malnutrition and malabsorption syndromes, alkali therapy and the use of inappropriate diets such as unmodified cows' milk or a combination of these factors *(Aggett, 1994).*

Clinical findings include neutropenia (1000/mm^3), Normocytic hypochromic anemia, pallor, hypopigmentation and failure to thrive. In addition to psychomotor retardation, hypotonia and hepatosplenomegaly. Radiological findings may include oesteopenia, fraying, cupping and splaying of the metaphyses of long bones, prominent scalp viens in periosteal depression on X-ray study, along with fractures. Bone marrow shows vacuolated erythroid and myeloid cells with iron deposition in the vacuoles. Plasma Cu usually <30μg/100ml *(Lucas, 1992).*

Menkes' kinky hair disease is a progressive neurodegenerative condition inherited as a sex-linked recessive trait. In the newborn, the disease is characterized by generalized myoclonic seizures, hypothermia and hypotonia. The hair may not appear kinky, although if present, it has the characteristic sandy brown color. A defect in Cu absorption and transport across the gut has been postulated as the cause of the condition *(Haslam, 1992).*

Diagnosis is made by demonstration of decreased serum levels of Cu and ceruloplasmin and the characteristic gross and microscopic apperance of hair *(Kuban and Filiano, 1991).*

Requirements:

Cu deficiency does not appear to occur in breast-fed term infants. Hence, human milk provides a good

first estimate of Cu requirements. In the 1st month of lactation human milk contains 0.4 to 0.7mg/L of Cu, declining to 0.1 to 0.2mg/L in term mature milk *(Casey et al., 1989).*

The Cu needs for tissue growth (retention of 20μg/kg/day) are much lower than in-utero retention rate *(Salmenpera et al., 1986).*

Infant formulas for term and preterms should contain 60 and 90μg of Cu/100kcal respectively *(Espgan, 1987).*

The American Society of clinical Nutrition recommended a parenteral Cu dose of 20μg/kg/day *(Greene et al., 1988).*

Subjects & Methods

SUBJECTS AND METHODS

The present study was conducted on 80 neonates in the neonatal intensive care unit of gynecology and obstetric hospital, Ain Shams University. They were classified into two groups:

Group I:

Comprised 40 full term neonates born to diabetic mothers, their gestational ages ranged from 37-40 (38.17 ± 0.78) weeks, they were 17 males and 23 females.

They were subdivided into two subgroups according to the control of maternal diabetes.

Group Ia: 34 neonates of controlled diabetic mothers.
Group Ib: 6 neonates of non controlled diabetic mothers.

Group II:

Comprised 40 full term neonates of healthy mothers serving as a control group. Their gestational ages ranged from 37-41 (39.37 ± 1.14) weeks. They were 17 males and 23 females.

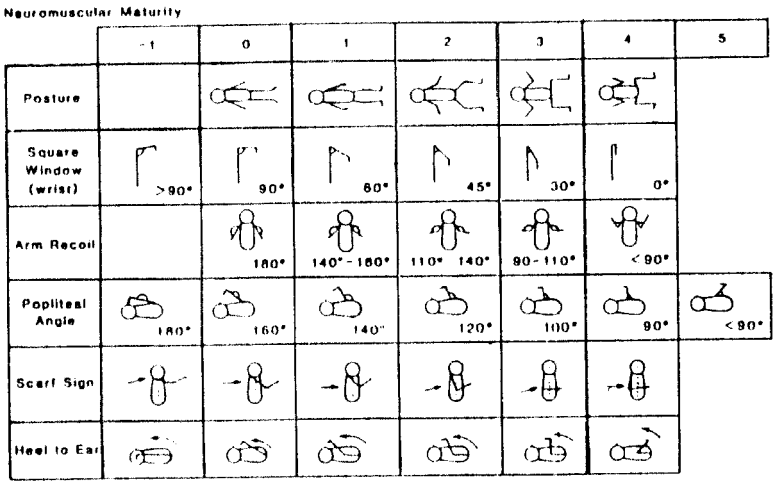
All the infants were subjected to the following:

I. Thorough history taking lying stress on:

- Maternal, perinatal and family histories.
- History of maternal diabetes regarding the type, onset, duration of the disease and treatment received.
- Age of the mother and parity.
- Mode of delivery.

II. Complete clinical examinations:

- Estimation of 1 and 5 minutes Apgar score *(Apgar, 1953).*
- General examination, looking for any congenital anomalies.
- Assessment of gestational age according to Ballard score *(Ballard et al., 1991).*



Physical Maturity

Skin	sticky friable transparent	gelatinous red, translucent	smooth pink visible veins	superficial peeling &/or rash, few veins	cracking pale areas rare veins	parchment deep cracking no vessels	leathery cracked wrinkled
Lanugo	none	sparse	abundant	thinning	bald areas	mostly bald	
Plantar Surface	heel toe 40-50 mm: -1 <40 mm: -2	>50mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole	
Breast	imperceptible	barely perceptible	flat areola no bud	stippled areola 1-2mm 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	sl. curved pinna; soft; slow recoil	well-curved pinna; soft but ready recoil	formed & firm instant recoil	thick cartilage ear 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	prominent clitoris small labia minora	prominent clitoris enlarging minora	majora & minora equally prominent	majora large minora small	majora cover clitoris & minora	

Maturity Rating

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

Fig. (4): Estimation of gestational age according to Ballard score (Ballard et al., 1991).

III. Anthropometric measurements:

1. Weight (Kg):

The birth weight was assessed with Easiweight electronic scale (0 to 10Kg). The newborn was placed on the scale without any clothing.

2. Length (Cm):

A special board was used, caliberated in millimeters.

3. Skull circumference (Cm):

It was measured at the largest occipito-frontal diameter.

IV. Laboratory investigations:

1. Blood glucose level at birth using glucose-oxidase/ peroxidase reaction. Haemo-Glucotest* 20-800R strip react specially to glucose.

Obtaining the blood:

Wash hands/heel with soap and warm water, dry thoroughly. Make sure that the puncture site is dry before optaining the blood to avoid erroneous results.

Prick the lateral side of the heel with a lancet, wipe off the first drop of blood obtained, then gently squeeze the heel so as to obtain a second large suspended drop of blood.

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* Boehringer Mannheim GmbH. Mannheim, Germany.

Applying the blood:

Apply the drop of blood to the center of the twin-zone test area, making sure that both test zone are covered. Don't spread or smear the blood on the test area. After 1 minute wipe then wait for another one minute.

Visual color determination:

By using the color blocks printed on the test-strip vial label. The test area consists of two test zones with different sensitivities to glucose. The lower test zone (nearer the "handle") allows clear differentiation of values in the range 20-120mg/dL (1-7 mmol/L) and the upper test zone values above 120mg/dL (7mmol/L).

2. Determination of serum Ca, Mg, Zn and Cu by atomic absorption spectrophotometry technique and P by autoanalyser method:
   Within 5 minutes of delivery, 8cc of cord blood were collected in clean sterile glass tubes which were prepared as follows:
   1. Washed by distelled water and soap.
   2. Washed by non ionized water.
   3. Dried in hot oven.

The collected samples were centrifuged to optain the serum. The serum was kept in polyetheline tubes and freezed. Serum concentrations of Ca, Mg, P, Zn and Cu levels were determined at Atomic Authority laboratories

Atomic Absorption Spectrophotometry (AAS):

Principle:

Energy excites atoms through transfer of electrons from lowest energy level (ground state) to higher energy orbits in which they are unstable so, they tend to move back to ground state emitting light. Some atoms in the ground state absorbs this emitted light.

On this basis, if light of wave lengths corresponding to the lines of emission spectrum is passed through the flame, they are absorbed by the ground state atoms which are not excited. Fall in absorption is measured corresponding to the concentration. This is the basis of flame photometry. Flameless AAS uses the electrothermal energy instead of flame.

Applications:

It is applied for measurement of Ca and Mg which are poorly excited, but it is better for measurement of trace elements such as zinc, iron, copper, manganese, chromium, cobalt, cadmium and lead. Flameless AAS using minute amounts of serum is useful in ultratrace element determination of levels less than 50ng/g.

Caliberation:

It is a comparative method, response of instrument to test solution is compared to that obtained by several standard solution. Creation of caliberation curves at specific time intervals is mandatory.

Draw backs:

1. This is a one element at a time technique.
2. Sample preparation is necessary.
3. Nebulizers are frequently partially clogged with protein or metal residues.
4. Contamination by dust is easy and dust particles on the burner exhibit coloured glow in the flame.

(Jacobson and Lockitch, 1988).

Estimation Of Calcium:

Reagent for standards preparation:

Aqueous : Calcium carbonate AR.

Non aqueous : Calcium 2-ethylhexanoate.

Preparation of 1000µg / ml standard:

Dissolve 2.497g of dried CaCo3 in 25ml of 1N hydrochloric acid and dilute to 1 litre to give 1000µg/ml Ca.

Atomic absorption:

Lamp current : 10.0 mA.

Flame type : Nitrous oxide-acetylene (oxidizing)

Optimum technique.

Wave length nm.	Slit width nm.	Working range µg/ml	Sensitivity µg/ml
422.7	0.5	1-4	0.02
239.9	0.5	180-760	4.0

Interferences:

Chemical interferences are common for air-acetylene. Addition of a releasing agent (2000-5000μg/ml strontium or lanthonum) help to remove the interference, as does a lean flame. In nitrous oxide-acetylene an ionization buffer (2000μg/ml potassium) is needed.

Flame emission:

Wavelenght : 422.7 nm.
Slit width : 0.2 nm.
Flame type : Nitrous oxide-acetylene (reducing).

(Khayam et al., 1977).

Estimation Of Magnesium

Reagent for standards preparation:

Aqueous: Magnesium metal ribbon, or tumings (99.99%).

Preparation of 1000μg / ml standard:

Dissolve 1.0000g of Mg metal in 50ml of 5N hydrochloric acid and dilute to 1 litre for 1000 μg/ml Mg.

Atomic absorption:

Lamp current: 3.0 mA.
Flame type : Air-Acetylene (oxidizing).

Optimum technique.

Wave length nm.	Slit width nm.	Working range μg/ml	Sensitivity μg/ml
285.2	0.5	0.1-0.4	0.003
202.6	1.0	5-20	0.1

Interferences:

Chemical interferences are common for the air-acetylene flame. Addition of a releasing agent (2000-5000μg/ml strontium or lanthanum) helps to remove the interference. In the nitrous oxide-acetylene flame an ionization buffer (2000μg/ml K) is needed.

Flame emission:

Wavelenght : 285.2 nm.

Slit width : 0.2 nm.

Flame type : Nitrous oxide-acetylene (oxidizing).

(Khayam et al., 1977).

Estimation Of Zinc:

Reagents for standard preparation:

Non aqueous: Zinc 4-cyclohexylbutyrate.

Preparation of 1000μg/ml standard:

Dissolve 1 gram of Zn metal in 40ml of 5N hydrochloric acid and dilute to 1 litre to obtain 1000μg/ml Zn.

Atomic absorption:

Lamp current : 5mA.

Flame type : Air acetylene (oxidizing).

Optimum technique.

Wave length nm.	Slit width nm.	Working range μg/ml	Sensitivity μg/ml
213.9	0.5	0.4-1.5	0.008
307.6	0.5	3000-12000	66

Interferences:

Non-atomic absorption should be corrected at 213.9 by use of a continuum lamp.

(Makino and Takahara, 1981).

Estimation Of Copper:

Copper was estimated using the flame atomic absorption, on 902 double beam.

Reagents for standard preparation:

Non-aqueous: Copper 4-cyclohexylbutyrate.

Preparation of 1000μg / ml standard:

Dissolve 1 g of Cu in 50ml of 6 N nitric acid and dilute to 1 litre to give 1000μg/ml Cu.

Atomic absorption:

Lamp current: 3 mA.

Flame type : Air-acetylene (oxidizing).

Optimum technique.

Wave length nm.	Slit width nm.	Working range μg/ml	Sensitivity μg/ml
324.7	0.5	1-5	0.025
327.4	0.5	2.5-10	0.050
217.9	0.2	7.5-30	0.16
222.6	1.0	45-180	1.0
249.2	0.5	180-730	4.0
244.2	1.0	400-1700	9.0

Interferences:

Few interferences have been reported for copper *(Johnson and Milne, 1991).*

Estimation Of Phosphorus:

Inorganic P was measured on Express-550 Autoanalyzer.

Principle:

The modification method of Dalay and Ertingshausen is used, the equation is:

P_i + H_2SO_4 + Ammonium molybdate → unreduced phosphomolybdate complex which absorbs light maximally at 340nm.

(Grabber and Miller, 1983).

Statistical Analysis:

The clinical and laboratory data were recorded on an "investigative report form". These data were transferred to IBM cards using IBM personal computer with statistical program "Microstate Version 2.0" to obtain:

Descriptive statistics:

1. Mean ($\overline{X}$)
2. Standard deviation (S.D).
3. Minimum and maximum values (range).

Analytical statistics:

1. Student's "t" test to compare between two independent means.
   P value = level of significant
   P >0.05 → insignificant
   P ≤0.05 → significant
   P ≤0.001 → highly significant
2. Correlation matrix and coefficient of correlation (r) for relationship of different variables by Pearson's method. Variables were correlated in all possible combinations against each other.

   The interpretation of "r":

   - <0.20 very poor; almost negligible relationship.
   - 0.2-0.4 poor correlation; definite but small relationship.
   - 0.4-0.7 fair correlation; substantial relationship.
   - 0.7-0.9 strong correlation; marked relationship.
   - >0.9 very strong correlation; very dependable relationship.

(Williams, 1986).

Research design

Study of some minerals in cord blood of infants of diabetic and non diabetic mothers

The objectives of the study was to estimate the serum levels of total Ca, Mg, P, Cu and Zn in cord blood of IDMs compared to that of normal neonates and to find out possible relationships between gestational age and growth variables (birth weight, length and head circumference)and the concentrations of these minerals.

Sample

Main study;case contol study
40 cases,40 control
Time table :
The practical part of main study started in April 1995 and closed in October 1995.

Methodology

*Questionnaire;
history of illness
*Clinical examination
*Anthropometric assessment.
*Biochemical study
Ca, Mg ,P, Cu,Zn

Criteria for inclusion:

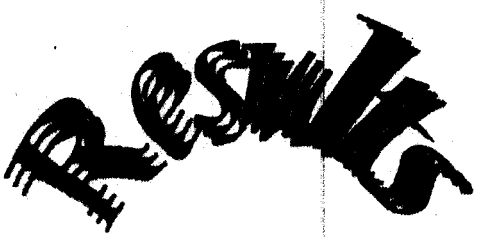
Full term IDMs 37:40 weeks
Full term normal neonates
37:41 weeks
Both sexes

Criteria for exclusion:

Preterms

Conclusion:

It is concluded that diabetes mellitus in women causes significant variations in their infants' growth.
Cord serum copper level being the most significant variable affecting growth in healthy infants however this relationship was noticed to be disturbed in IDMs.


Results

RESULTS

The results of the present study are presented in tables (7-11) and in figures (5-30).

This study was conducted on 80 full term neonates. They were classified into 2 groups:

Group I: Included 40 full term infants of diabetic mothers. 30 neonates were delivered by CS, while 10 neonates were delivered vaginally.

They were subdivided into two groups:

Group Ia: Included 34 full term infants of controlled diabetic mothers.

The duration of treatment was ranging from 2-3 years except one mother with IDDM, she was under insulin treatment for 10 years (No. 32).

Group Ib: Included 6 full term infants of non controlled diabetic mothers.

Group II: Included 40 full term neonates born to healthy mothers as a control group, only three infants were delivered by CS.

No apparent congenital anomalies in all the neonates.

Table (7): Comparison between IDMs and normal neonates as regards the clinical data and blood glucose levels.

Variables / Groups	Gest. age (Weeks)	Weight (Kgms)	Length (Cm)	Skull circ. (Cm)	Apgar 1st min	Apgar 5th min	Parity	Mat. age (Years)	Blood glucose mg/dL
IDMs: (Group I)									
Number	40								
Range	37-40	3.0-5.200	47-52	33-38	3-9	8-10	0-7	20-42	20-120
Mean	38.17	3.96	50.62	35.13	6.82	9.35	3.12	32.35	56.50
± SD	0.78	0.50	1.39	1.28	1.73	0.86	1.87	6.14	23.04
Normal neonates: (Group II)									
Number	40								
Range	37-41	2.5-5.750	48-52	33-36	7-9	8-10	0-5.0	19-37	40-80
Mean	39.37	3.51	49.77	34.75	8.25	9.80	2.15	27.10	61.0
± SD	1.14	0.60	1.14	1.03	0.58	0.46	1.54	6.03	14.28
t-test value	5.46	3.65	2.98	1.48	4.91	2.9	2.54	3-85	1.04
P value	**<0.001	**<0.001	*<0.05	>0.05	**<0.001	*<0.05	*<0.05	**<0.001	>0.05

P value >0.05 is non significant * P value <0.05 is significant ** P value <0.001 is highly significant

Table (7) clarified the following:

- There were highly significant differences as regards the mean of gestational age and Apgar score at 1min. ($P<0.001$) but a higher significant difference as regards Apgar score at 5 min ($P<0.05$) in normal neonates than in IDMs.
- The differences were highly significant in mean weight and length of IDMs than those of normal neonates ($P <0.001$ and $P <0.05$ respectively) but there was no significant difference in mean skull circumference between both groups although it was increased in IDMs than the normal one.
- As regards the parity it was significantly higher in diabetic mothers than that of normal neonates ($P<0.05$). Meanwhile there was a highly significant difference in mean age of diabetic mothers than that of normal neonates ($P<0.001$).
- Although the difference in mean blood glucose levels between both groups was not significant ($P>0.05$) yet it was lower in IDMs than the control group.

Table (8): Comparison between IDMs and normal neonates as regards serum trace elements levels.

Variables / Groups	(Ca) mEq/L	(Mg) mEq/L	(P) mg/dL	(Zn) µg/dL	(Cu) µg/dL
Group I					
Number	40				
Range	1.38-3.88	0.14-2.27	5.27-6.60	50.5-97.0	18-130
Mean	2.46	1.43	6.00	69.43	70.15
± SD	0.59	0.50	0.23	13.20	28.03
Group II					
Number	40				
Range	2.4-4.9	1.2-2.94	5.55-6.71	27-112.5	45-125
Mean	3.78	2.09	6.29	70.04	84.07
± SD	0.57	0.48	0.25	17.89	22.34
t-test	10.07	6.01	5.26	0.27	2.45
P-value	**<0.001	**<0.001	**<0.001	>0.05	*<0.05

P value >0.05 non significant ** Highly significant. * Significant.

Table (8):

- The differences between both groups were highly significant as regards the mean serum levels of Ca, Mg, P ($P<0.001$) but only significant as regards serum Cu levels ($P<0.05$) being lower levels in IDMs than in normal neonates.
- The mean serum Zn levels showed no significant statistical difference between both groups ($P>0.05$).

Table (9): Comparison between IDMs (controlled and non controlled groups) and normal neonates as regards the clinical data and blood glucose levels.

Variables / Groups	Gest. age (Weeks)	Weight (Kgms)	Length (Cm)	Skull circ. (Cm)	APGAR 1st min	APGAR 5th min	Parity	Mat. age (Years)	Bl. glu. mg/dL
Group Ia:									
Number	34								
Range	37-40	3.00-5.20	47-52	33-38	3-9	8-10	0-6	20-42	20-120
Mean	38.08	3.88	50.55	34.89	6.97	9.41	2.94	31.67	58.23
± SD	0.75	0.49	1.46	1.15	1.58	0.85	1.85	6.14	23.80
Group Ib:									
Number	6								
Range	38-40	3.80-4.60	50-52	35-38	3-9	8-10	2-7	27-42	20-60
Mean	38.66	4.41	51.0	36.50	6.00	9.00	4.16	36.16	46.66
± SD	0.81	0.31	0.89	1.22	2.44	0.89	1.72	4.99	16.32
Group II:									
Number	40								
Range	37-41	2.5-5.75	48-52	33-36	7-9	8-10	0-5.0	19-37	40-80
Mean	39.37	3.51	49.77	34.75	8.25	9.80	2.15	27.10	61.0
± SD	1.14	0.60	1.14	1.03	0.58	0.46	1.54	6.03	14.28
Group Ia Vs. Ib									
t-value	1.71	2.53	0.71	3.11	1.27	1.07	1.5	1.68	1.13
P-value	>0.05	*<0.05	>0.05	*<0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Ib Vs. II									
t-value	1.45	3.58	2.50	3.78	5.16	3.44	2.94	3.49	2.25
P-value	>0.05	**<0.001	*<0.05	**<0.001	**<0.001	**<0.001	*<0.05	**<0.001	*<0.05
Ia Vs. II t-value	5.59	2.89	2.58	0.57	4.73	2.47	2.00	3.22	0.61
P-value	**<0.001	*<0.05	*<0.05	>0.05	**<0.001	*<0.05	*<0.05	**<0.001	>0.05

Table (9) showed that:

- The differences between the controlled and non controlled groups of IDMs were significant with respect to the mean weight and skull circumference ($P<0.05$) being heigher in non controlled group.
- As regards the mean of gestational age, length, Apgar score at 1 and 5 min., parity, maternal age and blood glucose levels of IDMs, there were no significant differences between the controlled and non controlled groups as the $P>0.05$ for all.

- There were highly significant differences between the non controlled group and normal neonates as regards the mean of weight, skull circumference, Apgar score at 1 and 5 min. and maternal age where $P<0.001$ respectively. The non controlled group of IDMs tended to be macrosomic with increased skull circumference, lower Apgar score at 1 and 5 min. and had older mothers than the normal neonates.
- The mean lenght and parity were significantly higher in non controlled group of IDMs than the normal ones ($P<0.05$).
- The mean blood glucose level was significantly lower in the non controlled group than the normal ones ($P<0.05$).

- On comparing the controlled group of IDMs to normal neonates the following were observed:
  - * There were highly significant differences as regards the mean of gestational age and maternal age between both groups ($P<0.001$ respectively). The gestational age was higher in normal neonates while the maternal age was increased in the controlled diabetic mothers.
  - * The parity was increased in the mothers of the controlled group than that of normal neonates. The difference was significant ($P<0.05$).
  - * The mean Apgar score at 1 and 5 min. showed a significant statistical difference between group Ia and group II being lower in group Ia ($P<0.001$ at 1 min., $P<0.05$ at 5 min.).
  - * There were significantly higher differences in mean weight and length of group Ia than those of group II (both $P<0.05$).
  - * No significant differences were found between both groups as regards the mean skull circumference as well as the mean blood glucose levels where $P>0.05$ repsectively.

Table (10): Comparison between IDMs (controlled and non controlled groups) and normal neonates as regards serum trace elements levels.

Variables / Groups	(Ca) mEq/L	(Mg) mEq/L	(P) mg/dL	(Zn) µg/dL	(Cu) µg/dL
Group Ia:					
Number	34				
Range	1.38-3.31	0.54-2.27	5.27-6.60	50.5-97.0	18-130
Mean	2.45	1.41	6.00	69.57	69.73
± SD	0.56	0.45	0.24	13.75	29.04
Group Ib:					
Number	6				
Range	1.63-3.88	0.14-2.07	5.74-6.21	50.5-80.0	44-98
Mean	2.47	1.49	6.01	68.66	72.5
± SD	0.83	0.76	0.17	10.49	23.52
Group II:					
Number	40				
Range	2.4	1.2-2.94	5.55-6.71	27-112.5	45-125
Mean	3.78	2.09	6.29	70.04	84.07
± SD	0.57	0.48	0.25	17.89	22.34
Group Ia Vs. Ib					
t-test	0.06	0.33	0.07	0.21	0.22
P-value	>0.05	>0.05	>0.05	>0.05	>0.05
Ib Vs. II					
t-test	4.88	2.6	2.56	0.04	1.17
P-value	**<0.001	*<0.05	*<0.05	>0.05	>0.05
Ia Vs. II					
t-test	9.96	6.13	4.94	0.23	2.39
P-value	**<0.001	**<0.001	**<0.001	>0.05	*<0.05

Table (10) showed the following:

- On comparing the non controlled to the controlled subgroups of IDMs, there were no significant differences between both groups as regards the mean serum levels of Ca, Mg, P, Zn and Cu where $P>0.05$ respectively.

- A comparison between the non controlled group of IDMs to normal neonates showed that:

  * The non controlled IDMs were hypocalcemic, hypomagnesemic and hypophosphatemic ($P<0.001$ $P<0.05$ and $P<0.05$ respectively).

  * There were no significant differences between both groups as regards serum Zn and Cu levels ($P>0.05$ respectively).

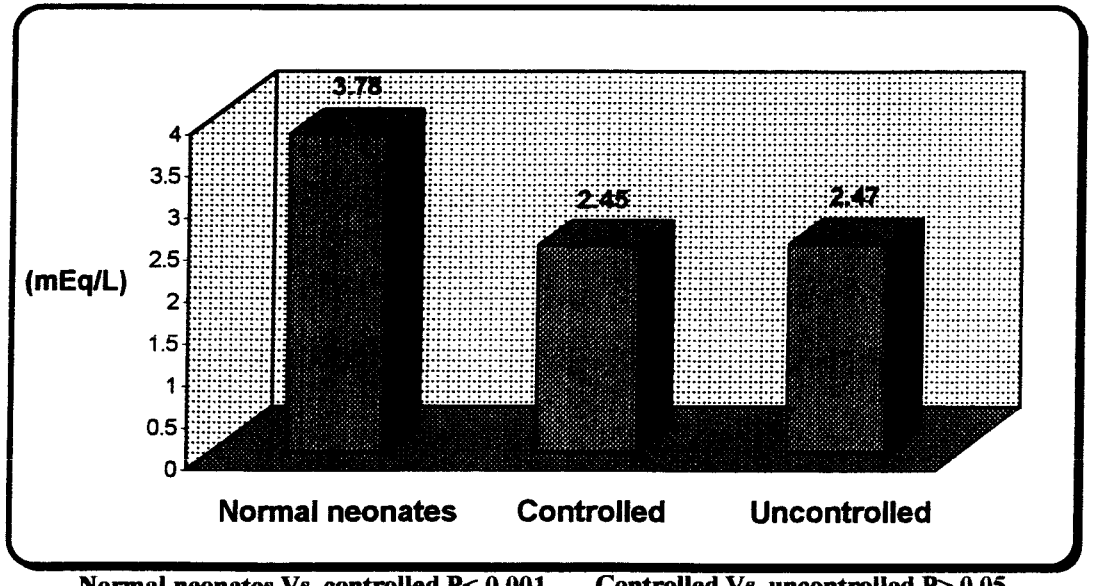
- On comparing the controlled group of IDMs (Ia) to the normal neonates (II) it was found that:

  * The mean serum levels of Ca, Mg and P were lower in group Ia compared to group II. The differences were highly significant ($P<0.001$).

  * There was a statistical significant difference between both groups regarding the mean serum level of Cu being lower one in group Ia ($P<0.05$).

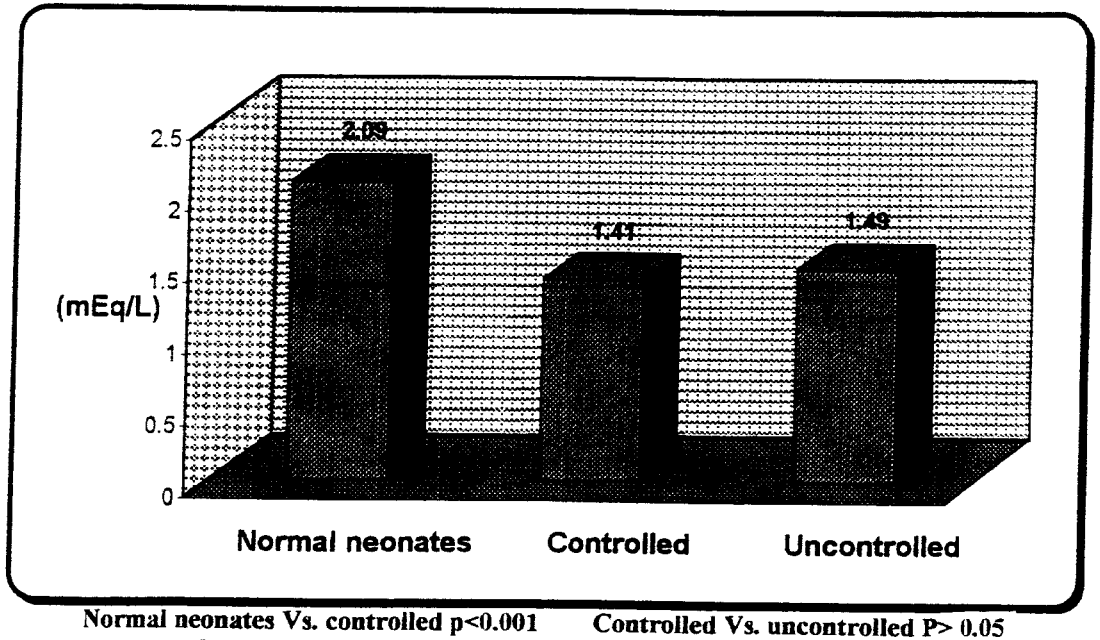
  * There was no significant difference between both groups regarding the mean serum Zn level ($P>0.05$).

Fig.(5):Shows a comparison between subgroups of IDMs and normal neonates as regards the mean serum calcium levels



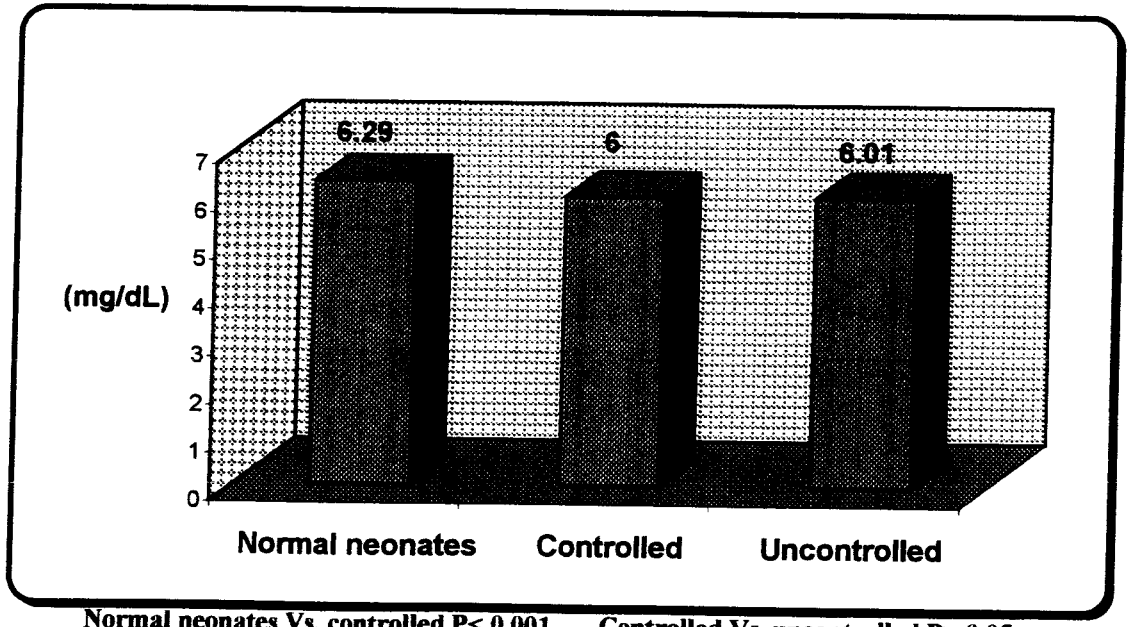
Normal neonates Vs. controlled P< 0.001 Controlled Vs. uncontrolled P> 0.05
Normal neonates Vs. uncontrolled P < 0.001

Fig.(6): Shows a comparison between subgroups of IDMs and normal neonates as regards the mean serum magnesium levels



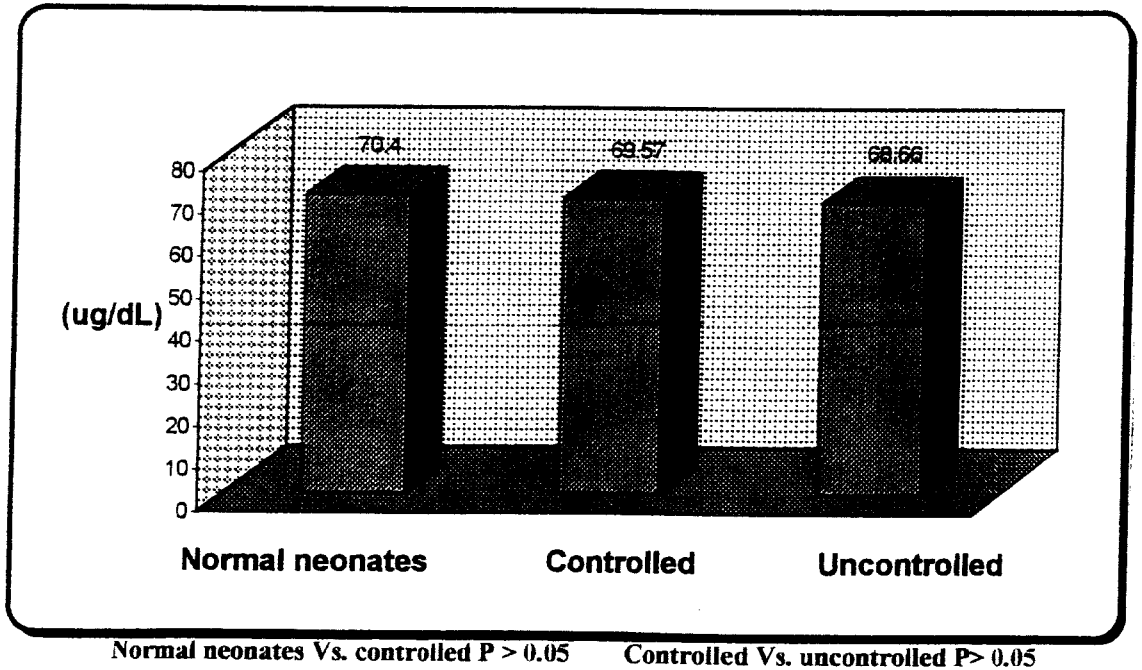
Normal neonates Vs. controlled p<0.001 Controlled Vs. uncontrolled P> 0.05
Normal neonates Vs. uncontrolled P< 0.05

Fig.(7) :Shows a comparison between subgroups of IDMs and normal neonates as regards the mean serum phosphorus levels



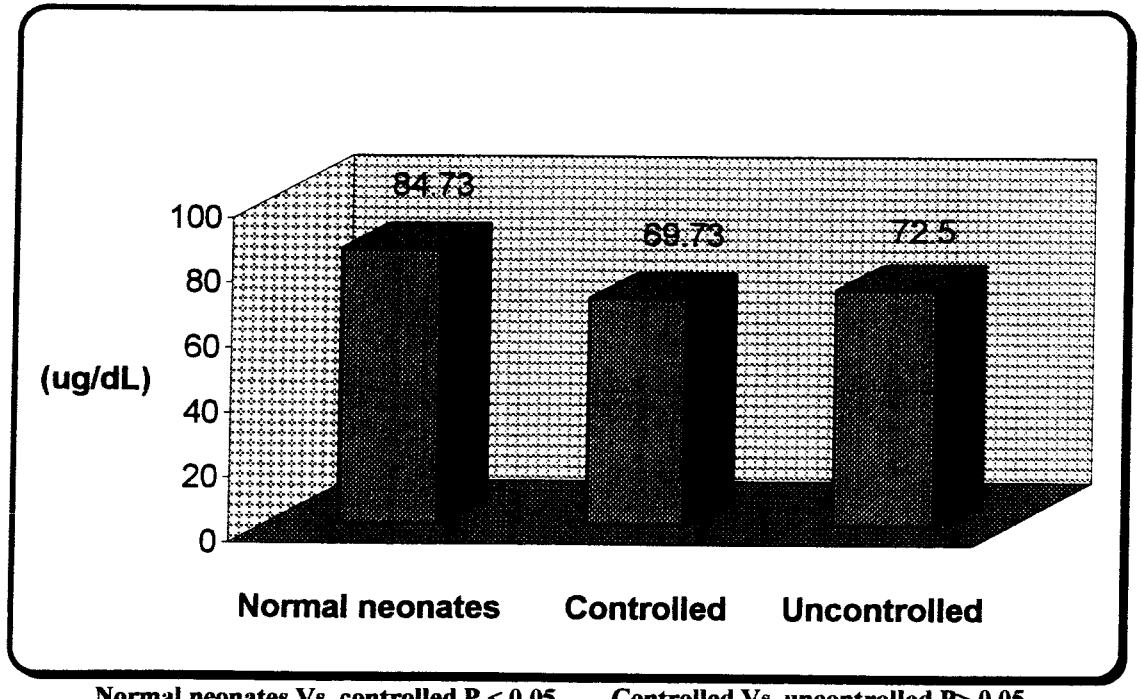
Normal neonates Vs. controlled P< 0.001 Controlled Vs. uncontrolled P> 0.05
Normal neonates Vs. uncontrolled P< 0.05

Fig.(8) :Shows a comparison between subgroups of IDMs and normal neonates as regards the mean serum zinc levels



Normal neonates Vs. controlled P > 0.05 Controlled Vs. uncontrolled P> 0.05
Normal neonates Vs. uncontrolled P> 0.05

Fig.(9): Shows a comparison between subgroups of IDMs and normal neonates as regards the mean serum copper level



Normal neonates Vs. controlled P < 0.05 Controlled Vs. uncontrolled P> 0.05
Normal neonates Vs. uncontrolled P> 0.05

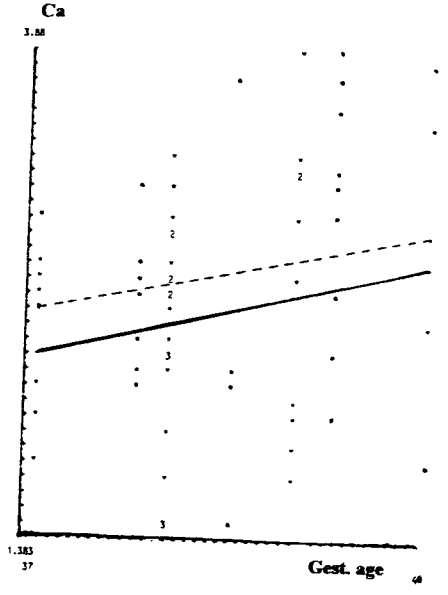


Fig. (10): Correlation between gestational age and calcium level in both IDMs and normal neonates.

IDMs
INTERCEPT= -3.889309148265 SLOPE= .16632702418507
r = 0.2170
Normal neonates
INTERCEPT= -.6024817518249 SLOPE= .1114598540146
r = .2210 r squared = .0489

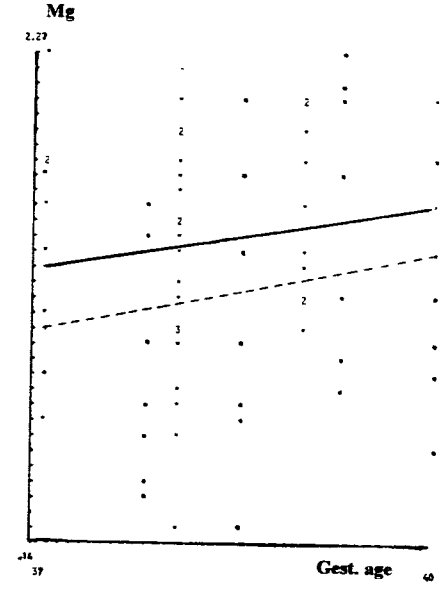


Fig.(11):Correlation between gestational age and magnesium level in both IDMs and normal neonates.

IDMs
INTERCEPT= -2.2859936908517 SLOPE= 9.73606729758l5E-02
r = 0.1519
Normal neonates
INTERCEPT= -.9924919708029 SLOPE= .07830900243309
r = .1865 r squared = .0348

* & (____) = IDMs
● & (-----) = Normal neonates

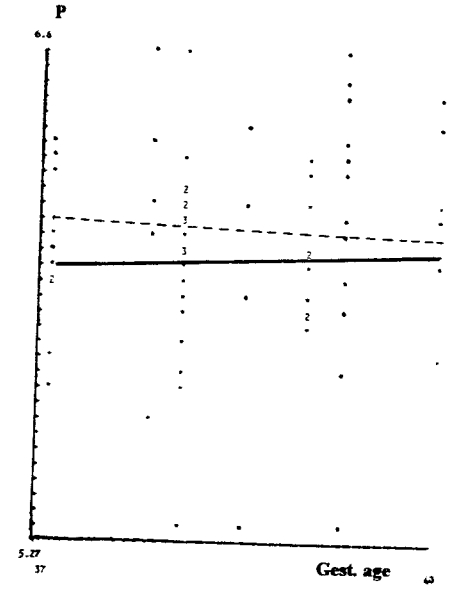


Fig.(12):correlation between gestational age and phosphorus level in both IDMs and normal neonates.

IDMs
INTERCEPT= 5.308832807571 SLOPE= 1.8275499474238E-02
r = 0.0616
Normal neonates
INTERCEPT= 6.6620671532847 SLOPE= -9.294403892944E-03
r = -.0410 r squared = .0017

The following statistical correlations were detected in this study.

Fig. (10):

A poor positive correlation between serum Ca level and gestational age in both IDMs and normal neonates. ($r = 0.21$ and $r = 0.22$ respectively).

Fig. (11):

A very poor positive correlation between serum Mg level and gestational age in both IDMs and normal neonates ($r = 0.15$ and $r = 0.18$ respectively).

Fig. (12):

A very poor positive correlation between serum P level and gestational age in IDMs and a very poor negative correlation in normal neonates ($r = 0.06$ and $r = -0.04$ respectively).

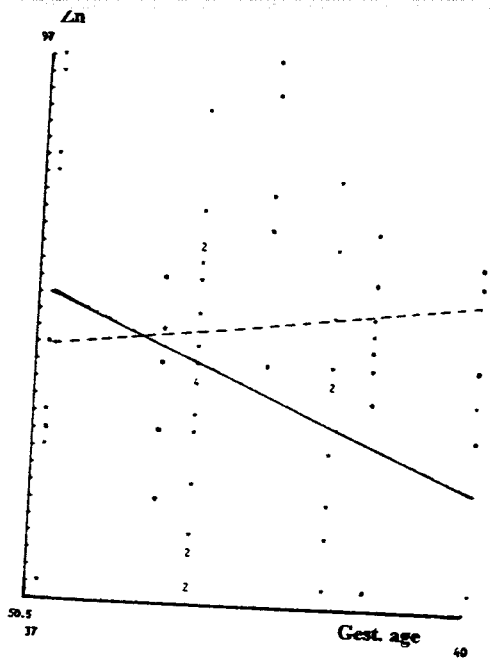


Fig.(13):Correlation between gestational age and zinc level in both IDMs and normal neonates.

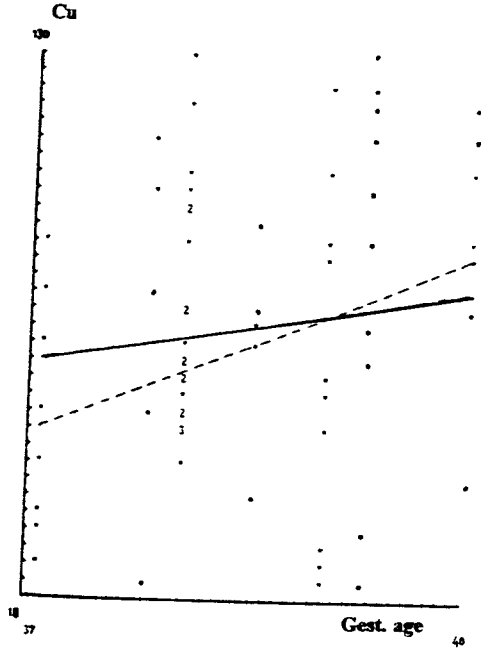


Fig.(14):Correlation between gestational age and copper level in both IDMs and normal neonates.

IDMs
INTERCEPT= 269.44479495268 SLOPE= -5.239221871714
r = -0.3098

Normal neonates
INTERCEPT= -23.486861313869 SLOPE= 2.3844282238443
r = .1529 r squared = .0234

* & (_____) = IDMs
• & (-----) = Normal neonates

IDMs
INTERCEPT= -149.7476340694 SLOPE= 5.7602523659306
r = 0.1604

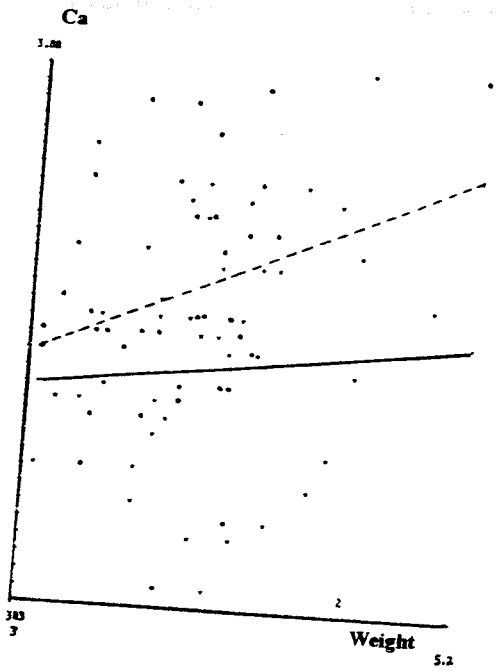
Normal neonates
INTERCEPT= -178.71240875913 SLOPE= 6.6739659367397
r = .3428 r squared = .1175

Fig. (13):

A poor negative correlation between serum Zn level and gestational age in IDMs (r = - 0.309) and a very poor positive correlation in normal neonates (r = 0.152).

Fig. (14):

A very poor positive correlation between serum Cu level and gestational age in IDMs (r = 0.160) and a significant positive correlation in normal neonates (r = 0.342).



g.(15):Correlation between birth weight and
lcium level in both IDMs and normal neonates.

IDMs
EPT= 1.9389432853763 SLOPE= .13145007776168
r = 0.1107

Normal neonates
CEPT= 2.8433489855586 SLOPE= .26844156994773
r = .2790 r squared = .0778

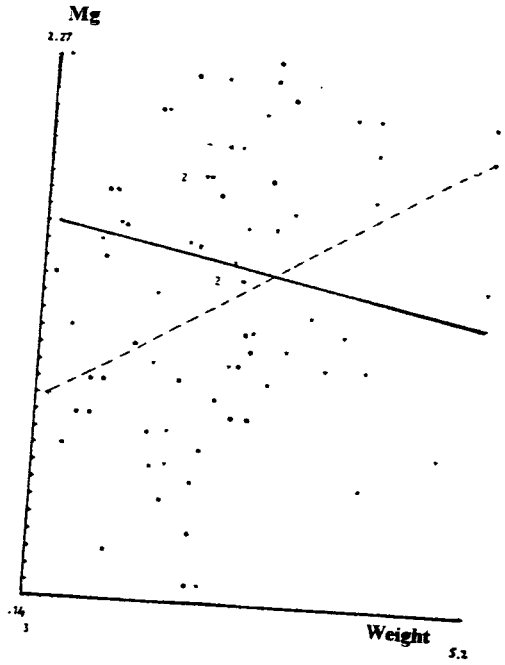


Fig.(16):Correlation between birth weight and magnesium level in both IDMs and normal neonates.

IDMs
INTERCEPT= 2.0227548230697 SLOPE= -.14928411614051
r = -0.1504

Normal neonates
INTERCEPT= 1.2165219367414 SLOPE= .24894037388146
r = .3107 r squared = .0965

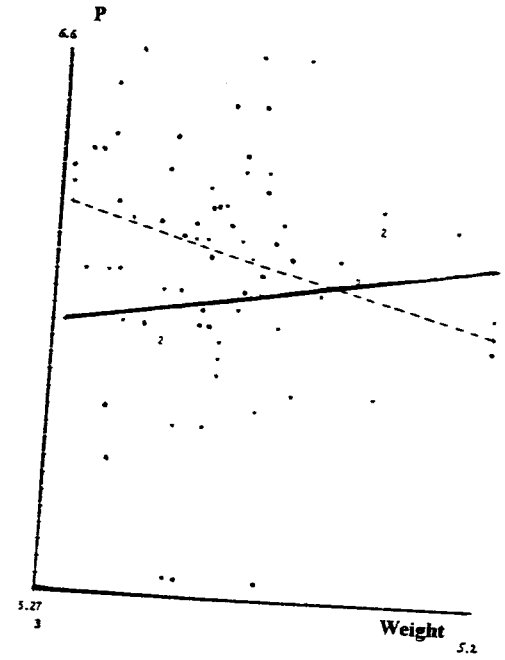


Fig.(17):Correlation between birth weight and phosphorus level in both IDMs and normal neonates.

IDMs
INTERCEPT= 5.7088646908985 SLOPE= 7.5053821050018E-02
r = .1634

Normal neonates
INTERCEPT= 6.5973279170727 SLOPE= -.08575883760078
r = -.1985 r squared = .0394

Fig. (15):

A very poor positive correlation between serum Ca level and birth weight in IDMs ($r = 0.110$) and a poor positive correlation in normal neonates ($r = 0.279$).

Fig. (16):

A very poor negative correlation between serum Mg level and birth weight in IDMs ($r = 0.150$) and a poor positive correlation in normal neonates ($r = 0.310$).

Fig. (17):

A very poor positive correlation between serum P level and birth weight in IDMs ($r = 0.163$) and a very poor negative correlation in normal neonates ($r = -0.198$).

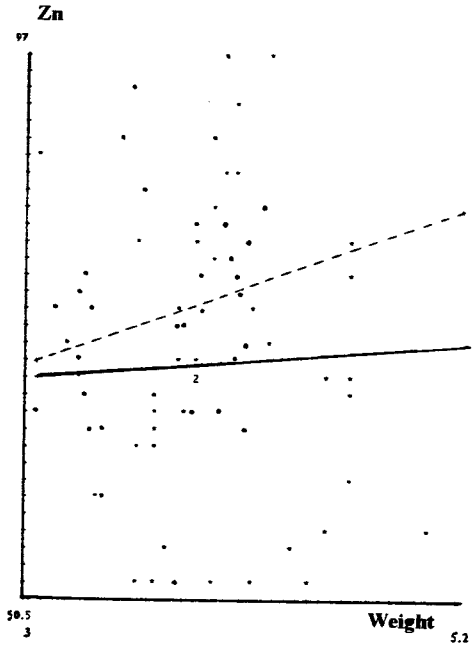


Fig.(18):Correlation between birth weight and zinc level in both IDMs and normal neonates.

IDMs

INTERCEPT= 62.630006351563 SLOPE= 1.7166256639086

r = 0.0655

Normal neonates

INTERCEPT= 42.57883405688 SLOPE= 7.9206166386108

r = .2662 r squared = .0709

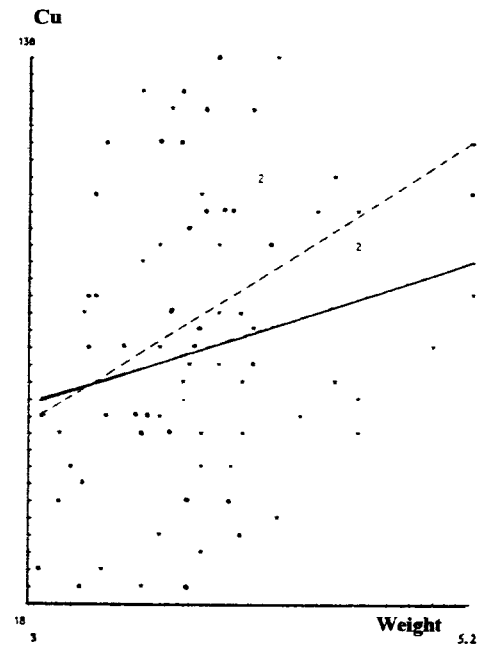


Fig.(19):Correlation between birth weight and copper level in both IDMs and normal neonates.

IDMs

INTERCEPT= 17.568446082242 SLOPE= 13.259335897307

r = 0.2384

Normal neonates

INTERCEPT= 38.188748117302 SLOPE= 13.063701603615

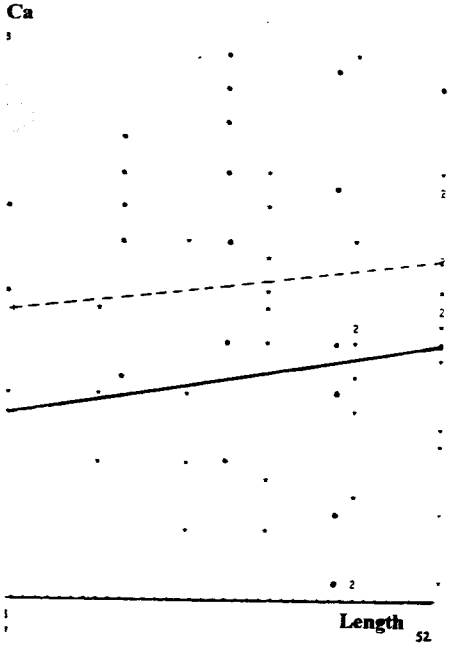
r = .3517 r squared = .1237

Fig. (18):

A very poor positive correlation between serum Zn level and birth weight in IDMs (r = 0.065) and a poor positive correlation in normal neonates (r = 0.266).

Fig. (19):

A poor positive correlation between serum Cu level and birth weight in IDMs (r = 0.238) and a significant positive correlation in normal neonates (r = 0.351).



g.(20):Correlation between length and calcium evel in both IDMs and normal neonates.

IDMs

PT= -.8424895522388 SLOPE= 6.5238805970149E-02
r = 0.1515

Normal neonates

T= .8410053948014 SLOPE= 5.9171162334478E-02
= .1169 r squared = .0137

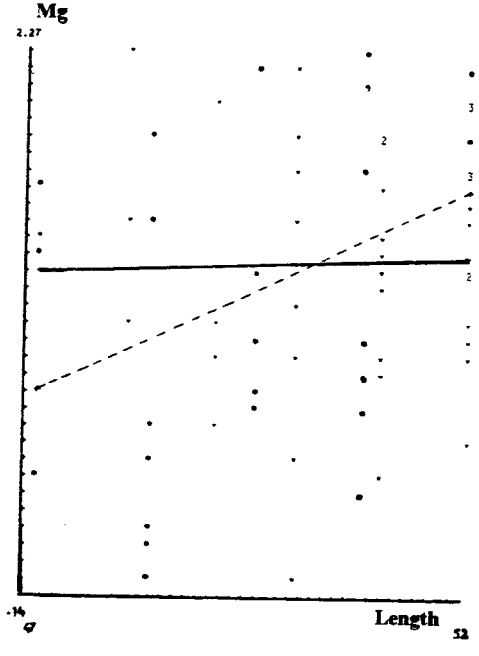


Fig.(21):Correlation between length and magnesium level in both IDMs and normal neonates.

IDMs

INTERCEPT= .4090149253732 SLOPE= 2.0182421227197E-02
r = 0.0561

Normal neonates

INTERCEPT= -6.3489279058363 SLOPE= .16956007846984
r = .4022 r squared = .1618

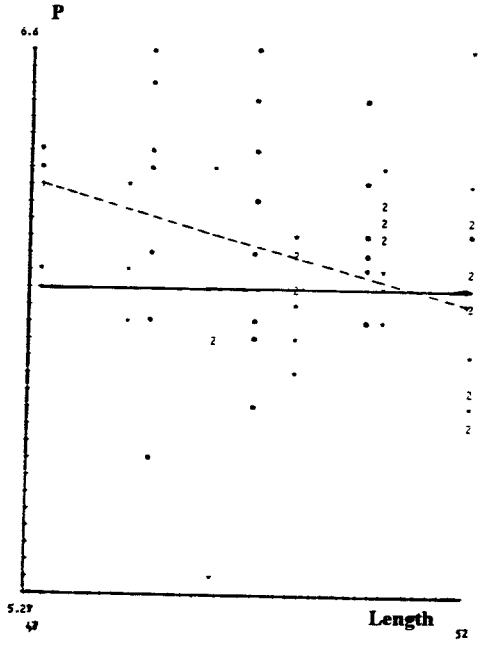


Fig.(22):Correlation between length and phosphorus level in both IDMs and normal neonates.

IDMs

INTERCEPT= 5.7731044776119 SLOPE= 4.6102819237148E-03
r = 0.0277

Normal neonates

INTERCEPT= 9.904213830309 SLOPE= -7.2488474742521E-02
r = -.3188 r squared = .1017

Fig. (20):

A very poor positive correlation between serum Ca level and length in both IDMs and normal neonates ($r = 0.151$ and $r = 0.116$ respectively).

Fig. (21):

A very poor positive correlation between serum Mg level and length in IDMs ($r = 0.056$) and a significant positive correlation in normal neonates ($r = 0.402$).

Fig. (22):

A very poor positive correlation between serum P level and length in IDMs ($r = 0.027$) and a significant negative correlation in normal neonates ($r = - 0.318$).

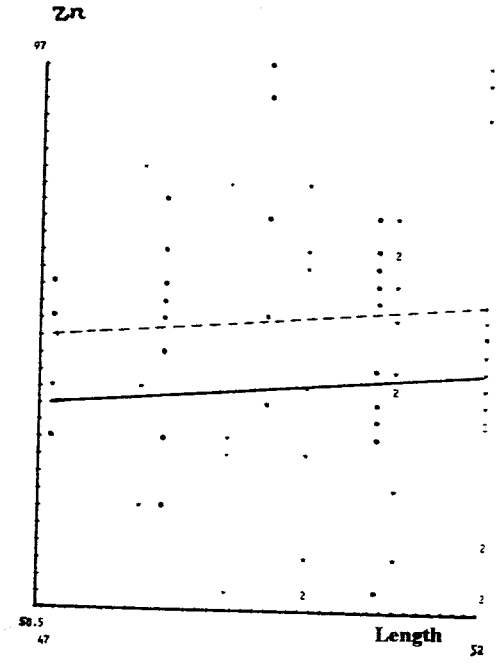


Fig.(23):Correlation between length and zinc level in both IDMs and normal neonates.

IDMs

INTERCEPT= 42.194029850746 SLOPE= .53814262023217

r = 0.0567

Normal neonates

INTERCEPT= 9.761893084844 SLOPE= 1.2182442373713

r = .0778 r squared = .0061

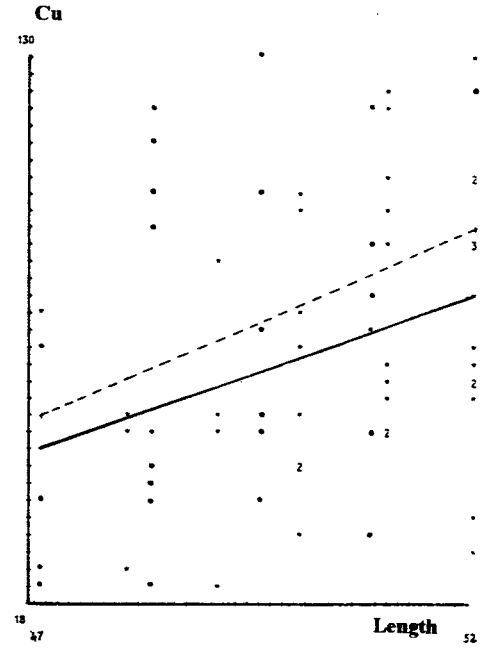


Fig.(24):Correlation between length and copper level in both IDMs and normal neonates.

IDMs

INTERCEPT= -260.46567164179 SLOPE= 6.530679933665

r = 0.3239

Normal neonates

INTERCEPT= -277.87395782246 SLOPE= 7.271701814615

r = .3721 r squared = .1384

Fig. (23):

A very poor positive correlation between serum Zn level and length in both IDMs and normal neonates ($r = 0.056$ and $r = 0.077$ respectively).

Fig. (24):

A significant positive correlation between serum Cu level and length in both IDMs and normal neonates ($r = 0.323$ and $r = 0.372$ respectively).

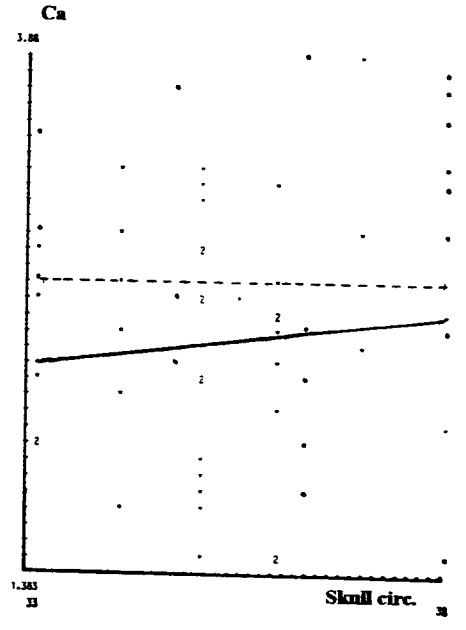


Fig.(25):Correlation between skull circumference and calcium level in both IDMs and normal neonates.

IDMs

INTERCEPT= 1.1778475627483 SLOPE= .03649597829247

r = 0.0784

Normal neonates

INTERCEPT= 3.265 SLOPE= .015

r = .0267 r squared = .0007

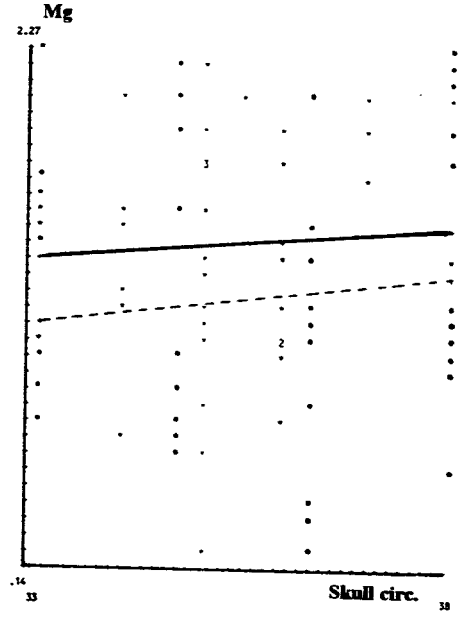


Fig.(26):Correlation between skull circumference and magnesium level in both IDMs and normal neonates.

IDMs

INTERCEPT= .2616338792519 SLOPE= .03327260393449

r = 0.0855

Normal neonates

INTERCEPT= .1279686746988 SLOPE= 5.6487951807229E-02

r = .1209 r squared = .0146

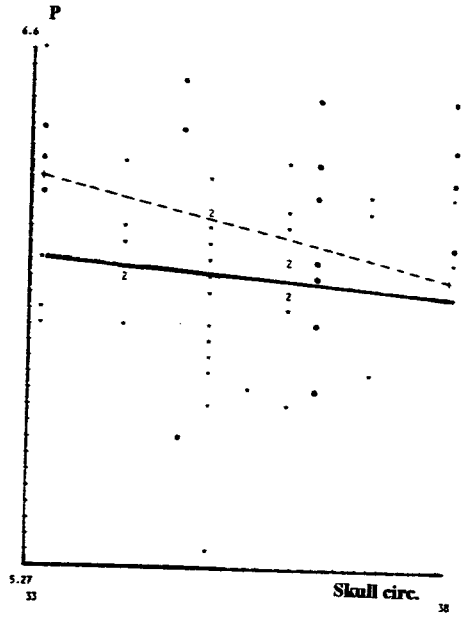


Fig.(27):Correlation between skull circumference and phosphorus level in both IDMs and normal neonates.

IDMs

INTERCEPT= 6.4264201957554 SLOPE= -1.1950770423491E-02

r = -0.0664

Normal neonates

INTERCEPT= 8.9664072289157 SLOPE= -7.6843373493976E-02

r = -.3050 r squared = .0930

Fig. (25):

A very poor positive correlation between serum Ca level and skull circumference in both IDMs and normal neonates (r = 0.078 and r = 0.026 respectively).

Fig. (26):

A very poor positive correlation between serum Mg level and skull circumference in both IDMs and normal neonates (r = 0.085 and r = 0.120 respectively).

Fig. (27):

A very poor negative correlation between serum P level and skull circumference in IDMs (r = - 0.066) and a poor negative correlation in normal neonates (r = - 0.305).

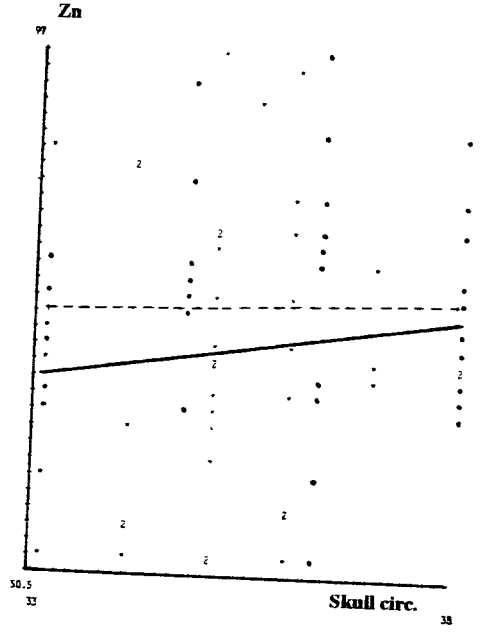


Fig.(28):Correlation between skull circumference and zinc level in both IDMs and normal neonates

IDMs

INTERCEPT= 32.338647155733 SLOPE= 1.0558193623413

r = 0.1028

Normal neonates

INTERCEPT= 14.716265060242 SLOPE= 1.6024096385542

r = .0924 r squared = .0085

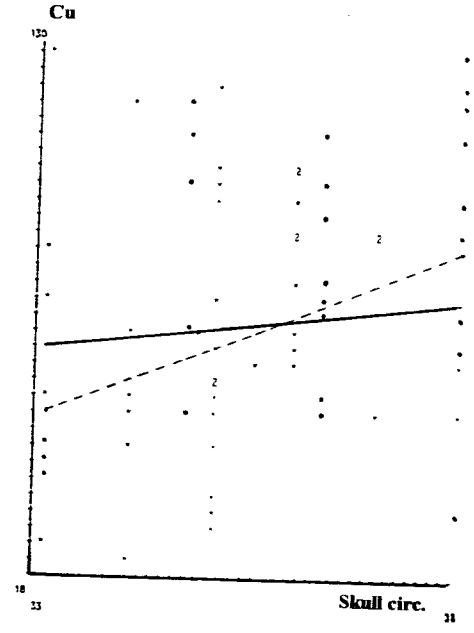


Fig.(29):Correlation between skull circumference and copper level in both IDMs and normal neonates.

IDMs

INTERCEPT= 4.676228316697 SLOPE= 1.863358852602

r = 0.0855

Normal neonates

INTERCEPT= -220.5108433735 SLOPE= 8.7650602409639

r = .4047 r squared = .1638

Fig. (28):

A very poor positive correlation between serum Zn level and skull circumference in both IDMs and normal neonates (r = 0.102 and r = 0.092 respectively).

Fig. (29):

A very poor positive correlation between serum Cu level and skull circumference in IDMs (r = 0.085) and a significant positive correlation in normal neonates (r = 0.404).

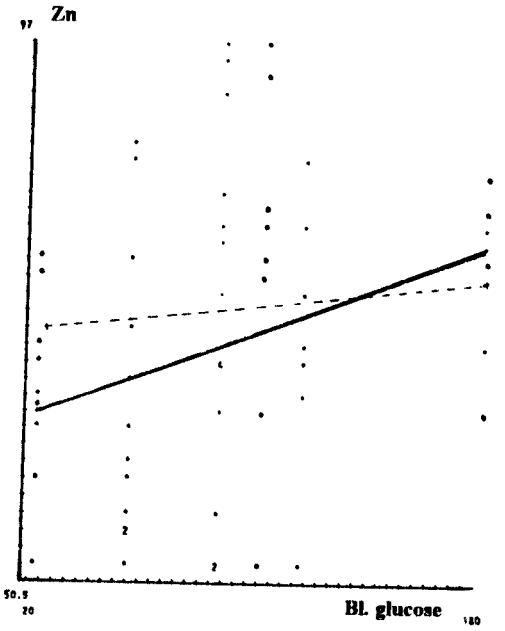


Fig.(30):Correlation between blood glucose level and zinc level in both IDMs and normal neonates

IDMs
INTERCEPT= 60.785852245292 SLOPE= .15312650893288
r = 0.2672

Normal neonates
INTERCEPT= 55.732412060302 SLOPE= .24045226130653
r = .1920 r squared = .0369

Fig. (30):

A poor positive correlation between serum Zn level and blood glucose level at birth in IDMs (r = 0.267) and a very poor positive correlation in normal neonates (r = 0.192).

Table (11): Summay of the correlations between gestational age, anthropometric measurements and serum levels of Ca, Mg, P, Zn and Cu in IDMs and normal neonates.

Subjects	IDMs "r"	Normal neonates "r"
Gestational age:		
Vs. Ca	0.2170	0.2210
Vs. Mg	0.1519	0.1865
Vs. P	0.0616	- 0.0410
Vs. Zn	- 0.3098	0.1529
Vs. Cu	0.1604	0.3428*
Birth weight:		
Vs. Ca	0.1107	0.2790
Vs. Mg	- 0.1504	0.3107
Vs. P	0.1634	- 0.1985
Vs. Zn	0.0655	0.2662
Vs. Cu	0.2384	0.3517*
Length:		
Vs. Ca	0.1515	0.1169
Vs. Mg	0.0561	0.4022*
Vs. P	0.0277	- 0.3188*
Vs. Zn	0.0567	0.0778
Vs. Cu	0.3239*	0.3721*
Skull circumference:		
Vs. Ca	0.0784	0.0267
Vs. Mg	0.0855	0.1209
Vs. P	- 0.0664	- 0.3050
Vs. Zn	0.1028	0.0924
Vs. Cu	0.0855	0.4047*

* Significant (P <0.05). Critical value +/- 0.311

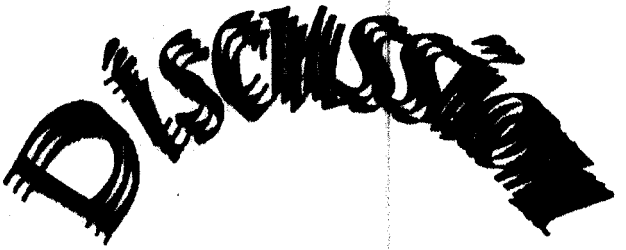
Table (11) showed the following:

- The most contributing variable affecting gestational age was serum Cu level in normal neonates

- The most contributing variable affecting birth weight was serum Cu level in normal neonates .

- The most contributing variables affecting length was serum Cu level in IDMs and serum Mg ,Cu and P levels in normal neonates .

- The most contributing variable affecting skull circumference was serum Cu level in normal neonates.


DISCUSSION

DISCUSSION

Pregnancy may occur either in diabetic women or in one who develops transient or permanent diabetes during pregnancy. GD presents a special problem, because the diagnosis may be missed or unsuspected unless pregnant women are routinely screened by urine analysis and subsequent oral glucose load *(Molsted, 1984).*

Macrosomia is a characteristic feature outcome of diabetic pregnancy. The IDMs (especially those with poorly controlled IDDM or GD) have increased body fat and selective organomegaly, including cardiomegaly but normal sized brains and kidney *(Schwartz, 1990).*

In this study the mean of gestational age in IDMs (38.17±0.78 wks.) was less than that of the normal neonates (39.37±1.14 wks.) and this difference was statistically significant where $P<0.001$. This was explained by the high frequency of elective CS; 30 out of 40 IDMs (75%). This is much higher than the 22% reported by *Berk et al. (1989)* who stated that the examination of indications for CS revealed that macrosomia was the major one.

In this study, there was a strong positive significant correlation between the parity and the maternal age in both diabetic and healthy mothers (critical value +/- 0.311, r = 0.721 and 0.884 respectively). Also the parity and maternal age were significantly higher in the diabetic mothers than the healthy ones ($P<0.05$ and <0.001 respectively).

Although the birth of a large infant increases the likelihood of subsequent diabetes in the mother, most macrosomic infants are born to non diabetic mothers. Other factors associated with fetal macrosomia are multiparity, previous delivery of a macrosomic infant, and excessive weight gain during pregnancy *(Cordero and Landon, 1993).*

In this study 17 out of 40 IDMs (42.5%) were macrosomic compared to 7 out of 40 normal neonates (17.5%). This is in agreement with the work of *Berk et al. (1989)*, who reported that, the rate of macrosomia is still significant in the IDMs (43%) and much higher than that observed in their general population (11.4%).

In another study carried by *Ballard et al. (1993)* on diabetic fetal macrosomia, it was found that 45% of IDMs had macrosomia compared with 8% of control infants. This was concordant to the previous findings. Meanwhile, neonatal macrosomia was observed in 27% of infants of mothers with GD in a study carried out by *Stenninger et al. (1990)*, who reported that macrosomia

was frequent, being found in one fourth of the infants of mothers treated with insulin during pregnancy.

Macrosomia has been explained by a long-standing maternal hyperglycemia resulting in fetal hyperinsulinemia but the condition has also been reported to occur in well-controlled diabetic pregnancies *(Visser et al., 1984)*, this supported our result as the mean weight of the controlled IDMs (3.88±0.49 kg) was significantly higher than that of the normal neonates (3.51±0.60 kg) since $P<0.05$.

Moreover, the non controlled IDMs were heavier (4.41±0.31 kg) than both the controlled IDMs and normal neonates ($P<0.05$ and $P<0.001$ respectively). The generally held view is that, badly controlled diabetics are more likely to have macrosomic babies and by controlling maternal blood glucose levels closely macrosomia can be avoided *(Brudenell and Doddridge, 1989)*.

In our results the mean weight of the IDMs was higher than that of the normal neonates (3.96±0.5 kg and 3.51±0.6 kg respectively $P<0.001$), and the mean length in IDMs (50.62±1.39 cm) was more than that of the control group (49.77±1.14 cm) $P<0.05$, while there was no significant statistical difference in mean skull circumference between both groups ($P>0.05$).

Aziz et al. (1994) studied the anthropometric assessment of IDMs. They reported that although the

mean of weight in IDMs was of statistically significant increase compared to control infants (P<0.001), yet, the mean of length and head circumference in IDMs were statistically not significant as compared to the control group.

Also, *Gerlini et al. (1986)* found that poor metabolic control during pregnancy resulted in excessive and abnormal prenatal growth. The fetal weight increased progressively during the last 3 weeks of gestation, while little or no increase was obseved in fetal length or the head circumference.

These findings document the traditional definition of macrosomia on the basis of birth weight, which has long been recognized in the IDM who typically has a disproportionate increase in such insulin-sensitive tissue as adipose, liver and muscle but not in tissue such as bone, skull and brain in which growth is relatively insulin insensitive *(Landon et al., 1989)*.

The present study showed a statistically significant lower Apgar scores at 1 and 5 minutes in the controlled IDMs compared to the control group (P<0.001 and P<0.05 respectively). Furthermore, the present study revealed lower Apgar scores at 1 and 5 minutes in the non controlled IDMs compared to normal neonates (P<0.001 for each).

This was supported by the work of *Hazzaa et al. (1994)*, who reported a significantly lower Apgar score

at 5 minutes in macrosomic infants compared to the control group.

These low Apgar scores were correlated with increased rate of CS, prolonged labor, and instrumental delivery *(Meshari et al., 1990).*

Brudenell and Doddridge (1989) had mentioned that chronic hypoxemia may be related to the effect of poor maternal glycemic control including hyperglycemia, hyperketonemia and changes that occur in the placenta of diabetic mothers leading to intrapartum distress low Apgar scores or both, even in the well controlled diabetic pregnancy, a degree of hypoxia exists and is associated with fetal macrsomia.

In this work, there was no significant statistical difference as regards the mean blood glucose levels between the controlled IDMs (58.23±23.80 mg/dL) and the normal neonates (61.0±14.28 mg/dL), $P>0.05$. Meanwhile, the mean blood glucose level of the non controlled IDMs (46.66±16.32 mg/dL) was lower than that of the normal neonates (61.0±14.28 mg/dL) and the difference was statistically significant ($P<0.05$).

Hay and Sparks (1985), declared that hypoglycemia of neonates is facilitated by poor control of maternal diabetes, and administration of large doses of intravenous glucose to diabetic mothers during labor.

Furthermore, there was no significant correlation between the blood glucose levels of the IDMs and the birth weight in our study (critical value +/- 0.311, r = 0.013, P>0.05).

Supporting our results *Stenninger et al. (1991)*, found no significant correlation between the blood glucose concentration of the diabetic mothers at delivery and the blood glucose concentration or its decline two hours after delivery in their neonates. They did not find any correlation between either weight or macrosomia and the neonatal hypoglycemia.

Berk et al. (1989), concluded that the policy of strictly controlled maternal blood glucose concentration during labor may have blunted the evidence of the relationship between fetal macrosomia and neonatal hypoglycemia.

For healthy intra-uterine development the fetus requires adequate amounts of major, minor and trace elements which are only obtinable from the maternal blood via the placenta *(Hyvönen-Dabek et al., 1984)*.

Active placental transport of Ca ions from the mother to the fetus against a concentration gradient, making the fetus hypercalcemic relative to his mother, results in the release of calcitonin and may inhibit secretion of parathyrin, which would be conductive to fetal skeletal formation *(Pitkin, 1985)*. Mg is marginally

higher and P is substantially so, in cord blood as compared with maternal blood *(Kuoppala et al., 1986)*.

In our study, circulating concentrations of serum Ca, Mg, and P levels in cord blood of IDMs were highly significantly lower than that of the normal neonates $P<0.001$ for each.

Moreover, serum Ca level was the most discriminating variable between the non controlled IDMs and the normal neonates where the difference was highly significant $P<0.001$, being lower in the non controlled group. This is supported by *Mimouni et al. (1988)*, who found significantly decreased bone minerals contents is IDMs.

Also, a significant correlation did exist, between hypocalcemia and hypomagnesemia in IDMs ($r = 0.424$). A similar result was found by *Mimouni et al. (1986)*.

Actually, the diabetic pregnant women, exhibited persistently low serum Mg levels throughout most of gestation due to maternal Mg losses and failed to demonstrate the normal increase in PTH level leading to relative hypoparathyroidism in both mother and fetus with the resultant propensity to hypocalcemia *(Pitkin, 1985)*.

Another explanation of this hypocalcemia is macrosomia which increases neonatal Ca demands

producing a more profound and prolonged hypocalcemia *(Rubin, 1991).*

As in our result, the study of *Mahmoud et al. (1994)* reported that, in the group of IDMs, the mean serum Mg level (1.725±0.186 with a range of 1.4-2.1mg%) was significantly lower than that of normal full term newborns.

Mg catalyzes or activates more than 300 enzymes in the body. It acts as an essential cofactor for enzymes concerned with cell respiration, glycolysis and transmembrane transport of other cations such as Ca and Sodium. It is generally accepted that fetal and perinatal Mg homeostasis depend on endocrine and nutritional factors *(Milne, 1994).*

Mg deficiency in IDMs may cause a functional hypoparathyroidism that could result in neonatal hypocalcemia when the newborn is no longer provided with Ca of maternal origin through the placenta *(David et al., 1983).*

Regarding P level our result showed that, in IDMs the mean serum P concentration (6.00±0.23 mg/dL) was lower than that of normal neonates (6.29±0.25 mg/dL) and this difference was statistically significant $P<0.001$.

In contrast to our result, *Salle et al. (1982)* found no significant difference in comparison between IDMs and control newborn regarding plasma P concentration.

Pitkin (1985) reported that changes in P are influenced strongly by dietary factors with higher values when feeding is delayed because of tissue catabolism.

While *Tsang and Kleminnan (1972)* stated that, the failure to increase PTH level after birth was associated with both hypocalcemia and hyperphosphatemia and occasionally hypomagnesemia.

Physiological changes occur during pregnancy include decreased plasma Zn and increased plasma Cu concentrations. The decrease in Zn reflects a maternal-fetal transfer, an expansion of maternal plasma volume, decreased Zn binding affinities or transport protein concentrations, and increased Zn requirements or inadequate Zn intake *(Bros et al., 1988).*

The increase in Cu can be attributed to increased ceruloplasmin which is the result of increased estrogen concentration *(Noubah and Al Awgati, 1990).*

In our study, the mean serum Zn and Cu concentrations in the IDMs (69.43±13.20μg/dL and 70.15±28.03μg/dL respectively) were lower than those in normal neonates (70.04±17.89μg/dL and 84.07±22.34 μg/dL respectively). The difference was significant regarding serum Cu level ($P<0.05$) but not for serum Zn level ($P>0.05$).

Wibell et al. (1985) and *Speich et al. (1992)* reported no differences in serum Zn concentrations between IDMs and normal newborns.

Bros et al. (1988), stated that, at birth, plasma Zn values in infants are higher and plasma Cu values are lower than those of pregnant and nonpregnant women. The high plasma Zn level may reflect an active transfer of Zn across the placenta. The low plasma Cu concentration may be associated with the decrease in the fetal liver ability to synthesize adequate amounts of ceruloplasmin *(Sikorski et al., 1988)*.

In this work, a significant positive correlation was found between gestational age and serum Cu concentration in the normal neonates (r = 0.342) but not in the IDMs.

On the contrary *Pop-Jordanova and Bogdanova (1992)* reported that the serum Cu level is not correlated with gestational age of the newborns.

Furthermore there was a significant positive correlation between serum Cu level and length in both the IDMs and the normal neonates (r = 0.323 and r = 0.372 respectively). Also, there was a positive correlation between serum Zn level and weight in the normal neonate although not significant (r = 0.230).

In concordance to our results, *Speich et al. (1992)* reported that, plasma Cu proved to be the most

significant variable in the stepwise-regression equation for birth length as the dependent variable and the most significant regressor accounting for birth weight was plasma Zn.

Zinc is an essential trace mineral for all mammals. The activity of many enzymes, including those needed for protein synthesis, are Zn dependent *(Khoshoo, 1992).*

As in our work, *Jeswani and Vani (1991) and Neggers et al. (1991),* found the same results regarding serum Zn and weight, the larger the fall in serum Zn during pregnancy, the smaller the infant.

Meanwhile, the study of *Arumanayagam et al. (1986) and Lao et al. (1990)* found no significant correlation between serum Zn level and birth weight.

In this work there was a significant positive correlation between serum Cu level and skull circumference in the normal neonates (r = 0.404 and critical value +/- 0.311). Meanwhile *Speich et al. (1992)* found no significant regression for head circumference.

Moreover, in this work the length was correlated positively with serum Mg level and negatively with serum P level in the normal neonates. Both were significant (r= 0.402 and r= -0.318 respectively) indicating that both Mg and P were important for bone growth.

Summary & Conclusion

SUMMARY AND CONCLUSION

The deleterious effects of maternal diabetes mellitus on development and outcome of the fetus and newborn have long been recognized, and the opportunity to improve this outcome has been one of the first challenges to be met by co-ordinate perinatal-neonatal approach to management.

For healthy intra-uterine development the fetus requires adequate amounts of major, minor and trace elements which are only obtained from the maternal blood via the placenta.

The objectives of the present study was to estimate the serum levels of total Ca, Mg, P, Cu and Zn in cord blood of IDMs compared to that of normal neonates and to find out possible relationships between gestational age and growth variables (birth weight, length and head circumference) and the concentrations of these minerals.

This study was conducted on 80 full term neonates in the neonatal intensive care unit, Ain Shams University. They were classified into 2 groups:

Group I: Included 40 full term IDMs with gestational ages ranging from 37-40 (38.17±0.78 wks). They were 17 males and and 23 females. CS

delivery was detected in 30 neonates while 10 neonates were delivered vaginally.

According to being controlled mothers or not this group was subdivided into two groups:

Group Ia: Included 34 full term infants of controlled diabetic mothers.

The duration of treatment was ranging from 2-3 years except one mother with IDDM. She was under insulin treatment for 10 years.

Group Ib: Included 6 full term infants of non controlled diabetic mothers.

Group II: Included 40 full term neonates born to healthy mothers as a control group with gestational ages ranging from 37-41 (39.37 ±1.14 wks). They were 17 males and 23 females, only 3 neonates were delivered by CS.

All the newborn included in this study were subjected to the following procedurs:

- Thourough history taking.
- Complete clinical examination; Apgar score, estimation of gestational age, measurement of birth weight, length, and skull circumference.
- Investigation done included:
  * Determination of cord serum Ca, Mg, P, Zn and Cu.

* Blood glucose level at birth by glucosticks.

The results of the present study revealed the following:

- The gestational age in IDMs (38.17±0.78 wks) was less than that of the normal neonates (39.37±1.14 wks) P<0.001. This was associated with high frequency of CS; 30 out of 40 diabetic mothers (75%) compared to 3 (7.5%) CS in the healthy mothers.
- The percentage of macrosomia was much higher in IDMs 42.5% compared to 17.5% in normal neonates.
- The non controlled IDMs was heavier (4.41±0.31 kg) than both the controlled IDMs (3.88±0.49 kg) and the normal neonates (3.51±0.60 kg) P<0.05 and P<0.001 respectively.
- The mean weight (3.96±0.5 kg) and length (50.62±1.39 cm) of IDMs are higher than that of normal neonates (3.51±0.60 kg and 49.77±1.14 cm) P<0.001 and P<0.05 respectively.
- The Apgar scores were significantly lower in IDMs compared to normal neonates at 1 and 5 minutes (P<0.001 and P<0.05) and much lower in the non controlled IDMs at 5 minutes (P<0.001).
- The non controlled group was hypoglycemic compared to the normal neonates (P<0.05).

- There was no significant correlation between blood glucose levels of IDMs and their birth weight (P>0.05).
- The cord blood levels of Ca, Mg, P and Cu were significantly lower in IDMs compared to normal neonates but was not significant regarding serum Zn level.
- A significant positive correlation was found between length and serum Cu levels in the IDMs (r = 0.323).
- Also there were significant positive correlations between serum Cu level and each of birth weight (r=0.351), length (r=0.372), skull circumference (r=0.404) and gestational age (r=0.342) in the normal neonates.
- Moreover the length was significantly positively correlated with serum Mg level (r = 0.402) and was negatively correlated with P level (r = - 0.318) in the control group.

Conclusion:

- It is concluded that diabetes mellitus in women causes significant variations in their infants' growth as in birth weight and length but not in skull circumference inspite of being under control.
- IDMs are at increased risk of hypoglycemia, hypocalcemia and hypomagnesemia.

- Factors associated with fetal macrosomia are multiparity, previous delivery of a macrosomic infant, excessive weight gain during pregnancy and maternal diabetes.
- Cord serum copper concentration being the most significant variable affecting growth in healthy infants, however this relationship was noticed to be disturbed in the IDMs.
- There was no significant difference in cord blood zinc level between normal neonates and IDMs.
- We accept the hypothesis that the controlled diabetic mothers have favorable effects on their infants' growth and minerals concentrations than the non controlled diabetic mothers.

Recommendations

RECOMMENDATIONS

In view of the implications of this study, we would like to make the following recommendations:

- A good antenatal care, good maternal blood glucose control and adequate treatment of maternal diabetes are mandatory for healthy intrauterine growth.
- Ultrasonography should be done serially to exclude any malformations, for diagnosis of fetal macrosomia or intrauterine growth retardation, and for deciding the mode of delivery to avoid faulty management.
- The overall prognosis for IDM is good but expert pediatric care is an essential for their management.
- The diagnosis of trace elements deficiency should be done early and treatment should start before major clinical features occur.
- Further follow up study to identify the relationship between anthropometric assessment and other minerals values.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Appendix

Table (12): Descriptive clinical data of infants of controlled diabetic mothers.

No.	Sex	Gest. age (wks)	Weight (kg)	Length (cm)	Skull cir. (cm)	Apgar		Parity	Mat. age (years)	Mode of delivery
						1 min	5 min			
1	F	38	5.132	52	36	7	9	P5	35	CS
2	F	37	3.600	50	34	7	8	P3	30	CS
3	M	38	4.100	51	36	5	8	P6	35	VD
4	F	38	3.800	50	35	9	10	P6	23	VD
5	F	38	3.950	50	35	8	10	P6	20	VD
6	F	38	4.625	51	35	8	10	P2	22	CS
7	M	37	5.200	52	38	8	10	P3 + 1	30	CS
8	F	38	4.300	50	34	8	10	P4	33	CS
9	F	37	3.950	50	34	8	10	P2 + 2	25	CS
10	M	39	3.500	49	33	3	10	P6	41	VD
11	M	37	3.600	52	36	3	10	P2 + 4	35	CS
12	M	38	3.740	52	35	7	10	P3	35	VD
13	F	39	3.547	49	34	6	8	P6 + 2	36	VD
14	M	39	3.320	48	33	7	9	P3 + 1	32	VD
15	F	37	3.600	50	35	8	10	P4	37	CS
16	F	38	3.800	51	36	8	10	P3	35	CS
17	F	38	3.100	48	35	7	9	P2	33	CS
18	F	38	3.200	47	33	8	10	P1	41	CS
19	M	39	3.700	52	35	8	10	P1	24	CS
20	F	38	4.00	52	35.5	8	10	P2	25	CS
21	F	37	4.200	52	35	9	10	P3	30	CS
22	M	38	4.600	51	35	8	10	P6	42	CS
23	F	38	3.660	51	34	9	10	P2	26	CS
24	M	37	3.000	48	33	7	10	P1	30	CS
25	M	38	3.700	51	36	8	10	PG	23	CS
26	F	38	3.900	51	35	7	9	P3	38	CS
27	M	39	3.500	51	35	5	10	P5	35	CS
28	F	38	4.200	52	36	6	8	P1	30	CS
29	M	39	4.000	49	36	4	8	P6	38	CS
30	F	38	3.900	52	36	5	8	P5	37	CS
31	F	40	4.100	52	35	6	8	P4	36	CS
32	M	38	3.600	49	35	6	8	P1	25	VD
33	F	39	3.800	52	35	8	10	P2	24	VD
34	M	39	4.475	52	36	8	10	P3	37	CS
Mean		38.08	3.886	50.55	34.98	6.97	9.41		31.67	-
± SD		0.753	0.491	1.460	1.153	1.58	0.85		6.14	-
Range		37-40	3-5.20	47-52	33-38	3-9	8-10	0-6	20-42	-

Table (13): Descriptive laboratory data of infants of controlled diabetic mothers.

No.	Blood glucose mg/dL	Ca mEq/L	Mg mEq/L	P mg/dL	Zn µg/dL	Cu µg/dL
1	60	2.769	0.7	6.19	54.5	68
2	20	2.729	0.6	5.98	51	67
3	60	2.511	0.96	5.9	75	104
4	60	3.153	2.22	5.79	69	100
5	60	2.883	1.92	6.13	79	74
6	40	1.394	0.54	6.17	59.5	59
7	60	2.606	1.35	5.94	95	79
8	40	3.316	1.26	6.01	54	53
9	40	2.475	1.6	6.08	87	44
10	40	1.913	1.0	5.86	51	85
11	80	2.078	1.79	5.67	66	89
12	20	2.667	1.78	5.64	65.5	66
13	20	3.005	2.07	5.86	62	18
14	40	2.661	1.57	5.91	57.2	23
15	40	2.662	1.76	5.97	63	30
16	60	2.624	1.35	6.2	69	52
17	60	2.246	1.14	6.04	69	52
18	80	2.267	1.48	6.06	69	76
19	80	3.224	1.79	6.25	75	56
20	60	2.678	2.07	5.71	93	62
21	60	1.7	1.07	5.75	97	32
22	120	1.383	1.04	6.05	81	98
23	40	2.225	1.5	6.13	53	120
24	40	1.967	2.27	6.24	88	54
25	120	2.362	1.92	6.13	70	63
26	60	2.587	1.43	6.31	84	66
27	80	1.778	1.29	6	81	121
28	10	2.951	1.64	6.6	71	130
29	80	1.602	1.2	6.31	86	51
30	80	1.42	1.04	5.97	51	92
31	60	2.938	1.59	6.19	50.5	104
32	60	2.259	0.76	5.27	64	54
33	80	3.316	1.36	5.83	70	26
34	40	3.21	1.2	6.04	55	103
Mean	58.235	2.457	1.419	6.00	69.57	69.735
± SD	23.80	0.563	0.453	0.242	13.75	29.045
Range	20-120	1.38-3.31	0.54-2.27	5.27-6.6	50.5-97	18-130

Table (14): descriptive clinical data of infants of non controlled diabetic mothers.

No.	Sex	Gest. age (wks)	Weight (kg)	Length (cm)	Skull cir. (cm)	Apgar		Parity	Mat. Age (years)	Mode of delivery
						1 min	5 min			
1	M	38	4.400	50	35	3	8	P5+2	36	CS
2	M	39	4.600	51	37	7	10	P2	38	CS
3	F	40	4.600	52	37	9	10	P4	36	CS
4	F	39	4.500	52	38	3	8	P7	42	CS
5	F	38	4.600	51	37	7	9	P4	38	CS
6	M	38	3.800	51	35	7	9	P3	27	VD
Mean		38.66	4.416	51	36.5	6	9		36.16	
± SD		0.816	0.312	0.894	1..224	2.44	0.89		4.99	
Range		38-40	4.8-4.6	50-52	35-38	3-9	8-10	2-7	27-42	

Table (15): Descriptive laboratory data of infants of non controlled diabetic mothers.

No.	Blood glucose mg/dL	Ca mEqL	Mg mEq/L	P mg/dL	Zn µg/dL	Cu µg/dL
1	60	1.903	1.04	6.07	50.5	98
2	20	3.88	1.9	6.15	69	92
3	40	2.468	2.07	5.74	66.5	90
4	60	1.992	2.07	6.04	68	60
5	40	2.973	1.75	6.21	78	51
6	60	1.634	0.14	5.87	80	44
Mean	46.666	2.475	1.495	6.013	68.666	72.50
± SD	16.329	0.835	0.765	0.176	10.496	23.526
Range	20-60	1.63-3.88	0.14-2.07	5.74-6.21	50.5-80	44-98

Table (16): Descriptive clinical data of the control group.

No.	Sex	Gest. age (wks)	Weight (kg)	Length (cm)	Skull cir. (cm)	Apgar		Parity	Mat. age (years)	Mode of delivery
						1 min	5 min			
1	F	39	3.600	49	35	9	10	P3 + 1	32	VD
2	F	40	3.750	50	36	9	10	P2	28	VD
3	M	41	4.000	51	35	8	10	PG	22	C.S
4	M	40	3.800	50	36	9	10	P3	26	VD
5	F	40	3.550	51	35	8	9	P4 +2	35	VD
6	F	38	2.850	48	33	8	9	P3	23	VD
7	F	39	3.300	49	34.5	8	10	P1	22	VD
8	F	41	3.400	51	36	7	9	PG	20	VD
9	M	38	2.900	49	34	7	8	P3	25	VD
10	F	39	3.700	50	35	8	10	PG	19	VD
11	M	40	3.750	49	34	8	10	PG	20	VD
12	M	40	4.100	51	36	8	10	P4	35	VD
13	F	40	2.850	50	35	8	10	P3 + 1	33	VD
14	F	37	2.700	49	33	8	10	P2	29	VD
15	M	39	3.450	51	36	9	10	PG	20	VD
16	M	40	3.900	50	35	8	10	P1	22	VD
17	F	41	3.950	51	35	9	10	P3	27	VD
18	F	40	2.800	49	34	8	9	P4	35	VD
19	M	40	3.550	52	36	7	10	P2	30	VD
20	F	40	4.200	51.5	36	8	10	PG	21	C.S
21	M	39	3.650	48	34	9	10	PG	20	VD
22	M	38	3.000	49	35	9	10	P3	28	VD
23	F	37	2.900	48	33	8	10	P5	35	VD
24	M	38	3.600	48	34	8	10	P4	33	VD
25	F	40	3.250	49	35	9	10	P4	36	VD
26	F	41	4.100	51	36	8	10	P2	24	VD
27	F	39	3.200	50	34	9	10	PG	19	VD
28	M	40	3.750	50	35	8	10	P2	22	VD
29	F	40	4.000	51	36	9	10	P3	30	VD
30	M	38	2.650	48	33	8	10	PG	20	VD
31	M	37	2.500	48	33	8	10	PG	19	VD
32	F	38	3.000	49	34	9	10	P3	31	VD
33	M	40	3.100	50	35	8	9	P3	35	VD
34	M	41	2.800	49	33	9	10	PG	20	VD
35	F	40	4.100	52	36	8	10	P3 + 1	33	C.S
36	F	40	3.450	50	34	8	10	P2	27	VD
37	M	39	3.900	50	35	8	10	P4	36	VD
38	F	40	4.000	51	36	8	10	P5	37	VD
39	F	38	3.600	49	35	8	9	P2	30	VD
40	F	40	3.850	50	35	8	10	PG	25	VD
Mean		39.37	3.512	49.77	34.75	8.25	9.8	-	27.1	-
± SDF		1.14	0.601	1.143	1.031	0.58	0.46	-	6.03	-
Range		37-41	2.5-4.2	48-52	33-36	7-9	8-10	0-5	19-37	-

Table (17): Descriptive laboratory data of the control group.

No.	Blood glucose mg/dL	Ca mEq/L	Mg mEq/L	P mg/dL	Zn µg/dL	Cu µg/dL
1	40	3.1	1.2	6.12	61.5	100
2	60	4.6	1.8	6.59	70.5	103
3	40	3.6	1.75	6.24	76	85
4	60	4.03	1.95	6.47	99	125
5	60	3.3	2.3	6.12	27	112
6	60	3.7	2.24	6.39	77	90
7	80	3.2	1.57	6.51	90	71
8	80	3.6	1.5	6.31	57.5	113
9	60	3.2	1.885	5.82	71	104
10	60	3.7	2.5	6.39	84	83
11	80	4.2	2.64	6.34	77	117
12	60	3.5	2.94	5.55	83	84
13	80	2.98	2.48	5.92	56	81
14	40	4	1.75	6.48	65.5	62
15	60	2.4	1.85	5.56	55.5	87
16	80	3.4	1.935	6.71	85	101
17	80	2.75	2.06	6.62	80	89
18	60	4.31	1.75	6.63	74	46
19	80	4.7	2.66	6.15	68.5	121
20	60	4.12	2.8	6.28	88	96
21	40	3.7	1.66	6.37	55	82
22	40	3.6	1.35	6.71	41	72
23	60	3.6	2.5	6.21	53	88
24	80	4.2	1.55	6.38	67	45
25	80	3.6	1.69	6.44	83	67
26	80	4.8	2.57	6.2	53	118
27	60	4.7	2.76	6.34	107.5	70
28	60	4.9	2.76	6.06	89	105
29	80	4.22	2.02	6.42	61.5	69
30	60	3.8	1.67	6.48	72	58
31	60	3.6	2.21	6.45	53.5	48
32	40	3.4	2.38	6.35	50.5	111
33	60	3.5	1.977	6.11	98.5	81
34	60	4.5	1.85	6.54	62	60
35	40	4.3	2.9	6.31	65	78
36	60	4.3	2.9	6.34	55	67
37	60	3.7	2.23	6.28	112.5	59
38	40	4.1	1.98	6.19	74	54
39	60	3.14	1.35	6.27	63.5	59
40	40	3.4	1.78	6.19	53.5	102
Mean	61	3.786	2.09	6.296	70.4	84.07
± SD	14.28	0.578	0.482	0.259	17.89	22.34
Range	40-80	2.4-4.9	1.2-2.94	5.55-6.71	27-112.5	45-125

ABESTRACT

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Study Of Some Minerals In Cord Blood Of Infants Of Diabetic And Non Diabetic Mothers

This study was done in the neonatal intensive care unit of gynecology and obstetric hospital ,Ain Shams University. It was started in April 1995 and closed in October 1995.Concentration of total calcium (Ca), magnesium (Mg), phosphorus (p), copper (cu) and zinc (Zn) were investigated in plasma of venous cord blood of 40 infants of diabetic mothers (IDMs). Mineral results for IDMs were compared with those for 40 healthy full term newborns. The duration of gestation in the two groups was significantly different ($P<0.001$). The mean (± SD) differences between groups were significant for birth weight, length, plasma Ca (2.46 ± 0.59 for IDMs vs. 3.78 ± 0.57 mEq/L for control group), plasma Mg (1.43 ±0.5 vs. 2.09±0.48 mEq/L) , plasma P (6.00± 0.23 vs . 6.29± 0.25 mg/dL) ,plasma Cu (70.15±28.03 vs . 84.07 ± 22.34 μg /dL) but not for plasma Zn . The concentration of plasma Cu was significantly positively correlated with length of both groups, and were significantly positively correlated with the gestational age, weight and skull circumference in the control group ($P< 0.05$) but not in the IDMs.

Key words: IDMs - Minerals – Trace elements.

Arabic Summary

الملخص العربى

لقد عرفت الآثار الخطيرة لمرضى السكر أثناء الحمل ومدى تأثيره على نمو الجنين والوليد بعد ذلك منذ زمن بعيد.

وكانت الفرصة لتحسين النتائج واحدة من أهم التحديات التى يمكن مواجهتها عن طريق العناية المتكافئة ما قبل وأثناء فترة الحمل وما بعدها.

من أجل نمو سليم يحتاج الجنين إلى كميات كافية من المعادن الكبيرة والصغيرة والنادرة والتى يتم الحصول عليها فقط عن طريق الأم من خلال المشيمة.

يهدف هذا البحث إلى قياس نسبة المعادن مثل الكالسيوم والماغنسيوم والفسفور والنحاس والزنك فى الحبل الوريدى للأطفال حديثى الولادة لأمهات مرضى السكر مقارنتا بأطفال لأمهات أصحاء واكتشاف وجود علاقات ممكنة بين العمر الرحمى ومتغيرات النمو مثل الوزن والطول ومحيط الرأس ونسبة هذه المعادن فى كلا من المجموعتين.

أجريت هذه الدراسة فى وحدة الرعاية المركزة لحديثى الولادة بمستشفى أمراض النساء والولادة جامعة عين شمس.

وقد إشتملت على مجموعتين من الأطفال حديثى الولادة.

المجموعة الأولى:

تحتوى على ٤٠ طفل حديث الولادة لأمهات مرضى السكر يتراوح العمر الرحمى لهم من ٣٧-٤٠ أسبوع (٣٨,١٧ ± ٠,٧٨).

وكانت ولادة ٣٠ طفل منهم ولادة قيصرية، بينما ولد ١٠ أطفال عن طريق الولادة الطبيعية وتم تقسيمهم مرة أخرى إلى مجموعتين وذلك على أساس وجود الأمهات تحت التحكم بالعلاج بالإنسولين أم لا.

مجموعة (أ) تحتوى على ٣٤ طفل لأمهات تحت العلاج بالأنسولين.

مجموعة (ب) تحتوى على ٦ أطفال لأمهات غير خاضعين للعلاج.

المجموعة الثانية:

إشتملت على ٤٠ طفل حديثى الولادة لأمهات أصحاء كمجموعة ضابطة يتراوح العمر الرحمى لهم بين ٣٧-٤١ أسبوع (٣٩,٣٧ ± ١,١٤).

وقد خضع كل طفل فى هذه الدراسات إلى:

- أخذ تاريخ مفصل مع التركيز على عمر الأم والعمر الرحمى وعدد مرات الولادة ومدة السكر عند الأم ونوعه وما إذا كانت تحت العلاج.
- فحص إكلينيكى شامل مقياس ابجار عند الولادة، تحديد العمر الرحمى عن طريق مقياس بلارد.
- قياس كلا من الوزن والطول - محيط الرأس.
- لقياس نسبة المعادن فى اللازما يتم سحب العينة من حبل الوريد فى خلال خمس دقائق من الولادة ثم يتم فصل العينة وحفظها فى أنابيب جافة ونظيفة ويتم القياس بواسطة جهاز السبكتروفوتومتر.
- قياس نسبة السكر بالدم عند الولادة.

وقد أظهرت هذه الدراسة النتائج الآتية:

- إنخفاض متوسط أعمار الأطفال لأمهات مرضى السكر عنه فى الأطفال للأمهات الأصحاء حيث أن الطريقة الأكثر شيوعا لولادة هؤلاء الأطفال كانت الولادة القيصرية، قبل الميعاد المحدد للولادة الطبيعية بأسبوعين أو ثلاثة أسابيع.
- وكانت نسبة كبر الحجم فى الأطفال لأمهات مرضى السكر (٤٢,٥٪) أكثر منها فى الأطفال لأمهات أصحاء (١٧,٥٪).
- وكان وزن الأطفال للأمهات غير الخاضعين للعلاج أثقل من كلا من الأطفال للأمهات الخاضعين للعلاج وكذلك الأمهات الأصحاء.
- كانت متوسطات الطول والوزن فى الأطفال لأمهات مرضى السكر أكثر منها فى الأطفال الأصحاء.
- وجد فرق إحصائى من حيث مقياس ابجار الذى انخفض بدرجة ملحوظة فى الأطفال للأمهات تحت العلاج عنه فى الأطفال لأمهات أصحاء وكانت معدلاته أكثر إنخفاضا فى الأطفال لأمهات غير خاضعين للعلاج.

- إنخفض مستوى السكر بالدم فى الأطفال للأمهات غير الخاضعين للعلاج عنه فى الأطفال للأمهات الأصحاء كما لم توجد دلالة إحصائية بين كلا من نسب السكر والوزن عند الولادة فى الأطفال لأمهات مرضى السكر. بإضافة إلى إنخفاض نسبة كلا من الكالسيوم والماغنسيوم والفسفور والنحاس فى الحبل الوريدى فى الأطفال لأمهات مرضى السكر عنها فى الأطفال لأمهات أصحاء، بينما لم تختلف نسبة الزنك فى كل من المجموعتين.
- وجدت علاقة إيجابية ذات دلالة إحصائية بين مستوى النحاس والطول فى الأطفال لأمهات مرضى السكر.
- كما وجدت علاقات ذات دلالة إحصائية إيجابية بين مستوى النحاس وكل من العمر الرحمى والوزن والطول ومحيط الرأس فى الأطفال الأصحاء. بالإضافة إلى وجود علاقة إيجابية ذات دلالة إحصائية بين الطول ومستوى الماغنسيوم وعلاقة سالبة ذات دلالة إحصائية بين الطول ومستوى الفسفور.

مما سبق يتضح لنا أن المشكلة الرئيسية فى أطفال الأمهات المصابات بمرض السكر تكمن فى مدى الاهتمام والرعاية التى تحظى بهما الأم قبل وأثناء وحتى بعد فترة الولادة مباشرة فمن الضرورى إستمرار التحكم الأمثل فى مستوى السكر خلال هذه الفترات.

وأيضا يتضح لنا أهمية العناية بأطفال هؤلاء الأمهات بالمتابعة الجيدة وإهتمام كل من طبيب الأطفال وطبيب الولادة للإقلال من نسبة حدوث المشاكل التى يتعرضون لها أثناء وبعد الولادة.

من الضرورى متابعة نسبة المعادن مثل الكالسيوم، والماغنسيوم والفسفور والنحاس فى الدم لكى يمكن علاجها فى وقت مبكر.

ونوصى بعمل دراسات متابعة لمقاييس النمو المختلفة مع معادن أخرى لإيجاد علاقات جديدة.

مستخلص الرسالة

جامعة عين شمس–معهد الدراسات العليا للطفولة – قسم الدراسات الطبية

أسم الباحث /هدي عبد الرحمن محمد إسماعيل

دراسة لبعض المعادن في الحبل السري في الأطفال حديثي الولادة لأمهات مرضي السكر والأمهات الأصحاء

أجريت هذه الدراسة في وحدة الرعاية المركزة لحديثي الولادة بمستشفى أمراض النساء و الولادة جامعة عين شمس علي ٤٠ طفل حديثي الولادة لأمهات مرضي السكر مقارنتا ب ٤٠ طفل حديثي الولادة لأمهات أصحاء وتم مقارنة كل من نسبة الكالسيوم والماغنسيوم و الفسفور و النحاس والزنك في بلازما الحبل الوريدي وكذلك الطول والوزن ومحيط الرأس في كلا من المجموعتين .وقد أوضحت النتائج نقص نسبة كل من الكالسيوم(٢,٤٦±٠,٥٩)والماغنسيوم(١,٤٣± ٠,٥)و الفسفور(٦± ٠,٢٣)و النحاس(٧٠,١٥±٢٨,٠٣)وكذلك العمر الرحمي وزيادة الوزن والطول في الأطفال حديثي الولادة لأمهات مرضي السكر عنها في الأطفال للأمهات الأصحاء .كما وجدت علاقة إيجابية ذات دلالة إحصائية بين مستوي النحاس والطول في كلا المجموعتين بينما وجدت علاقات إيجابية ذات دلالة إحصائية بين مستوى النحاس وكل من العمر الرحمي والوزن ومحيط الرأس في الأطفال للأمهات الأصحاء فقط

الكلمات المفتاحية :

الأطفال حديثي الولادة لأمهات مرضي السكر

المعادن –العناصر النادرة

جامعة عين شمس

الكلية :

شكر

اشكر السادة الأساتذة الذين قاموا بالأشراف

وهم :

١) أ.د. مجدية محمد عبد الفتاح ... جامعة عين شمس

٢) د. محمد كامل محمد إبراهيم .....

٣) د. عزة عبد اللطيف إمام ... المركز القومي للبحوث .

٤) .....

ثم الأشخاص الذين تعاونوا معي في البحث

وهم :

١) ... د. نبيلة إسماعيل عطية .....

٢) .....

٣) .....

وكذلك الهيئات الآتية :

١) .....

٢) .....

٣) .....

" جامعة عين شمس "

الكلية : معهد الدراسات العليا للطفولة

إسم الطالب : هدى عبد الرحمن محمد إسماعيل

عنوان الرسالة: دراسة لبعض العادات في الفم لبعض أطفال حديثي الولادة لأمهات مرضى السكر والأمهات الأصحاء.

إسم الدرجة : (~~ماجستير~~ / دكتوراه)

لجنة الإشراف

١- الإسم / أ.د. بشيرية محمد عبد الفتاح ٢- الوظيفة / أ.ط. طب الأطفال جامعة عين شمس

١- الإسم / د. مجدي كرم الدين علي ٢- الوظيفة / مدرس دراسات الطفولة جامعة عين شمس

الإسم / د. عزة عبد اللطيف إمام الوظيفة / مدرس بوحدة الأطفال بقسم البحوث الصحية بالمركز القومي للبحوث.

تاريخ البحث : ٢٠ / ٢ / ١٩٩٦

الدراسات العليا

ختم الإجازة

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أجيزت الرسالة بتاريخ

٩٧/ ٩/ ١٦

موافقة مجلس الكلية

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موافقة مجلس الجامعة

/ / ١٩٩

" جامعة عين شمس "

الكلية : معهد الدراسات العليا للطفولة

صفحة العنوان

إسم الطالب : هدى عبد الرحمن محمد إسماعيل

الدرجة العلمية : دكتوراة الفلسفة في دراسات الطفولة الطبية

القسم التابع له : الدراسات الطبية

إسم الكلية : معهد الدراسات العليا للطفولة

الجامعة : عين شمس

سنة التخرج : ١٩٩٧

سنة المنح : ١٩٩٧

شروط عامة

يوضع شعار الجامعة على الغلاف الخارجى

معهد الدراسات العليا للطفولة
قسم الدراسات الطبية
جامعة عين شمس

دراسة لبعض المعادن فى الحبل السرى فى الأطفال حديثى الولادة لأمهات مرضى السكر والأمهات الأصحاء

رسالة مقدمة
للحصول على درجة دكتوراه الفلسفة
فى دراسات الطفولة الطبية

مـن
الطبيبة/ هدى عبدالرحمن محمد إسماعيل
ماجستير طب الأطفال - جامعة عين شمس

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د/ مجدى كرم الدين على
مدرس دراسات الطفولة - جامعة عين شمس

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مدرس بوحدة الأطفال بقسم البحوث الصحية
بالمركز القومى للبحوث وتكنولوجيا الإشعاع

١٩٩٧