Comparative Study on Electrophoretic Pattern of Serum Proteins in Peptic Ulcer Disease in Pregnancy.

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Abstract: *This study was undertaken to evaluate correlation between level of serum proteins in pregnant women with peptic ulcer .100 cases were compared with 50 normal pregnant women and 50 nonpregnant women. Age, parity, BMI, co-morbidities, endoscopic findings , serum protein and their differential fractions were recorded. Gastric biopsies were examined histopathologically using Giemsa stain. .patients with peptic ulcer disease showed decrease persistent decrease in albumin,a2globulin and b globulin and just slight decrease or no decrease in levels of a1 and gamma globulin when compared with pregnant controls. .value of a/g was persistently low in pregnant cases and control.malnutrition and inflammatory response in peptic ulcer disease was found to be causative in low level of serum proteins present in cases with peptic ulcer disease.*

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I. Introduction

There are no gastrointestinal diseases specifically caused by pregnancy. However, pregnancy may complicate most gastrointestinal diseases, particularly gastroesophageal reflux and peptic ulcer disease . Symptoms such as nausea, vomiting, and dyspepsia occur in 50–90% of all patients.[1] Most of these symptoms are a manifestation of normal altered physiology in which changes occur both functionally and anatomically. These changes may cause new symptoms, worsen preexisting disease, or mask potentially deadly disease.Several hypothesis have been postulated regarding etiology of peptic ulcer disease(neurogenic theory,genetic,blood group,endocrine,malnutiton,vitamin deficiency,inadequate mastication,irregular meals).Albumin fraction of plasma protein reflects the actual protein statusof an individual.The aim of this paper ELECTROPHORETIC PATTERN OF SERUM PROTEINS IN PEPTIC ULCER DISEASE IN PREGNANCY is to see how far nutritional deficiency as reflected by serum proteins has bearing on peptic ulcer disease.

II. Materials And Methods

Between January, 2015 and JANUARY, 2017 pregnant women presenting to the OUTPATEINTS DEPARTMENT at RIMS, RANCHI, were screened for eligibility. Patients WITH SYMPTOMS OF PEPTIC ULCER DISEASE(CASES) AND PREGNANT WOMEN WITH NO SYMPTOMS(CONTROLS) until 12 weeks of their pregnancy were included in the study.

STUDY DESIGN : COMPARITIVE STUDY

STUDY METHODOLOGY: The study was carried out according to ethical principles for medical research involving human subjects outlined in the Helsinki Declaration. Written informed consent was obtained from all patients.Patients data including age, parity, gestational age, documented past medical and surgical history as well as their presenting medical problems, were recorded. Patients' weight and BMI were recorded. Blood investigations including COMPLETE BLOOD COUNT ,ELECTROPHORETIC ESTIMATION OF SERUM PROTEINS and abdominal ultrasonography findings were TRACED All participants completed a Questionaire regarding severity of symptoms,dietary habits,regularity of meal,anxiety factors,socioeconomic conditions,severity of daily activities and so on.

Upon presentation to the endoscopy unit, all patients provided informed consent after being interviewed by a gastro-enterologist. Endoscopies were performed by experienced gastroenterologist using video gastroscopes. Precautions were taken to minimize possible risks to the patients and their fetuses. These include the employment of an anesthetist and the positioning of patients in left lateral positions. Whether the patients were positive for H. pylori was investigated by the rapid urease test then by obtaining two mucosal samples each from antrum and corpus. Histopathological analysis was performed by a pathologist specialized in the gastrointestinal tract using Giemsa stain Blood is collected in a tube with clot activator. After separation from blood components, serum is placed on paper treated with agarose gel, followed by exposure to an electric current in the presence of a buffer solution (electrophoretic cell). Various serum proteins are then separated based on charge. After a predetermined exposure time to an electric field, the paper is removed, dried, and placed on a fixative to prevent further diffusion of specimen components, followed by staining to visualize various protein bands. Coomassie brilliant blue is a common staining agent used to visualize bands in serum protein electrophoresis. Then using a densitometer, each fraction is quantitated: for both cases and control group of patients.The serum protein components are separated into five major fractions(albumin,alpha1 globulin,alpha2 globulin,beta globulin,gamma globulin): for both cases and control group of patients and subsequent comparison was done.

INCLUSION CRITERIA
singleton pregnancy detection of fetal heart activity gestational age of UPTO 12 weeks verified by ultrasound.

EXCLUSION CRITERIA
patients with history of any systemic disorder drug use except ordinary supplementation, known thyroid disease, diabetes mellitus multiple gestation, fetal malformation, chromosomal abnormality, gestational trophoblastic disease psychiatric disease, previous gastrointestinal disease previous upper gastrointestinal surgery,
previous treatment of H. pylori. Statistical analysis SPSS SOFTWARE VERSION 20.

III. Results

This study was undertaken at rims ranchi from jan 2015 to jan 2017.100 pregnant women with symptoms of peptic ulcer disease were taken as cases.controls composed of 50 normal pregnant women and 50 non pregnant women of same age group.

Table1.Incidence with age

Maximum no of cases belonged to age group 24-26 yrs.

Age group	cases
20-22yrs	10
22-24yrs	20
24-26yrs	40
26-28yrs	30

Table 2.incidence with parity

No association was found between primi and multigravida as equal no of cases were present.

parity	incidence
primigravida	40
>1 live issue	20
multigravida	40

Table 3.incidence with BMI

Association with greater bmi and peptic ulcer disease was seen

BMI	incidence
20-22kg/m^2	20
22-24kg/m^2	20
24-26kg/m^2	35
26-28kg/m^2	25

Table 4.incidence of religion

Cases mostly belonged to muslim category

religion	No of cases
1.hindu	30
2.muslims	50
3.others	20

Table 5 Socioeconomic strata

Maximum casesbelonged to socioeconomic strata IV (KUPPUSWAMY CLASSIFICATION).

Social class	cases
I	5
II	25
III	30
IV	40
TOTAL	100

Table 6 Dietary habit

CASES MOSTLY BELONGED TO LOW PROTEIN VEGETERIAN DIET

habit	cases
Non veg diet	33
Veg diet	67
total	100

Table 7 Periodicity of meal.

MAX CASES DID NOT TAKE MEALS AT REGULAR INTERVALS

Periodicity of meal	No of cases
At regular intervals	36
No fixed interval	64

Table 8.anxiety factors

STRESS AND ANXIETY WAS SEEN IN SOME CASES

Significant history	No of cases
present	46
absent	54
total	100

Table 9.family history of peptic ulcer diathesis

Significant history	No of cases
present	16
absent	84
total	100

Table10 .helminthic and protozoal infestation

smear	cases
positive	56
negative	44
total	100

Table 11.distribution of haemoglobin

CASES PRESENTED WITH ANEMIA IN QUITE A CONSIDEARBLE NO.

haemoglobin	cases
<8gm/dl	32
8-9gm/dl	36
9-10gm/dl	16
>10gm/dl	16
total	100

Table12 .period of gestation with incidence of pud

MAX CASES BELONGED TO 8 -12 WEEKS.

Period of gestation	Incidence of pud in cases
preconception	nil
<8 weeks	32
8-12weeks	68

Table 13.incidence of pud with H.pylori infection

infection	cases
present	40
absent	60

Table 14.endoscopic dx features

Endoscopic findings	cases
Erythematous gastritis	40
Erosive gastritis	10
Peptic ulcer	45
duodenitis	5

Table 15.level of serum proteins in cases and controls(figure1)

Cases with peptic ulcer disease showed more decrease in serum protein level than normal pregnant controls.

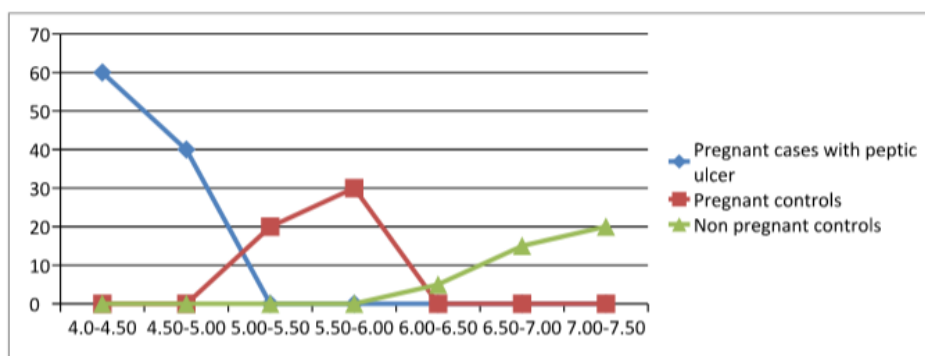|	Pregnant cases with peptic ulcer	Pregnant controls	Non pregnant controls
4.0-4.50	60	nil	nil
4.50-5.00	40	nil	nil
5.00-5.50	nil	20	nil
5.50-6.00	nil	30	nil
6.00-6.50	nil	nil	5
6.50-7.00	nil	nil	15
7.00-7.50	nil	nil	20
total	100	50	50

FIGURE 1.

Table 16.range of total serum protein in g/dl and its differential fractions SEEN IN ELECTROPHORESIS.(figure 2)

In normal pregnant women albumin showed decreased value,alpha1 globulin and gamma globulin didn't show much alteration in value,alpha2and beta globulin showed rise in value.
In pregnant women alpha 2 and beta globulin showed decrease in value .Rest parameters didn't show much alteration.

	albumin	Alpha1globulin	Alpha2globulin	betaglobulin	Gamma globulin	Total protein	A/Gratio
Non pregnant controls	3.6-4.8	0.09-0.27	0.24-0.59	0.41-0.87	0.61-1.32	6.12-7.8	1.7-2.4
Mean value in nonpregnant controls	4.25	0.19	0.39	0.57	1.06	6.46	1.92
Pregnant controls	3.5	0.24	0.43	0.69	0.94	5.8	1.52
Pregnant cases with peptic ulcer disease	3	0.22	0.30	0.52	0.90	4.8	1.54

Figure 2.
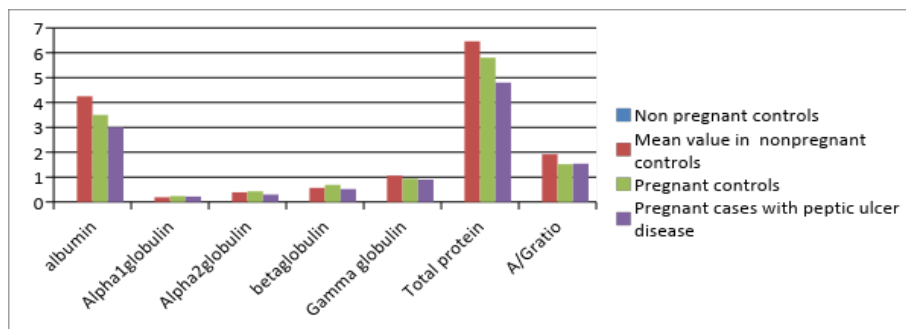
IV. Discussion

Peptic ulcer disease in pregacy is a challenge to obstetricians . A total of100 patients with peptic ulcer disease met our inclusion criteria.under the present work an attempt has been made to study total serum proteins and their differential fractions in cases of peptic ulcer disease diagnosed clinically and endoscopically .For the purpose of study 100 pregnant women with symptoms of peptic ulcer disease were compared with 50 normal pregnant women and 50 normal non pregnant women .

Patients ranged in age from 20 to 28 years.Maximum number of patient(40%) belonged to age group 24-26 yrs.Mathur et al(1969)[1]found 83% of patients belonged to age group 21-40yrs.No specific age prevalence was found for peptic ulcer disease in pregnancy. The mean body mass index was24.3 kg/m2 (range 20 – 28 kg/m2) Primi-gravidas comprised 40% of patients.Approximately 50% of cases were muslims30%were hindus and the rest belonged to miscellaneous religions.The increased prevalence of peptic ulcer in muslims can be traced to their dietetic habit of consuming spicy food(chatterjee et al).40% of cases in this study belonged to socioeconomic class IV.Mahadevan(1967)[2]reported that stress and strain(46% of cases) seemed to play a dominant role in the causation of ulcer in the western world ,while in India malnutrition played a dominant role(HARRISON 1958)[3].Doll,Jones and Bucket zeck(1951)[4]observed that it was present in professional classes subjected to stress and strain.In the present study 67%cases had vegetarian diet deficient in proteins resulting in ulcer prevalence(Malhotra et al1964)[5].Spicy,irregular and hurried(64%)meals may in someway or the other cause trauma result in ulcers as stressed by Malhotra et al.56% of the cases were carrying helminthic infestation which may interfere with the process of absorption .32% of cases had<8gm%haemoglobin and 36% of cases had haemoglobin between 8-9gm% which again points to malnutrition as causative factor for devlopement of peptic ulcer disease. The rapid urease test and the histopathological examination of gastric biopsies using giemasa stain had confirmed H. pylori in 40% of cases. Data in the existing medical literature are consistent regarding a possible connection between peptic ulcer disease and H. pylori infection.(JAMA 1994,272:65-9)[6]

In our study of 100 cases,erythematous gastritis was present in 40,erosive gastritis in 10,peptic ulcer in 45 and duodenitis in 5 as per endoscopic diagnosis. The most common diagnosis was peptic ulcer which occurred in 45%; this can be explained by malnutrition,irregularity of meal and stress factors in this study.Erythematous and erosive gastritis occurred during pregnancy from increased intra-abdominal pressure and decreased LES pressure mediated by gestational hormones.

Endoscopy is useful for diagnosing gastroesophageal reflux disease (GERD), gastritis, Helicobacter pylori (H. pylori) infection, peptic ulcer disease, esophageal varices, and malignancy (Friedele et al., 2014)[7]. A mailed survey of ACOS members, which included information over 73 upper endoscopies performed during pregnancy. Endoscopic diagnoses included esophagitis, gastritis, ulcers, Mallory-Weiss tears and normal findings in descending order(Frank, 1994)[8]which correlates well with this study.

Chack and his colleagues found that the pregnant women has lower rate of peptic ulcer diseases but higher rate of reflux esophagitis compared to non-pregnant patients(chack et al 2001)[9]One of the most important points in endoscopic procedures of pregnant patients is to avoid maternal hypoxia and hypotension which can cause placental hypoperfusion and potential fetal injury (O'Mahony[10], 2007, Cappell, 2011).In our study, pregnant patients were positioned in the left lateral position and prompt intravenous hydration with normal saline was made..

In this piece of work the total serum protein has been compared in pregnant women with peptic ulcer disease,normal pregnant women and non pregnant women of same group.   In this study non pregnant has serum protein mean value 6.46g/dl,normal pregnant had value 5.8 g/dl and our study group pregnant with peptic ulcer had value 4.8g/dl Changes in maternal plasma proteins during pregnancy are now well documented. These changes may be quantitative, as seen in the electrophoretically separated fractions of serum and in the various binding globulins; or they may be represented by the appearance of a protein which is present only in the serum of pregnant women.

Differential fraction of proteins showed the following trend(values in g/dl)

group	albumin	Alpha 1globulin	Alpha2 globulin	Beta globulin	Gamma globulin	A/G ratio
Pregnant cases	3	o.22	0.3	0.52	0.90	1.54
Pregnant controls	3.5	0.24	0.43	0.69	0.94	1.58
Non pregnant controls	4.25	0.19	0.39	0.57	1.06	1.92

A fall in the concentration of total protein occurs during pregnancy. The extent of this fall and the pattern of change were the major differences encountered in numerous investigations. In some cases a continuous reduction in total protein during pregnancy was seen[11] while in others a stable period after the second trimester, or a rise in concentration prior to delivery, or a drop in concentration after delivery were encountered with values returning to normal in 6 to 12 weeks postpartum.in this study we have taken into account pregnancies upto 12weeks of gestation[12]. The fall in protein concentration seen during pregnancy most likely is a result of the dilution of the plasma, since total protein concentration is inversely related to plasma water concentration.

In this study further decreased value of total serum protein was found in pregnant case which can be correlated with malnutrition Albumin represents the major component of serumproteins and may be decreased due to anabolic failure orcatabolic metabolism. It is produced by the liver under normal physiologic conditions. pregnancy. The concentration of albumin also decreases in pregnancy and malnutrition. The total amount of albumin decreases in concentration are thought to be the result of an increase in plasma volume.In this study further decrease in serum albumin can be correlated with malnutrition which further was causative in peptic ulcer disease.

The extent of change in the globulin fractions varied from study to study. A slight but significant rise in α1-globulin from early pregnancy to delivery, followed by a return to normal values by four weeks postpartum was found in some studies. In others, no significant variation during pregnancy was found, but rather an increase within the first week postpartum and a return to normal levels six to seven weeks after delivery. The α 1 protein fraction is comprised of AFP, α1 -glycoprotein,thyroid-binding globulin, and transcortin. A decreasedband is seen in deficiency states such as AFP deficiency,nephrotic syndrome and liver failure from cirrhosis.Bence Jones protein from multiple myeloma maybind to and retard the α 1 -band and thus also lead to a decreased α1 zone, whereas in other malignancies or duringinflammatory responses an increase of the α1 –protein band may result from acute-phase reactants.in our study cases with peptic ulcer had significant change in alpha 1 globulin level compared to normal pregnant counterparts,there was slight rise as compared to non pregnant counterparts.

The changes in α 2-globulins are similar. A significant rise in α 2-globulin occurs throughout pregnancy, especially during the third trim ester. A rise in concentration in the first week postpartum has been observed with values returning to normal within several weeks. Ceruloplasmin, α 2 -macroglobulin, and haptoglobin contribute to the α 2 -protein band. The α 2 -zone is typicallydecreased in hemolytic anemia when haptoglobinbinds with free hemoglobin from red blood cells and these complexes are rapidly removed by phagocytes.Haptoglobin[13] may also be elevated, especially during inflammationas part of the acute-phase response.peptic ulcer causes inflammatory response hence increase in haptoglobulin and decrease in serum α2 globulin is seen in this study.

βGlobulins also rise during pregnancy. T he elevation is significant throughout pregnancy . One study, however showed no change in β-globulin until shortly before delivery, at which time an abrupt rise until the first week postpartum was seen, with a return to normal by six weeks after delivery. When β-globulin concentration was expressed as percent total protein, the increase was seen in the first trim ester. The βfraction may be separated into a β1 -band and a

β 2 -band but on graphical data is often represented as a single band. Transferrin comprises the β 1 -band. An increaseof β1 -proteins is typical for iron-deficiency anemia due to elevated levels of free transferrin, pregnancy and estrogen therapy. The β2 -band is formed by complementprotein 3 (C3) and β -lipoprotein. IgA (immunoglobulinA), IgM, and

sometimes IgG also can be identified in theβ-fraction. βfraction shows decrease in level in cases of protein malnutrition which is seen in this study caused due to peptic ulcer disease.

There is a fall in the concentration of y-globulin during pregnancy with a return to normal in 6 to 12 w eeks. This is apparently a result of a decrease in the concentration of IgG[14]. The various immunoglobulinclasses (IgG, IgA, IgM, IgD and IgE) are usually of gamma -mobility and make up most of the gamma -band, but they

can also be found in the β _gamma and βregions, and may occasionally even extend into the α2 -globulin area. However, when -y-globulin concentration is expressed as percent total protein, little change is seen.in this study no significant change in level of gamma globulin between cases and normal pregnant controls were found.

Since album in concentration decreases and the α andβ-globulin concentrations increase, there is a sharp decline in the albumin/globulin ratio during pregnancy.In this study a/g was slightly less than normal pregnant controls and remarkably less than non pregnant controls which is due to alteration of respective albumin and globulin values explained above.

V. Conclusion

[1]. estimation of serum proteins by electrophoresis was undertaken in 100 pregnant women with symptoms of peptic ulcer with 50 normal pregnant women and 50 non pregnant women

[2]. patients with peptic ulcer disease showed decrease persistent decrease in albumin,a2globulin and b globulin and just slight decrease or no decrease in levels of a1 and gamma globulin when compared with pregnant controls

[3]. normal pregnant women showed increase in level of a1.a2 beta andgamma globuin and decrease in albumin when compared with non pregnant controls.

[4]. value of a/g was persistently low in pregnant cases and control

[5]. persistently low value of albumin in peptic ulcer ds in pregnancy points to association of malnutrition and inflammatory response attributes to decrease in globulin in peptic ulcer in pregnancy.

[6]. serum protein level more so albumin reflects actual protein status of peptic ulcer patients in this study.

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