Dermatology Section

Assessment of Nailfold Capillaroscopy Findings in Pregnant Women having Preeclampsia: A Research Protocol

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ABSTRACT

Introduction: Pregnancy causes significant vascular and cutaneous changes in a woman's body. Preeclampsia is one of the life-threatening conditions associated with high blood pressure and proteinuria after the 20th week of pregnancy. It can cause placental hypoperfusion and placental insufficiency, leading to foetal defects or, in severe cases, foetal loss, which can be prevented by early diagnosis and treatment. There are many ways to observe and study the microcirculation non invasively the safest and most accessible method is nailfold capillaroscopy. Nail-fold Video Capillaroscopy (NVC) is a hand-held digital microscope used to observe the microcirculation at the nailfold of the hands. Thus, comparing the capillary status with healthy subjects will help establish an early diagnosis and manage cases to prevent further complications in the mother and newborn.

Need of the Study: The pathophysiology states that preeclampsia is related to systemic endothelial dysfunction, causing the release of Tumour Necrosis Factor (TNF) alpha, a proinflammatory mediator, leading to hypoxia of the placenta and the loss of endothelial cell-lined capillaries. Thus, there is a need to find if there is an established correlation in association of decreased Capillary Density (CD) in individuals with preeclampsia. Although evidence supporting a link between decreased CD and preeclampsia is limited, timely assessment and prevention are crucial. Nailfold capillaroscopy, an accessible and non invasive imaging method, holds promising calibre for understanding microvascular changes in preeclampsia. This could facilitate post-conception monitoring and early interventions to identify and address circulatory issues in affected women with preeclampsia.

Aim: To study and compare the nailfold capillary changes in women diagnosed with preeclampsia and women having normal and uneventful pregnancies.

Materials and Methods: A comparative cross-sectional study will be done in the Outpatient Department (OPD) and Inpatient Department (IPD) of Obstetrics and Gynaecology and the Outpatient Department of Dermatology at AVBRH Sawangi Meghe, Wardha, Maharashtra, India, from March 2023 to March 2025. A total of 150 pregnant women will be considered in the study, with 75 women being normal pregnant women (controls) and 75 pregnant women diagnosed with preeclampsia (cases). In order to confirm the gestational age of the patients, fundal height and abdominal circumference measurements will be taken. Demographic data, Basal Metabolic Index (BMI), weight gain during pregnancy, laboratory reports including Complete Blood Count (CBC), coagulation profile (Prothrombin Time, International Normalised Ratio, Activated Partial Thromboplastin Time), liver function tests, kidney function tests, urine examinations, and serial ultrasonography reports available for the patients will be noted. Pre-examination blood pressure will be recorded and compared with the baseline to confirm the status of preeclampsia after obtaining written consent from the patients. Nailfold capillaroscopy will be performed using a (Dinolite -AF4115ZT) dermoscope equipped with a 200X magnification, high-resolution lens in a non polarised light setting with oil immersion as a fluid coupling. The observations will be used to interpret the results of the study. Results will be calculated for finding differences between the two comparative groups of cases and controls at a p-value of ≤ 0.05.

Keywords: Blood pressure, Gestation, Nailfold microcirculation, Non invasive

INTRODUCTION

Pregnancy involves cutaneous and vascular changes in a female's body. The shift in blood volume and the adaptations required for the growing foetus pose challenges for a mother, as a hypercoagulable state is witnessed from the 8th week of pregnancy itself. Vasoconstriction due to increased sodium concentration, plasma expansion, and retrograde trophoblastic invasion of spiral vessels, especially in the latter half of the first trimester, are the reasons for strong uteroplacental vascular compliance [1]. Preeclampsia is a life-threatening condition in pregnant females associated with high blood pressure ($\geq 140/90$ mmHg) along with proteinuria (urinary albumin ≥ 300 mg/24 hours), usually beginning after 20 weeks of pregnancy. It has a prevalence rate of 5-8% of total pregnancies globally, making it the second leading cause of foetal and maternal deaths [2].

One of the mechanisms that also contributes to preeclampsia is the Capillary Bed (CB), a composite of CDe and Capillary Diameters (CDi), which is lower in the third trimester than in the first trimester, leading to cardiovascular risk [3]. Women who are pregnant and have preeclampsia are twice as likely to be at risk of experiencing cardiovascular problems and three times more likely to experience hypertension in the future [1]. Patients with extreme grades of preeclampsia may present with typical symptoms such as headache, epigastric pain, or visual disturbances, along with signs of uncontrollable high blood pressure, ankle oedema and proteinuria [4]. Preeclampsia is a recurrent pregnancy complication that disrupts placental perfusion and releases soluble factors such as Tumour Necrosis Factor (TNF) α into the bloodstream. As a result, the placenta experiences hypoxia and hypoperfusion. Endothelial dysfunction may also cause symptoms of preeclampsia such as raised blood pressure and maternal and child distress, thus additionally damaging the maternal vascular endothelium, leading to heat stress and multiple organ damage. The risk of Small Gestational Age (SGA) is prevalent in such pregnancies, and the Haemolysis, Elevated Liver Enzymes, Low Platelet Count (HELLP) syndrome is an additional complication in mothers aged 35 years or more [4]. Nailfold capillaroscopy is a Universal Serial

Bus (USB) enabled hand-held device designed to visualise the microvasculature [5] and can be used to observe the changes seen in pregnant women with preeclampsia. It can be done on the patient's bedside with the USB-enabled NVC device; in this case, the Dinolite AF4115ZT is used. Presently, the aim to carry out this research is to study and compare the nailfold capillary changes in women diagnosed with preeclampsia and women having normal and uneventful pregnancies.

Primary objectives: To study the nail vasculature findings in pregnant women with a normal uneventful hypothesis pregnancy and in women with preeclampsia.

Secondary objectives: To compare the nail vasculature findings obtained in women diagnosed with preeclampsia and women with a normal uneventful pregnancy.

REVIEW OF LITERATURE

According to a study by Antonios TFT et al., quantifying the structural rarefaction of skin capillaries in pregnancy is a potentially useful clinical marker for predicting preeclampsia [6]. In May 2022, Armstrong JL from Ontario, Canada hypothesised that preeclampsia is associated with a decline in the number of nailfold capillaries per 1 mm^2 that persists postpartum. These microvascular changes may help identify women at the highest risk for future cardiovascular disease and who may benefit from cardiovascular disease screening, lifestyle modification, and pharmaceutical intervention. There is evidence of functional, but not structural, differences in CD found between women with preeclampsia and pregnant women aged 18 to 40 years with intact capillary concentrators [7]. Thevissen K and Gyselaers W studied NVC in pregnant women with and without cardiovascular risks and concluded that capillary rarefaction precedes the onset of hypertension, becoming the primary phenomenon and can be a positive predictor in the early diagnosis of preeclampsia [8].

The present study represents an early exploration of answering the question of whether capillary changes can be significant in predicting circulatory defects in preeclamptic women and preventing complications. The results derived from previous studies are not clear, possibly due to the preliminary nature of the research and the limited sample size, which further constrains the main findings. Here, we aim to establish a relationship between changes in macro and microcirculations. Preeclampsia is known to increase blood pressure, but its effect on microcirculatory CD remains unclear.

MATERIALS AND METHODS

A comparative, cross-sectional study will be done in the outpatient and inpatient Departments of Obstetrics and Gynaecology and the Outpatient Department of Dermatology at AVBRH Sawangi Meghe, Wardha, Maharashtra, India from March 2023 to March 2025. Written informed consent will be taken from all study participants. Institutional Ethics Committee consent has been obtained (IEC Number: Ref. No. DMIMS (DU)/IEC/2023/742). The Clinical Trials Registry-India (CTRI) trial registration has been done (Trial Registration: Reg No: CTRI/2023/09/057807).

- **Inclusion criteria:** Pregnant patients recruited for the study will be between the ages of 18 and 40 with a singleton pregnancy diagnosed with preeclampsia, a gestational age of 20 weeks or more, and willing to deliver at Acharya Vinoba Bhave Rural Hospital.

- **Exclusion criteria:** Pregnant patients diagnosed with any pre-existing systemic illness such as high blood pressure, diabetes, lupus, kidney disease, gestational diabetes, coronary heart disease, Raynaud's syndrome, scleroderma, arthritis, or collagen-vascular diseases will be excluded from the study. Pregnant patients who are consuming drugs or have a drug history that may interact with or disrupt the study protocol will also be excluded. Additionally, patients with onychophagia,

onychotillomania, or any other nail disease will be excluded from the study.

Sample size calculation:

$n = (Z\alpha/2)^2 \times P(1-P)/ d^2$

Where, $Z\alpha/2$ is the level of significance at 5%, i.e., 95%

Confidence Interval (CI)=1.96

p=Prevalence of preeclampsia. =5 %=5.0=0.05 [2] (prevalence rate of preeclampsia ranging between 5-8% of total pregnancies globally)

d=Desired error of man = 0.05

$n = (1.96)^2 \times 0.005 \times (1-0.05)/(0.05)^2$

n=73

n=75

Hence, two groups will be formed:

Group-A (cases): Patients diagnosed with preeclampsia in pregnancy with a gestational age of 20 weeks or more.

Group-B (controls): Patients with normal, uneventful pregnancies with a gestational age of 20 weeks or more.

A sample size (n) of 75 in each group will be considered, making a total sample size (n) of 150.

Study Procedure

Demographic descriptions such as age, marital status, hypertensive status, Gravida, Preterm, Living child, Abortion (GPLA) score, BMI, and total weight gain during pregnancy will be noted. A detailed blood workup will include laboratory values such as coagulation profile {including Prothrombin Time (PT), International Normalised Ratio (INR), Activated Partial Thromboplastin Time (APTT)}, CBC, liver function test (including Serum Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxaloacetic Transaminase (SGOT), Alkaline Phosphatase (ALP), total bilirubin values), kidney function test values (including urea, creatinine, serum sodium, serum potassium), and urine examination showing microscopy and albumin. Serial ultrasound results available with the patient will also be noted.

The patient will be counselled and explained about the procedure. Written informed consent will be obtained, and the patient will be settled in a sitting/lying position for the examination process. Fundal height, abdominal girth, and blood pressure will be measured. The examination will be conducted at room temperature to exclude additional vasoconstriction. The patient may use acetone to remove the varnish. The appropriate cap on the nail body will be selected, attached to the device, and a small amount of infused oil will be applied to the nailfold of each finger (except the thumb) to improve vision and visibility of capillaries. Nailfold capillaroscopy will be performed using (Dinolite- AF4115ZT) in a non polarised mode with oil immersion as a fluid coupling. The contact angle and direction of the capillary microscope will be manually adjusted to reduce the light according to the observer's perception [9].

Nailfold findings will be evaluated as quantitative findings such as CD (width), mean CD, and qualitative findings such as cross-linked capillaries (sinus or twisted) and capillary morphology, which will combine to form the overall pattern evaluated while examining the capillaroscopic pattern [10,11]. Comparison and assessment of probabilities for the occurrence of circulatory defects will be conducted through statistical analysis.

Outcomes: To evaluate and compare the capillaroscopy results by measuring CD, mean CD, the number of cross-linked capillaries (sinus or twisted), and capillary morphology in both the case and control groups.

STATISTICAL ANALYSIS

All results will be calculated using R Studio software version 3.2. Demographic descriptions such as age, marital status, hypertensive status, GPLA score, and BMI, over the baseline characteristics,

will be tabulated and described by frequency and percentage for categorical data and mean standard deviation for quantitative data such as total weight gain during pregnancy and laboratory values including coagulation profile (PT, INR, APTT), CBC, liver function tests including SGPT, SGOT, ALP, total bilirubin, kidney function test values including urea, creatinine, serum sodium, serum potassium, urine examination showing microscopy, and urine albumin.

Inferential statistics will be tested using an independent t-test analysis for nailfold findings as quantitative/numerical measurements, such as CD (width) and mean CD. The Chi-square/Fisher's-exact test will be used for qualitative/morphological findings, such as capillary morphology and cross-linked capillaries (sinus or twisted), to find the significant difference between the two comparative groups: preeclampsia (cases) and normal pregnant women (controls). Results will be calculated for a significant difference at a p-value of <=0.05 with a 95% CI.

Authors Contribution: Conceptualisation: All authors, Data Collection: Dr Shreya Gupta, Revising the manuscript for intellect content: All authors, All the authors have read and agreed to the final manuscript.

Proforma

Parameters
OPD/IPD no.
Name
Age
Sex
Address
Contact no.
Socio-economic status
Marital Status
Last menstrual period:
Gestational period of patient in weeks:
Current weight of the patient:
Height of the patient
BMI
GPLA score:
Blood pressure:
Blood workup parameters:
Complete Blood Count (CBC)
Coagulation profile:
PT
INR
APTT
Liver function test:

SGPT
SGOT
ALP
Total Bilirubin
Kidney function test:
Urea
Creatinine
Sodium
Potassium
Urine examination: microscopy and albumin
Fundus examination
Abdominal girth
Ultrasonography findings
Nailfold examination findings
Quantitative parameters:
Capillary Diameter (CD)
Mean Capillary Density (MCD),
Qualitative parameters:
Cross-linked capillaries (sinuous or twisted arrangement)
Capillary morphology
Clinical diagnosis

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