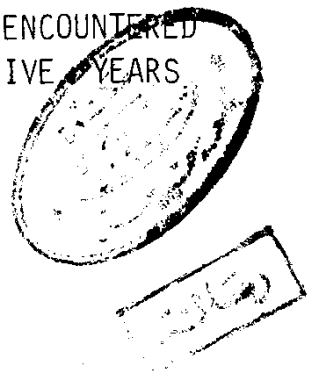
THE STUDY OF DIFFERENT FETAL ANOMALIES ENCOUNTERED IN OBSTETRIC PRACTIC IN THE LAST FIVE YEARS "1975 - 1979"



THESIS
SUBMITTED IN PARTIAL
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BY
MOHAMED SERRY ALY ESSA

UNDER SUPERVISION OF

Prof. Dr.: Bahi El Deen El Ganzory
Asst. Prof.Dr.: Sobhi Khalil Abu Louz.

FACULTY OF MEDICINE
DEPARTMENT OF OBSTETRIC AND GYNEECOLOGY
AIN SHAMS UNIVERSITY

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Dr. Mohamed Serry Aly

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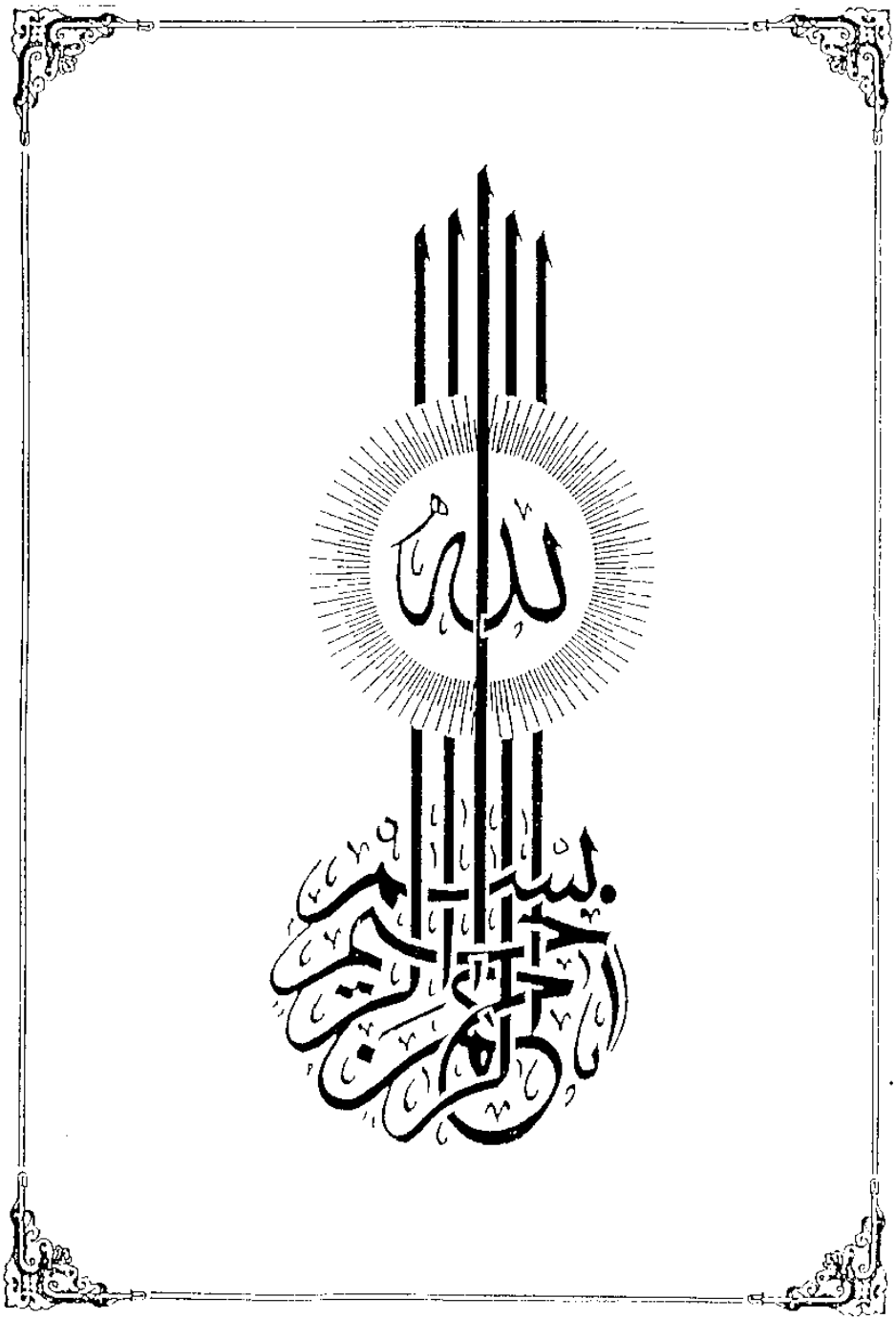

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CONGENITAL MALFORMATIONS

Definition: May be defined as visible or easily detectable structural abnormalities which hasgrown with increasing knowledge of their origins and the steady improvement in neonatal surgery.

Alan Brews (2)

Fetal malformations account for 10 to 20 % of the deaths of fetuses and infants weighting more than 500 gm. They are also an important cause of intrauterine deaths during the first trimester of pregnancy and of many instances of crippling and death appearing months and years after birth.

Probably less than half of the congenital malformations which will ultimately lead to permanent disability or death are apparent at birth. The overall incidince is, therefore, not well defined, but it is estimated to be in excess of 3% of all births.

Lethal anomalies incompatible with life occur in about 0.5% of infants born alive. If all minor malformations are included, the frequency of occurance may be as high as 10%

Greenhill Friedman(17).

Most malformations probably result from complicated interactions between genetic predispositions and subtle factors in the intrauterine enviroment "Fraser 1959"(15).

Wilson "1959" had been outlined these principles:

1. The susceptibility of an embryo to a teratogen depends upon the developmental stage at which the agent is applied. All organs and systems seem to have an early a susceptible period in the differentiation of their primordio and decreases as organs formation advances and become neligible after organogenesis is substantially completed.

2. Each teratogenic agent acts on a particular aspect of cellular metabolism, therefore different teratogenic agents, tend to produce different effects although acting at the same period of embryonic development and on the same system-moreover the same agent may produces different effects when acting at different stages of embryonic development.

3. The genotype influences to a degree of the animal's reaction to a teratogenic agents, therefore both a genetic predisposition and a teratogenic agents are required to produce an anomaly.

4. An agent capable of causing malformations also causes an increase in embryonic mortality.

5. Teratogenic agent needs not to be deleterious to the maternal organism. Subclinical maternal rubella may

leads to congenital malformations. Pritchord Mac Donald "30".

All the proven specific teratogens probably account for less than 5% of all anomalies of human development "Lowe, 1973" (24).

THE AIM OF THE THESIS.

1. The evaluation of the etiology of the congenital malformations as regards the heridietry factors or the diseases complicating pregnancy, drugs, X-Ray and other factors affecting fetal growth.

2. Evaluating the methods of Diagnosis either the modern methods or the old one.

3. Enumerating the methods of prevention in the future. and Management of cases antenatal and postnatal.

4. Comparison our statistical analysis with other countries.

AETIOLOGY

Malformations present at birth have a varied aetiology. Aminiority appear due to purely enviromental factors such as Fetal infection or teratogenic drugs, aminiority are due almost entirely to genetic factors such as chromosome anomalies or mutant genes of large effect, most whoever, the types of malformation with a relativily high incidence are probably due to a complex interaction of genetic predisposition and enviromental triggers. (Carter C.O.(6).

A) Malformation due to chromosome anomaly:

1. Non-disjunction:

In particular chromosome non-disjunction, "the failure of members of a chromosome pair to spearate at cell division. "during the formation of ovum or sperm, is common. The effect is the production of an ovum or sperm, with one missing, or extra chromosome. The zygot in turne will have one missing chromosome "monosomy" or one extra chromosome "triosomy".

For example, non disjunction of the sex chromosome pair at the first or second stages of meiosis may lead to zygotes with monsomy for a single X-chromosome, called the XO genotype, or triosomy for the sex chromosomes in the form of XXX or XXY genotype-similarly non-disjunction, at the second meiotic division, of the Y chromosome may produce the XYY genotype.

Most zygotes with the XO genotype abort-and this genotype is one of the most common found in early spontaneous abortions. Those XO fetuses that reach term, about 3 in 10,000 female births, have some or all of the congenital malformations characteristic of Turner's syndrome. There is probably no fetal loss with the trisomies of the sex chromosomes, and a little over 1 in 1000 Females have the XXX genotype and about 2 per 1000 of males the XXY genotype, but neither of these have any striking incidence of structural congenital malformations.

- No estimation is yet available of the population incidence XYY genotype.
- No complete monosomies of the autosome are viable. Most trisomes of the autosomes are also non-viable and abort, but about 2 in 1000 fetuses which reach term have a trisomy of chromosome 21 and have Down's syndrome "Mongolism". Appreciable fewer, perhaps 0.3 in 1000 have trisomy of chromosome 18, and a simillar number of trisomy 13. as with trisomy 21,13 and 18 are characterized by a specific syndrome of malformations Patau and Edward's syndrome respectively.

A striking feature of the Trisomic genotypes is that they occur with increasing frequency as maternal age increases . The reason for this maternal age effect has not yet been found. Elliot E. Phillipp (12).

2. Structural change:

Syndromes may also occur due to the absence of part of a chromosome or the presence of extra charmosome material followed by loss of chromosome material, or by anomlous rejoining of raw ends. There being neither gain nor loss but only rearrangement of chromosome material and so no clinical effects are produced. The best known example is an interchange between a 14 and 21 chromosome to give a chromosome with most of the material of both the 14 and 21 chromosomes-such individual may form germ cells:

- With normal 14 and 21 chromosomes, giving a normal zygote.
- With normal 14 and no 21 chromosome giving not viable zygote.
- With the 14/21 translocated chromosome, giving a zygote witch develops into clinically normal individual but with the same genotype as the parent.
- With the 14:21 and a 21 chromosome which since on extra 21 chromosome is present gives a zygote that develops into a child with Down's syndrome. A woman carrying a 14/21 translocation appears to have about a 1 in 5 chance-where the pregnancy goes to term of having a child with Down's syndrome.

The Load of chromosomal anomalies:

Most of the abortions associated with chromosome anomalies are due to fresh mutations. "Usually non-disjunction" and is only rarely that repeated abortions can be attributed to a balanced chromosome interchange in one or other parent.

Malformations due to gene mutations:

1. The Nature of gene Mutation:

Gene mutations, unlike chromosome mutations, are not visible under the microscope. The most likely effect of the base change in a structural gene is to substitute one amino-acid for another in the peptide. The effect of a gene mutation is, then essentially a single specific chemical change. The most typical conditions due to mutant genes are the haemglobinopathies and in born errors of metabolism such as phenylketonuria, amaurotic family idiocy and galactosaemic., mutant genes no doubt by similar mechanisms, may also produce anomalies which may be classed as malformations.

If the protein product of the gene is required for structural development a mutation in that gene will cause malformation. Gene mutations are individually much rare than chromosome mutations. There are however, a great many genes that may mutate and it is estimated that about

1 live-born child in 100 is affected by conditions, however, do not involve congenital malformation.

3. Dominant, Recessive and X linked conditions:

When a gene mutation first occurs in a germ cell, the zygote will nearly always receive anormal gene on the corresponding chromosome coming from the other germ cell- the zygote is then said to be heterozygous for the mutant gene. If this heterozygous state causes clinical abonrmality the condition so caused is called a dominant condition.

Clinical abnormality occurs only when zygotes are formed homozygous for the mutant gene because both parents happen to be heterozygous for that mutant gene, and increased if they are blood relatives. Recessive mutants genes build up in the population to relatively high frequencies, most individuals are heterozygous for one or more such genes.

Mutant genes on the X-chromosome have the special feature that since males have only one X-chromosome a boy or man will be clinically affected if this X-chromosome carries the mutant gene. A woman however may be heterozygous for the gene and in many instances such heterozygoutes will be clinically liffle affected.

Examples of straight forwards dominant congenital malformations are:

Classical a chondroplasia - mandiblafacial dysostosis-acrocephalosyndactyly "Apert's syndrome" - cleidocranial dysostosis, polydactyly and brachy dactyly, polycystic kidney of the type which usually does not cause renal failure till a dult lif - subvalvalar aortic stenosis, cleft lipcleft palat - congenital cataract.

Straight forward recessive congenital malformations include:

Congenital deafness - severe microcephaly - infantile polycystic kidney with cysts in the liver.

Straight forward X-linked congenital malformations include:

- Congenital hydrocephalus due to aque duct stenosis, anhidrotic congenital ectodermal dysplasia - Albright's hereditary osteodystrophy, megalocornea one form of microphthalmia, and mal pseudohermaphrodism due to testicular feminization syndrome.

Patau, Smith (28)

More complex Determination of Common Malformations.

Of the conditions simply genetically determined described above only Down's syndrome, spina bifida cystica and anencephaly, cardiac malformations - "If these are considered as a whole" cleft lip with or without cleft plate, talipes equinovarous, congenital dislocation of the hip and infantile pyloric stenosis are considered a common malformations.

The best evidence that both genetic and enviromental factors are concerned in the atiology of these common malformations comes from twin studies. For example, a large scale twin study from southern Germany showed that only 25% of the monozygotic twins of patients with talipes equinovarus were similarly affected. So the intra-uterine enviromental factors must be important, but that an even smaller proportion of like - sexed dizygotic twins were also affected, so that genetic factors must also be important in the aetiology of the condition. The same situation applies for congenital dislocation of the hip- pyloric stenosis and cleft lip ± cleft-palate.

Nosatisfactory twin studies for neural tube or cardiac malformations are yet available. Large scale family studies support the hypothesis that these common malformat-