SERUM NONESTERIFIED (FREE) FATTY ACIDS IN PREGNANCY

by

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and

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Introduction

Advancement of pregnancy is accompanied by the extra demand of energy. An adjustment of the subject to this increased energy demand is accomplished by enhancing the mobilization of glucose from glycogen and lipids in the form of free fatty acids from adipose tissue or fat depot. The present concept is that lipid is the most important fuel. About 50-70% of the oxygen consumption is accounted for by the oxidation of lipids. The enzymes required for direct oxidation of fatty acids are present in peripheral tissues. The oxidative needs of the brain, however, are supplied by glucose alone.

Free fatty acids exist in plasma primarily as anions, though at the plasma pH 7.4 one would expect to find less than that of 1% of the fatty acids in the undissociated state. The free carboxyl group of this fatty acid is involved in the formation of ester bond, so, this is referred to as non-esterified or unesterified acid.

Mobilisation of the lipid means the net release of free fatty acids from triglycerides, stored in the adipose tissue for transport to other organs of the body.

The presence of free fatty acids in the plasma was first shown by Szent-Gyorgyi and Tominaga in 1924. Kelsey and Longenecker (1941) showed the recovery of free fatty acids from their fractionation of lipids, extracted from the bovine plasma. They observed primarily palmitic, oleic and linoleic acids with small amounts of stearic, myristic and arachidic acids. Acids which have been identified include saturated acids from C_{10} to C_{18} and also oleic, palmito-oleic, linoleic and longer chain polyethenoic acids; fatty acids of short chain occur in plasma, particularly in that of runinants. In 1947 Davis noted the presence of free fatty acids in human plasma. Free fatty acids were uniformly present in the albumin fractions isolated from human plasma by Cohn and his co-workers (1947).

The amount of free fatty acids pool in adipose tissue which is the resultant of two continuous processes going on, viz. hydrolysis and re-esterification provide the source and determine the free fatty acid level in circulation.

The overall effect of glucose in reducing the free fatty acid level is due to the provision of alpha glycero-phosphate which enhances esterification of free fatty acids, via acyl-Co. A.

This work is from Ph.D. Thesis of Dr. A. V. V. Potnis accepted by Bombay University in February 1971.*

The paper was read at Teaching Pathology meeting held on 25th March 1971 at Seth G. S. Medical College.

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Received for publication on 21-5-1971.

Grossman, *et al*, (1955) reported that the concentration of non-esterified fatty acids in plasma rose from 500 to 700 μEq per litre during periods of alimentary lipemia. The level of non-esterified fatty acids appears to be intimately and inversely related to the level of carbohydrate utilization, being increased in diabetes and depressed after insulin, glucose, fructose or tolbutamide administration. Bierman, *et al* (1957), Dole (1956), Dole (1958). A slow increase in the level of free fatty acids is observed in fasting conditions, Dole *et al* (1957), Gordon and Clerkes (1956). Isotopic tracer experiments with C^{14} tagged palmitic acid indicate that insulin administration decreases the outflow of non-esterified fatty acids from fat (Bierman *et al* 1957). Dole has interpreted so simply the relation between non-esterified fatty acids and glucose utilization by suggesting that carbohydrate utilization inhibits the release of free fatty acids (Dole 1958).

Gorden *et al* (1956) have suggested that free fatty acids by their prompt responses in the changes in carbohydrate utilization provide for "caloric Homeostasis".

Burt (1960) has noted the elevation of free fatty acids at the 33rd week of normal gestation and in the third trimester. The study of free fatty acids is undertaken to have a better understanding of the importance of this lipid fraction during normal gestation and at the time of delivery.

Material and Methods

Majority of subjects were selected from the patients attending antenatal clinic of Dr. B. N. Purandare's Maternity Hospital and the rest of the patients were selected from patients attending K. E. M. Hospital and Wadia Maternity Hospitals. Subjects were classified according to their trimesterwise gestational period.

Normal non-pregnant control group included 50 healthy cases belonging to medium socio-economic class and having normal menstrual function with no evident hormonal deficiency.

Thirty cases in the first trimester, 31 cases in the 2nd trimester and 51 cases in the 3rd trimester in normal pregnancy were studied. These patients had systolic pressure 130 mm of Hg. or less and diastolic pressure 100 mm Hg or less. Cases of anaemia and threatened abortion were excluded. The symptoms of nausea and vomiting was observed in two thirds of cases in the 1st trimester and the incidence of glycosuria was recorded at the onset of 3rd trimester.

Thirty cases of pre-eclamptic condition were studied who had high blood pressure (systolic pressure 140 mm of Hg. or more and diastolic pressure 100 mm of Hg or more than 100 mm). Patients had oedema on feet and on body and albuminuria was observed. Fasting blood samples were collected from above patients and the sera were separated. Serum free fatty acid estimations were done according to the method of Fredrick and Mossinger.

Results

Table I represents serum non-esterified fatty acids in normal gravidas pre-eclamptic conditions and in normal non-pregnant control group. Though the fall in first trimester is not significant, yet there is a definite decrease in level. (577.4 μEq/L) than the normal non-pregnant control group. (593.3 μEq/L). The progressive rise in level is observed from 2nd trimester to the third trimester. In pre-eclamptic group, the level is much elevated (1184.2 μEq/L). All differences except

TABLE I

Serum Non-esterified Fatty Acids (Free Fatty Acids)

Group	Normal Non-pregnant	1st Trimester	2nd Trimester	3rd Trimester	Pre-eclampsia
Number of cases	50	30	31	55	30
Serum non-esterified (Free) Fatty Acid μEq/L	593.3	577.4	792.6	948.6	1184.2
Standard deviation (SD)	± 30.3	± 34.20	± 39.9	± 56.8	± 43.6
Standard error (SE)	± 4.30	± 6.24	± 7.17	± 7.66	± 7.9
Co-efficient of variation	± 5.1	± 5.9	± 5.0	± 5.9	± 3.6

Except between first trimester and normal non-pregnant groups, all differences ($P < 0.001$) are significant as the standard errors are very small compared to the differences observed.

in 1st trimester and in control group are statistically significant ($P < 0.001$).

Table II represents the t-test for significance.

TABLE II

t-Test for Significance (Non-Esterified Fatty Acids)

Group Difference	t	df	Probability
Normal non-pregnant — 1st trimester	2.097	78	N. S.
Normal non-pregnant — 2nd trimester	23.840	79	<0.001
Normal non-pregnant — 3rd trimester	40.375	103	<0.001
Normal non-pregnant — pre-eclampsia	64.934	78	<0.001
1st trimester — 2nd trimester	22.652	59	<0.001
1st trimester — 3rd trimester	37.877	83	<0.001
1st trimester — pre-eclampsia	60.079	58	<0.001
2nd trimester — 3rd trimester	14.857	84	<0.001
2nd trimester — pre-eclampsia	36.598	59	<0.001
3rd trimester — pre-eclampsia	11.04	83	<0.001

N.S. = Not Significant.

Dicussions

The trimesterwise study of serum non-esterified fatty acids is done in the present work in normal gestation and pre-eclamptic conditions and the values are compared with normal non-pregnant control group. Many of the observers have studied the non-esterified fatty acids just before and after parturition. They have reported the elevation of free fatty acids at the time of delivery but the etiology of this elevation is not explained.

Patil *et al* (1965) have done the work on 23 mothers who had full term normal deliveries and have compared the results with 32 normal non-pregnant women and 18 men. Their results both for control non-pregnant group and last trimester agree with our results. Nelson *et al* (1966) state that maternal blood at delivery, when the non-esterified fatty acids

are dramatically elevated, contains about 3% of its lipid as non-esterified fatty acids. They further state that this suggested "that non-esterified fatty acids play an integral part in placental lipid metabolism and perhaps the non-esterified fatty acids is supplying a significant portion of the energy requirements of the placenta.

Fabian *et al* (1968) have investigated the level of plasma free fatty acids and the activity of the heparin activated plasma lipolytic enzymes in a group of 21 women towards the end of pregnancy, between 33rd and 38th weeks. The results were compared with 10 non-pregnant women. The level of plasma free fatty acids before delivery noted by these workers were 704 ± 140 μEq/L while the level of free fatty acids for non-pregnant group determined was 502 ± 151 μEq/L.

In the present studies even if there is not a significant fall in serum non-esterified fatty acid value in the first trimester 577.4 ± 34.20 μEq/L) from that of non-pregnant control group (593.4 ± 30.4 μEq/L), yet there is a definite decrease in non-esterified fatty acids level in the first trimester. This decrease might be attributed to the vomiting which is usually observed in the first three months of pregnancy.

The symptom of vomiting, accompanied by nausea creates a semistarvation state. Continuous or frequent vomiting will lead to the condition of starvation. Starvation metabolism should be given due consideration and is one of the etiological factors for the decrease of non-esterified fatty acids in the first trimester of pregnancy. Because of starvation, the carbohydrates will not be in sufficient amount to supply the energy to the tissue. As the role of free fatty acids (non-esterified fatty acids) is to supply the energy to tissue cells, the free fatty acids are utilised in providing energy to the tissues, resulting in lower levels of non-esterified fatty acids level in the blood. After the first trimester, there is a rise in free fatty acids level until term.

The rate at which the fatty acids are released from tissues and the rate at which they are utilised by body tissues, determines the level of non-esterified free fatty acids. Non-esterified fatty acids in circulation have a half time of only a few minutes and, therefore, their concentration responds almost immediately to any change of turnover rate. Elevation of free fatty acid during pregnancy is probably because of reversion of albumin and globulin ratio. Free fatty acids fraction is carried with albumin and when less albumin is available, less of free fatty acids, are seen in combined form, with the result that free fatty acid level is elevated in circulation.

The present studies have noted a high value of (1182.2 ± 43.6 μEq/L) non-esterified fatty acids in pre-eclamptic conditions ($P < 0.001$). Thus it suggests that estimation of serum non-esterified fatty acids will be the diagnostic and prognostic test in addition to other clinical manifestation which occur during toxaemic conditions. The elevation of non-esterified fatty acids might be the natural compensation of energy which the mother requires at the time of parturition.

In protracted labour, prolonged first and second stages, lead towards starvation stage accompanied by vomiting.

During prolonged labour the excessive increase in non-esterified fatty acids may have an adverse effect on the intensity and rhythm of the uterine contractions, rendering them less effective and thus prolonging labour.

Summary

1. Estimation of serum non-esterified fatty acids were carried out in normal

gravidas during first, second, and third trimesters and in pre-eclamptic cases in the third trimester. The results are compared with normal non-pregnant control group.

2. A definite fall in level is observed in the first trimester of normal gravidas from that of control group. This fall is attributed to vomiting in the first trimester.

3. Progressive rise in level is observed from second trimester until term. Level of non-esterified fatty acids is considerably elevated in pre-eclamptic group ($P < 0.001$).

Acknowleldgements

The authors wish to thank the Dean, Seth G. S. Medical College and K. E. M. Hospital for the facilities extended to them.

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