A STUDY ON SERUM LIPIDS AND LIPOPROTEINS PATTERN IN DOWN'S SYNDROME

THESIS

Submitted For Partial Fulfilment for
The Master Degree of Pediatrics

BY

ALI ABDEL FATTAH ABDALLAH
M.B., B.Ch.

Supervisors

Dr. RABAH M. SHAWKY
Prof. of Pediatrics

Dr. ALI KHALIFA ALI
Assist Prof. of Biochemistry

Dr. NAGIA MOUSTAFA BAHGAT
Lecturer of Pediatrics

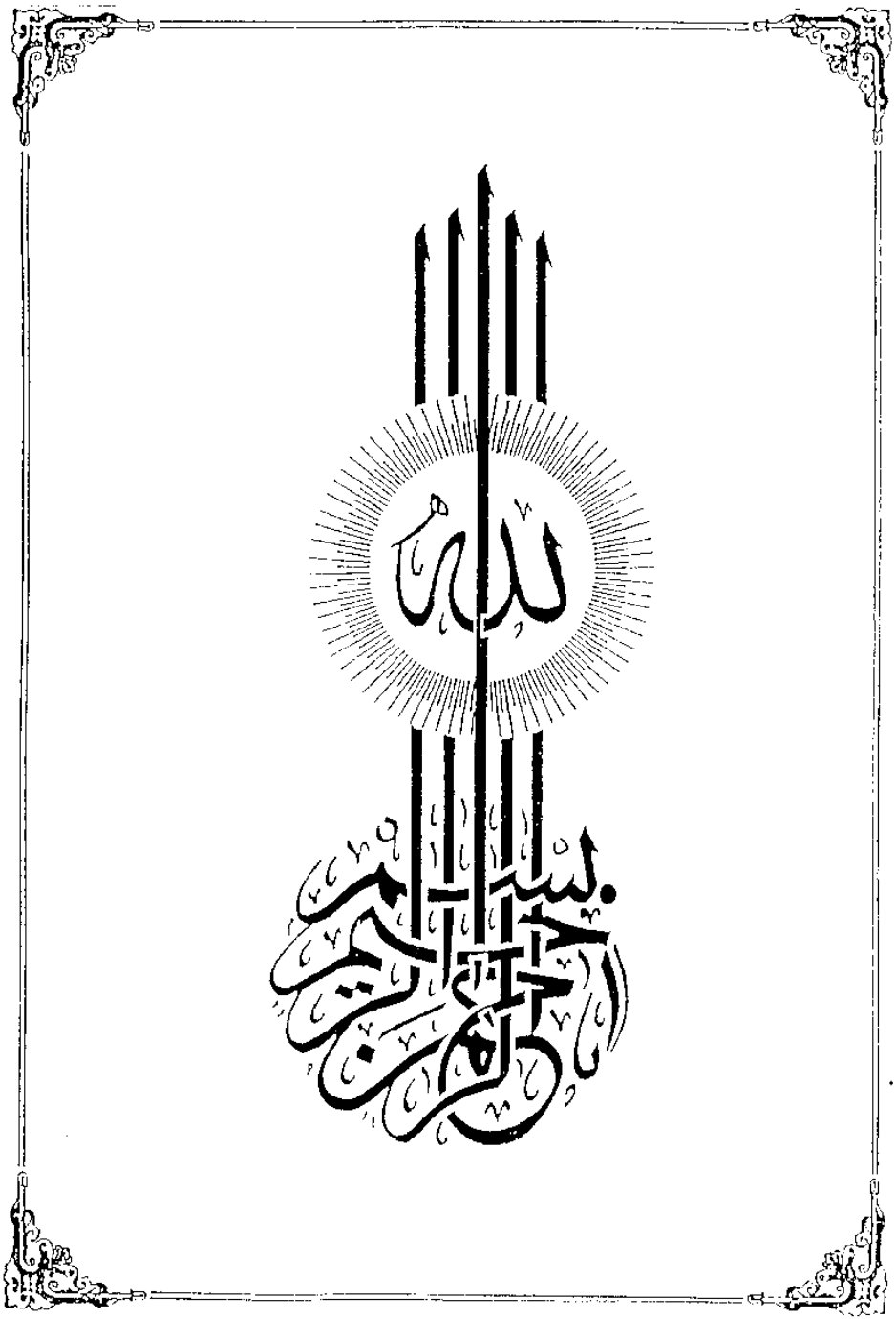
FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

1985

وقل رب زدني علما

صدق الله العظيم

سورة طه آية ١١٣



CONTENTS

ACKNOWLEDGEMENT

I am greatly honoured to express my sincere gratitude to Dr. **RABAH MOHAMED SHAWKY**, PROFESSOR OF PEDIATRICS, Faculty of medicine, Ain Shams University, for her very valuable supervision, fruitful guidance and kind help throughout the course of the work.

I would like to express my sincere thanks to Dr. **ALI KHALIFA ALI**, assistant professor of Biochemistry, Faculty of medicine, Ain Shams University, for his kind care. He gave me much of his unlimited experience in scientific research which helped me to perform the practical part.

I wish to express my sincere thanks to Dr. **NAGIA MOUSTAFA**, Lecturer of pediatrics, Faculty of medicine, Ain Shams University, for her kind care enabling me to complete this work.

I will always remeber the kind help and encouragement of Dr. **MOUSTAFA EL-RASSED**, Lecturer of Biochemistry, Faculty of medicine, Ain Shames University.

INTRODUCTION

Down's syndrome is the most common autosomal abnormality compatible with life. It's importance is indicated by the fact that it accounts, for about 10% of mentally retarded individuals in institutions (abdel-Salam, 1982). It's incidence among live births has been estimated as one in 700 births (Smith and Berg, 1976).

The causation of mongolism includes several deviations from normal chromosomal mechanisms such as primary and secondary non-disjunction of chromosome number 21, translocation involving chromosome number 21, and mosaicism. (Hagemeijer and Smit, 1977).

Various predisposing factors have been accused in this syndrome among these is the role of maternal age in non-disjunction type which is age dependent type (Abdel-Salam et al., 1979).

There is deviation of biochemical , pharmacological and metabolic processes in patients with Down's syndrome. (Kucera, 1969).

Mongoloids have been reported to differ from other patients with mental retardation and from healthy controls by being virtually free of atherosclerosis. (Salo et al., 1979).

AIM OF THE WORK

the aim of this work is to study pattern of lipids and lipoproteins among children with Down's Syndrom in comparison with that of a healthy control group to detect any possible metabolic error.

This work will include:

- Full history and clinical examination of twenty children with Down's syndrome and ten children as control group.

- Estimation of serum lipids and lipoproteins in each group.

Down's syndrome

Terminology:

Down's Syndrome is one of the commonest trisomies compatible with life (Abdel-Salam, 1967). It's importance is indicated by the fact that it accounts for about 10% of mentally retarded individuals in institutions (Abdel-Salam, 1982). The first description of this trisomy was given by "Langdon Down" in 1866 while classifying some mental defectives on an ethnic basis and named it "Mongolian idiocy a term which remained until the discovery of the chromosome abnormalities by Lejune 1959. The disease is now Called Down's syndrome but others prefer the more precise term of 21 trisomy. (Grouchy and Turleau, 1983)

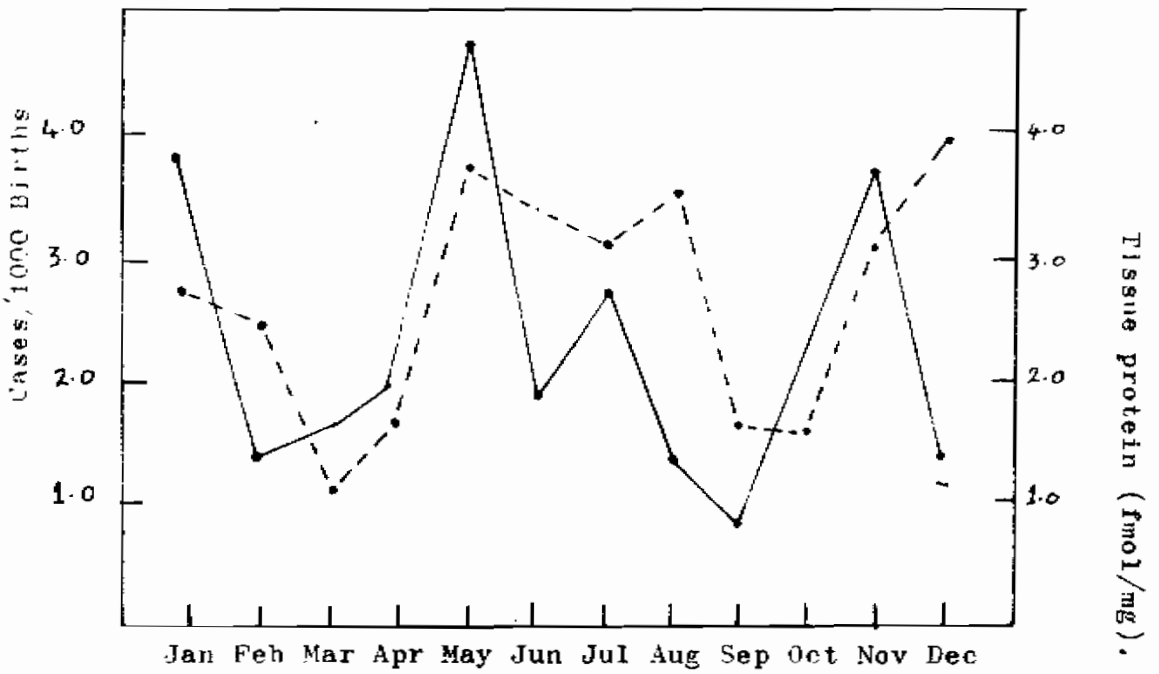


Fig.(2) Changing monthly rate of conception of foetuses with Down's syndrome(Broken line) compared with monthly variation in oestradiol receptor levels in mammary tumour(Solid line).
"Adapted from Janerich and Jacobson,(1977)."

Epidemiology:

Incidence:

The incidence of 21 trisomy is 1.45 per 1000 or about 1 for every 700 births. It will however tend to change slightly with the development of prenatal diagnosis (Smith and Berg, 1976). Adams (1981), made a study on the effect of maternal age distribution on Down's syndrome incidence in the united states, with prediction of the potential impact of prenatal diagnosis, among women 35 years and older. He found that if 50% of women 35 years and older had prenatal diagnosis, the predicted drop in the crude incidence would be about 10%. So, the most common indication for prenatal diagnosis remains advanced maternal age because of its associated increased risk for offspring with autosomal trisomy (Hamerton and Simpson, 1980).

The incidence of Down's syndrome rises continually with maternal age, as illustrated in Fig. 1. After the age of 35, the rise becomes increasingly rapid (Kelley, 1974).

In Egypt, there is a high prevalence of paternal consanguinity with an expected high level of chromosomal aberrations. The prevalance of Down's Syndrome in Egypt is estimated to 1.2/1000 in general population.

(Abdel-Salam, 1967).

Sex ratio:

The sex ratio at birth is 1.24 males to 1.0 female (Bain, 1979).

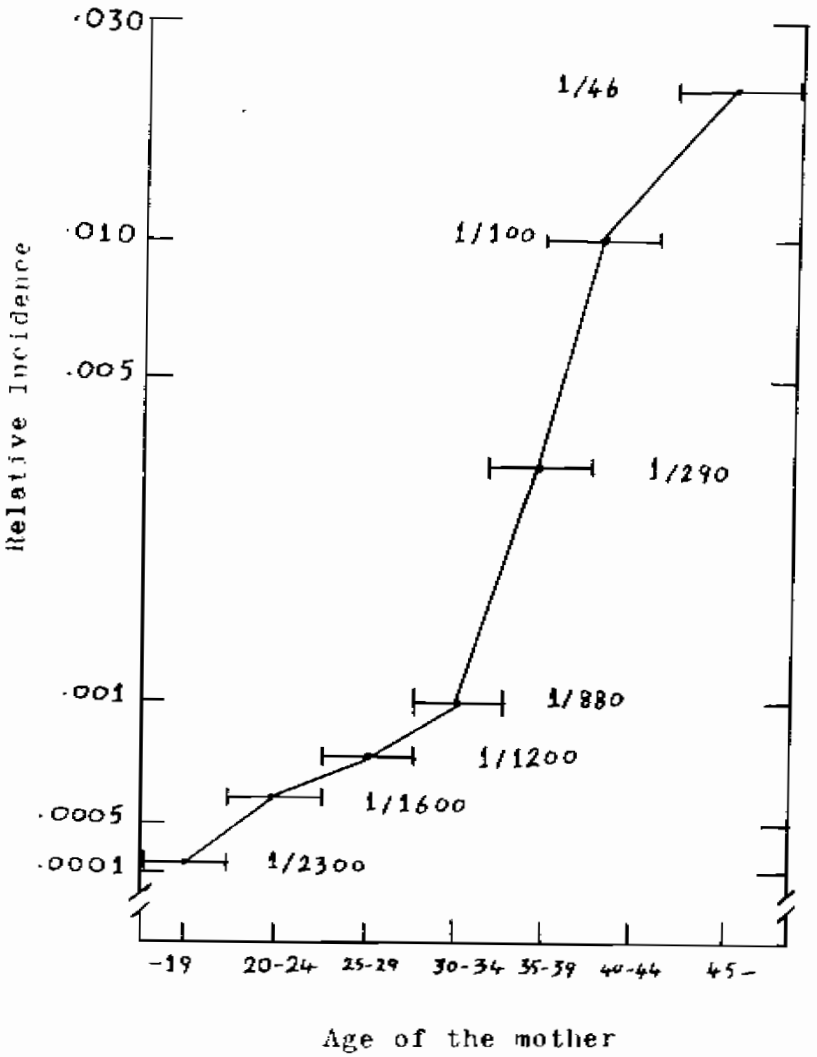


Fig.(1) Incidence ofDown's syndrome at birth according to age of the mother, from a survey of 780,168 births.
"Based on data from Collmann, and Stoller, Am. J. Public health 52:813, 1962."

Seasonality:

There is a strong bimodal seasonal trend in the birth incidence of Down's syndrome that indicate minimum rates of Down's syndrome conceptions in early spring and early autumn. The explanation of this seasonality is the status of mother's endocrine system during the meiotic divisions which take place just before conception. The evidence for this conclusion were: first, exogenous hormones as contraceptive pills taken by the mother before pregnancy can cause chromosome abnromalities in the zygot; and second, seasonal tissue changes occur in the oestrogen target cells of the female endocrine, these changes coinciding seasonally with the conception of foetuses with Down's syndrome. Fig 2 shows a plot of the months of conception of Down's syndrome cases from Harlap's report superimposed on monthly plot of oestradiol-receptors level from human mammary-tumour tissue. (Janerich and Jacobson, 1977).

Races and Goegraphical Distributions:

It is found in all racial groups and in all areas of the world with limited variability (Fabia and Drolette, 1970).

Aetiology:

The maternal age effect is a well known aetiological factor. Mean maternal age is 34.4 years as compared to 28.2 years in the general population. The distribution curve of maternal ages Fig 1 shows a first peak near 28 year which corresponds to the peak for all births and includes most sporadic or inherited translocations. A second peak at 36 to 37 years is responsible for the strong correlation with maternal age. The biological

basis of the maternal age effect is far from being understood. Many mechanisms have been suggested, such as delayed fertilization and ageing of the ovum, but non is entirely convincing (Grouchy and Turleau, 1983).

Paternal age has always been considered of no aetiological importance (Hook, et al . 1981), although Magenis, (1977), suggested that most cases of Down'ssyndrome result from an error in the first meiotic division in the mother , but a significant proportion were paternal in origin.

Other factors have been suggested, such as oral contraceptives, or gene mutations favouring non-disjunction but their true importance is still a matter of debate(Alfi, et al ., 1980). Another factor have been suggested such as maternal radiation exposure. (Alberman, et al ., 1972).

Cytogenetics of Down's syndrome:

It is now generally acknowledged that every patient with Down's syndrome has the supernumerary chromosome either as free trisomy 21, or within a translocation chromosome such as No. 21,22,13,14 or 15. Observations on some rare cases with reciprocal translocation suggest that the distal part of the long arm of chromosome 21, and especially the band 21q,22 is responsible for the characteristic phenotype of Down's syndrome. (Hagemeijer and Smit, 1977).

Free Trisomy 21:

In most cases, 21 trisomy is due to free trisomy which occurs in 92.5% to 95% of cases. It results from non-disjunction during meiosis

in one of the parents, and is correlated with advanced maternal age . Before the age of 33 years, the risk of giving birth to a trisomic child is relatively constant at about 0.9 per 1000 live births. The risk increases to approximately 2.8 per 1000 at ages 35-38,. It then increases steeply to 38 per 1000 at 44 years (Trimble and Baired., 1978).

It has been suggested that there are at least two different origins of non-disjunction. The first would be the same in both sexes and affects both meiotic divisions. The second would be limited to the first meiotic division in the mother (Mattei, et al ., 1979).

Maternal age is the only well documented aetiological factor in free 21 trisomy. Other factors have been suggested such as oral contraceptive or gene mutations favouring non-disjunction but their true importance is still a matter of debate (Alfi et al ., 1980).

Translocation in Trisomy 21:

In minority of cases, 21 trisomy is due to a translocation which occurs in 4.8% of the patients (Giraud and Mattei, 1975). Translocations can either appear de novo in the trisomic newborn, or be transmitted from one of the parents. These translocations are essentially centric fusion or Robertsonian translocations and occur between a 21 and a D-group chromosome, usually a 14 [t(14q 22q], or another 21[t(21q 21q]. When the translocation is transmitted, maternal age has no effect (Grouchy and Turleau, 1983).

The chance that a translocation once found will prove familial depends

n the type of translocation; about 40% of D/21 and only 8% of G/21 translocations re familial (Wright et al., 1967).

own's Syndrome Mosaicism:

Down's syndrome mosaicism represents about 2-3% of 21 trisomy cases. t is usually expected when the phenotype is not fully expressed or when he I.Q. is higher. Mosaicism cases result from mitotic non-disjunction fter the first cleavage in either a normal or 21 trisomic zygote by anaphase ag . (Kohn, et al 1970).

Usually two cell lines are detected, one normal and one with 21 trisomy. he relative proportions of these cell lines may vary according to the issues examined. It is considered that mosaicism is a postzygotic event ccuring after fertilization. (Grouchy and Turleau., 1983).

While it is frequently assumed that the extra chromosome 21 in mosaic own's syndrome individuals arises from mitotic non-disjunction in a chromosomally ormal zygote, evidence from maternal ages suggest that a large proportion f such cases arise from meiotic non-disjunction (Norio and Tadashi., 984).

amilial Mongolism:

It means the presence of mongolism in 2 or more members of family ither siblings or other close relatives. In two large surveys,a total of 168 families with 2 affected siblings were found (Carter and Evans 1961).