

Proposed Plan to Investigate the Impact of Amniotic Fluid Index on Pregnancy Outcome at Selected Obstetrics & Gynecology Clinics, Jeddah, Saudi Arabia

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Abstract: Background: Amniotic fluid is vital to the well fetus. It cushions the fetus from injury, helps to prevent compression of the umbilical cord, and allows room for it to move and grow. The current study amid at introducing a Proposed Plan to Investigate the Impact of Amniotic Fluid Index on Pregnancy Outcome at Selected Obstetrics & Gynecology Clinics, Jeddah, Saudi Arabia. The purposes in its utilization are evaluation of maternal serum interleukin-6 (il-6) as an early marker of subclinical chorioamnionitis in patients with preterm premature rupture of membranes. Hoping to improve maternal and neonatal outcome in PPRM and to bring about changes in management strategies in PPRM. Objective: To provide a framework of Proposed Plan to Investigate the Impact of Amniotic Fluid Index on Pregnancy Outcome at Selected Obstetrics & Gynecology Clinics, Jeddah, Saudi Arabia. Method: An experimental research design is proposed to be utilized in the current study in which the participants will be divided into two groups a study group presenting with PPRM between 24 and 34 weeks gestation and a control group of healthy pregnant women without PPRM (matched for age, parity, and gestational age. Serum IL-6 levels will be determined by solid-phase sandwich enzyme-linked immunosorbent assay. Results: This study finding will include the data related to evaluation the clinical usefulness of maternal serum IL-6 as early marker for detection of subclinical chorioamnionitis in patients with preterm premature rupture of membranes. Secondly to compare interleukin 6 with total leukocyte count and C reactive protein as a method for earlier detection of subclinical chorioamnionitis in patients with preterm premature rupture of membranes. Conclusions: The current study results aiming to reveal the data beyond the achievement the objectives Assessment of need for additional markers in the maternal serum, simpler and less invasive than amniocentesis to predict intrauterine infection. Secondly, Early diagnosis of subclinical infection and inflammation that may therefore aid clinicians to institute interventions focusing on adverse outcomes. Finally, Subjective and objective assessment of early onset of complications and/or side effects.

Keywords: Proposed Plan, Amniotic Fluid Index & Pregnancy Outcome

1. Introduction

According to Hulter et al., (2010), an antepartum or intrapartum amniotic fluid index of ≤ 5.0 cm is associated with a significantly increased risk of cesarean delivery for fetal distress and a low Apgar score at 5 minutes. There are few reports linking amniotic fluid index and neonatal acidosis, the only objective assessment of fetal well-being. A multicenter study with sufficient power should be undertaken to demonstrate that a low amniotic fluid index is associated with an umbilical arterial pH < 7.00 . With the advent of real-time ultrasonography, assessment of amniotic fluid has been possible, resulting in earlier recognition of abnormal conditions and possible intervention. Since, these disorders of liquor amine has a significant impact on pregnancy and fetus, it prompted us to carry out this study with sincere efforts to find out its effect on pregnancy outcome .

Premature rupture of membranes is defined as spontaneous membrane rupture that occurs before the onset of labor. When membrane rupture occurs before 37 weeks gestation it is referred to as Preterm Premature rupture of membranes (PPROM). Noor, et al., (2007). According to Nava, et al., (2003), premature rupture of membranes continues to be a leading cause of neonatal morbidity and mortality. It occurs in approximately 2-8% of all pregnancies but it is associated with 20% of per-natal deaths. Complications include

maternal and fetal infection, preterm labor, asphyxia and if earlier in pregnancy pulmonary hypoplasia and anatomic distortion as a result of amniotic bands.

Furthermore Goldenberg, Culhane& Romero, (2008), mentioned that subclinical intrauterine infection has been implicated as a major etiological factor in the pathogenesis and subsequent morbidity associated with PPRM, but once clinical chorioamnionitis is present, there is a fourfold increase in neonatal mortality. Early infection is not reliably predicted by commonly used laboratory variables such as erythrocyte sedimentation rate, white blood cell count, neutrophil count, or vaginal bacterial culture. Clinical signs such as fever and fetomaternal tachycardia usually appear late. (Trochez, Smith & Lamont , 2007). To the greatest of our understanding, current study amid at introducing a Proposed Plan to Investigate the Impact of Amniotic Fluid Index on Pregnancy Outcome at Selected Obstetrics & Gynecology Clinics, Jeddah, Saudi Arabia. Consequently, conducted this study will assist in providing a framework for evaluation the clinical usefulness of maternal serum IL-6 as early marker for detection of subclinical chorioamnionitis in patients with preterm premature rupture of membranes. Secondly to compare interleukin 6 with total leukocyte count and C reactive protein as a method for earlier detection of subclinical chorioamnionitis in patients with preterm premature rupture of membranes.

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2. Participants and Methods

Gathered data will be processed using suitable statistical package. Quantitative data will be expressed as means \pm SD while qualitative data will be expressed as numbers and percentages (%). Student t test will be used to test significance of difference for quantitative variables and Chi Square will be used to test significance of difference for qualitative variables. A probability value (p-value) < 0.05 will be considered statistically significant. Other statistical tools may be used when appropriate and applicable. Data will be analyzed and appropriately presented in tables and figures.

This is a case-control study enrolled persons will be divided into two groups a study group presenting with PPRM between 24 and 34 weeks gestation and a control group of healthy pregnant women without PPRM (matched for age, parity, and gestational age. Serum IL-6 levels will be determined by solid-phase sandwich enzyme-linked immunosorbent assay. A total of 54 women will be recruited for the study. Patients will be divided into two equal groups, 27 in each. Group A (case group): consisted of 27 patients at 24-34 weeks' gestation with preterm PROM without any clinical chorioamnionitis at time of hospitalization and inclusion in the study. Group B (control group) : consisted of 27 women at 24-34 weeks' gestation without ROM.

Inclusion Criteria

Selection of patients:-Diagnosis of PPRM will (24-34 weeks gestation) based on:

- History of sudden gush of clear fluid from the vagina.
- Presence of pool of fluid in posterior fornix during sterile speculum examination.
- Escape of amniotic fluid from cervix on coughing or applying abdominal pressure.
- Positive nitrazine test.
- Positive fern test.

Exclusion Criteria:

- Patient exceed 34 weeks of gestation and before 24 weeks of gestation
- Evident clinical chorioamnionitis.
- Patients with pregnancy-induced hypertension.
- Antepartum hemorrhage.
- Multiple gestation.
- Polyhydramnios.
- Immunological disorders.
- Medical disorders such as anemia, heart disease, hypertension, and diabetes mellitus.
- Those with evidence of any other infection such as urinary tract infections will be excluded from the study.

Every subject will be subjected to:

- Clinical assessment.
- Complete history to diagnose preterm PROM and to exclude any symptoms suggestive of infection.
- General examination of pulse and temperature to exclude any signs of infection.

- Abdominal examination to exclude any signs of infection and feel uterine contractions or tenderness.
- Sterile speculum examination to diagnose preterm PROM and to exclude labor.

Laboratory assessment: withdrawal of 5 ml venous sample for measurement of:

- Complete blood count.
- C reactive protein .

-IL-6 estimation Sera will be separated and immediately stored at -70°C until they will batch analyzed. Single blood samples will be taken for assessing serum IL-6 levels from the control group while three blood samples (at the time of admission, at 48 hr, and on day 7 of admission or onset of labor whichever was earlier) will be taken from PPRM group. Serum IL-6 levels will be determined by solid-phase sandwich enzyme linked immunosorbent assay.

Conservative inpatient management consisting of:

- Antibiotics in form of erythromycin 500 mg tablet orally every 6 hours for 7 days.¹²
- Corticosteroids in the form of dexamethasone 8 mg ampoule intramuscular injection every 8 hours for 3 doses.
- Temperature chart.
- Tocolysis will not be given.
- Frequent observation of maternal and fetal wellbeing until termination of pregnancy is decided.
- Termination of pregnancy will be done when:¹²
- Delivery should be considered at 34 weeks of gestation. Where expectant management is considered beyond this gestation, women should be informed of the increased risk of chorioamnionitis and the decreased risk of respiratory problems in the neonate.
- Appearance of evidence of clinical chorioamnionitis, accidental hemorrhage or fetal distress.
- Spontaneous onset of labor pains.

After delivery, the followings will be assessed:

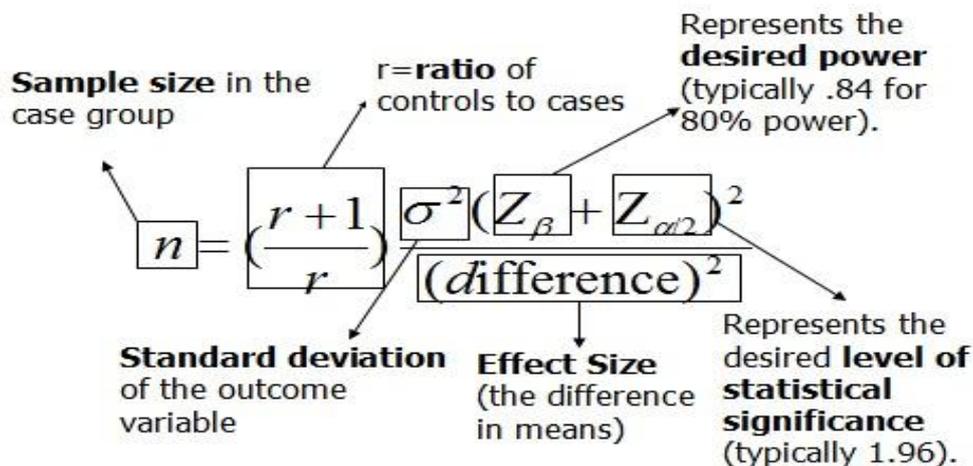
- Maternal outcome:
- Occurrence of puerperal sepsis.
- Occurrence of wound infection.
- Fetal outcome:
- APGAR score at 1 and 5 minutes.
- Fetal weight.
- Need for NICU admission.

Occurrence of Neonatal Complications:

- TTN
- RDS.
- Deep jaundice
- Histopathological examination of placenta and membranes a marker of histological chorioamnionitis.

3. Sample Size Estimation

The sample size is calculated from this equation:



- For 80% power, $Z_{\beta}=.84$
- For 0.05 significance level, $Z_{\alpha}=1.96$
- $r=1$ (equal number of cases and controls)
- $\sigma= 11.8$
- Difference of the mean serum IL-6 value between the case and control = 9
- **Framework Adopted from a previous study by (Gulat S et al., 2012).**

4. Discussion

Various studies have shown that chorioamnionitis leads to a rise of several cytokines in amniotic fluid, fetal cord blood, and maternal serum. This study findings congruent with the result of the research carried out by Resnick, et al., (2002), who focused on Calcitropic hormones in pre-eclampsia: a renewal of interest, it was reported that Limited sun exposure is the main reason beyond vitamin d deficiency among the pregnant women. On the other hand, the study carried by Seely, (2007), focused on Chronic continuous PTH infusion results in hypertension in normal subjects., showed that only 96% of the studied sample from the pregnant women were had vitamin D deficiency due to limited sun exposure and Mal-absorptive syndromes (cystic fibrosis, cholestatic liver disease, inflammatory bowel disease, short gut syndrome), which constant with the current study results.

In cases of intrauterine infection, cytokines produced within the uterine cavity first mount a local inflammatory response and then reach the maternal circulation and the liver to stimulate the synthesis of C-reactive protein (CRP) by hepatocytes or bone marrow targets to induce leukocytosis. Hence, rise in cytokines occurs earlier than that of CRP. IL-6 is a very well-known infection/inflammation marker and it is found to be significantly elevated in maternal serum , amniotic fluid and vaginal secretion in preterm labour and PPRM patients .

This cytokine as well as other pro-inflammatory markers have been studied to predict the interval to delivery and maternal and neonatal outcomes. Amniotic fluid IL-6 levels have been proposed as marker for evolving chorioamnionitis but it requires amniocentesis, which is an invasive procedure. A simpler and less invasive method of measuring IL-6.cytokine in maternal serum would be useful for the identification of asymptomatic intrauterine infections in patients with PPRM. In addition to the parameters routinely used for the detection of infection (CRP,

leukocytosis, body temperature, and fetal heart rate), there is a need to investigate whether serum IL-6 levels can supplement or even replace routine inflammatory parameters in diagnosis of subclinical chorioamnionitis and help to decide timely delivery of the fetus.

However clinical signs of infection are subtle and usually not present in early patients. Currently there are no reliable clinical markers to adequately indicate impending intrauterine infection in patients with premature rupture of membranes so a more sensitive test which is capable of identifying intrauterine infection soon after it occurs is needed.

The anticipated benefits: Improving pregnancy outcome in patients with subclinical chorioamnionitis .Furthermore , The potential risks: no suspected risk .As well as , condut follow up such as ongoing monitoring of possible side effects.Each participant has the right to abstain or withdraw at any time without any reprisals.

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