

MATERNAL PLASMA HOMOCYSTEINE LEVEL, 24-HOUR URINARY PROTEIN AND HAEMOGLOBIN IN PRE-ECLAMPTIC PATIENTS: IS THERE ANY RELATIONSHIP?

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Background: Anaemia is very common in developing countries especially during pregnancy. Hyperhomocysteinaemia can result from genetic or nutrient-related disturbances in the transsulfuration or remethylation pathway for homocysteine metabolism. Inadequate intake of vitamin B₁₂, B₆ or folate may underlie some cases of elevated homocysteine levels. The aim of this study was to investigate the possible relationship between plasma homocysteine level, haemoglobin level and 24-hour urinary protein in pre-eclamptic patients. Folic acid deficiency is one of the major causes of hyperhomocysteinemia which is one of the major risk factor for pre-eclampsia [PET]. Severe proteinuria of several grams/day occurs in pre-eclamptic toxemia.

Methods: A cross-sectional comparative study was carried out on 90 primigravida attending the "antenatal clinic" of Services Hospital, Lahore. Out of these 60 primigravida 30 were mildly pre-eclamptic and 30 were severely pre-eclamptic at 30-38 weeks of pregnancy. 30 primigravida [30-38 weeks of pregnancy] having uncomplicated pregnancy were taken as control.

Results: The results show that in mild PET and in severe PET, the plasma homocysteine level shows a significant relationship with 24-hour urinary protein and haemoglobin level.

Conclusion: Anaemia [folic acid deficiency] is one of the important risk factor in the causation of hyperhomocysteinemia which is one of the major chronic risk factors for eclampsia.

Keywords: Hyperhomocysteinemia, anaemia, mild PET, severe PET.

Introduction

Anaemias of diminished erythropoiesis are caused by an inadequate supply of some substances to the bone marrow which are necessary for erythropoiesis. The most common deficiencies are those of iron, folic acid and vitamin B₁₂. It is essential that 10% of the population in developed countries and as much as 25-50% in developing countries are anaemic. Iron deficiency accounts for most of this prevalence. Increased demands not met by normal dietary intake occur around the world during pregnancy and infancy. When iron deficiency develops there is a decrease in circulating iron, with a low level of serum iron and a rise in serum transferrin iron binding capacity. Ultimately, the inadequacy makes its impact on haemoglobin, myoglobin and other iron compounds.

There are two principal types of megaloblastic anaemia. One caused by a folate deficiency and another caused by lack of vitamin B₁₂. These anaemias may be caused by a nutritional deficiency [folic acid] or may result from impaired absorption [vitamin B₁₂]. Both of these vitamins are required for DNA synthesis and hence the effect of their deficiency on erythropoiesis are quite similar. High risk of clinically significant folate deficiency associated with poor diet

and increased metabolic needs [as in pregnant woman and patients with chronic haemolytic anaemias]. Inadequate levels of vitamin B₁₂ or cobalamin in the body results in pernicious anaemia. The metabolic defects induced by vitamin B₁₂ deficiency are intertwined with folate metabolism. Vitamin B₁₂ is required for recycling of tetrahydrofolate and hence its deficiency reduces availability of the form of folate that is required for DNA synthesis. Both folate and vitamin B₁₂ deficiency give rise to megaloblastic anaemia.¹ So iron deficiency, folic acid deficiency and vitamin B₁₂ deficiency lead to anaemia and all these deficiencies are common in developing countries especially in pregnancy when metabolic demand is increased.

Homocysteine, a sulfur containing amino acid is an intermediate product of methionine metabolism. It is metabolized through the pathways of transsulfuration and transmethylation.² In transmethylation pathway methionine can be regenerated by the transfer of methyl group to homocysteine from N 5-methyltetrahydrofolate, a reaction catalyzed by homocysteine methyltransferase (methionine synthase). The co-enzyme that mediates this transfer of a methyl group is methylcobalamin derived from vitamin B₁₂.

In transsulfuration pathway, homocysteine is an intermediate in the synthesis of cysteine.³ Hyperhomocysteinaemia means increased concentration of homocysteine and it indicates that homocysteine metabolism is compromised causing the export mechanism to remove excess of homocysteine in tissue to blood.⁴ Inadequate intake of vitamin B₁₂, B₆ or folate may underly some cases of elevated homocysteine levels.⁵

Hyperhomocysteinemia is associated with cardiovascular and cerebrovascular diseases as well as recurrent miscarriages, placental abruption, pre-eclampsia, intrauterine growth restriction and perinatal death.⁶

Pre-eclampsia is pregnancy induced hypertension which includes a triad of clinical signs and symptoms, hypertension, proteinuria and pathologic edema.⁷ It is demonstrated that elevated levels of maternal plasma homocysteine are present in pre-eclampsia. Elevated maternal plasma homocysteine plays a role in the pathogenesis of vascular disease in the uteroplacental circulation in placental insufficiency.

This role may be locally limited to the placenta when only fetal manifestations are present. In severe pre-eclampsia the role may be extended throughout the maternal vascular tree.⁵

The aim of this study was to investigate the possible relationship between plasma homocysteine level, haemoglobin level and 24-hour urinary protein excretion in mildly pre-eclamptic primigravida and severely pre-eclamptic primigravida.

Materials and Methods

Following approval by the Local Ethical Committee and patients informed written consent sixty pre-eclamptic patients were included in the study. This cross-sectional comparative study was carried out at Services Hospital, Lahore. Patients were recruited from those attending the "antenatal clinic" and admitted in the "antenatal ward and labour room" of the Services Hospital, Lahore between July 2003 to January 2004.

Out of the sixty pre-eclamptic patients thirty patients were of mild pre-eclampsia and thirty patients were suffering from severe pre-eclampsia. All the patients were primigravida and were analyzed in the third trimester of pregnancy (30-38 weeks of pregnancy). All the patients were taking vitamin supplementation irregularly with no history of essential hypertension, diabetes mellitus and jaundice. An initial interview by a specialist (in Gynaecology Department) determined the subjects suitability for the trial. Inclusion and exclusion criteria were applied at the interview.

A recent blood sample and urine sample were sent to the laboratory for urine analysis, blood sugar level, serum creatinine level and liver function test to exclude renal disease, diabetes mellitus and liver disease.

Twenty-four hours urine was collected according to the standard instructions to the subjects. At the end of each 24-hour collection period, the subjects were asked to empty their bladder completely. 24 hour urinary protein estimation was done by Randox Kit Method.

Inclusion Criteria

For mild pre-eclampsia.

1. Primigravida (30-38 weeks of pregnancy)
2. A diastolic blood pressure 90-100mm Hg and a systolic blood pressure at or above 140mm Hg on at least 2 occasions 6 hours apart.
3. Significant proteinuria more than 300 mg/24 hour.

For severe pre-eclampsia.

1. Primigravida (30-38 weeks of pregnancy)
2. A diastolic blood pressure more than 110mm of Hg on at least 2 occasions 6 hours apart.
3. Significant proteinuria of 4 gram/24 hour or more with any signs and symptoms of impending eclampsia.

Exclusion Criteria

1. Essential hypertension
2. Renal diseases
3. Diabetes mellitus
4. Jaundice

Each patient was given a full explanation of the study and after taking informed consent a 5ml venous blood was obtained from antecubical vein of patient into vacutainer tubes containing tripotassium EDTA (for preparation of plasma) after an overnight fast. The plasma was removed within an hour and stored at -20°C until analyzed for homocysteine.

Plasma total homocysteine level was estimated by a Bio-Rad enzyme linked immunoassay (EIA), microtiter method.

Statistical Analysis

All mean values were expressed as mean \pm standard deviation (SD). Values of various groups were compared using analysis of variance [ANOVA]. Students "t" test was used to compare means with two categories of study variables. Statistical analysis was carried out using the SPSS® (Statistical Package for Social Sciences), software version 10 for

relationship with eclampsia because haemoglobin level is decreased in eclampsia group as compared to control group. So plasma homocysteine level mean 24-hour urinary protein, haemoglobin level and eclampsia have a significant relationship with each other.

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