PREVALENCE OF CONGENITAL MALFORMATIONS AMONG EGYPTIAN NEWBORN INFANTS

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of Master Degree in Pediatrics

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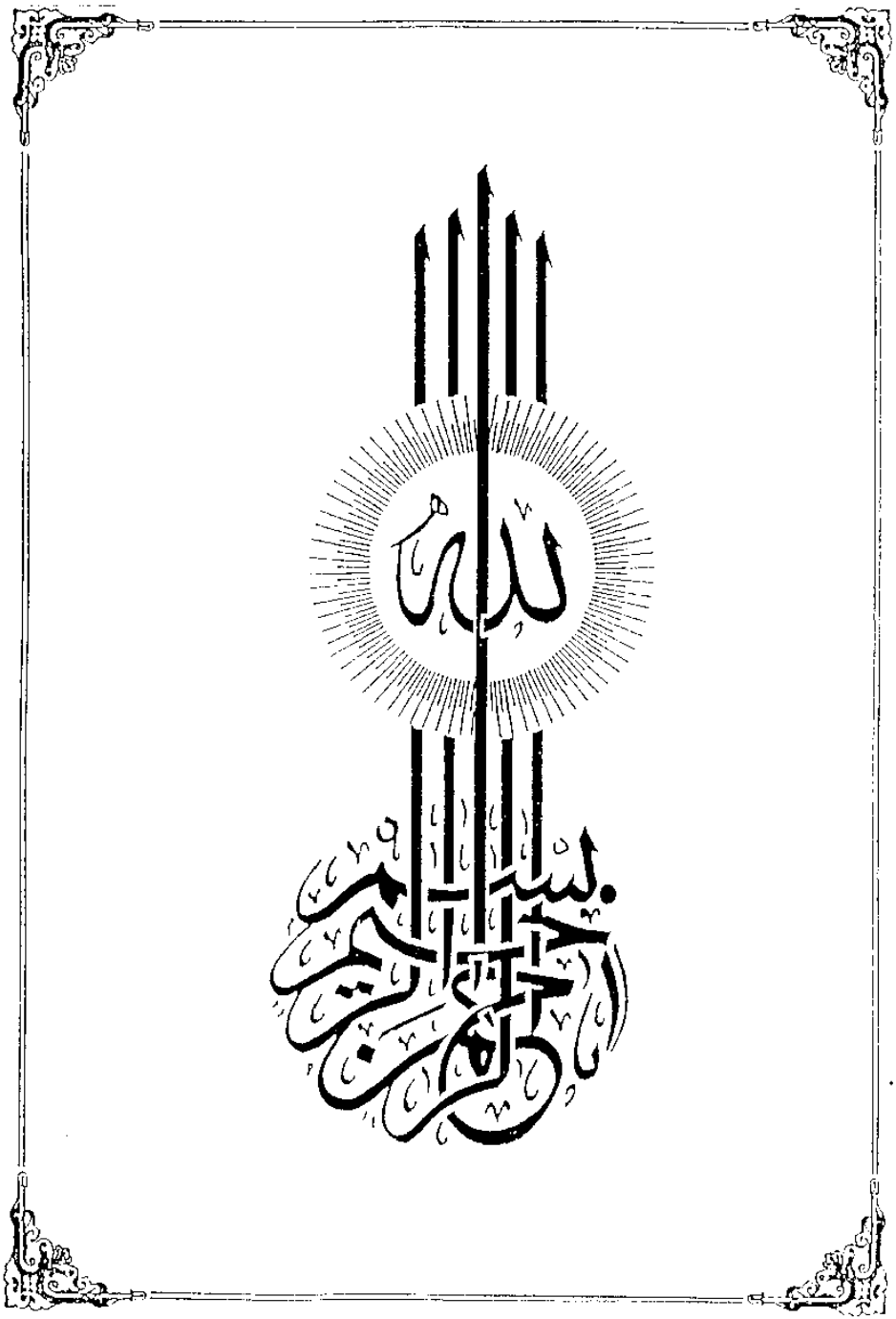

LIST OF ABBREVIATIONS

<	Less than.
>	More than.
AA	Ascorbic Acid.
AFP	Alfa Feto Protein.
ASD	Atrial Septal Defect.
CHD	Congenital Heart Disease.
CMV	Cytomegalovirus.
CNS	Central Nervous System.
CRS	Congenital Rubella Syndrome.
CVS	Chorionic Villus Sampling.
DHA	Dehydroascorbic Acid.
DM	Diabetes Mellitus.
DNA	Deoxyribonucleic Acid.
EDTA	Ethylene Diamino Tetracetic Acid.
FHS	Fetal Hydantoin Syndrome.
GD	Gestational Diabetes.
GDM	Gestational Diabetes Mellitus.
GIT	Gastrointestinal Tract.
HbA_{1c}	Glycosylated Hemoglobin.
HIV	Human Immuno-deficiency Virus.

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AIM OF THE WORK

INTRODUCTION

The term birth defect is used to describe dysmorphologies visible at birth; these may occur in 2-3% of infants (Manchester et al., 1991) .

Genetic causes account for 20% to 25 % of human birth defects, but the largest proportion of birth defects have no definitive etiology and some of these malformations may be due to intrinsic, " nonpreventable " spontaneous errors of development .

Environmental causes, which include maternal disease states, maternal infections, mechanical factors, problems of constraint, chemicals, drugs and physical agents, are responsible for only about 10% of human birth defects (Brent et al., 1993) .

The stage of gestation is critical to the effects that are expected of teratogens, and all stages of embryogenesis and fetogenesis can have vulnerability to environmental toxicants .

Also, the response of the embryo and fetus is characteristic for each teratogenic agent (Brent et al., 1993) .

In a study done by Chen and Li, (1993), the first six causes of neonatal deaths were respiratory diseases, prenatal asphyxia, infection, scleredema, congenital malformations and intracranial haemorrhage .

AIM OF THE WORK

Assessment of the prevalence of congenital malformations in 1000 Egyptian newborns delivered in the Maternity Hospital - Ain Shams University .

Also, the effect of metabolic control as reflected by the level of glycohemoglobin (Hb A1c) in the first trimester of diabetic pregnancies on the fetal outcome will be evaluated .

REVIEW OF LITERATURE

Morphogenesis

Definition :

After fertilization, the zygote undergoes several steps which involve increase in cell number by cell proliferation, specialization of different tissues by differentiation of cells and achievement of normal shape .

This process is called morphogenesis (Abdel Salam, 1990) .

It includes the following stages :

1) Gametogenesis and fertilization.
2) Blastogenesis . This stage is completed by 13-14 days post-fertilization .
3) Organogenesis . It extends from the second to the eighth week following conception .
4) Fetal development. It extends from 9 to 38 weeks following conception (Manchester et al., 1991) .

Sensitive Periods Of Prenatal Development

A) Gametopathies

Defects of gametogenesis (gametopathies) occur before day 1 (postfertilization) of development in man .

(1) Radiation

Ovarian or testicular irradiation before conception can lead to point mutations and cytogenetic changes, which may, in turn, lead to congenital malformations .

The risk of trisomy 21, or of a chromosomally abnormal fetus that is spontaneously aborted, is slightly increased after maternal and possibly paternal preconceptional irradiation . (David, 1983) .

(2) Viruses

Various viruses induce chromosome abnormalities in experimentally infected cells, and similar aberrations have been found in peripheral blood cells of humans who have contracted chicken pox, measles and mumps or have been vaccinated with live measles virus preparations (David, 1983) .

(3) Delays during reproduction

Preovulatory ageing of ova explains a relationship between increased maternal age and Down's syndrome (David, 1983) .

B) Blastopathies

These are defects which occur in the period of blastogenesis . There are two potential types of local damage to an embryo at this stage .

Either the embryo consists of a small number of very similar cels which are equally susceptible to a teratogen, the teratogen exerting its action locally and therefore only damaging part of the embryo, or the embryo has developed further so that some of the cells have become differentiated, and have developed a differential susceptibility to a teratogen (David, 1983) .

C) Embryopathies

These are defects which occur in the period of organogenesis . As far as the production of congenital malformations is concerned, organogenesis is the most vulnerable period for the embryo .

The effect of a teratogen will vary according to the day or days on which the embryo is exposed to it .

A good example is the consistent correlation between the time of intake of thalidomide and the type of malformation. The earliest damage caused by thalidomide in man occurs on about the 35th day after the beginning of the last menstrual period and results in the absence of the ears. The overall sensitive period of thalidomide lasts for about 16 days from the 35th to the 50th day .

Another example of the importance of timing is hypospadius . It appears that the closer the time of treatment with progestins and oestrogens to the beginning of penis formation, the more severe the hypospadius (David, 1983) .

D) Fetopathies

These are defects which occur in the period of fetal development .
At the end of the period of embryogenesis the embryo becomes the fetus .
Various adverse influences can damage the fetus at this stage and these comprise :

1) **Infections** as toxoplasmosis, varicella infection and herpes zoster (David, 1983) .

2) **Drugs** such as tetracycline, antithyroid drugs, radioactive iodine and progestins (David, 1983) .

3) **Vascular factors** such as jejunoileal atresia, atresia of the appendix, atresia of the colon, and gastroschisis (David, 1983) .

4) **Mechanical factors**
If amniotic fluid is removed from pregnant rats prior to palatal closure, oligohydramnios causes fetal compression including the chin, which forces the tongue upwards preventing palatal closure . Oligohydramnios also causes limb defects ranging from ring constrictions to phocomelia (David, 1983) .

5) **Amniotic bands**

Congenital ring constrictions are sometimes associated with malformations of the digits e.g. digital constriction rings, amputation and syndactyly of the finger tips, and occasionally other gross and bizarre defects of the face and skull (severe microcephaly, encephalocele, microphthalmia and distortion of the palpebral fissures, unilateral proboscis, facial cleft, and aberrant bands of tissue across the face) (David, 1983) .

Interference with normal development at any one of these stages is likely to produce a structural defect (congenital malformation) . The major mechanisms to be considered are the following :

1) Disruption of normal migration of cells
2) Interaction of tissues and cells
3) Growth
4) Cell death

(David, 1983) .

1) Disruption of normal migration of cells

During the development of the embryo, morphogenesis is accompanied by a series of synchronized migration of cells, as well as random motility of certain cells . Congenital abnormalities can result from interference with directed movements of cells .

Because distortion of one tissue may have a profound effect on neighbouring tissues, the end result of interference with cell migration may be a whole series of failures of normal synchronized development. Two examples of abnormalities resulting from disordered morphogenetic movement are described below (David, 1983) .

a) Closure of the palatal shelves

During the 8th week, the palatine shelves approach each other in the midline, fuse, and form the secondary palate . At the same time as the palatine shelves fuse, the nasal septum grows down and joins the newly formed palate . Inhibition of these morphogenetic movements or of the process of fusion leads to development of a cleft palate (David, 1983) .