T.R.

KAHRAMANMARAŞ SÜTÇÜ İMAM UNIVERSITY

GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCE

ISOLATION AND IDENTIFICATION OF GROUP B STREPTOCOCCUS FROM TRIMESTER OF PREGNANT WOMEN

DLZAR BAYZ RAHMAN

MASTER THESIS

DEPARTMENT OF BIOENGINEERING AND SCIENCES

KAHRAMANMARAS - TURKEY 2015

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M.Sc thesis entitled “Isolation and Identification of Group b Streptococcus From 35 to 37 gestation age of Pregnant Women ” and prepared by DLZAR BAYZ RAHMAN ,who is a student at Bioengineering and Sciences Department, Graduate School of Natural and Applied Sciences, Kahramanmaraş Sütçü İmam University, 20 / 10 / 2015 was certified by all the majority jury members, whose signatures are given below.

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DECLARATION

I hereby declare that all information in the thesis has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

DLZAR BAYZ RAHMAN

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ÇEŞİTLİ KLİNİK ÖRNEKLERDEN İZOLE EDİLEN *STREPTOCOCCUS AGALACTIAE* SUŞLARININ ANTİBİYOTİK DUYARLILIKLARI

(YÜKSEK LİSANS TEZİ)

DLZAR BAYZ RAHMAN

ÖZET

Bu çalışma, Erbil-Kurdistan bölgesindeki doğum hastahanesinde Haziran- Aralık 2014 tarihleri arasında gerçekleştirildi. Gebeliklerinin 35-37. haftaları arasındaki arasındaki kadınlardan 157 vajinal sürüntü örnekleri alındı.

Prospektif bir çalışma olan bu araştırmada, gebe kadınların vajen örneklerinde GBS kolonizasyonu ve etkenlerin antibiyotik duyarlılıkları belirlendi. Vajinanın giriş alanından alınan sürüntü örneklerine, kanlı agar kültürü ve standart bakteriyolojik teknikler uygulanmıştır. Kültürel, morfolojik ve biyokimyasal özelliklerine göre *Streptococcus agalactiae* türleri tanımlanarak antibiyotiklere duyarlılık testleri yapılmıştır.

157 gebe kadına ait vajinal örneğin 19'undan (%12.10) GBS türü izole edildi. Çalışmamızda suşların tamamı penicillin, vancomycin ve amoxicilline duyarlı bulunurken, chloramphenicol'e %94.44, clindamycine %94.11, erythromycine %93.75, ciprofloxacin'e %89.47 ve cefatoxime %83.33 oranında duyarlı bulundu. Suşların tamamı (%100) doxycycline ve oxacilline dirençli idi.

Anahtar cümleler: Grup B Streptococ, hamileler, yenidoğanlar.

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ISOLATION AND IDENTIFICATION OF GROUP B STREPTOCOCCUS FROM TRIMESTER OF PREGNANT WOMEN

(MSc THESIS)

DLZAR BAYZ RAHMAN

ABSTRACT

The present study was carried out between June – December 2014 One hundred fifty seven vaginal swab specimens were obtained patient has pregnant gestation age between 35 to 37 week from maternity teaching hospital in Erbil- Kurdistan region .

A prospective study was performed to determine the prevalence of GBS colonization in the vagina of pregnant women and the antibiotic susceptibility pattern of the isolates. We also aimed to identify risk factors associated with GBS colonization. Low vaginal swabs were collected and cultured on the blood agar , a presumptive identification of isolates was made using standard bacteriological methods. Identify of *Streptococcus agalactiae* according to the cultural characteristics, morphological features and biochemical reaction.Sensitivity tests for these isolated bacteria to antibiotics which include ten antibiotics were done.

GBS strains were isolated from 19out of 157 patients, corresponding to a colonization rate of 12.10%. In our study showed that the sensitivity of GBS to penicillin, vancomycin and amoxicillin (100%), chloramphenicol (94.44), clindamycin (94.11%), erythromycin(93.75), ciprofloxacin(89.47) , cefatoxime (83.33). And all isolates were resistant 100 % to doxycycline and oxacilline.

Key Words: Streptococcus group b, pregnant woman, neonates.

Kahramanmaraş Sütçü İmam University

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LIST OF ABBREVIATIONS

GBS :	Group b Streptococcus
S.agalactiae:	*Streptococcus agalactiae*
CDC :	Center of infectioncontrole
CPS:	Capsular polysaccharide
EOD :	Early onset infection
LOD :	Late onset infection
GI :	Gastro intestinal
LGT :	Lower genital tract
STI:	Sexuall transmitted infection
CAMP:	Christie, Atkins, Munch-Petersen
UTI :	Urinary tract infection
GIT:	Gastrointestinal tract
IAP .**:**	Intrapartum antibiotic prophylaxis
EOGND:	Early onset group b neonatal disease
PROM:	Preterm rupture of membrane
UGT:	Uper genital tract
EOGNS:	Early onset GBS neonatal septicemia
DVE :	Digital vaginal examination
LAB :	Lactıc acidic bacteria
CLSI:	Clınıcal and laboratory standard institute

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1. INTRODUCTION

Streptococcus agalactiae (synonym S. difficile) is a Gram-positive, cocci-shaped bacterium which typically occurs in pairs or in long chains. The colonies are small, translucent, round, and slightly raised, pinpoint, measuring 1-2 mm in diameter and appear yellowish to grey in color when grown on solid agar (Plumb, 1999; Buller, 2004).

S. agalactiae strains are α-, β- or non-haemolytic (γ) when cultured on blood agar (Kitao *et al.,* 1981; Buller, 2004). They typically not produce capsule niether spore, none motile, oxidase negative and catalase negative. These bacteria can grows between the temperature not less than 10°C and more than 45°C, with the optimal pH of 9.6. The presence of 40% (v/v) bile salts or in the presence of 6.5% NaCl inhibits the growth of bacteria (w/v) (Inglis *et al.,* 1993; Plumb, 1999; Buller, 2004).

According to Lancefield serogrouping method this bacterium is related to the group B Streptococcus (GBS) species (Devriese, 1991; Facklam, 2002).Lancefield's group B streptococci (GBS) (Lancefield and Hare, 1935), also referred to as *S. agalactiae*, produces a colonization thats asymptomatic to adult humans. It is commonly found in the gastrointestinal and the genitourinary tracts, However within the neonates it typically cause an invasive bacterial infectionleading to septicemia, meningitis and pneumonia. It is responsible for two to three cases per 1000 live births. It is also leads to high mortality or morbidity in non-pregnant adults, particularly in elderly persons and those with underlying diseases (Schuchat, 1998; Nizet and Rubens, 2000; Farley, 2001).

Group B streptococci (GBS), which is a beta-hemolytic streptococci that has been linked to human diseases since 1938 (Lancefield, 1938) which afterward it has become the common pathogen causing serious neonatal infections like sepsis and meningitis (Hood *et al.,* 1961; Eickhoff *et al.,* 1964). Nearly 15-20% of pregnant women has GBS in the lower vaginal tract (Hoogkamp-Korstanje *et al.,* 1982). Which then it infects the neonates as they going through pass through birth canal and colonization occurs (Baker *et al.,* 1973; Baker *et al.,* 1977). The womes birthcanal is the big reservoir of this infectious agent for newborn (Franciosi *et al.,* 1973).

Group B *Streptococcus* (GBS; *Streptococcus agalactiae*) is asymptomatic bacterium found in the genital and lower intestinal tracts, thats contribute to isolted between 10 to 30% of pregnant women (Regan *et al.,* 1991; Yancey *et al.,* 1996; Campbell *et al.,* 2000).

Reports suggesting that nearly 50 % of the GBS transmetted from the carrier mother to the neonates at the deliver in which 1-3% of this rate developes severe GBS infections, such as neonatal pneumonia, sepsis, and meningitis.(Baker and Barrett, 1974; Schrag *et al.,* 2000; Dermer *et al.,* 2004; Phares *et al.,* 2008).

GBS typically transfere from mother to the neonates through aspiration of infected amniotic fluid or during the passage through the birth canal. Monitoring for the colonization of the female genital tract with GBS is very important as its significantly associated with this infection (Garcia *et al.,* 2003; Larcher *et al.,* 2005).

Group B streptococci (GBS) remain a major cause of leading neonatal bacterial infections (Centers for InfectionControl and Prevention, 1996). Babies with early-onset GBS infections get infected with the bacteria from the birth canal of their mothers (Yow *et al.,* 1980). Reports suggesting that one-fifth of pregnant women are vaginally colonized with GBS at the time of delivery, which leads to colonization of a high percentage of babies with the organism and many develop potentially fatal infections (Regan *et al.,* 1996). Over th past years Group B Streptococcus has become as a common pathogen leading to neonatal sepsis (Eickoff *et al.,* 1964; McCracken, 1973).

Group B Streptococcus (GBS) are known increase the risk of adverse obstetric outcomes within pregnant womens hence it increase the neonatal morbidity and mortality (Breed, 1957; Baker and Edwards, 1995; Alttoparlak *et al.,* 2004).

Group B streptococci (*Streptococcus agalactiae*) make up one of the various microorganisms that grow and multiply in human beings. GBS are also associated with significant maternal peripartal infectionincluding bacteremia, endocarditis, chorioamnionitis, endometritis, UTI, arthritis, and responsible for serious bacterial illness and some times leading to deaths in nonpregnant women that have underlying diseases and in elderly adults (Dzowela *et al.,* 2005; Tazi *et al.,* 2008; Phares *et al.,* 2008; Sendi *et al.,* 2009). GBS can also pass through the cervix without causing serious cervicitis, and cross-intact amniotic fluid causing amnionitis thereby infecting the foetus in the uterus (Dzowela *et al.,* 2005).

Group B streptococci are sub classified into serotypes according to the immunologic reactivity of the polysaccharide capsule. Of the nine serotypes stated so far, the types Ia, Ib, II, III, and V are accountable for the majority of invasive human GBS diseases. Serotype III GBS is specially notable due to the fact that it causes

a huge percentage of initial invasion disease (i.e. infectionhappening within the first week of life) and the majority of late-onset infection(i.e. infection occurring after the first week of life). Overall, the capsular serotype III is responsible for greatest cases (80%) of neonatal GBS meningitis (Schuchat, 1998; Nizet and Rubens, 2000).

Colonization of the rectum and vagina of pregnant ladies with GBS, which causes contamination of the amniotic cavity, is connected with GBS sepsis in babies with ahead of schedule onset sickness. In this situation, newborns are colonized intrapartum by aspiration of contaminated amniotic fluid. The lung is a plausible entryway passage for GBS into the circulatory system as these microscopic organisms can hold fast to and attack alveolar epithelial (Rubens *et al.,* 1992) and endothelial cells (Gibson *et al.,* 1993). Pneumonia results from local infections, whereas sepsis and meningitis may be due to the spread of spread of microscopic organisms took after by systemic disease. *Streptococcus agalactiae* is the species designation for streptococci belonging to Lancefield group B. This bacterium is a facultative gram-positive diplococcus with an ultrastructure like that of other gram-positive cocci. Prior to Lancefield's arrangement of hemolytic streptococci in 1933 (Lancefield, 1933), this microorganism was known to microbiologists by its characteristic colonial morphology, its restricted zone of b-hemolysis encompassing settlements on blood agar plates, and its twofold zone of hemolysis that appeared when plates were refrigerated an extra 18 hours past the beginning incubations (Brown, 1937) .

Occasional strains (approximately 1%) are determined to be a-hemolytic or nonhemolytic. GBS can grow in various bacteriologic media. Isolation from different body sites (respiratory, genital, and gastrointestinal tracts) can be enhanced by use of broth medium supplied with antimicrobial agents that inhibit growth of other bacterial species indigenous to these sites (Baker *et al.,* 1973; Lim *et al.,* 1987).

The diagnostic standard is the culture of anal and genital specimens obtained at 35 - 37 weeks of gestation or at delivery when at least one risk factor associated with neonatal infection is present. So as to recognize GBS in vaginal examples, effective standard culture and a quick screening strategy is required to distinguish carriage of GBS in pregnant ladies at the season of delivery (Artz *et al.,* 2003).

Numerous studies have been done on streptococcal contamination of the female genital tract with emphasis on Group B streptococci. Around 10 to 30 % of pregnant ladies

are colonized with GBS in the vaginal or rectal region. Of all babies conceived of these ladies, 1 to 2 % will grow early onset intrusive sickness (EOD) (Motlová *et al.,* 2004).

GBS neonatal contamination is partitioned into two classes, early-onset (<7 days old) and late-onset (7 to 90 days old) illness. Because of the genuine way of GBS contamination, pregnant ladies in the United States are routinely screened for GBS vaginal colonization late in the third trimester of pregnancy; a positive test results in the organization of anti-infection agents amid conception to diminish the danger of GBS exchange to the infant.

Regardless this intervention, the occurence of early-onset GBS infection in the United States remains at 1 in 3,000 live births, relating to around to approximately 1,200 infected newborn per year (Verani *et al.,* 2010). There is additionally confirm that contamination rate are much higher among some ethnic gatherings and in newborn children conveyed at _37 weeks of development (Schuchat *et al.,* 1990; Schuchat *et al.,* 1994; Zalezink *et al.,* 2000; Verani *et al.,* 2010). Additionally, antibiotic prophylaxis does not prevent late-onset diseases. GBS is available in up to 33% of ladies of childbearing age, and one in every thousand live births will be affected by group B streptococcal infection (Artz *et al.,* 2003).

In the 1970s, the bacterium group B Streptococcus (GBS) emerged as the leading infectious cause of early neonatal morbidity and mortality in the United States (Baker *et al.,* 1973; Barton *et al.,* 1973; Franciosi *et al.,* 1973; McCracken, 1973).

Initial case series reported case-fatality ratios as high as 50% (Baker and Barrett, 1974). Maternal colonization with GBS in the genitourinary or gastrointestinal tracts is the essential danger element for disease. Beginning in the mid-1980s, several clinical trials and well-designed observational studies showed that administering intravenous antibiotics in the time of labor to women at risk for transmitting GBS to their neonates could prevent invasive infectionin the first week of life (i.e., early-onset disease) (Allardice *et al.,* 1982; Boyer and Gotoff, 1986; Lim *et al.,*, 1986; Tuppurainen and Hallman, 1989; Garland and Fliegner, 1991; Matorras *et al.,* 1991).

Group B Streptococcus is an important cause of maternal and neonatal morbidity and mortality in several parts of the world. The last few decades have seen intensified efforts in the Western hemisphere in the prevention of this serious infection by identifying and treating pregnant women who carry group B streptococci or who are at highest risk of

transmitting the organism to neonates. The intrapartum use of antibiotics in these women has led not equally to adecrease in the rate of neonatal group B streptococcal disease.(Shet and Ferrieri, 2003).

1.1. The Aim of the Study

1. To identify the *Streptococcus agalactiae* from pregnant women
2. To detect the percentage of colonized *Streptococcus agalactiae* from 35 to 37 gestation age pregnant women.
3. To differentiate between the rate of positive *S. agalactiae* and different age.
4. To detect the rate of group B streptococcus before and after delivery.
5. To identify the better antibiotic for the infectious pregnant women to control the bacterial infection.
6. To decrease the risk factor for the pregnant mother and also for the new born at early onset time because all the pregnant from my country not doing any test from laboratory for detect the streptococcal infection and know about the risk factor of this bacteria to her baby.

2. LITERETURAL REVIEW

2.1. What Is Streptococci

Streptococci typically are Gram-positive, non-motile, catalase-negative, cocci of which happen within stores or frames (Medical micro kaisary). Streptococcus is often a genus that is certainly categorised based on the hemolytic components in to about three types: Alpha-Hemolytic Streptococci, Beta-Hemolytic Streptococci, as well as Non-Hemolytic Streptococci. *Streptococcus agalactiae*, Streptococcus agalactiae, frequently alluded as Group B *Streptococcus* (GBS), is one of four Beta-Hemolytic streptococci, which results in complete rupture of blood cells shown in wide and clear areas surrounding bacterial colonies on blood agar. (Patterson *et al.,* 1996).

Streptococcal species of clinical importance are divided into six groups depended on pathogenic and clinical characteristics. *Streptococcus agalactiae* descents into the pyogenic group. The pyogenic streptococci are recognized on blood agar plates by the classical zone of β haemolysis surrounding colonies. Further classification of the B-haemolytic streptococci is by serological typing of the polysaccharide capsule, a method developed by Rebecca Lancefield in the 1940s. *Streptococcus agalactiae* is serologically grouped as Lancefield Group B, hence it being commonly called Group B *Streptococcus* or GBS (Greenwood *et al.,* 2002; Madigan *et al.,* 2006).

2.2. *Streptococcus Agalactiae*

S. agalactiae is really a diplococcal (a couple of cocci, spherical, pair) gram-positive, non acid-fast germs (2 μm) it does not form spores, isn't motile, and it is catalase-negative (catalase is definitely an enzyme in which catalyzes the lowering regarding hydrogen peroxide). It appears in pairs or short chains and has group B Lancefield antigen current (Timoney et al., 1973).

Streptococcus agalactiae (b-haemolytic streptococcus group B) is identified to cause numerous infections in adults, but clinical attention in these bacteria chiefly relates to their capability to cause serious neonatal sickness, especially meningitis and sepsis. Although neonates born by caesarian section have presented with *S. agalactiae* infection, representative ascending transmission of the micro-organism from the vagina of their moms, in the majority of cases the neonate acquires the infection during labour through

contact with the vaginal discharges of the mother colonized by *S. agalactiae* (Regan *et al.,* 1981; Boyer *et al.,* 1983; Ross,1984; Schwartz *et al.,* 1991; Farley *et al.,* 1993; Edwards *et al.,* 1990).

Group B streptococci (GBS) are typically pathogens which typically havebeen linked to preterm labour. (Regan *et al.,* 1981; Moeller *et al.,* 1984; Thomsen *et al.,* 1987), premature rupture of membranes (Regan *et al.,* 1981; Moeller *et al.,* 1984), and neonatal sepsis (Baker and Edwards, 1983). Children born in order to women with rectal, genital, as well as urinary tract associated with GBS have possibility with regard to colonization (Baker *et al.,* 1973; Boyer *et al.,* 1979; Gardner *et al.,* 1983). along with infection inside the peripartum period. Intrapartum directory tranny along with earlier onset GBS infection have been prevented. (K. M., *et al.,* 1983) through administration of ampicillin in order to targeted populations thought to be at danger for infant infection(Yow *et al.,* 1979; K. M., *et al.,* 1983; Morales *et al.,* 1986; Thomsen *et al.,* 1987).

Within the last few Fifty years, *Streptococcus agalactiae* (Group B Streptococcus – GBS) has been defined as an important pathogen in newborn and pregnant women. Vaginal colonization with GBS in pregnancy is significantly coupled with infections in newborns, and requires analysis (Schuchat, 1999; Schrag *et al.,* 2002; Phares *et al.,* 2008).

Group B streptococcus (GBS, *Streptococcus agalactiae*) infection in adults is being recognized with increased frequency. The infection initiates from soft-tissue infections, bacteremia and also pneumonia (Schwartz *et al.,* 1991). Include those with reduced immunity through diabetes or even most cancers have a very 10- to be able to 15-fold greater connected with GBS infection (Schwartz *et al.,* 1991). In adults, GBS infection has a high case-fatality level; it is also one of the most important causes of neonatal infection. Reports since the 1930s had linked GBS with neonatal meningitis, but the scope of perinatal and neonatal GBS infection did not become distinct until the 1960s, when associations were completed between maternal genital GBS foundation and spontaneous abortions, stillbirths, and preterm carriages (Hood *et al.,* 1961).

Group B Streptococcus (GBS) provides re-emerged as being a significant virus over the last several decades (Kulkarni *et al.,* 2001). The actual vagina and the peri-anal regions/rectum would be the significant reservoirs pertaining to GBS, and the colonization of such parts can be a threat issue pertaining to subsequent contamination in women that are pregnant and also her babies (Nwachukwu *et al.,* 2007).

Group B beta-hemolytic streptococcus (GBS) as well as *Streptococcus agalactiae* can be a varieties with the normal bacterial flora with the gut and also woman urogenital tract (Brooks *et al.,* 2004). GBS infectionoccur as early onset infectionof the newborns on the first week after birth or late onset infectionon the first week after birth to three month. Perinatalinfection reasons septicemia, meningitis or pneumonia,which are supplementary with a high mortality (Schrag , 2002).

2.3. History of Group B Streptococcus (GBS)

S. agalactiae, actually identified as being a cause of bovine mastitis, will be area of the normal microbe flora colonizing the gastrointestinal (GI) system and genitourinary system of the considerable ratio on the population. However, it often gets a great infectious pathogen colonizing the uterus, our blood, mind, and meninges. This kind of pathogen is among the major factors behind invasive attacks in non-pregnant immunocompromised men and women plus will cause bacteremia, septicaemia, meningitis, and pneumonia. Colonization on the rectum and vagina involving women that are pregnant together with GBS will be correlated together with GBS sepsis in infant newborns together with beginning oncoming condition (Glaser *et al.,* 2002).

GBS was initially discovered in 1887 as being a source of infection for bovines; a cause of bovine mastitis. (Schuchat and Wenger, 1994) as well as was first noted as being a individual pathogen in 1953 (Schuchat, 1998). GBS has been classified while normal individual local flora asymptomatically colonising the particular gastrointestinal as well as genitourinary tracts connected with both men and women (Schuchat, 1995; Jeffery and Royal, 2002). his living thing in addition has also been out of the way from throat as well as respiratory tract connected with humans (Schuchat and Wenger, 1994; James, 2001). It is proposed that the gastrointestinal system may be the reservoir regarding GBS in both equally humans and animals which in turn asymptomatically bring pathogenic GBS (Sneath, 1986a) letting this kind of opportunistic living thing for you to transiently colonise the lower genital tract (LGT) connected with females and thus this kind of micro-organism could be present from one particular stage but consequently not recognized actually a short time or maybe 2 or 3 weeks afterwards (Chua *et al.,* 1995b; Bliss *et al.,* 2002; Jeffery and Royal, 2002). This bacterium is a sexually transmitted infection (STI) as it has been present in 31 to 65% of male urethras (Centre, 1996; James, 2001; Bliss *et al.,* 2002). Hence the latest way of revealing GBS in expectant mothers isn't a genuine signal

connected with maternal GBS colonisation during time and also the neonatal illness potential. Various other microorganisms of which furthermore generally asymptomatically colonise the feminine LGT which could cause a negative carrying a child end result incorporate; *Ureaplasma parvum, U. urealyticum, Mycoplasma hominis*, other sexually transmitted and pathogenic bacteria (Knox, 1997) but of such microorganisms, GBS postures the greatest danger for the neonates (Isaacs and Royle, 1999).

Streptococcus agalactiae, generally known as Group B streptococcus (GBS) is among the leading factors that cause neonatal morbidity along with fatality throughout the world (Isaacs and Royle, 1999; Mullaney, 2001; Mehr *et al.,* 2002; Pinar, 2004). In Sydney, within the 1990's, GBS was noted because the many widespread organism leading to neonatal sickness (Garland and Fliegner, 1991; Isaacs *et al.,* 1995; Isaacs and Royle, 1999). Likewise inside United states (USA) this specific microorganism has become the class leading reason behind neonatal sickness since the 1970's (Mullaney, 2001; CDC, 2004a; Dermer *et al.,* 2004). This bacterium is commonly proven to cause sickness inside children, ladies, this immunocompromised mature and also the seniors (Schuchat, 1998; Amaya *et al.,* 2004; Palazzi *et al.,* 2004).

2.4. General Charecteristic Of *Streptococcus Agalactiae*

Streptococcus agalactiae (group B streptococcus was first recognized as a significant cause of neonatal sepsis and meningitis in the United States in the 1970s (Puopolo *et al.,* 2005).

Streptococcus agalactiae (synonym *S. difficile*) is described as a Gram-positive, cocci-shaped bacterium which commonly occurs in pairs or in long chains. They produce small, translucent, round, and slightly raised, pinpoint colonies, measuring nearly 2 mm in diameter and appear yellowish to grey in colour when grown on solid agar (Plumb, 1999; Buller, 2004).

Strains belonging to *S. agalactiae* are described as α-, β- or non-haemolytic (γ) when cultured on blood agar (Kitao *et al.,* 1981; Buller, 2004). They are termed as non-motile, non-capsulated, non-spore forming and are negative for the presence of oxidase and catalase enzymes. These bacteria are ability to grow at pH 9.6 but not at 10°C nor at 45°C nor in the presence of 40% (v/v) bile salts or in the presence of 6.5% NaCl (w/v) (Inglis *et al.,* 1993; Plumb, 1999; Buller, 2004). This bacterium is divided as belonging to the group

B Streptococcus (GBS) species using the Lancefield serogrouping technique (Devriese, 1991; Facklam, 2002). At present, depended on the conformation of the capsular polysaccharide antigen, GBS organisms have been divided into ten serotypes (Ia, Ib and II to IX) (Chaffin *et al.,* 2000; Persson *et al.,* 2004; Slotved *et al.,* 2007).

2.5. Morphology In Addition To Identification Connected With GBS

GBS is a beta haemolytic facultative Gram positive diplococcus which able often be initiate growing in more long chains of paired streptococci (Schuchat and Wenger, 1994). GBS cells are spherical or ovoid from 0.6 to 1.2μm in diameter; however, colonies grown on blood agar plates range in size from 3 to 4mm, they are greyish-white in colour, flat and appear mucoid (Stevens and Kaplan, 2000). GBS produces a distinctive narrow β–haemolytic zone which sometimes may only be observed when the colony has been removed from the blood agar plate (Stevens and Kaplan, 2000). Non haemolytic or β–haemolytic strains account for 1 to 2% of GBS isolates and α-haemolytic or double zone GBS strains are occasional (Stevens and Kaplan, 2000). Typically β–haemolysis is caused by the production of haemolysins O as well as S which diffuse into the media and causes haemolytic activity. However, some strains produce a characteristic opaque β– haemolytic zone which is different from the zones produced due to hemolysin O as well as S. It has been suggested that opaque β–haemolytic zone may be due to a soluble haemolysin which has a low haemolytic activity (Sneath, 1986a).

Colonies of GBS grown on sheep blood agar medium are 3 to 4 mm in diameter, produce a narrow zone of b-hemolysis, are gray-white, and are flat and mucoid. B hemolysis for some strains is apparent only when colonies are removed from the agar. Tests for presumptive identification include bacitracin and sulfamethoxazole-trimethoprim disk susceptibility testing (92% to 98% of strains are resistant), hydrolysis of sodium hippurate broth (99% of strains are positive), hydrolysis of bile esculin agar (99% to 100% of strains fail to react), pigment production during anaerobic growth on certain media (96% to 98% of strains produce an orange pigment), and CAMP (Christie-Atkins- Munch-Petersen) testing (98% to 100% of strains are CAMP-positive) (Facklam *et al.,*1979 ; Tapsall and Phillips, 1987).

Several virulence factors have been identified and include: capsular polysaccharides which avoids the hosts' defences; enzymes such as C5a peptidases and hyaluronidases which spread and destroy the host; beta haemolysins/cytolysin toxins,

lipotechoic acid and superficial protein antigens which are recognised in human infections (Sneath, 1986a; Doran *et al.,* 2003).

The CAMP factor is a thermostable extracellular protein that, in the presence of the B toxin of *Staphylococcus aureus*, produces synergistic hemolysis when grown on sheep blood agar. Hippurate hydrolysis is an accurate method for presumptive identification of GBS, but the condition for 24 to 48 hours of incubation parameters its uselessness. GBS can be distinguished from other streptococci by a combination of the CAMP test, the bile esculin reaction, and bacitracin sensitivity testing (Facklam *et al.,* 1979) .

Biochemical micro methods recognize GBS with reasonable inaccuracy after a 4-hour incubation period (Facklam *et al.,* 1985). Definitive identification of GBS requires recognition of the group B–specific antigen usuall to all of the strains through use of hyperimmune grouping antiserum. Lancefield's special method required acid treatment of large dimensions of broth-grown cells to extract the group B antigen from the cell superficial (Lancefield, 1938).

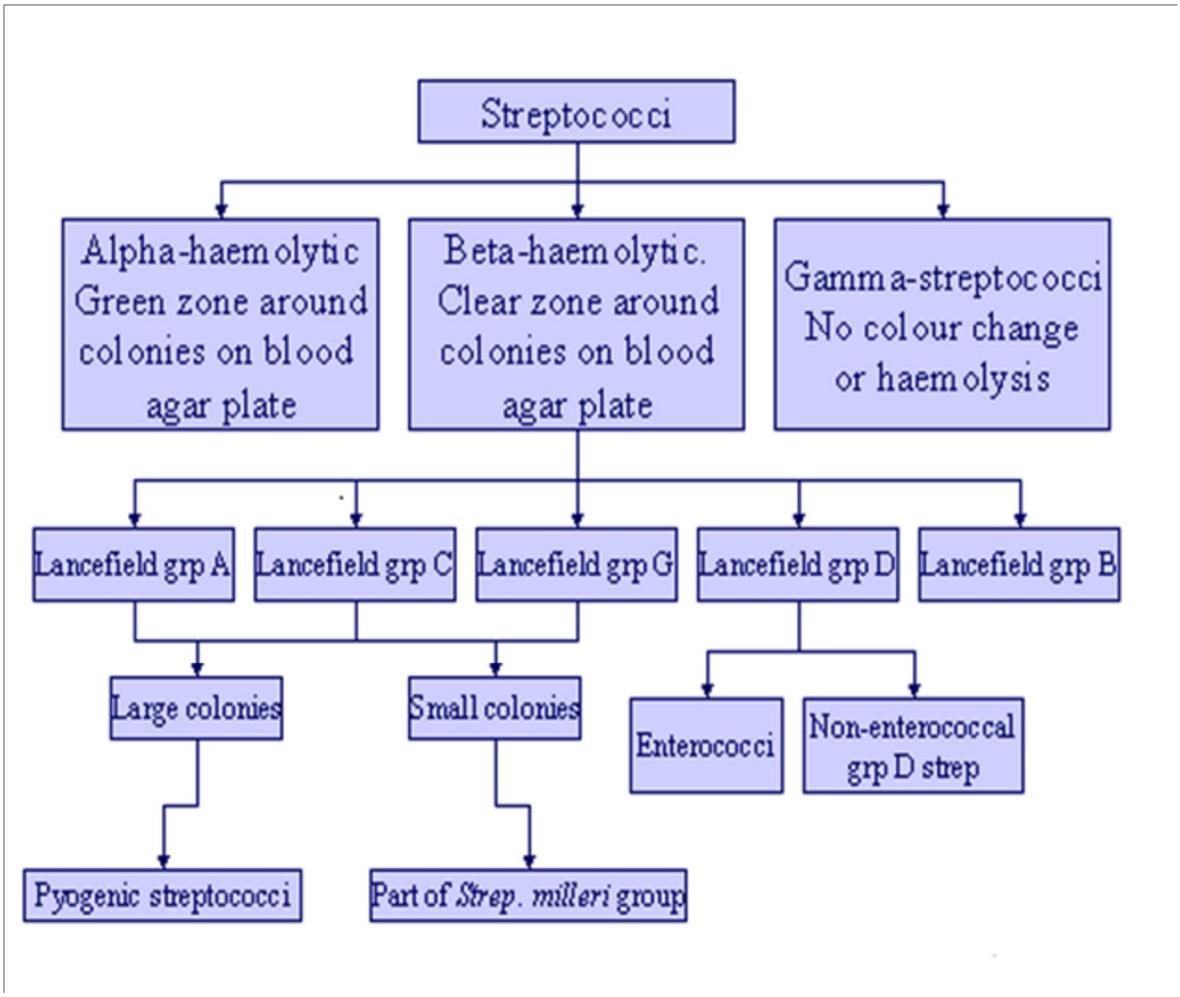
Streptococcus agalactiae (Group B streptococcus; GBS) is the species description for streptococci be in the right place to the Lancefield group B. GBS are facultative anaerobic gram positive cocci and form chains of adjustable length that able to grow on different media. Colonies are 1-3 mm in diameter and greyish-white in colour when it grown on the media of sheep blood agar. The flat mucoid colonies are surroundes superficial s by a clear zone, produced by lysis of RBC in the agar media, produced by bacterial haemolysins (β-hemolysis). Streptococci which generate β- hemolysis are also called β-haemolytic streptococci. 1-2 percent of the GBS strains are non hemolytic (Kilian *et al.,* 2007).

2.6. Classification Of Streptococci

The genera Streptococcus and Enterococcus comprise a big number of species. Table 2.1 lists the most important. a-, b-,and none-hemolysis. a-hemolysis. Colonies on blood agar are walled by a green zone. This "greening" is produced by H_2O_2, which translates hemoglobin into methemoglobin b- hemolysis. Colonies on blood agar are walled by a huge, yellowish hemolytic zone in which no additional intact erythrocytes are current and the hemoglobin is decomposed c- hemolysis. This (illogical) term shows the nonappearance of macroscopically visible hemolytic zones. Numerous streptococci and

enterococci have a polymeric carbohydrate (C substance) in their cell walls superficial named the Lancefield antigen. They are divided in Lancefield groups A-V depended on differenciation in the antigenicity of this antigen. Lancefield described 2 cell wall carbohydrate antigens employing hydrochloric acid–extracted cell supernatants as well as hyperimmune rabbit antisera: the group B–specific or "C" substance usuall to completely strains and the typespecific or "S" substance that allowable classification into types, spacially types I, II, and III (Lancefield and Hare 1935; Freimer, 1967).

Table 2.1. Show the classıfıcatıon of Streptococci



GBS in history designated type Ic were characterized when strains having type Ia capsular polysaccharide (CPS) were exposed also to hold a protein antigen usuall to type Ib, greatest type II, and some type III strains(Wilkinson and Eagon, 1971). Almost wholly clinical isolates of GBS bring a capsular polysaccharide (CPS) and can be divided into ten distinct serotypes or CPS types; Ia, Ib and II-IX(Farley *et al.,* 1993; Slotved *et al.,*

2007). The type specific polysaccharides are repeating units of 5 to 7 monosaccharides (glucose, galactose, glucosamine, and N-acetylneuraminic acid, or sialic acid). The chief serologic method used for serotype determination was antigen extraction and precipitation responses with adsorbed entire -cell antisera introduced by Lancefield in 1934 (Tettelin *et al.,* 2002; Glaser *et al.,* 2002).

2.7. *S. agalactiae* Virulence Factors

GBS products more extra cellular substances, some of which have a role either in virulence or as defensive antigens (Edwards *et al.,* 2006). The finest characterized are the capsular polysaccharides, which converse serotype specificity to GBS (Jennings *et al.,* 1983). The capsule converse virulence to the organism, at least in some, by preventing the deposition of whole composition on the surrounded of the organism in the nonappearance of serotype-specific antibody. Defensive immunity is related to antibodies directed at these serotype specific capsular polysaccharide component (Baker *et al.,* 2000). Candidate group B streptococcal capsular polysaccharide-protein conjugate vaccines for types la, Ib, and III have been advanced and have been tested for protection and immunogenicity in healthy women (Kasper *et al.,* 1996). Conjugate vaccines for serotype II and the newly developed type V also have been developed and have undergone stage 1 clinical trials (Baker *et al.,* 1999).

The pathogenic mechanisms of GBS are not completely understood. Several virulence factors have been described and include: capsular polysaccharides which avoids the hosts' defences; enzymes such as C5a peptidases and hyaluronidases which increase and destroy the host; beta haemolysins/cytolysin toxins, lipotechoic acid and surrounded protein antigens which are recognised in human infections (Sneath, 1986a; Doran *et al.,* 2003). In order to initiate an infection the GBS microorganism must be able to connect to many different cell types within the human body and avoid the body's immune defence structures. Firstly the microorganism must be able to adhere to the cells of the mucous membranes, the epithelial cells lining the vagina and the rectum. Once attached to the body's superficial areas and avoiding the body's immune defences GBS can be vertically transmitted to the neonate during delivery causing invasive infections rapidly after birth which may end in death within 48 hours. Otherwise, once GBS colonisation of the vagina is recognized, GBS can invade the placental membranes and enter the amniotic fluid causing adverse pregnancy outcomes (Katz and Bowes, 1988). From a focus of infection in

the lungs of the foetus or neonate GBS can gain access to the circulatory system causing a rapid bacterial systemic infection and at birth can result in a serious postnatal fatality or prior to birth result in stillbirth or miscarriage (Katz and Bowes, 1988; Nizet *et al.,* 2000).

One of the most important known virulence factors in Group B *Streptococcus* is the β-hemolysis/cytolysin (b-h/c), a superficial associated pore forming toxin which is responsible for the characteristic zone of haemolysis on blood agar plates (Nizet *et al.,* 1996; Nizet, 2002). The b-h/c toxin is expressed by *cylE,* a single open reading frame on the *cyl* operon (Forquin *et al.,* 2007). *cylE* deletion mutants have been shown to be less virulent than wild type GBS in animal models (Liu *et al.,* 2004). Four main roles in pathogenicity have been ascribed to the *cyl* operon, (i) apoptosis in macrophages (Fettucciari *et al.,* 2000, Ulett and Adderson, 2005) (ii) induction of a pro-inflammatory host response (Lembo *et al.,* 2010), (iii) increased resistance to phagocytic killing (Liu *et al.,* 2004) and (iv) induction of cytolysis.

GBS be able to reach the foetus in uteri through ascending infection of the placental superficial as well as amniotic fluid. Alternatively, the neonates may become polluted with the organism on passage through the birth canal. Invasive neonatal infectionmay be caused by both virulence factors in GBS and host factors. The GBS virulence includes factors that obstruct immunological defence mechanisms and the ability to penetrate epithelial and endothelial cellular barriers to reach the bloodstream and deeper tissues. GBS produce toxins that directly injure or disrupt host tissue, and also create factors that cause inflammatory pathways which may irritate the infection(Wibawan *et al.,* 1992; Beckmann *et al.,* 2002). GBS colonisation of pregnant ladies and lack of maternal defence to GBS are also essential factors contributing to invasive newborn disease.

2.8. GBS Serotyping

All GBS serovars are ability of causing neonatal infection and possess a polysaccharide cell superficial antigen composed of rhaminose, N-acetylglucosamine along with galactose (Sneath, 1986a). Differences within these antigens are used to differentiate eight antigenic GBS serovars (I–VIII) (Schuchat, 1998). Type I has been classified into 3 subtypes Ia, Ib, (Schuchat, 1998) and Ia/c (Mullaney, 2001). In addition, a small number of strains do not respond with hyperimmune sera; therefore, they are divided in a separate group called non typeable (Schuchat, 1998). At present, both human along with other animal GBS species are divided together, as taxonomical differences between

them have not been recognized. However, recently the human serovar III has been classified into four distinct phylogenetic lineages which suggests that the human serovar III is largely unrelated to the bovine serovar III (Bohnsack *et al.,* 2004).

2.9. Ultra Structure Of GBS

Early concepts suggested a thick, rigid peptidoglycan layer external to the cytoplasmic tissue layer surrounded by concentric layers of cell wall structure antigens. The group specific carbohydrate was thought to be "covered" by a type-specific CPS. Evidence now supports a model in which the group B carbohydrate as well as the CPS are accompanying independently to cell wall structure peptidoglycan (Deng *et al.,* 2000).

S. agalactiae contains genes expressing various extracellular products, such as capsular polysaccharide and superficial proteins. This bacterium seems to use those polysaccharide and superficial proteins to stick to epithelial cells of host and to evade host defense system (Glaser *et al.,* 2002).

Best GBS strains express a diversity of superficial proteins. Numerous of the superficial protein antigens induce protective immunity in animal models and are possible vaccine candidates (Larsson *et al.,* 2006). The first superficial protein identified in GBS was the c antigen (Wilkinson and Eagon, 1971). The c antigen is composed of the trypsin resistant α-protein and the trypsin sensitive beta protein (Bevanger, 1985).

GBS, like most other bacterial pathogens, often haven bacteriophages. Bacteriophages of GBS were at first isolated from bovine strains of the bacteria in 1969 (Russell *et al.,* 1969). Phages were subsequently related to be ubiquitous in human GBS strains and they formed the basis for various phage-typing systems for GBS (Stringer,1980; Haug *et al.,* 1981). Double-stranded DNA bacteriophages commonly utilize a two-component lytic system that includes together a holin and a lysin (Grundling *et al.,* 2001). A phage holin unconfined intracellular first disrupts the bacterial cell surface, exposing the peptidoglycan to the degradative action of the lysine, which leads to cell lysis and the release of progeny phage. The lysin alone, however, is often sufficient to lyse the bacteria when they are exposed to preparations of the enzyme outside (Loeffler *et al.,* 2001).

2.10. Etiology

Zaleznik, *et al.,* (1999) from 1993 to 1996, revealed that the attack amount for peripartum maternal infection different generally by city and may have been influenced by the frequency of administration of intrapartum antibiotics or of evaluating febrile ladies by performance of blood cultures. Pregnancy loss or GBS infectionin the newborn occurred in 28% of these maternal cases. Among neonatal and maternal GBS isolates, serotypes Ia (34%–37%) and III (25%–26%) predominated, and type V was frequent (14%–23%). These results provide a description of invasive GBS perinatal infection during the period in which guidelines for inhibition were actively disseminated.

Khadijeh Nasri *et al* ., (2013) discovered that advantageous traditions associated with GBS ended up being observed in 04.1%. Initially adverse GBS end result ended up being identified not to ever modify once check-up. Yet constructive civilizations ended up adverse with 1. 6% connected with women of all ages soon after a digital vaginal check-up. After 24 hrs only two. 7% connected with primarily adverse GBS ended up being constructive no one having initially constructive GBS received adverse traditions. Tenderness to penicillin along with vancomycin ended up being 100%, erythromycin 74%, ampicillin 65%, cefazolin 62. 8%, cefotaxime fifty four. 2% along with ceftizoxime ended up being 40%.

Hajare *et al* .,(2012) established that this two hundred expecting mothers screened-in, 7.5% ended up colonized by simply GBS. Number of cases connected with GBS colonization were being higher Amongst expecting mothers inside the finally trimester who were 20 years along with primigravida. The many isolates ended up very sensitive to Ampicillin, erythromycin and penicillin nevertheless ended up resistant to gentamicin along with kanamycin.

Berkowitz, *et al.,* 1990 in (New York) showed that on the list of 156 vaginal along with cervical isolates connected with GBS ended up being analyzed for resistance to penicillin, ampicillin, clindamycin, cefoxitin, gentamicin, along with erythromicin. Zero resistance to penicillin as well as ampicillin ended up being identified, neither ended up being penicillinase creation proven. A high amount of resistance to gentamicin ended up being famous (91%). On the isolates analyzed, 9, 9.5, and 15. 3% demonstrated possibly resistance as well as advanced beginner susceptibility to erythromycin, clindamycin, along with cefoxitin, respectively. Thirty traces (19%) demonstrated a many antibiotic resistance

design. Given the particular excessive penicillin along with ampicillin treatment failing costs while wanting to eradicate vaginal GBS colonization along with our own studies connected with higher along with many pill resistance patterns connected with GBS, picking a an alternative antibiotic strategy can be connected with considerable specialized medical value.

Onipede *et al.,* (2012) in Nigeria discovered revealed that prevalence of 11.3% GBS vaginal colonization which high with age. There was no significant association between GBS colonization status and age (p >0.05), gestational age (p >0.05), gravidity (p >0.05) and obstetric risk factors (p >0.05)). There was no occurence of GBS infection observed. Although, all (17) the GBS isolates were 100% resistance to penicillin, ampicillin, cefoxitin and clindamycin. Resistance to cefotaxime (11.8%), erythromycin (64.7%) and vancomycin 70.6% were observed. Group B Streptococcus colonization in vagina in late pregnancy has been established in the antenatal clinic of the teaching hospital with the attendant risk to the fetus in the population of those affected. There were high and multiple resistance patterns of the GBS isolates to different antibiotic cs in this study. This calls for a review of the present hospital policy to include the routine screening of GBS during antenatal visits and surveillance.

Jannati *et al.,* (2012) showed that each isolates ended up susceptible to ampicillin, vancomycin along with penicillin. One particular isolate(1.7%) showed diminished susceptibility design topenicillin (MIC; 0.20 μg/ml). There was 3 (5.3%) isolates semi-sensitive(0.25-1 μg/ml) to erythromycin (2; 0.5 μg/ml along with 1; 0.38 μg/ml) along with only two (3.5%) isolates to clindamycin (1; 0.5 μg/ml, 1; 0.38 μg/ml). Moreover, only two (3.5%) isolates ended up resistant to clindamycin (1;04 μg/ml, 1;2 μg/ml). According to the hard disk drive diffusion test out, 47 (83.9%), 8 (14.2%) along with 7 (12.5%) isolates ended up resistant to Cotrimoxazole, ciprofloxacin along with ceftriaxone respectively.

2.11. Epidemiology

Several other species of b hemolytic streptococcus in group b, c, and d live among the normal flora of humans and other mammals and can be isolated in clinical spacemence from diseased human tissue. The GBS represented by the sp *Streptococcus agalactiea* demonstrated clearly how the spreading of a parasite can modificate in arelativly short time. It regularly resides in the ladies vagina, pharynx, and large intestine . A straine found in cattle is a frequent cause of bovine and mastitis .the major result of human colonization

has been a sudden increase in serious infections in newborn and compromised people. Five serotypes (Ia, Ib, II, III and V) are responsible for 85% of neonatal GBS infectionworldwide and the distribution of these serotypes is the same across all WHO regions (Edmond *et al.,* 2012).

Streptococcus agalctiea has been chiefly implicated in neonatal, wound, and skin infections and in endocarditis. human suffering from diabetes and vascular infectionare particularly at risk to wound infections. Because of its location in the vagina, GBS can be transferred to the baby during born, sometimes with dire consequence. An early – onset infection develops a few days after birth and is accompanied by sepsis, pneumonia and high mortality (Kathleen, 2005).

Previous studies on the epidemiology of infections due to the group B *Streptococcus* have shown a high amont of colonization of the female genitourinary tract by this micro organism. Therefore, most investigators implicated the vaginal canal as the primary cause of infection for neonates. (Colonization of the anorectal area in women by the group B *Streptococcus* was reported by Franciosi *et al.,* 1973).

This bacterial pathogen is the most prevalent cause of neonatal pneumonia, sepsis and meningitis in the united states and Europe. Approximately 15000 babies a year acquire infection, with 5000 deaths in the united states(USA) only. A later complication comes on in 2 to 6 weeks with symptoms of meningitis – fever, vomiting and seizures. About 20% of kid have extended term neurological harm. Because most cases occur in the hospital, personnel must be aware of the risk of passively transmitting this pathogen, especially in the neonatal and surgical units. Pregnant women should be screened for colonization in the 35 to 37 gestation age and immunized with globulin and treated with a course of antibiotics if infection is found (Kathleen, 2005).

Group b streptococci occasionally source of infections of the skin and connective tissues, sepsis, urinary tract infections, pneumonia, and peritonitis in immuno compromised individuals. About one in 1000 neonates suffers from a sepsis with or without meningitis. These infections manifest in the first days of life (early onset infection) or in the first weeks of life (late onset infection). In the early onset infection, the infection is caused intra partum by B streptococci colonizing the vagina. Potential predisposing factors include birth complications, premature birth, and a lack of antibodies to the capsule in mother and neonate (Kayser *et al.,* 2005).

The association between GBS strains of human and bovine origin has been queried for years. There is no compelling evidence to suggest that cattle serve as a reservoir for human disease, and transmission of GBS from cows to humans is exceedingly odd (Finch and Martin 1984). In addition, during the past decades when group B Streptococcus has been a leading human pathogen in the United States, most of the population has lacked exposure to the two possible modes of transmission: (1) proximity to dairy cattle (direct contact) and (2) ingestion of unpasteurized milk. Application of molecular techniques to type III strains from bovine sources and strains infecting human neonates supply the assertion that these lineages are unrelated. Phylogenetic lineage determination does indicate, however, that some clonal complexes of invasive or colonizing strains in humans are related to "ancestral" lineages of bovine GBS (Bohnsack, *et al.,* 2004).

Infection is extent between cows and/or sheep through the milker's hand, connected to instrument, and the mouth of calves. Once infected, these mammals are likely to lose their reproductive ability due to blocked milk channels through inflammation (Timoney *et al.,* 1973).

GBS colonization is typically asymptomatic in ladies, this is a known source of infection in neonates and typically baby. The most common cause of infection in newborns is GBS. Vertical transmission typically occurs at the beginning of labor or after rupture of membranes during delivery (Schrag *et al.,* 2002). This microorganism has been shown to be effective in adverse outcome during pregnancy including preterm labor, premature rupture of membranes, and chorioamnionitis, postpartum sepsis, pneumonia and meningitis. Also there are certain reports of osteomyelitis and mastitis with GBS in the mothers after delivery (Cunningham *et al.,* 2010).

Group B Streptococcus has appeared over the past decade as a common pathogen in the etiology of neonatal sepsis (Eickoff *et al.,* 1964 ; McCracken, 1973). Previous studies on the epidemiology of infections due to the group B Streptococcus have shown a high amount of colonization of the female genitourinary tract by this organism. Therefore, most investigators implicated the vaginal canal as the primary source of infection for neonates. Colonization of the anorectal area in lady by the group B Streptococcus was reported by Franciosi *et al.,* 1973.

2.12. Maternal GBS Colonization

Significantly GBS was defines as being a virus with expecting mothers creating: i) reproductive system area connected such as; postpartum endometritis (10 to 20%), puerperal sepsis along with chorioamnionitis; along with, ii) postpartum complications such as: UTI's, bacteremia, injury attacks regarding caesarean shipping and delivery, along with sometimes meningitis (Gibbs and Blanco, 1981; Faro, 1981; Persson *et al.,* 1988; Fletcher and Gordon, 1990;Farley *et al.,* 1993a).

Group B Streptococcus can be part of the regular human being microbiota along with somewhere around 30% in the people typically are colonized on a single moment. Colonization is significant since it appears to precede obtrusive disease. GBS continues to be separated from the rectum, perianal area, vagina, cervix along with urethra (Melin, 2011). Most of the frequency scientific tests considering colonization are actually carried out on expecting mothers along with coming from most of these it can be acknowledged that colonization costs typically are higher with sexually lively persons, in particular people that have many sex companions, along with improves having maternal era (Sendi *et al.,* 2008, Rocchetti *et al.,* 2010). It is acknowledged that this vaginal bacteria is definitely an essential aspect with being pregnant outcome along with GBS colonization can be regarding earlier impulsive abortion (Rocchetti *et al.,* 2010).

GBS is additionally an important virus with maternal intrapartum along with postpartum attacks. The actual likelihood connected with puerperal septicemia because of GBS is approximately one to two in thousand deliveries (Blanco *et al.,* 1981; Pass *et al.,* 1982). In a single study, GBS ended up being separated coming from 15% connected with constructive blood civilizations extracted from postpartum sufferers. thirty three In the related proportion connected with women of all ages having postpartum endometritis, GBS ended up being separated from the endometrium (Rosene *et al.,* 1986c). Just one more study identified that, inspite of the management connected with antibiotic prophylaxis, endometritis generally created with women of all ages who were initially identified to get GBS inside the endometrium throughout cesarean segment (Watts *et al.,* 1991).

The actual frequency along with healthy heritage connected with GBS colonization in the feminine decrease vaginal area are actually carefully researched throughout being pregnant. GBS ended up being restored from the vagina along with cervix with somewhere around 19% (range, 9% to 26%) connected with 8000 expecting mothers applying

discerning traditions medium (Regan *et al.,* 1991). The actual gastrointestinal area would be the main water tank connected with GBS, along with vaginal colonization happens secondarily from the gastrointestinal source. The actual frequency connected with GBS isolation can be greatest inside the rectum, advanced beginner inside the vagina, along with most affordable inside the cervix. A plan vaginal-rectal traditions is currently proposed to find GBS with expecting mothers (Schuchat *et al.,* 1996). Around 20% (range, 10% to 30%) connected with expecting mothers have got GBS with vaginal along with rectal civilizations with scientific tests applying discerning media (Boyer *et al.,* 1983; Hoogkamp-Korstanje *et al.,* 1982; Comple *et al.,* 1979; Merenstein *et al.,* 1980; Gardner *et al.,* 1979). Colonization costs can vary by simply era, ethnicity, and various geographic spots. GBS can even be restored from the urethra connected with 45% to 63% in the men companions connected with feminine carriers, revealing that sex sign may also occur (Franciosi *et al.,* 1973; Gardner *et al.,* 1979).

In 1938, Fry explained three lethal conditions connected with endocarditis with postpartum women of all ages. This was your initial insight that group B Streptococcus ended up being a human being virus and might result in puerperal contamination. Postpartum attacks such as septic abortion, bacteremia, chorioamnionitis, endometritis, pneumonia, along with septic osteoarthritis were saved sporadically after that, nevertheless group B streptococcal attacks with postpartum women of all ages, as with neonates, ended up uncommonly described reported before of 1970 (Ramsay and Gillespie, 1941; Butter and Moor; 1941; Hood *et al.,* 1961).

Pregnant women have the similar prevalence of GBS as non-pregnant women. The amont of colonization does not differ with gestational age (Yow *et al.,* 1980; Dillon *et al.,* 1982). The diffusion of GBS serotypes also remains constant throughout gestation and the puerperium. Approximately one third of isolates are type I, one third type II, and one third type III. Although the degree of GBS remains constant, throughout pregnancy either intermittent or transient carriage happens in 35% to 40% of pregnant GBS carriers. Persistent GBS carriage with multiple consecutive positive cultures happens in only 30% to 50% of pregnant GBS carriers. Approximately 30% of pregnant GBS carriers do not fall into these categories (Anthony *et al.,* 1978Yow *et al.,* 1980; Hoogkamp-Korstanje *et al.,* 1982).

Group B Streptococcus is part of the normal human micro biota and nearly 30% of the population are colonised at any one time. Colonisation is very important as it occure to

lead invasive disease. GBS has been isolated from the rectum, perianal area, vagina, cervix and urethra (Melin, 2011). Many of the prevalence studies looking at colonisation have been transported out on pregnant women and from these it is known that colonisation amounts are higher in sexually active person, specifically those with multiple sexual partners, and increases with maternal era (Sendi, *et al*., 2008, Rocchetti *et al*., 2010)

Relapse as well as recurrence connected with group B streptococcal contamination happens within the estimated 0. 5% to 3% connected with newborn. Indicators can build throughout treatment with the primary event as well as on the phase connected with 3 days and nights to three months soon after completion connected with therapies (Atkins *et al.,* 1998; Moylett, *et al.,* 2000).

Many of the prevalence studies considering at colonization have been passed out on pregnant ladies and from these it is known that colonization amount are biger in sexually active persons, specifically those with multiple sexual partners, and multiplications with maternal age (Sendi, *et al.*, 2008, Rocchetti, *et al.*, 2010). It is recognized that the vaginal flora able to an very important factor in pregnancy outcome and streptococci colonization is supplementary with previous spontaneous abortion (Rocchetti, *et al.*, 2010).

2.13. Signs And symptoms With GBS Colonization

A mother may direct signs and symptoms of GBS colonization during gestation as well as in labour. Through gestation urinary genital tract GBS disease may results in miscarriage, preterm rupture of membranes (PROM) (before the onset of labour) (Jeffery and Royal, 2002) and recurrent urinary tract infections (Persson *et al.*, 1986a; Persson *et al.*, 1986b; Fletcher and Gordon, 1990; Schuchat, 1995). Through labour in particular instances, the lady may presence signs or indicators of streptococuus colonization. The obstetric dangers factors that can be checked through labour include: PROM for 18 hours or more (OR 2.39, 95% CI, 1.38-4.14) (Adair *et al.*, 2003); an intrapartum fever of 38 ^{0}C or greater (OR 4.65, 95% CI, 2.48-8.69) (Adair *et al.*, 2003); preterm birth (less than 37 weeks) (OR 10.4, 95% CI, 3.9-27.6) (Oddie and Embleton, 2002) and/or low birth weight (≤2500gm); and, preterm labour (Jeffery and Royal, 2002). Postpartum a mother earlier colonised with urinary genital tract GBS may development clinical chorioamnionitis (Benitz *et al.,* 1999a; Oddie and Embleton, 2002; Schuchat, 1995; Weisman *et al.,* 1992).

The mother can be asymptomatically colonized with GBS through labour and the baby can still be at danger of GBS colonization and potential EOGND disease. The occurence of neonatal EOGND is lower; however, the following seven maternal complications have been associated with EOGND diseases and adverse pregnancy outcomes. A neonate is at a big risk of EOGND when the mother is heavily colonized with GBS at the time of delivery (Jeffery and Royal, 2002) or when the neonates is delivered preterm (Garland and Kelly, 1995; Jeffery and Royal, 2002). A preterm baby has an OR 10.4 (95% CI, 3.9 to 27.6) greater chance of GBS disease associated to a term delivered infant (Schuchat, 1995).

A neonate born to a mother through symptoms of PROM for further than 18 hours (Garland and Kelly, 1995) has an OR of 25.8 (95% CI, 10.2 to 64.8) (Oddie and Embleton, 2002) chance of contracting EOGND. In contrast, neonates born to mothers with a ruptured membrane before the onset of labour (Benitz *et al.*, 1999a) have an OR of 11.1 (95% CI, 4.8 to 25.9) chance of increasing EOGND (Oddie and Embleton, 2002). The neonate is also at danger of EOGND if the mother expressed signs of fever during of labour. These infants have an OR 10.0 (2.4 to 40.8) of developing a GBS disease (Oddie and Embleton, 2002). Again the danger of EOGND would be increased when their mothers were diagnosed through maternal GBS sepsis (Garland and Kelly, 1995).

2.14. Exactly How GBS Transported To Neonates

Boyer and associates found that amount of vertical transmission were substantially higher in lady with heavy than in women with light colonization (65% versus17%) and that colonization at multiple sites and development of early-onset infection were more likely between infants born to heavily colonized mothers. The probability of colonization in a infants born to a woman who is culture-positive at time of delivery is unconnected to maternal age, race, parity, or blood type or to duration of labor or procedure of delivery (Boyer, *et al.,* 1983).

The neonate is at greatest danger of GBS disease upon delivery, and premature infants are at the greatest danger of death and disease (Schuchat and Wenger, 1994; Schimmel *et al.,* 1998; Mullaney; 2001). Normally the particular infants gets to be colonised having GBS throughout manual effort as a result of vertical sign from the GBS colonised mother. Directory sign connected with GBS coming from colonised mothers may lead to 50 to 75% in their neonates growing to be colonised having GBS (Boyer *et al.,*

1983; Dillon *et al.,* 1987; Jeffery and Royal, 2002). During labour a healthful mother colonised with GBS will not all times show signs or symptoms of colonisation along with, therefore, vertical transmission from mother to infant at the time of delivery may present unnoticed and result in neonatal infection. Maternal recognition of GBS during pregnancy and administration of medication to the mother during labour will lead to a reduced occurence of neonatal GBS colonisation and subsequently a decrease in the occurence of neonatal GBS infection.It is not yet determined whether or not preterm as well as minimal beginning bodyweight neonates are in higher chance for colonization coming from maternal solutions than time period baby. Most neonates exposed as a result of their mothers to GBS have got contamination that is limited by exterior as well as mucous tissue layer web sites (colonization) that results coming from toxins in the oropharynx, gastric items, as well as gastrointestinal area by simply taking connected with afflicted amniotic fluid as well as maternal vaginal secretions. Healthy baby colonized from your maternal source show tenacity connected with contamination on mucous tissue layer web sites for months (Paredes *et al.,* 1976; Baker and Edwards, 1988).

GBS can ascend into the upper genital tract (UGT) and pass through placental membranes into the amniotic fluid where the GBS infected amniotic fluid may be aspirated by the neonate causing miscarriages, preterm delivery and stillbirths (Katz and Bowes, 1988; Garland, 1991; Nizet, 2002). Neonates able also to acquire GBS, although less frequently than previously described; from infected breast milk (Mullaney, 2001); through nosocomial (Mullaney, 2001) or public acquisition (Baker and Kasper, 1977); or as a recurrent disease in a new line after antimicrobial medication (Schuchat, 1998). Alternatively, GBS disease may present when neonates are medicated for an illness and administered antibiotics. This changes the infants normal flora and easily to invasive GBS infection (Schuchat, 1998).

The distribution of CPS types in group B streptococcal isolates from mothers is comparable to that in isolates from healthy infants. Other sources for group B streptococcal colonization in neonates have been recognized. Horizontal transmission from hospital or community major to neonates is an very important, albeit decrease frequently proved, mode for transmission of disease (Paredes, *et al.,* 1976 and Anthony, *et al.,* 1983). Cross-contamination from maternally infected to uninfected neonates can happen from hands of nursery personnel staff (Easmon*, et al.,* 1981).

The actual mode connected with sign likely can be fecal-oral. No matter whether obtained by simply vertical as well as horizontal mode, colonization connected with mucous tissue layer web sites with neonates along with fresh baby generally lasts for months as well as a few months (Hansen *et al.,* 2004).

2.15. Invasive GBS InfectionWith Newborn

Neonatal sepsis refers traditionally to sepsis in newborn children during the therty day of life. However, greater survival of immature and premature infants has caused in a big group of baby with a great susceptibility to disease for a more time after birth, and the inclusion time for neonatal sepsis and meningitis regularly covers the whole hospital time (Baltimore, 1988; Ferrieri *et al.,* 2004). Two specialized medical syndromes occur amid fresh baby having group B streptococcal infectionwhich might be epidemiologically and distinct relate to age at onset (Franciosi *et al.,* 1973 and Baker *et al.,* 1973).

Neonatal infection is preceded by the asymptomatic colonisation of the mother genital tract at time pregnancy and thirty to seventy percntage of infants born to colonised mothers will be colonised themselves. One to three percent of infants born to colonised mothers will advance disease infection(Schuchat, 1999; Heath and Schuchat, 2007; Melin, 2011; Daniels *et al.,* 2011;).

In times past, the attack amount for the first of these syndromes, designated early-onset because it happen within the first 6 days of birth (mean onset 12 to 18 hours), ranged from 0.7 to 3.7 per 1000 live births. The attack levels for late onset infection (mean onset 7 to 89 days of age) ranged from 0.5 to 1.8 per 1000 live births. Multistate actual surveillance that described cases of invasive infection in a population of 10.1 million in 1990 reported an occurence of 1.6 and 0.3 per 1000 live births for early-onset and late onset infection (Zangwill,*et al*., 1992).

Two different clinical syndromes present between neonates with GBS disease. These differ in the age at onset, pathogenesis, and outcome. Early-onset disease occurs within the first 7 days of life. The mean age of clinical onset is the first few hours of life. A significant percentage percentage of these infections are apparent at birth (14%) or become symptomatic within the first 90 minutes of life (29%), representing that in utero GBS exposure and infection often occur (Baker, 1979). In fact, approximately 70% of blood cultures are positive at birth in early-onset GBS disease (Boyer *et al.,* 1983).

2.16. GBS InfectionWith Neonates

Maternal asymptomatic LGT GBS colonization could potentially cause the particular foetus to abort or possibly a neonate to get created stillborn so they can being delivered preterm (Katz and Bowes, 1988). To avoid most of these adverse being pregnant outcomes women of all ages along with their companions have to be screened-in prior to conceiving and also early on inside the being pregnant with the profile of this bacterium. GBS screening in the mother should to go on through the being pregnant because GBS may possibly recolonize the particular LGT in the mother after the management connected with antibiotic treatment (Knox *et al.,* 1997; Jeffery and Royal, 2002). Possibly a protocol for early on gestational detection linked with GBS has to be intended along with executed which might lead to the particular lessening in adverse being pregnant outcome conditions. This protocol can help to reduce the amount of miscarriages that occur, in particular in instances where a woman has received a earlier miscarriage. Preterm job may be attributable to the particular profile connected with GBS inside the amniotic fluid (Kenyon *et al.,* 2001). Kenyon *et al.,* (2001) researched microbial colonization in the cervicovaginal along with amniotic fluid with women of all ages having preterm manual work and they identified GBS was being provide.

Group B Streptococcus emerged as being a reason behind neonatal meningitis, sepsis along with pneumonia inside the 1970's (Anthony and Okada, 1977). GBS was previously recently been informed they have the particular probable to result in human being contamination, nevertheless it will be possible that in those times the particular clonal extension of the profitable sponsor used lineage greater the particular frequency in the disease. It's recently been witnessed recently having ST-17 clones (Sorensen *et al.,* 2010). With The United Kingdom, Wales and Northern Ireland the particular rate connected with GBS bacteraemia such as neonatal disease can be only 2.8 per 100 000 people (HPA, 2011).

They concluded that preterm delivery capable present when GBS has attacked the placental membranes reducing the membranes tensile strength and elasticity causing it to separation (Schuchat, 1998; Stoll *et al.*, 1996). It had also been suggested that GBS creates proteases that degrade the placental tissue and same mechanisms may promote membrane separate causing miscarriage and preterm passing (Kenyon *et al.*, 2001). Given that preterm delivered infants are at greater danger of EOGND (Oddie and Embleton, 2002)

and that GBS effects preterm delivery then early third trimester screening may reduce the occurence of infants that are born preterm and as a consequence lessening the associated GBS neonatal disease of those groups of infants.

2.17. Early Onset GBS Infection(EOD)

Early onset GBS neonatal disease(EOGND) can be attributable to GBS invading along with infecting the particular neonate's lung area, creating pneumonia, next later GBS may perhaps share systemically via the particular neonate's circulatory technique creating septicemia (sepsis) along with meningitis (Fletcher and Gordon, 1990; Mullaney, 2001). Prior to 2001, 15 to 50% connected with neonates systemically afflicted having GBS in high the bucket every year (Fletcher and Gordon, 1990; Mullaney, 2001). The actual fatality rate regarding EOGND continues to be as high as 50% (Anthony and Okada, 1977); on the other hand, latest info implies a neonatal fatality rate connected with 5 to 10% (Fletcher and Gordon, 1990; Isaacs and Royle, 1999; Mullaney, 2001; Dermer *et al.,* 2004;). Of these neonates having EOGND somewhere around half that endure can experience lasting sequelae (Fletcher and Gordon, 1990).

GBS reasons early onset GBS neonatal septicemia (EOGNS) with somewhere around 80% connected with GBS afflicted neonates whilst different manifestations connected with EOGND incorporate pneumonia along with meningitis which in turn occur with 7 along with 6% connected with afflicted neonates; respectively (Fletcher and Gordon, 1990; Mullaney, 2001). Complications connected with GBS attacks have also been described with 89% connected with GBS afflicted newborn along with little ones that lived with GBS sepsis having as well as without having pneumonia (CDC, 1997).

Individuals neonates having EOGND that undergo can experience neurodevelopmental flaws for example psychomotor retardation, spasticity, hemiparesis along with seizures (Fletcher and Gordon, 1990). They are able to in addition experience ability to hear as well as image loss along with an increased possibility connected with bronchopulmonary dysplasia (Fletcher and Gordon, 1990). Weisman *et al*. (1992) and Schuchat (1998) identified that nearly 83% off GBS afflicted neonates started to be characteristic quite rapidly inside the initial seventy two hours of life (Weisman *et al.,* 1992; Schuchat, 1998). EOGND just isn't limited by mothers that produce their children naturally (vaginal birth). Weisman *et al* (1992) researched the particular information connected with 245 neonates having GBS bacteremia coming from nine private hospitals

along the UNITED STATES along with identified that EOGND taken place with 37/149 (24. 8%) connected with time period caesarean provided children along with 29/96 (30. 2%) connected with preterm caesarean provided children.

Heavy colonization with GBS continues to be discovered more frequently with Black women of all ages than with white-colored National women of all ages as well as Oriental women of all ages. The actual possibility connected with EOD with Black newborn is additionally higher. The higher colonization rate may perhaps make clear the bigger chance connected with both equally early- along with late-onset GBS infectionamid African Americans, nevertheless whether or not socioeconomic components along with differentiated medical in addition have an effect on danger connected with GBS infectionjust isn't acknowledged. In addition, studies connected with excessive colonization costs with Scandinavian women of all ages may perhaps obstacle the particular theory connected with more GBS infectionwith populations having excessive colonization costs (Regan *et al.,* 1991; Bergseng *et al.,* 2007). Various other chance components gestational diabetes (Hakansson and Kallen, 2006) along with recurrent vaginal qualifications (Schuchat *et al.,* 2000), typically are described to improve danger connected with expecting having EOD.GBS reasons 60% off sepsis with preterm neonates along with sepsis would be the 2nd most popular reason behind dying with preterm children (behind dangerous malformations) (Doyle *et al.,* 1999; Mehr *et al.,* 2002). With Quotes GBS fatality with quite preterm newborn greater coming from 14% with 1980s to 44% with 1990s (Doyle *et al.,* 1999; Mehr *et al.,* 2002).

Preterm babies afflicted having GBS will also be at risk of lasting sequelae like the development connected with obvious ductus arteriousus, intraventricular hemorrhage, along with periventricular leukomalacia (Stoll *et al* ., 1996; Schuchat, 1998; Baker and Edward; 2003). Complications can include deficiency of air towards the brain and crucial parts in the human body such as the heart creating irreparable brain along with other body organ destruction.

An Australian study in 1999, discovered microbes which were jointly to blame for 50% off early onset neonatal sepsis infection conditions typically are different Streptococcal species for example *Streptococcus pneumoniae*, along with *Enterococcus faecalis* and also *Escherichia coli*, *Haemophilus influenzae* type B, *Listeria monocytogenes*, different Gram-negative bacilli, anaerobes, *Staphylococcus aureus* and Yeast infection spp. (Isaacs and Royle, 1999). This Foreign study in addition identified that

GBS on it's own ended up being to blame for 50% off EOGNS conditions (Isaacs and Royle, 1999).

In 48 hours soon after beginning almost all neonates afflicted having GBS can exhibit signs and symptoms connected with early on GBS obtrusive neonatal contamination, although 78% off conditions can show signs and symptoms inside the initial twenty four hours soon after beginning (Towers *et al.,* 1999) which implies intrapartum pathogenesis. Weisman *et al.,* (1992) identified somewhere around 22% connected with time period neonates, even with staying afflicted having GBS failed to show any symptoms connected with contamination inside the initial twenty four hours (Weisman *et al.,* 1992; Towers *et al.,* 1999). Research connected with Black neonates in addition identified that these neonates failed to constantly show signs connected with EOGND contamination (Towers *et al.,* 1999; Zaleznik *et al.,* 2000). Compared 100% connected with neonates that provided preterm indicated early on symptoms connected with EOGND (Weisman *et al.,* 1992). The most typical signal connected with EOGND can be respiratory hardship (Mullaney, 2001), which is often verified by simply x-ray along with established by simply GBS traditions. Respiratory system hardship happens with 80% off EOGNS conditions (Jeffery and Royal, 2002). Various other signs and symptoms incorporate cyanosis, bad perfusion, hypotension, listlessness, bad muscle mass tone and also bad serving, heat instability along with sugar instability (Mullaney, 2001; Weisman *et al.,* 1992). Becoming easily irritated along with hyperthermia (>37.2 ^{0}C) ended up described more frequently with time period children although listlessness as well as bad muscle mass tone as well as both equally, neutropenia, along with hypothermia (<36 ^{0}C) ended up more usual with preterm neonates (Weisman *et al.,* 1992). Neonates having EOGND meningitis may perhaps encounter recurrent seizures (Weisman *et al.,* 1992).

Streptococcus agalactiae group B streptococcus GBS was initially recognized as a tremendous reason behind neonatal sepsis along with meningitis in the USA in the 1970s. Numerous specialized medical studies have got proven that using intrapartum penicillin as well as ampicillin substantially minimizes the particular rate connected with neonatal colonization having GBS as well as the likelihood connected with early-onset neonatal GBS infection(EOGBS) (Boyer, *et al.,* 1983; CDC, 1996; Boyer and Gotoff; 1996).The particular Facilities for Condition Manage along with Reduction (CDC) posted opinion guidelines for preventing neonatal GBS infectionthat promoted using the maternal

screening-based as well as chance factor– based method to intrapartum antibiotic prophylaxis (IAP).

With early-onset GBS, there is a strong partnership between rate connected with neonatal assault along with the size of the particular inoculum along with quantity of colonized neonatal positions (Pass *et al.,* 1979). Occurrence connected with vagainal colonisation can be thought to be the most important chance element for early on starting point neonatal infection(Hansen *et al.,* 2004; Van Der Mee-Marquet *et al.,* 2009), though more maternal along with obstetric chance components with the development connected with EOD incorporate (Poyart *et al.,* 2008; Melin, 2011):

1. Premature beginning as well as minimal beginning bodyweight.

2. Extended rupture connected with amniotic membranes.

3. Maternal fever during labour as well as chorioamnionitis.

4. GBS separated coming from urine samples during pregnancy.

5. The earlier baby staying created having GBS disease.

The most typical manifestations connected with EOD typically are septicaemia, pneumonia along with meningitis. No matter what possition connected with effort, respiratory signs (apnoea, grunting respirations, tachypnea as well as cyanosis) are the specialized medical studies with more than 80% connected with neonates, along with they may be difficult to oxygenate (Weisman et *et al.,* 1992; Edwards *et al.,* 2006).

A differential diagnosis of GBS sepsis is RDS (Respiratory distress syndrome). As well as radiographically, topographies consistent with and indistinguishable from those of hyaline membrane infected are present in more than one half of infants with GBS and pulmonary disease. Treatment with surfactant improves gas exchange in a majority of these children , even though the response is slower than in non-infected the new borns (Herting *et al.,* 2000).

In the event the likelihood connected with neonatal contamination attributable to GBS greater dramatically inside the 1970s (Anthony and Okada; 1977) a bimodal supply connected with conditions based on era on starting point connected with signs started to be noticeable. 2 syndromes linked to era ended up explained with 1973 by simply Franciosi along with associates. (acute and delayed) along with by simply Baker along with co-workers (early and late). Early-onset contamination typically manifests inside of twenty

four hours connected with beginning (an estimated 85% connected with conditions; average era 12 hours), nevertheless it may become noticeable over the 2nd twenty four hours connected with existence (an estimated 10% connected with cases) as well as at any time over the succeeding 5 days and nights. Premature newborn typically encounter starting point on as well as inside of 6 hrs connected with beginning; newborn having starting point after the initial twenty four hours connected with existence tend to be connected with time period pregnancy (Baker, 1978).

In most reports, EOD establishes 60-80% of total invasive GBS disease in newborns. Published data from USA and Australia from the end of 1970s to the early 1990s reveal occurences of EOD of 1-3/1000 live births. Afterwards 1996 the occurence appeared to drop, and after 1998 to 2000 the average occurence has been about 0.5/1000 live births. The occurence of invasive GBS infectes among neonates in USA has been greater in newborn of African-American women than in neanates of white and Hispanic lady of all ages (Schrag *et al.,* 2002).

2.18. The EOGND Incidence

The UK/Ireland EOGND occurrence was described at 0.48 per 1000 live childbirths in 2002 (Heath *et al.,* 2004) along with previously a 2 years study concluding with 2000 reported the likelihood connected with 0.57 per 1000 live births (Oddie and Embleton, 2002). The two cases typically are twice the latest Australian EOGNS rate (Zangwill *et al.,* 1992; CDC, 1997; Isaacs and Royle, 1999;). If antenatal screening was generally practiced during the course of the UK and Ireland then the present EOGND occurrence may reduce further (Kenyon *et al.,* 2005). The UK rate is low in assessment to an EOGNS occurence of 0.7 to 1.0 per 1000 live births reported from the Czech Republic in 2004 (Strakova and Motlova, 2004) and 0.76 per 1000 live Evidence indicates that the GBS maternal colonisation amount has not changed over time; however, in certain countries the occurence of infantal GBS disease has changed significantly over the years (CDC., 1997; Gotoff, 2000a; Mullaney, 2001). Garland revealed in 1995 that 2 to 5% of mothers are transporters of GBS (Garland and Kelly, 1995) and a current EOGND occurence of 1.1 per 1000 live births has been reported in the USA (Boyer *et al.,* 1983; Chen *et al.,* 2001; Isaacs and Royle, 1999; Janek *et al*., 2004; Jeffery and Royal, 2002; Morales *et al.,* 1986). In 1998 and 2000 the USA EOGND occurence was reported as low as 0.6 per 1000 live births (Dillon *et al.,* 1987; Fletcher and Gordon, 1990; Schrag *et al.,*

2000). In 1999, Canada reported an occurence of 0.25 per 1000 (Davies et al., 2001) births reported as the Danish mean annual amont also reported in 2004 (Andersen *et al*., 2004).

In 1999 the USA EOGND amont reported was 0.6 per 1000 live births, just 0.1 per 1000 greater than the Australian EOGNS rate for the similar time period (CDC, 1997; Isaacs and Royle, 1999; Zangwill *et al.,* 1992). Prior to 1996 the USA EOGND different between one to four suitcases per 1000 live births (Jeffery and Royal, 2002). Despite the overall reduced in EOGND outside the USA some American populations are still at a higher danger of EOGND. During the past ten years infantes of African American descent have a higher amount of EOGND compared to other American population groups (Isaacs, 1998). African American infants are at an even higher risk if their mothers age is less than 20 (Isaacs, 1998).

2.19. Late onset GBS infection(LOD)

The source, the danger factors, and the methods of transmission associated with LOGD are unwell understood and as a consequence the true occurence of LOGD has not been recognized (Schuchat, 1998). This infantal disease able to cause similar illnesses to EOGND though most normally LOGD manifests as meningitis (Fletcher and Gordon, 1990; Schuchat, 1995). It has been reported that 20% of all babies who have contracted LOGD and who survive may suffer from long term illnesses such as simple neurological sequelae and other comparable sequelae affected from EOGND (Beardsall *et al.*, 2000; Towers *et al.*, 1999). A German study in 2003 revealed infantes with LOGD meningitis have a neurological sequelae amount of 40%, a rate couple that previously revealed (Haase *et al.*, 2003). Neonatal LOGD can also produced septic arthritis, osteomyelitis, cellulitis-adenitis, pneumonia, pleural empyema, endocarditis, urinary tract infection (UTI) and endophthalmitis (Fletcher and Gordon, 1990; Schuchat, 1995)

Furthermore, there were other reports of LOGD manifesting as newborn lymphadenitis (Fluegge *et al.*, 2003) and necrotizing fasciitis (Lang *et al.*, 2003). GBS serovar III has been reported in USA, England/Wales, and western Sweden from 1988 to 2004 as the more frequently isolated serotype producing LOGD (Baker, 1980; Mullaney, 2001;Bliss *et al.*, 2002; Martinez *et al.*, 2004; Persson *et al.*, 2004; Weisner *et al.*, 2004). In 1988 in the USA serovar III was then the most frequently isolated subtype causing 71% of all LOGD cases (Schuchat, 1998; Mullaney, 2001).

The mainly source of GBS disease in LOGD cases is thought to be the mother, because up to 50% of infants with LOGD had identical GBS serovars to their mothers (Towers *et al.*, 1999). GBS responsible for LOGD may have been acquired *in utero* or at time of birth; though, the baby may have had some defence system perhaps maternal resulting in the late the development of the infection (Boyer 1992). GBS infected breast milk has also been recorded as a main source of LOGD (Kotiw *et al.*, 2003). Kotiw used a PCR subtyping test and demonstrated serotypes goted from the mothers breast milk and the newborn were indistinguishable (Kotiw *et al.*, 2003). It is not understood how GBS infection of the breast milk incidence (Schuchat, 1998). Other sources for LOGD could include nosocomial transmission (Jeffery & Royal, 2002; Schuchat, 1998) and community transmission (Bingen *et al.* 1992).

LOGD has also been reported as a reappearance of EOGND (Schuchat, 1998; Kotiw *et al.*, 2003). It has also been described that LOGD may be the result of a reinfection and the amount for LOGD disease of previously medicated newborn was approximately 1% (Schuchat, 1998; Mullaney, 2001). It was also recognized that the disease site was new in fifty percent of re-infected newborn (Schuchat, 1998).

2.20. Signs, Symptoms, Treatment Of Neonatal LOGD

Symptoms connected with LOGD commonly look like after one week of life and able to include lethargy, poor feeding or irritability and fever (Mullaney, 2001). newborns connected with GBS meningitis may incidencne with upper respiratory tract disease, otitis media, facial cellulitis, septic arthritis and osteoarthritis (Mullaney, 2001). More serious LOGD “symptoms such as apnea, seizures, leukopenia or neutropenia are more likely to have a fatal outcome” (Mullaney, 2001). Thirty to 40% of neonates with LOGD will increase meningitis and a high number of these infants will suffer from permanent neurologic sequelae (Schuchat, 1998). Similar to EOGND meningitis sufferers, LOGD meningitis symptoms include frequent removals (Weisman *et al.*, 1992) and the infected babies require intense medical care and treatment.

Late-onset GBS disease most commonly results from horizontal transportation complete nosocomial spread in the nursery by colonized nursery personnel or other colonized newborns, or by acquisition from community foundation. Of all newborn, 3% to 12% are colonized by GBS within the seven day of life. The bearing of vertical transmission at birth on the total pool of colonized newborns at one week is lessened because of the large number of pregnant ladies without GBS. Approximately one third of neonates colonized at 4 days of age are born to noncolonized mothers (Christensen, *et al.,* 1981). Only approximately 45% of all newborn colonization is straightly attributable to vertical transmission (Anthony, *et al.,* 1979), and nosocomial spread is an important route of transmission, particularly in late-onset infection. Further, up to 35% of newborns initially colonized at delivery are culture-negative by the fourth day of life (Christensen, *et al.,* 1981).

More factors modify the danger of vertical transmission of GBS. Higher neonatal transmission rates incidence from lady persistently culture-positive and from lady with a high concentration of GBS (Ancona , *et al.,* 1980; Hoogkamp-Korstanje , *et al.,* 1982; Boyer, *et al.,* 1983). The site of motherly carriage is also very important: the amount of vertical neonatal transmission is higher when maternal GBS disease originates from the cervix (89%) compared to the rectum only (65%) (Hoogkamp-Korstanje , *et al*., 1982 ; Regan*, et al.*, 1991).

Late-onset group B streptococcal infection historically caused term newborns seven to eighty nine days of age who had an unremarkable motherly obstetric and early infantal history. Contemporary data indicate that at least half of newborns with late-onset infection now are born before 37 weeks of gestation age (Phares*, et al.,* 2008).

Late-onset infections has a lesser fatality amount (1% to 6%) than early-onset infections. Clinical expressions of late-onset disease include bacteremia without a focus of infection (65% of infants), meningitis (25%), bacteremic cellulitis or osteoarthritis (2% to 3% each), and pneumonia (3%) (Phares*, et al.,* 2008).

LOD frequently icidence along with hypothermia or hyperthermia, hyperglycaemia or irritability. Grunting respiration and apnoea are fewer frequent initial findings than in EOD (Bizzarro*, et al.,* 2005).

In contrast to early-onset infection, grunting respirations and apnea are fewer frequent initial findings, and their occurence suggests rapidly progressive, fulminant

infection. Apnea or hypotension is observed in fewer than 15% of patients, but there is a spectrum in clinical severity of sickness at presentation. Specific newborns appear clinically well a few hours earlier initial evaluation and occurence with seizures, poor perfusion, neutropenia, and high numbers of grampositive cocci in the CSF. These patients all times have a speedily fatal course, or if they survive, they are left with devastating neurologic sequelae. Leukopenia or neutropenia at the time of diagnosis has been correlated with fatal outcome in these newborns (Schrag, *et al.,* 2002).

LOD affects the newborns from one week to 90 days of age. Nosocomial disease of premature newborns in neonatal intensive care units (NICU) and transmission of virulent GBS strains from mother to newborn via skin or breast milk might explain some of the cases. However, most newborns with LOD have no known danger factors and an uneventful primary neonatal history, and in most of these newborns the mechanisms of disease are not showed (Edwards, *et al.,* 2006).

Infections in newborns greater than 89 days of age can account for 20% of cases of late-onset diseases. The terms very late onset or late late-onset, and beyond primerly infancy have been applied to diseases in these newborns . Most of these newborns have a gestational age of smaller than 35 weeks. The need for prolonged hospitalization and the undeveloped host status in these infants probably contributes to disease beyond the interval for term babies. Bacteremia without a focus is a normal presentation (Yagupsky, *et al.,* 1991).

Late-onset infections incidence in newborn after the seven day of life. The mean age at onset is 24 days (Baker, 1979). The overall attack amont is estimated to be 0.4 in 1000 live births (Schuchat, *et al.,* 1996). In contrast to early-onset infection, horizontal transmission through nosocomial passageways appears to be an important factor in late-onset infection. The serotype distribution of strains improved from late-onset infection does not reflect the serotypes occurent in the maternal genital tract; more than 90% of late-onset infection is caused by type III group b streptococci (Baker and Barrett, 1973). In more than 80% of newborns with late-onset infection, the infections manifests as meningitis, which has a mortality ampunt of approximately 20% (Baker, 1979) Between 15% and 30% of survivors have neurologic sequelae, including cortical blindness, diabetes insipidus, deafness or other cranial nerve shortfalls, and spasticity. Although the mainstream of late-onset infection incidence as meningitis, other manifestations include septic arthritis, osteomyelitis, empyema, endocarditis, cellulitis, and otitis media.

2.21. Relation Between GBS Colonization And Prematurity

The benefit connected with contamination as being a reason behind preterm shipping and delivery can be getting raising identification (Hillier *et al.,* 1988; Minkoff, 1993; Hillier, *et al.,* 1995). A recent writeup on the particular epidemiology connected with preterm beginning (Berkowitz and Papiernik, 1993) encouraged that distinct etiologic trails bring about impulsive preterm job along with preterm early rupture in the walls. Infection may perhaps may play a role with both of these trails, since intra-amniotic contamination costs typically are improved both equally with women of all ages having preterm job having undamaged walls and with people that have preterm early rupture connected with walls (Berkowitz and Papiernik, 1993). Research which in turn assessed the particular role connected with GBS colonization with prematurity have got discovered various results (Regan *et al.,* 1981; Alger, *et al.,* 1988; Matorras, *et al.,* 1989; Mc Donald *et al.,* 1989).

2.22. Transmission Of *Streptococcus agalctiae* To Blood Stream

Early-onset group B streptococcal infection can be heralded by simply respiratory symptoms, such as tachypnea, hypoxia, cyanosis, along with pulmonary hypertension (Payne *et al.,* 1988). 1/3rd to more than half connected with newborn typically are characteristic on beginning as well as inside of four to six hour soon after delivery. Autopsies with lethal early-onset conditions reveal that 80% have got histologic proof of lobar as well as multilobar pneumonia (Vollman *et al.,* 1976; Hemming *et al.,* 1976), characterized by thick microbe infiltration, epithelial cell destruction, alveolar hemorrhage, interstitial inflammatory exudate, along with hyaline tissue layer development (Ablow *et al.,* 1976; Katzenstein, *et al.,* 1976). Any time pneumonia grows with infant primates exposed by simply intra-amniotic treatment connected with GBS, microbe thickness actually reaches 109 to 1011 organisms per gram connected with lung tissues (Rubens *et al.,* 1991). While proven with rabbits, the particular lesser image resolution connected with pneumonia with preterm versus time period babies displays quantitative insufficient pulmonary alveolar macrophages, mandating the particular recruitment connected with neutrophils as being a secondary phagocytic protection process (Sherman *et al.,* 1992).

2.23. Capsular Polysaccharide and Immune Resistance

On penetration connected with GBS to the lung tissues as well as body in the infant toddler, the immunologic reaction can be recruited to apparent the particular organism. Main to the present reaction typically are sponsor phagocytic cells such as neutrophils along with macrophages. Successful subscriber base along with harming by simply most of these cells demand opsonization in the bacterium by simply particular antibodies inside the profile connected with match Neonates typically are in particular at risk of obtrusive infection because of their quantitative as well as qualitative an absence of phagocytic cell perform, particular antibody, as well as basic along with alternate match trails. In addition to most of these infant sponsor susceptibilities, GBS have got quite a few virulence determinants that seek out to combat all the crucial the different parts of successful opsonophagocytic harming. Main amid most of these components would be the sialylated group B streptococcal polysaccharide supplement (Shigeoka *et al.,* 1978; Edwards *et al.,* 1980; Anderson *et al.,* 1983).

2.24. Preterm And Low Birth Weight (LBW) Newborn

Preterm along with LBW newborn have an increased risk with EOD with a progressive increase with chance for neonatal sepsis having lessening gestational age (GA) along with beginning bodyweight (Schuchat *et al.,* 1994; Yancey *et al.,* 1996; Benitz *et al.,* 1999). Newborn created on 37 week GA received a three flip greater risk of EOD weighed with newborn created on 40 weeks (Hakansson and Kallen, 2006).

2.25. Extended Rupture In The Amniotic Walls

Prolonged rupture of the amniotic membranes (PROM) for >18-24 hours before the time of delivery is yhe main cause to increases the dangerosity of of newborn infected by colony of GBS disease. More published series revealed that PROM >18 hours incidence in 12.5% of deliveries and is associated with an OR of 7.28 (95% CI: 4.42-12.0) of invasive GBS infection (Boyer *et al.,* 1983; Boyer *et al.,* 1983; Schuchat *et al.,* 1994; Yancey *et al.,* 1996; Benitz *et al.,* 1999).

2.26. Fever

Intrapartum temperature >37.5ºC (Boyer, *et al.,* 1983) along with >38ºC (Adams *et al.,* 1993) typically are regarding an increased chance connected with neonatal GBS contamination (Boyer *et al.,* 1983; Boyer *et al.,* 1983; Benitz *et al.,* 1999; Schuchat *et al.,* 2000). It's not at all acknowledged perhaps the chance connected with EOD can be higher having a heat connected with 40 ºC than having a heat connected with 38.5ºC (Benitz *et al.,* 1999).

2.27.GBS Bacteruria

Newborns created to women of all ages having GBS bacteruria throughout being pregnant will be more often and even more to a great extent colonized having GBS, and may end up being on greater chance for obtrusive GBS infections, nevertheless the distinct scientific tests posted typically are not definite (Pass *et al.,* 1979; Persson *et al.,* 1985 Benitz *et al.,* 1999).

2.28. Maternal Antibodies

An neonates susceptibility to GBS can be greater while the quality of anticapsular antibodies towards the infecting serotype can be minimal. This is the case once the maternal antibody stage can be minimal as well as while newborn typically are created ahead of thirty four months pregnancy, since transplacental transfer connected with immunoglobulin G the is renduced just in gestation period (Baker and Kasper, 1976; Baker *et al.,* 1981).

Even with mature amounts of neutrophils, an important resistant insufficiency with neonates would be the diminished neutrophil response to contamination, thats in particular noticeable with pre-term children. The shortcoming connected with neutrophils to answer contamination can be thought to be as a result of restricted pool area connected with neutrophils, bad tissues puncture along with bad speeding connected with creation coming from bone fragments marrow. Neonatal polymorphonuclear leukocytes (PMN's) which might be definitely not triggered are actually encouraged to get flaws with creation connected with reactive air species along with lessened amounts of lactoferrin, lysozyme along with other degradative minerals (Henneke and Berner, 2006).

The actual supply connected with tissues resident macrophages with neonates matches inside the mature, apart from alveolar macrophages which can be minimal till ahead of time period, though this particular increases inside the initial 24-48 hours soon after beginning (Remington *et al.,* 2010). Phagocytosis along with antimicrobial operate connected with neonatal macrophages resemble that observed in parents, with the exception that they may be insensitive to IFN y activation. The capacity connected with macrophages to generate monocytes along with neutrophils to your site connected with contamination can be deferred with neonates (Remington *et al.,* 2010).

2.29. Earlier newborn Having Invasive GBS Disease

Just about all GBS serovars can handle creating neonatal infection and still have a polysaccharide cell wall structure antigen made up of rhaminose, N-acetylglucosamine along with galactose (Sneath, 1986a). Dissimilarities inside of most of these antigens utilized to tell apart eight antigenic GBS serovars (I–VIII) (Schuchat, 1998). Type one is classified in to three subtypes Ia, Ib, (Schuchat, 1998) and Ia/c (Mullaney, 2001).

Although having had a previous newborn with invasive GBS infection is accepted as placing a mother at high dangerous in subsequent pregnancies, only some of instances have been reported in which child having GBS infection followed more than one pregnancy in the similler mother (Faxelius *et al.,* 1988; Carstensen *et al.,* 1988). Nonetheless, women of all ages may perhaps continue being colonized while using identical tension connected with GBS for extended intervals and may fail to build safety amounts of type-specific serum antibodies even with long-term colonization (Dykes *et al.,* 1985). Therefore, it is likely that this chance with succeeding a pregnancy can be higher for females with received a child having EOD GBS disease, whether or not this particular chance cannot be quantified.

2.30. Detection Of GBS

The actual “gold standard” connected with GBS screening can be traditions carried out on 35-37 getation era of pregnancy coming from swabs obtained coming from the both vagina as well as the rectum. The use of discerning media (agar dishes along with broth) for traditions supplemented by simply antibiotics similar to colistin (10 μg/ml) as well as nalidixic acid (15 μg/ml) typically are proposed (Schrag *et al.,* 2002). The actual selective

agar dishes may be analyzed soon after twenty four hours as the inoculated discerning, enrichment broth can be incubated for 18-24 hrs and subcultured on top of sheep blood agar. In case GBS just isnt discovered after the incubation connected with 18-24 hrs, the particular blood agar platter should be reincubated along with analyzed on 48 hrs to recognize susspected organisms. susspected colonies may be analyzed applying glide agglutination assessments for particular identification(Laboratory practices for prenatal, 1999). Research demonstrate that using typical strong blood agar plating rather than discerning, enrichment medium causes bogus adverse traditions ends up with as much as 50% connected with expecting mothers colonised by simply GBS (Laboratory practices for prenatal, 1999).

The culture taken at 35-37 weeks of gestation age , may not accurately predict genital tract colonisation at time of labour because colonisation may be passing and colonisation may incidence after the time of screening. Studies have revealed that sensitivities of a positive test (the ability to predict vaginal colonisation at time of labour) in week 35-37 from 54% to 91% (Benitz *et al.,* 1999; Davies *et al.,* 2004; Valkenburg-van *et al.,* 2006).

2.30.1. Antigen tests

GBS traces can even be discovered with the creation connected with group B Lancefield antigen (Forbes *et al.,* 2002). Therefore, several latex agglutination assessments along with imunoassays that find this particular antigen for GBS identification are actually created for fast detection connected with GBS colonisations without having earlier traditions. Nonetheless, whether or not the particular specificity continues to be excessive (98-100%), the general sensitivity of those over the counter available immunological assays continues to be minimal but not completely exact for regimen utilization in the particular intrapartum detection connected with women of all ages colonized having GBS (Baker, 1996).

The actual sensitivity is significantly decrease while incubation can be reduced. Therefore, available probe hybridization procedures typically are suited to GBS id coming from instantaneously civilizations with discerning enrichment broth, nevertheless typically are inadequately very sensitive for strong detection along with id connected with GBS coming from recto vaginal swabs obtained from expecting mothers throughout manual work (Kircher *et al.,* 1996).

2.31. Immunity To Group B Streptococcal Infection

The actual profile connected with form particular antibodies against capsular polysaccharide continues to be proven may play a role with protecting persons against obtrusive GBS infection(Edwards *et al.,* 1979, Lin *et al.,* 2004). Capsule specific antibodies improve opsonophagocytic assassination of the organism in both infants and adults womens (Cheng *et al.,* 2001; Sendi *et al.,* 2008; Santi *et al.,* 2009b), and can offer you safety and protection as a result of neutralising attributes (Wessels *et al.,* 2011). Individuals who do not have strong or high levels of antibodies, for example the women is older in age and the very young, are at a greater risk of GBS disease infection(Amaya *et al.,* 2004).

The cells of the adaptive protected system are developed and able to start responding to challenges at delivery or birth . However levels of immunoglobulin are reduce in all infants , with the exception of IgG transferred placentally from the mother at the time of the third trimester of gestation age . Due to the poor immunogenicity of the GBS capsule just 10-20% of mothers have protective antibody levels (Melin, 2011).

leaving children at danger of infection. During birth the fetus travels from the sterile intrauterine environment direct to the vagina where it will encounter commensal bacteria such as GBS. The innate immune response will be the chief defence mechanism against these potentially pathogenic micro rorganism (Delves *et al.*, 2011, Kenzel and Henneke, 2006). PHD DK

The humoral support of the innate protected system is probably ineffective at removing Group B *Streptococcus*. Along with host deficiencies in complement levels, GBS superficial components BibA and the β protein GBS protect activation of complement and hinder the formation of the membrane attack compound (Santi *et al.*, 2007, Maisey *et al.*, 2008a).

2.32. EOGND Mortality Rate

EOGND acquired by vertical transmission from the mother at birth can be quickly fatal. In the primary 2000s, USA described an EOGND mortality rate varying from only 2.7% and as high as 14% (Weisman *et al.*, 1992; Lukacs *et al.*, 2004). In Australia, the EOGNS mortality rate prior to 2000 varying from only 6% to 15% (Garland and Kelly, 1995; Isaacs *et al.*, 1995; Isaacs, 1998; Isaacs and Royle, 1999; Connellan and Wallace,

2000; McLaughlin and Crowther, 2000). In Melbourne a 10 year study throug 1979 to 1988 was showed at the Royal Women's Hospital which resulted in 29/104 (28%) deaths (Garland, 1991). In 2004, the UK and Ireland described an amount of 9.7% while Canada from 1993 to 1997 described a rate of 13.6% which are dependable with USA and Australian data (Heath *et al.*, 2004).

Even however mortality rates were comparable between the USA, Australia, Canada and UK/Ireland, the mortality rates be different between full term and preterm delivered newborns and preterm infants are at a much biger danger of death (Towers *et al.,* 1999). In 2004, the USA described a reduction in mortality rates at 6.5% and 22.7% for term infants and preterm newborns; separately (CDC, 2004b). Since 1992, the informed USA mortality rates for complete term and preterm infants were at 2% and 28%; respectively (Weisman *et al.,* 1992).

2.33. Vaccine

Although vaccine technology possibly will provide complementary approach to the incidence management of GBS colonization and prevention of GBS neonatal infection, currently vaccines against GBS disease are still being produced and trialed. Vaccine technology in the future may significantly decrease the occurence of preterm delivery, stillbirths, EOGND and LOGD. At this present time, just partial maternal protection against some GBS serovars was succeeded if any of the following three groups of vaccines were implemented. Clinical trials for serovar Ia, II and III vaccines (depended on the capsular polysaccharide structures (CPS) were conducted. However, the immune responses in patients for serovar Ia 40% and III (60%) were low, while 88% of the patients developed an immune response for serovar II (Edwards and Baker, 2003). Protein conjugate vaccines for GBS serovars Ia, and Ib have also been developed and tested in healthy adults.

A type III CPS-protein conjugate vaccine was developed and phase 1 trials suggested that maternal immunization was possible (Edwards & Baker, 2003). Until now another CPS vaccine has been developed and clinically trialled, a conjugant vaccine for serovar V was clinically trialled and the results from this trial were same to the results obtained from earlier clinical trials of serovars Ia, Ib, and III vaccines (Baker and Edwards, 2003).

Baker and Edwards (2003), are working when it comes to a single dose pentavalent GBS conjugate vaccine. That they described that CPS vaccine resistant answers next to serovars Ia, Ib, II, III along with V were dependant upon quantity and that a four fold immune response intensification at eight weeks could be achieved in 80% to 93% of the adult population (Baker and Edwards, 2003). They also described that the type III conjugate vaccine administered to the mother throughout late pregnancy provided an immune response in the mother as well as the newborns. They recommended that the pentavalent GBS conjugate vaccine could have an efficacy of almost 90% (Baker and Edwards, 2003). These maternal vaccines or third trimester vaccines may in the next time be an effective method of reducing the incidence of EOGND; however, this type of vaccine preventative medication may not be established by pregnant ladies .

At this time there is not a vaccine available for Group B *Streptococcus,* although vaccination is an attractive preventative mechanism. It is known that high levels of capsular type definite antibodies are protective against invasive neonatal disease (Lin *et al.*, 2004). It could be expected that vaccination, unlike IAP, could also decrease the occurence of LOD and adult infection. Capsular polysaccharide vaccines with tetanus toxoid or CRM conjugates are in human clinical examinations, and protective levels of antibodies have been seen for up to twnty four month following vaccination (Heath, 2011).

Maternal antibody insufficiency to GBS can be regarding greater neonatal susceptibility to obtrusive GBS infection (Baker *et al.,* 1977). Immunization connected with women of all ages throughout as well as ahead of being pregnant may reduce peripartum maternal infectionalong with guard newborn coming from perinatally obtained contamination by simply transplacental exchange connected with safety IgG antibodies (Schuchat, 1998; Baker *et al.,* 2003).

The actual group B antigen, that's widespread to all traces, will not seem to be very important to particular immunity to GBS contamination. Maternal antibodies up against the group B particular antigen don't protect against neonatal contamination (Anthony *et al.,* 1985). Nonetheless, serotype-specific antibodies to GBS capsular polysaccharide (CPS), are actually proven to cross punch the particular placenta, promote opsonophagocytosis along with harming connected with GBS (Baker and Kasper, 1976; Kasper *et al.,* 1996).

Early on scientific tests showed minimal immunogenicity with response to the particular polysaccharide supplement connected with GBS alone (Baker *et al.,* 1976), nevertheless by simply merging the particular GBS polysaccharide having tetanus toxoid, a fantastic resistant reaction could possibly be made (Baker *et al.,* 2003; Baker *et al.,* 1985). Similarly several of the symptoms healthy proteins antigens induce safety immunity with animal models (Larsson, *et al.,* 2006). Vaccine trials have revealed that if superficial proteins are conjugated to CPS, they enhance the immunogenicity of the CPS (Madoff, *et al.,* 1992; Larsson *et al.,* 1996; Gravekamp, *et al.,* 1999). Alternative approaches to vaccines are based on superficial proteins of GBS (Larsson *et al.,* 1996; Immaculada *et al.,* 2009), around the identification connected with immunogenic pili that extend coming from the superficial of the bacterium (Immaculada *et al.,* 2009), along with on combination protiens (Stalhammar-Carlemalm *et al.,* 2007). A successful GBS vaccine could decrease mucosal bacterial colonisation and produce both humoral and mucosal immunity, and is expected to prevent additional cases of infantal disease than the current strategies with IAP (Colbourn, et al., 2007; Sinha, et al., 2005).

However, experiments of vaccine efficacy along with safety are required for licensing of the vaccines. Such ability trials are possible to use substitute outcomes depended on serological markers of a protective immune response, since trials to assess neonatal disease would need to be extremely great. Extensive post-marketing surveillance for effectiveness and safety would be an essential portion of a licensing strategy. The prime difficulty to the development and testing of a GBS vaccine is perhaps the specter of the liability associated with vaccine delivery in pregnant lady (Paradiso, 2001; Johri, et al., 2006).

Concerns for the safety of the mothers and fetuses require comprehensive and costly evaluation of candidate vaccines and the issue of responsibility is both serious and complex. Potential challenges other than medico-legal issues include lack of protection passed to newborn prematurely, the unknown effects on infants immune responses and regulatory issues (Brent, 2003).

In order to successfully proceed in this field of maternal immunization, it is necessary to describe the actual danger , so that studies can be appropriately designed to demonstrate protection. Studies of concerns that would be associated with GBS vaccination at the time of pregnancy from the perspectives of pregnant women and health care providers have been performed (Patten, *et al*., 2006). Given all the dynamics involved

in deciding whether to agree to take a vaccine or not, it appeared that being well informed about GBS was the most important dynamics. For any vaccine to be implemented, effective strategies for building public and individual trust are critical. These strategies need to be weighed against the pros and cons of the incidence IAP approach along with vaccination (Patten *et al.,* 2006).

2.34. Prevention Of Neonatal From GBS Infection

Theoretically, early-onset and late-onset group B streptococcal infectioncould be prevented if susceptible hosts were not exposed to the microorganism or if exposure occurred in the setting of protective immunity. Several approaches to prevention have been advocated; conceptually, these are directed at eliminating exposure or enhancing host resistance by chemoprophylaxis or immunoprophylaxis. Both strategies have limitations with respect to implementation,but could be targeted for the prevention of maternal and neonatal infections and are theoretically achievable (Baker, 1990; CDC, 2002).

The first attempt to prevent GBS infectionin neonates was giving antepartum antibiotics to pregnant women colonized with GBS (Lewin and Amstey, 1981). Oral and intramuscular regimens were examined , but were found to cause only a temporary drop in vaginal colonization. It is believed that GBS continue in the colon and recolonize the birth canal once the antibiotics are stationary. In 1979 a report demanded that a single dose of ampicillin given to the mother intrapartum could interrupt the transmission of GBS from mother to infants (Yow *et al.,* 1979). Later, Boyer and Gotoff demonstrated a decrease in EOD if antibiotics were given intrapartum.

Current prevention of GBS infectionin the UK is depended on the administration of antibacterial prophylaxis, proximately before and during the labour (Intrapartum prophylaxis or IAP) to lady who have been identified to have danger factors. If the antibiotics are able to be administered 4 hours before birth it has been revealed to significantly decrease the chance of newborns to colonised mothers becoming themselves colonised (from 40% to 25%) (Daniels *et al.,* 2011).

The main defense against GBS is antibody-dependent phagocytosis. Vaccines that produce antibodies against the capsule of GBS have been prepared (Schuchat and Wenger, 1994). Unfortunately vaccination to prevent GBS infantal sepsis necessaries to overcome numerous obstacles to have a place in clinical practice. Antibody levels can be achieved in

the majority of vaccines, but some vaccines do not induce antibody development (De Cueninck *et al.,* 1983).

Despite the reduction of early-onset neonatal infection by using antimicrobial intrapartum prophylaxis, mortality and permanent disability amount caused by GBS continue to be significant. However, GBS also has developed as an important pathogen in other patient groups such as children, young adults with underlying medical environments, and of advanced years individuals (Phares *et al.,* 2008).

Penicillin is the drug of choice for prevention and medication of GBS diseases, which remain universally susceptible. Erythromycin and clindamycin are recommended when danger of anaphylaxis or therapeutic miscarriage are present. However, resistance to erythromycin and clindamycin has greater than before in many countries in North America (Andrews *et al.,* 2000; Borchardt *et al.,* 2006; Desjardins *et al.,* 2006; Phares *et al.,* 2008), Europe (Poyart, *et al.,* 2003; Schoening, *et al.,* 2005; Gonzalez and Andreu; 2005; Gherardi *et al.,* 2007) and Asia (Hsueh, *et al.,* 2001), but not in Brazil (Duarte, *et al.,* 2005; Simões *et al.,* 2007) and other Latin American countries (Gonzalez *et al.,* 2002; Martinez *et al.,* 2004; Mollerach *et al.,* 2007). Such a resistance profile is chiefly due to two mechanisms, a methylase-mediated target site modification and an active efflux pump (Slotved *et al.,* 2002).

Antibiotics given more than a few weeks before labor has not decrease the maternal GBS colonization amount when labor begins (Anthony *et al.,* 1978; Gardner *et al.,* 1979) probably because the genital tract becomes recolonized with GBS from the rectal reservoir. Postnatal penicillin given to babies at birth has limitations because 70% of the infants with early-onset infection are infected before birth (Boyer; *et al.,* 1983). Preterm babies are particularly likely to be infected before birth, and postnatal penicillin given to preterm babies did not decrease early-onset GBS infection (Pyati; *et al.,* 1983). In another study, penicillin given at birth significantly decreased the amount of GBS sepsis, but the overall sepsis amount was not decreased in babies who received penicillin because they had an increased amount of infection from penicillin-resistant bacteria (Siegel *et al.,* 1980; Siegel *et al.,* 1982).

3. MATERIALS AND METHODS

3.1. Materials

3.1.1. The apparatuses

The apparatus used for preparing the appropriate experiments in the project are shown in table (3.1).

Table 3.1.The apparatus used in the present study.

Name	**Company**	**Country**
Autoclave	Witeg labortechnik	Germany
Electric oven	Melag	Germany
Incubator	Jrad	Syria
Microbiology safety cabinet	DLab Tech	Korea
Microscope	Olympus	Japan
Electronic balance	PSAW	India
Water distillator	DLabTech	Korea
Centrifuge	Kokusan	Japan
Micropipette different volumes	Eppendrof	Germany
Refrigerator	BEKO	Turkey
Camera	Canoon	Japan
UV lamp trolley air purification	DHgate	China
Vortex	Dragon lab	Germany
Table lamp	Turmed	Turkey
Bunzen burner	Flamefast	England

3.1.2. The equipments

The instruments and equipment's used for preparing the appropriate experiments in the present study are shown in table (3.2).

Table 3.2.The equipment's used in the present study.

Name	**Company**	**Country**
Loop	HiMedia	India
Beaker different size	Bro3.3	Germany
Conical flask different size	Bro3.3	Germany
Graduated cylinder	Bro3.3	Germany
Dropper	Plasti Med	Turkey
Disposable gel swab	Firat Med	Turkey
Filter papers (0.4) microns	SchleicherandSchuell	Germany
Microscope slide	Beromed GmbH	Germany
Cover slide	Beromed GmbH	Germany
Petri dishes	Plasti Lab	Lebanon
Forceps	Vantage	Pakistan
Aluminum foil	Sanita	Lebanon
Wooden stick	Citotest	China
Cotton	NCPI	Iraq
Micropipette tips	Plasti Lab	Lebanon
Centrifuge tube	Gemmey	USA
Thermos	KST	U.S.A.
Parafilm	Bemis	U.S.A.
Casco	Plasti Med	Turkey

3.1.3. Chemical agents

The chemical agents used for preparing the appropriate experiments in the present study are shown in table (3.3).

Table 3.3.Chemical agents and stains used in the present study.

Name	**Company**	**Country**
Crystal violet	Atom scientific	UK
Iodine	Atom scientific	UK
Ethanol 95%	Atom scientific	UK
Saffranin	Atom scientific	UK
Normal saline	ADWIC	Egypt
Oil emmersion	HiMedia	India
Catalase	Biomerieux	France
Slidex strepto plus	Biomerieux	France

3.1.4. Culture Media

The culture media used for identification of group B streptococcus in the present study are shown in table (3.4).

Table 3.4.Agar media whıch is used for culture

Culture Media	**Company**	**Country**
Blood agar base	HiMedia	India
Mueller Hinton agar	HiMedia	India

The composition and methods of preparation of different media used in this thesis are given below, performed as instructed by the manufacturer.

3.1.4.1. Blood agar base

It is a differential and enriched media supported with blood, promote the growth of most Gram-positive and Gram-negative organisms and are also use for the isolation, cultivation, and detection of hemolytic activity of staphylococci, streptococci, and other fastidious microorganisms (Atlas, 2010).

Directions :

1. Suspended 42 g of the medium in one liter of purified water.

2. Heated with frequent agitation and boil for one minute to completely dissolve the medium.

3. Autoclave at 121 ^{0}C for 15 minutes.

4. Prepare 5 - 10% blood agar by aseptically adding the appropriate volume of sterile defibrinated blood to melted sterile agar medium, cooled to 45 – 50 °C.

Principles of the Procedure

Nitrogen, vitamin, and carbon sources are provided by Enzymatic Digest of Casein and Enzymatic Digest of Animal Tissue in Blood Agar Base, Improved. Yeast Extract is a vitamin source. Corn starch is added to ensure any toxic metabolites produced are absorbed, and enhance organism growth (MacFaddin**,** 1985). Sodium Chloride maintains the osmotic balance of the medium. Agar is the solidifying agent.

Formula / Liter

Enzymatic Digest of Casein ..... 15 g

Enzymatic Digest of Animal Tissue..... 4 g

Yeast Extract ..... 2 g

Corn Starch ..... 1 g

Sodium Chloride ..... 5 g

Agar ..... 14 g

Final pH: 7.0 ± 0.2 at 25 °C

3.1.4.2. Mueller Hinton Agar

Mueller Hinton Agar is used in antimicrobial susceptibility testing by the disk diffusion method. This formula conforms to Clinical and Laboratory Standard Institute (CLSI), formerly National Committee for Clinical Laboratory Standards (NCCLS).

Principles of the Procedure Beef Extract and Acid Hydrolysate of Casein provide nitrogen, vitamins, carbon, and amino acids in Mueller Hinton Agar. Starch is added to absorb any toxic metabolites produced. Agar is the solidifying agent. A suitable medium is essential for testing the susceptibility of microorganisms to sulfonamides and trimethoprim. Antagonism to sulfonamide activity is demonstrated by para-aminobenzoic acid (PABA) and its analogs. Reduced activity of trimethoprim, resulting in smaller growth inhibition zones and inner zonal growth, is demonstrated on medium possessing high levels of thymide. The PABA and thymine/thymidine content of Mueller Hinton Agar are reduced to a minimum, reducing the inactivation of sulfonamides and trimethoprim.

Formula / Liter

Beef Extract .....2 g Acid

Hydro lysate of Casein..... 17.5 g

Starch..... 1.5 g

Agar ..... 17 g

Final pH 7.3 ± 0.1 at 25°C

Directions

1. Suspended 38 g of the medium in one liter of purified water.

2. Heat with frequent agitation and boil for one minute to completely dissolve the medium.

3. Autoclave at 121°C for 15 minutes. Cool to room temperature.

4. OPTIONAL: Supplement as appropriate. Pour cooled Mueller Hinton Agar into sterile petri dishes on a level, horizontal superficial to give uniform depth. Allow to cool to room temperature.

5. Check prepared Mueller Hinton Agar to ensure the final pH is 7.3 ± 0.1 at 25°C.

3.1.5. Reagents

3.1.5.1. Catalase reagent

It is consisting of 3% Hydrogen peroxide.

3.1.5.2. Gram stain

It is used in the identification of bacterial shape and in the typing of bacteria into the Gram-positive and Gram-negative bacteria.

3.1.6. Antimicrobial discs

The GBS isolates were tested for antimicrobial susceptibility by the Kirby-Bauer disk diffusion technique on Mueller Hinton agar plates (Bauer *et al*, 1966).

The antibiotics that commonly used in the treatment of pregnant women has infected by GBS and used in this study are shown in table (3.5).

Table 3.5.The antibiotic discs which are used to study the antibiotic susceptibility of the isolates.

Antibiotics discs	Symbol	Conc. (µg)	Company	country
Penicillin	P	10	Bioanalyse	Turkey
Vancomycin	VA	10	Bioanalyse	Turkey
Amoxicillin	AM	25	Bioanalyse	Turkey
Chloramphinicol	C	30	Bioanalyse	Turkey
Clindamycine	DA	10	Bioanalyse	Turkey
Bacitracin	B	10	Bioanalyse	Turkey
Erythromycin	E	15	Bioanalyse	Turkey
Ciprofloxacin	CIP	10	Bioanalyse	Turkey
Cyfatoxyme	CTX	10	Bioanalyse	Turkey
Doxacycline	DO	10	Bioanalyse	Turkey
Oxacilline	OX	5	Bioanalyse	Turkey

3.2. Methods

3.2.1. Study Area

This study was carried out in Erbil city- Kurdistan region, maternity teaching hospital. This facility for collecting the sample because of the first hospital it for born. A total of 157 sample from vaginal swab. The sample were obtained by sterile cotton swab and transformed gelatinized swab container then closed tightly and labeled correctly . After that all the samples were collected transformed to the microbiological rooms of the laboratory and cultured on the plate that we used in the study.

3.2.2. Study Population

The study included 157 samples taken from pregnant women aged between 17-50 years old without clinical signs of genitourinary infections. samples collected from Erbil Maternity teaching hospital in Erbil city – Kurdistan region. The period of sample collection was from June to December 2014 were included in this study. Samples had been taken before antibiotic use. A questionnaire list was already prepared to report all information’s concerning the patient's clinical symptoms, age, sex, geographical distribution and level of education.

3.2.3. Specimens collection

The specimens were collected from patients with vaginitis. The swabs were inserted into the upper part of the vagina and rotated there before withdrawing it, so that exudates was collected from the upper as well as the lower vaginal wall. An endocervical swab must be collected. A vaginal speculum must be used to provide a clear sight of the cervix and the swab was rubbed in and around the introits of the cervix and withdrawn without contamination from the vaginal wall. Swab for culture should be placed in tubes containing normal saline to maintain the swab moist until taken to laboratory. The swab has been inoculated on the blood agar and incubated anaerobically for 24hrs. at 37°C.

3.2.4. Isolation of GBS

The High vaginal swabs collected were cultured in the blood agar. Sterility test was done by incubating the last poured plate overnight at 37ºC. All media were prepared according to the manufacturer's specification. The swab was rotated over one-third of the superficial of a GBS agar plate and the inoculum was then spread over the plate using an inoculating loop. The plates were then incubated at 35-37°C under anaerobic conditions in an anaerobic jar (Hi-Media, India) with gas pack and read for the presence of orange pigmented colonies after 18–24 hours. Beta-hemolytic group B streptococci developed orange-red pigmented colonies in GBS agar plates. The pigment made the colonies readily distinguishable from other organisms that may be grown on the plate. Any degree of orange development would be considered a positive result. Negative plates were re-incubated for an additional 24-48 hours before being discarded.

3.2.5. Camp Test

This test is used for the presumptive identification of Group B Streptococcus (*Streptococcus agalactiae*). It is the only beta-hemolytic Streptococcus which yields a positive CAMP test. The test has been named after Christie, Atkins, and Munch-Peterson, who described it in 1944. This test detects a diffusible, heat-stable, extracellular protein produced by Group B Streptococcus that enhances the hemolysis of sheep erythrocytes by Staphylococcus aureus. Figure (3.1) show that the CAMP factor acts synergistically with the beta hemolysin produced by *S. aureus* to induce enhanced hemolysis of sheep or bovine RBCs but not human, rabbit or horse RBCs. A known hemolytic strain of *S. aureus* is streaked in a straight line across the centre of the sheep blood agar plate. Test inoculum is streaked in a straight line (2-3 cms in length) perpendicular to *S.aureus* streak but

without touching it. A known Group B Streptococcus may also be streaked similarly as a positive control. Four-five test organisms may be tested per plate. The plate is incubated at 37 c for 18-24 hours. A positive test for CAMP factor appears as “arrowhead” hemolysis between the junction of growth of *S.aureus* and Group B Streptococcus. There is no enhanced or “arrowhead” hemolysis if the test isolate is not Group B Streptococcus. A similar test has been described for Listeria ivanovii, where an “arrowhead” hemolysis occurs appear between streaks of *Listeria ivanovii* and *Rhodococcus equi*. Reverse CAMP test can be used for differentiation of *Clostridium perfringens* from other *Clostridium* species. Here, a CAMP positive Group B Streptococcus is streaked in the center of sheep blood agar, and Clostridium perfringens is streaked perpendicular to it. Following incubation at 37o C for 24-48 hours in anaerobic conditions, an “arrowhead” hemolysis is seen between growth of C. perfringens and Group B Streptococcus. This is because of alpha toxin produced by C. perfringens interacts with CAMP factor and produce synergistic hemolysis.

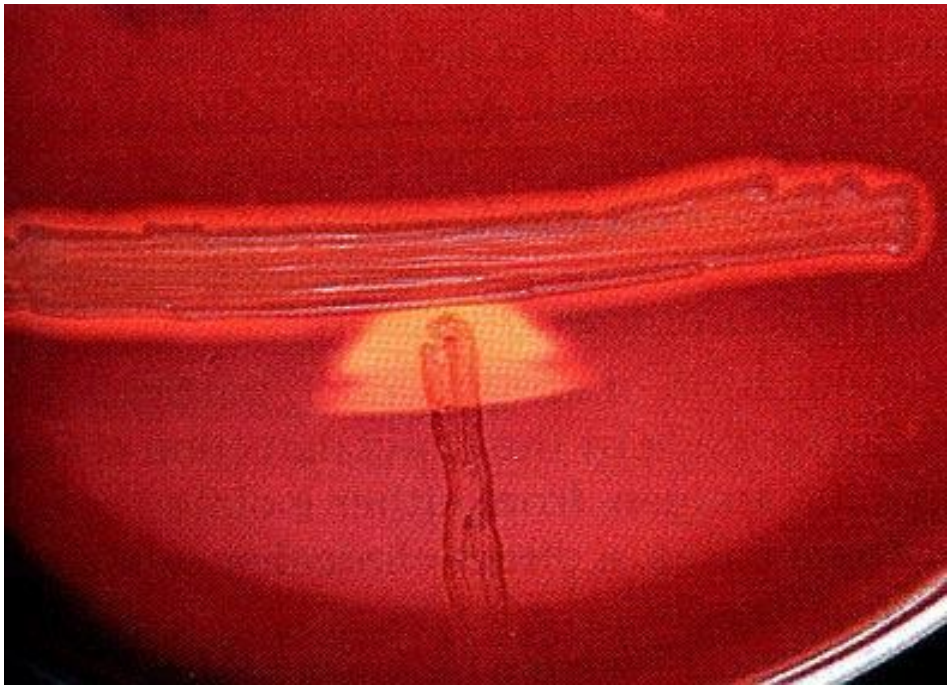


Figure 3.1. The hemolysis between the junction of growth of *S.aureus* and GBS

3.2.6. Bcitracin test

This test is used to determine the effect of a small amount of bacitracin on bacterial growth shaw in the figure (3.2). it is used for the differentiation of beta-hemolytic streptococci. The isolated colony inoculated by a sterile loop on blood agar plate, and then

using sterile forceps to place a bacitracin disk. Gently tapping the disk to ensure adequate contact with the agar superficial and incubated at 35°C for 24 hours. Appearance any zone of inhibition around disk indicates sensitive to bacitracin such as *Streptococcus pyogenes*. if does not observed any inhibition, and growth up to the disk was indicated resistant such as *Streptococcus agalactiae*.

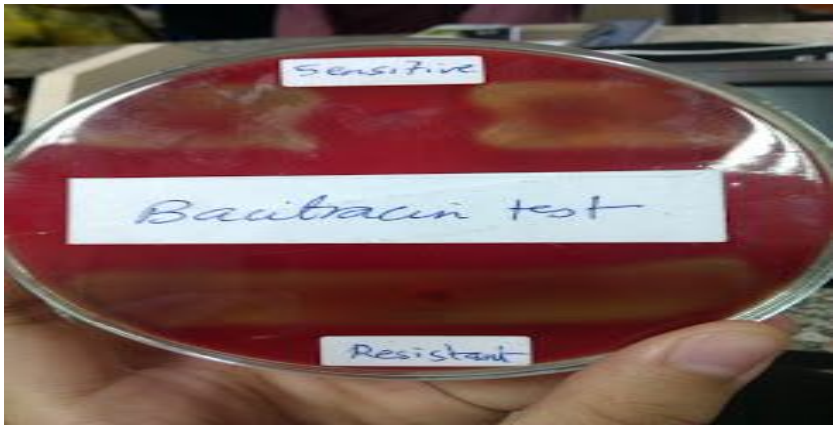


Figure 3.2. The Bacitracin test for distinguished between *Staphylococcus* and *Streptococcus* .

4. RESULTS AND DISCUSSION

GBS Was first in 1887 as a pathogen of bovines; a cause of bovine mastitis (Schuchat and Wenger, 1994) and was first reported as a human pathogen in 1953 (Schuchat,1998). GBS has been categorized as normal human regional flora asymptomatically colonizing the gastrointestinal and genitourinary tracts of both men and women (Schuchat, 1995; Jeffery and Royal, 2002). This has as also been isolated from the throat and respiratory tract of humans (Schuchat and Wenger, 1994; James, 2001).

Group B Streptococcus (GBS),also known as *Streptococcus agalactiae*, is a major cause of invasive infection in neonates, pregnant women, and non pregnant adults older than 65 years or those immunocompromised by underlying medical conditions.(Phares *et el*., 2008; Skoff *et al.,* 2009; Lamagni *et al.,* 2013).

Group B streptococcus (GBS) or *Streptococcus agalactiae* is a Gram- positive cocci that commonly Colonizes the female genital tract and rectum (Feuerschuette *et al.,* 2012). GBS can cause infections in women and men, presenting as cystitis, skin infections, among others. There can be major implications for pregnant women that cause Impairments in pregnancy, chorioamnionitis, abortion, intrauterine fetal death, premature membrane rupture, preterm delivery, postpartum endometritis, and sepsis (Choi *et al.,* 2012).

The bacterial flora of the female reproductive tract make up complex ecosystem consisting mostly of lactic Acid bacteria (LAB), represented by the Lactobacillus species, but also potentially pathogenic microbes (Bay *et al.,* 2002). A special threat among the microbes colonizing the vagina is posed by the beta- hemolytic Group B Streptococci (GBS) represented by *Streptococcus agalactiae*, which colonizes mainly the epithelial Cells of the lower gastrointestinal tract and the vagina. GBS carriage in pregnant women's reproductive tracts Reaches 10- 40% of subjects and as many as 40% develop so called asymptomatic bacteriuria. The digestive Tract is considered to be the main reservoir of *S. agalactiae*, which most probably constitutes the source of vaginal and urinary colonization (Schrag *et al.,* 2002).

A total of one hundred and fifty seven samples were collected from pregnant women between 35 to 37 gestation age or immediately after delivery , they were cultured and examined the samples for isolation and identified of B–hemolytic GBS from the maternity teaching hospital in Erbil- Kurdistan region between June 2014 to December

2014 . The results revealed that 19 (12.10%) were identified as group b streptococcus and, while 138 (87.89 %) samples showed culture negative, as shown in table (4.1) and figure (4.1). this study is comparable to findings in other parts of the world. In the USA, Regan *et al.,* (1981) reported GBS colonization rate of 10 - 35% (7) and In Malawi T, Dzowela *et al.,* (2005) reported a colonization rate of 16.5% (10) while in a local Kenyan study E. Were *et al.,* (using PCR method), found a colonization rate of 30.7% (12).

Table 4.1. The percentage of positive isolated result to GBS .

Samples (No. =157)	**Cultures results**	
	Positive. No. (%)	**Negative. No. (%)**
	19 (12.10 %)	138 (87.89 %)

N= number , % = percentage

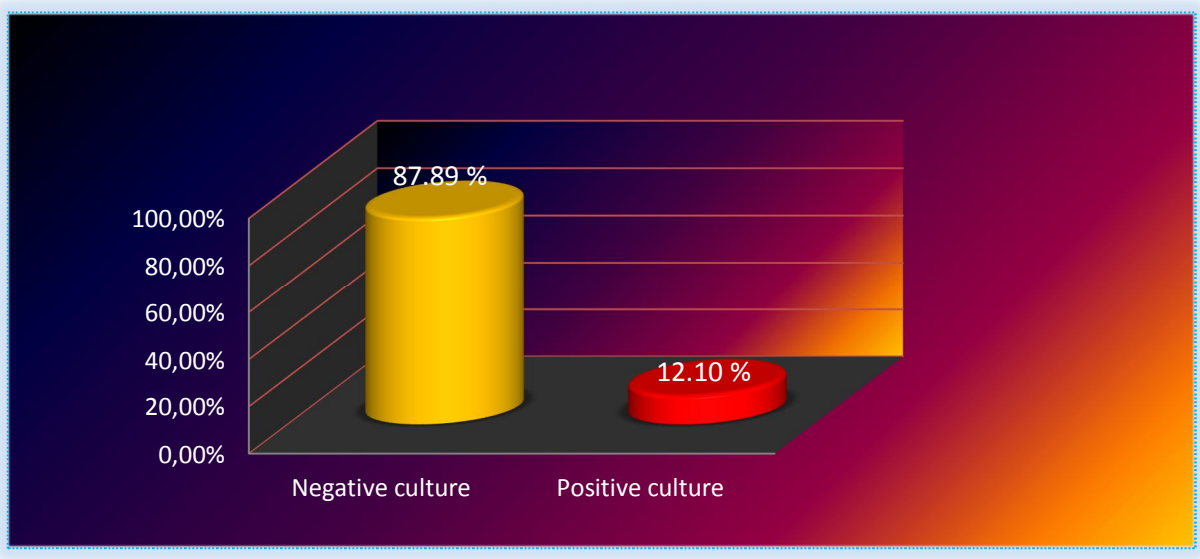


Figure 4.1. The percentage of positive GBS and negative from pregnant women

4.1. Identification of GBS

All isolates were further confirmed, characterized and identified by observing colony morphology and beta-hemolysis type on blood-agar, catalase, bacitracin disc,

CAMP, and serological tests (GBS were confirmed by specific-group (Streptococcal grouping kit, Oxoid) and specific-type antigen detection (Denka Seiken Co LTD, Japan) as described by (; Borger *et al.,* 2005; Cheesbrough; 2006).The isolates were diagnosed based on bacteriological and biochemical tests using standard procedures depending on the scientific sources (Alexander and Strete, 2001; Vandepitte *et al.,* 2003; Morello *et al.,* 2003; Forbes *et al.,* 2007) used for the diagnosis of bacteria, as follows:

4.2. Morphology

The GBS colonies were identified according to the morphology, pigment production, fermentation and hemolysis on the blood agar.

4.3. Microscopically

The bacterial isolates were further classified by Gram-staining to Gram-negative and Gram-positive bacilli and cocci.

4.4. Biochemical tests

Streptococcus agalactiae colonies were testing for their biochemical characteristics such as :

4.5. Catalase test

Catalase test was used to determine the organism′s ability to breakdown hydrogen peroxide (H_2O_2) into oxygen and water by action of the enzyme catalase. With a loop a small amount of bacterial colony of pure growth (preferably not more than 24 hours old and do not taken it from blood agar medium because red blood cells contain catalase) was transferred on to the superficial of a clean glass slide then immediately a drop of freshly prepared 3% hydrogen peroxide (3% H_2O_2) was placed on to apportion of colony on the slide. The evolution of bubbles of gas indicates a positive result and if not evolution of bubbles of gas indicated that is a negative result.

4.6. Slidex strepto plus test

This test was used to distinguished GBS from the other group of Streptococcus as follow :400 micron of EE + one loops of Streptococcal colony = put it in ependrof then take 10 mnts to uncubation at 37 ^{0}C then added one drop of this mixture to a slide paper

and added one drop of each group antigen and can show the positive result for anything that we want .

Figure 4.2. The slidex group test for GBS

The pattern of GBS encountered in this study correlates well with many studies conducted in different countries either in the regional or international settings. In a study conducted by Khadijeh *et al,* 2013 revealed that From 186 samples The vaginal culture was positive for GBS in 30 cases (16.1%) before DVE. After digital examination, from the 30 initially positive GBS subjects 27 (90%) were positive and the left 3 (10%) had negative culture result. None of the initially negative subjects had positive GBS results immediately after DVE After 48 hours of first sampling and digital vaginal examination,5 (2.7%) initially negative women were positive for vaginal GBS and the other 151 (81.2%) were negative.

Fatemi F *et al.,* 2009 showed that among the 330 women, the results of the culture were positive for GBS in 68 women (20.6%). Statistical analyses showed no significant relationship between demographics, reproductive histories and obstetric characteristics of subjects with the test results. The differences in these prevalence levels can probably be explained by the different populations studied, different gestational ages at culturing, differences in culture site, and in the use of different culture techniques .

The other study which is similar to my study is reported by Hassanzadeh P in 2011 among 310 pregnant women, 43 (13.8%) were colonized with GBS. There were no differences between GBS carriers and GBS-negative women in risk factors like preterm rupture of membranes ($p = 0.77$) and preterm labor ($p = 0.53$).

4.7. Smear preparation

Under the oil immersion power of light microscope *Streptococcus agalactiae* appears as Gram positive grow the outstanding morphologic characteristic of streptococci is their tendency to grow in chains. Because the individual cocci divide into pairs, a diplococcoid appearance of the members of a chain is often quite striking figure (4.3 and 4.4).

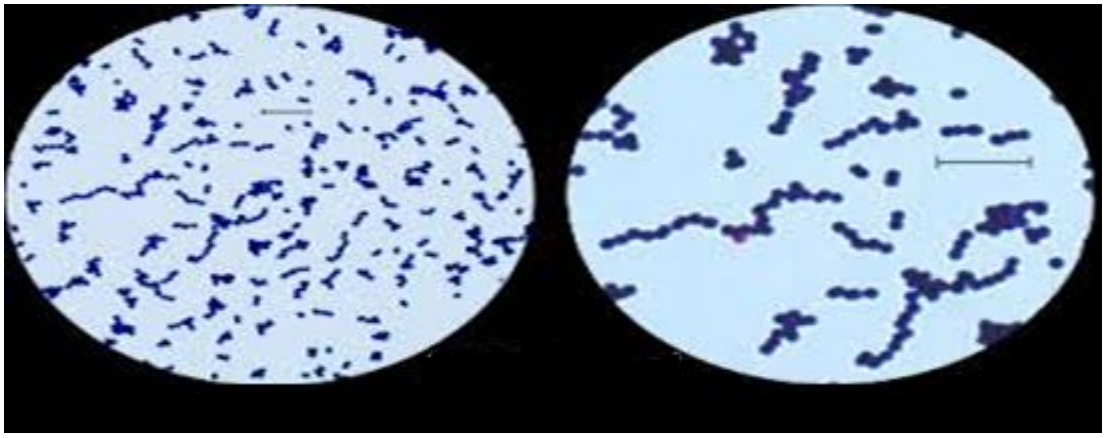


Figure 4.3. *Streptococcus* shape and colonial morphology under 100x light microscope

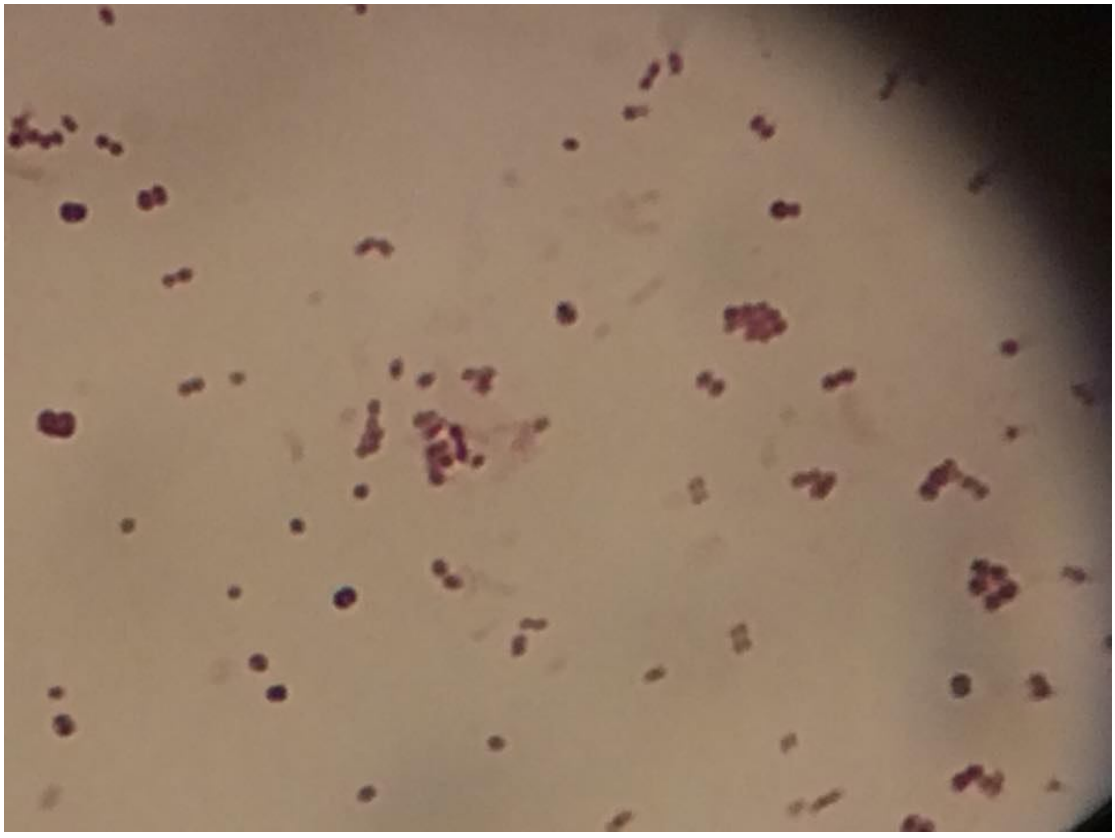


Figure 4.4. Gram stain of isolated GBS under 100x lightmicroscope

4.8. Morphological identification

Streptococcus agalactiae grow rapidly on the blood agar, most GBS colonies appear on blood plates as 1- to 2-mm, gray-white colonies surrounded by a zone of β-hemolysis, although 2% of strains are non hemolytic (figure 4.5).

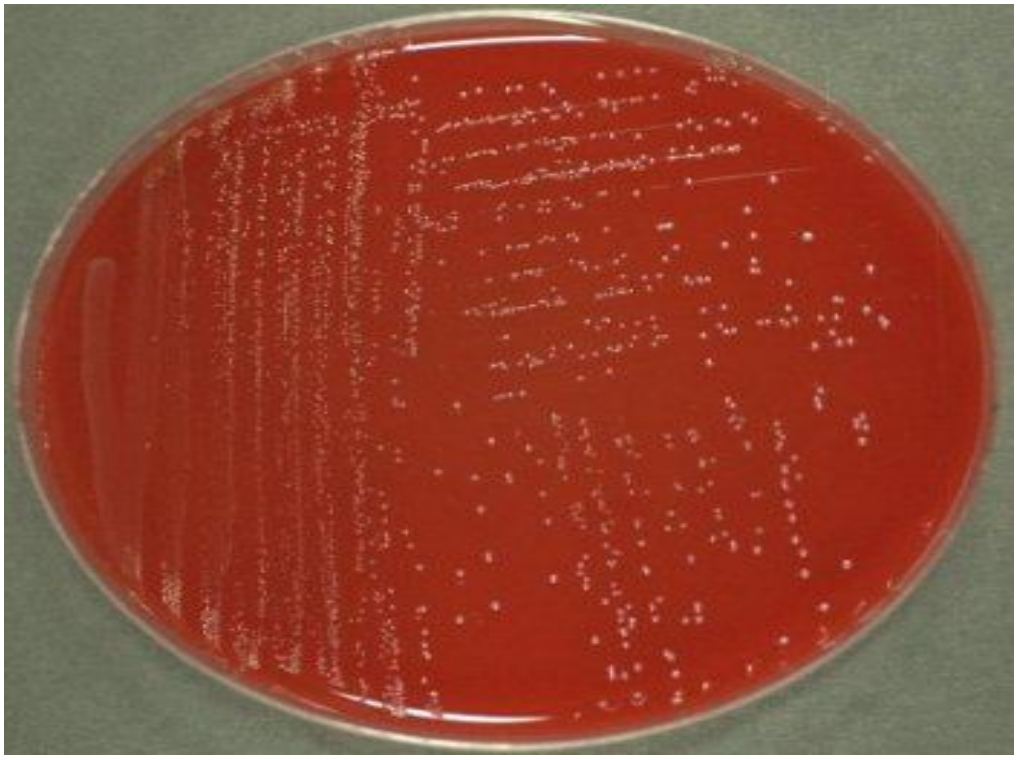


Figure 4.5. Colonial morphology of GBS on the blood agar

4.9. Biochemical identification

Catalase test :

Few drops of hydrogen peroxide solution (3%) were placed on a clean glass slide; good growth of the organism was taken and immersed in the hydrogen peroxide solution. The culture should not be more than 24 hours old and from a blood–free medium as nutrient agar. Immediate bubbling indicates positive results (Forbes; *et al.,* 2007). *Streptococcus agalactiae* are not produced this bubble so is negative for catalase test figure (4.6).

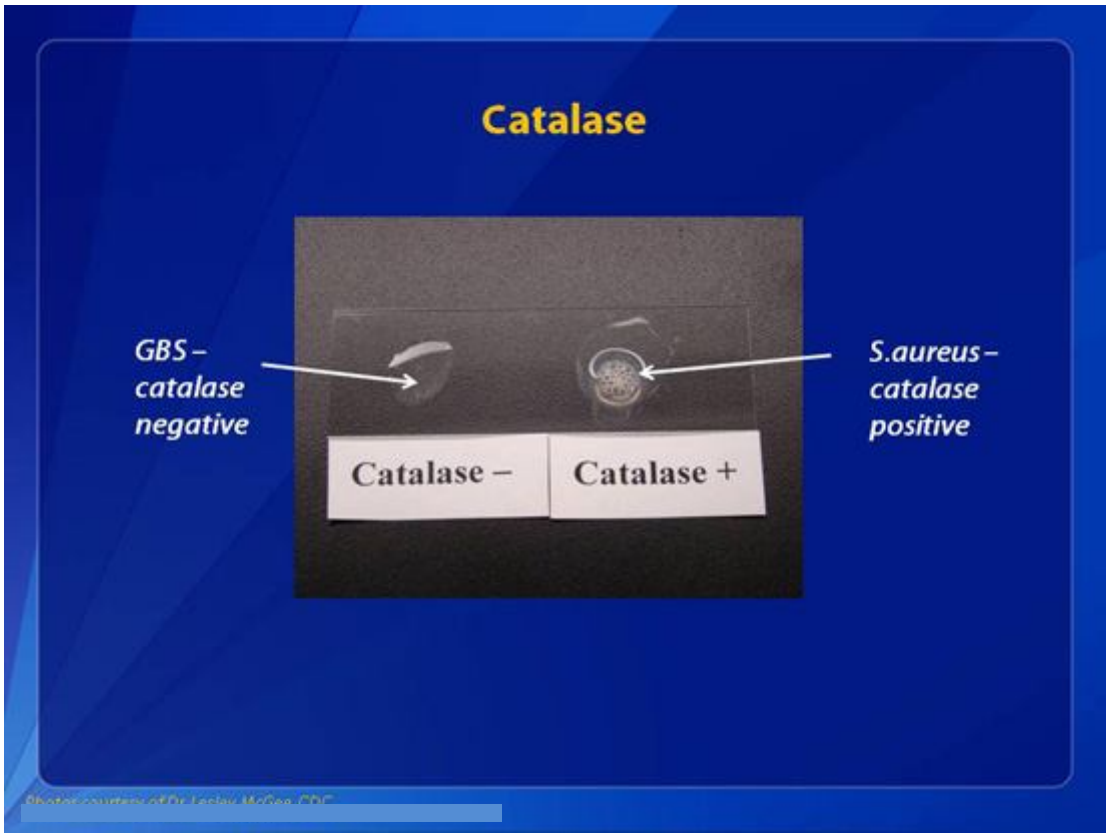


Figure 4.6. *Streptococcus agalactiae* catalase negative contrast to *S. aureus*

4.10. Lancefield group test

This test is used to identified of the grouping of streptococci by adding one drop of the solution of each group with the dilution colony of streptococci the positive agglutination reffered to this group of streptococcus (figure 4.7) .

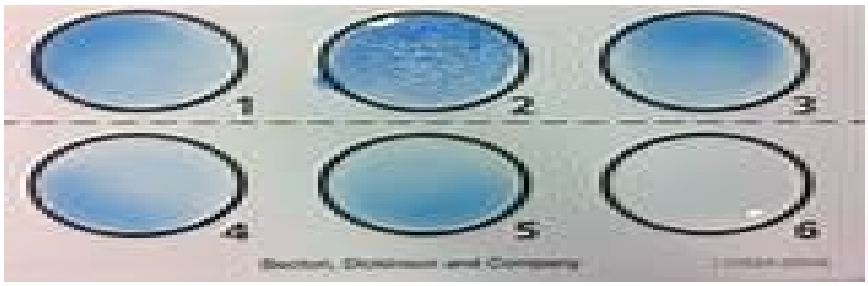


Figure 4.7. B- hemolytic streptococcal isolate agglutination with GBS

4.11. Relationship Between Age And Positive GBS

The distribution of *S. agalactiae* isolates among different age groups are presented in table 4.2. and figure (4.8), 5 (11.33 %) patients were between 18 to 20years, 11 (14.86%) patients were age between 23 to 34 years old, 2 (8.00%) patients were within the 35-40 years old and 1 (7.14%) patients were above 41 years old. However. Among these one hundred fifty seven samples isolates from *S.agalactiae* infection, the age range between 23-34 were found to be more predominant 11 (14.86%) than other age range .similar to our study and this results almost in agreement Orett (2003), also reported The prevalence of vaginal and rectal GBS colonization was 32.9%. Group B streptococci were isolated more frequently from women >24 years (36.6%) than those younger than 24 years (26.9%), and more so, from women of East Indian descent (37.3%) than women of African descent (27.2%).

Table 4.2 distribution of *S. agalactiae* among different age

Distribution age	Sample no	Positive *S.agalactiae*	%
18-22	44	5	11.33
23-34	74	11	14.86
35-40	25	2	8.00
41-50	14	1	7.14
Total	157	19	12.10

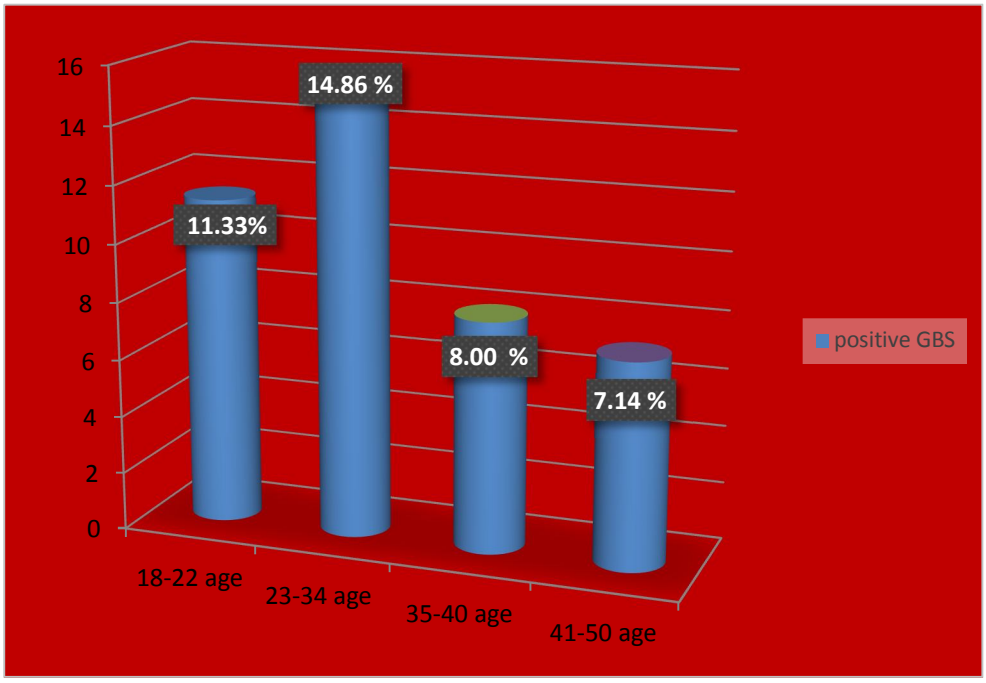


Figure 4.8. Correlation between age and GBS infection

In this work, the numbers and percentages of *Streptococcus agalactiae* isolates from pregnant women are presented in table (4.3) and figure (4.9) . Out of 157 different gestation age specimens, 19 (12.10 %) *Streptococcus agalactiae* were isolated, including 8 (5.09%) *S. agalactiae* isolates from 89 pregnant women with gestation age between 35 to 37 weeks, 11 (16.17%) isolates from 68 pregnant immediately after delivery .

The above results revealed that *S. agalactiae* were highly percentage rate isolated immediately after delivery than other sample were isolated before delivery, since about one-fifth of pregnant women are vaginally colonized with GBS at the time of delivery, a high percentage of babies are born colonized with the organism and many develop potentially fatal infections (Regan *et al.,* 1996).Neonates can acquire GBS from their mothers through aspiration of infected amniotic fluid or during the passage through the birth canal. The colonization of the female genital tract with GBS is significantly associated with this infection and should be carefully monitored (Garcia *et al.,* 2003; Larcher *et al.,* 2005)

Table 4.3. Numbers and percentages of *S. agalactiae* isolates from different gestation age .

Gestation age	Samples, n	*S. agalactiae*, n	%
Between 35-37 week	89	8	5.09
At delivery	68	11	16.17
Total	157	19	12.10

n: numbers, %: percentage

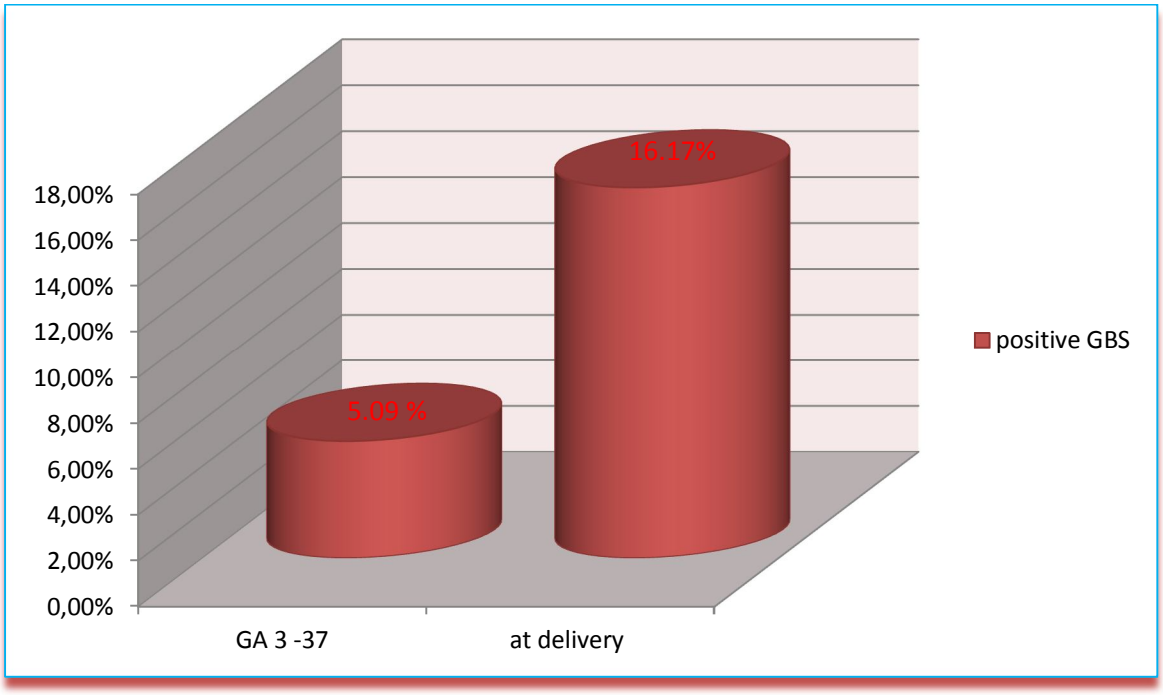


Figure 4.9. Distribution of GBS with different gestation age

4.12. Antimicrobial Susceptibility

Antimicrobial susceptibility tests are used to determine which specific antibiotics a particular bacterium is sensitive to. Most often, this testing complements a Gram stain and culture, the results of which are obtained much sooner. Antimicrobial susceptibility tests can guide the physician in drug choice and dosage for difficult-to-treat infections. (Levinson; 2010).

Constant survey of antimicrobial susceptibility testing plays a very important role in up to date informations about the sensitivities of GBS to the available drugs. Ideally, choice of treatment should be made after the susceptibilities of causative organisms had been determined in vitro. In a health care setting, very little extra studies on antimicrobial

susceptibility survey can facilitate to provide completely practical information of the resistance pattern (Abdulrazzaq, 2013). Continuous monitoring of sensitivity patterns is important, since this sensitivity is affected by the wide use of antimicrobials and this lead to the emergence of new resistant strains.

The antimicrobial susceptibility tested in this study of all nineteen clinical isolates. Of *S.agalctiae* collected during June 2014 to December 2014, was performed by the disk diffusion method according to the guidelines of the CLSI.

The minimum bactericidal concentration (MBC) is the lowest concentration of an antibacterial agent required to kill a particular bacterium. It can be determined from broth dilution minimum inhibitory concentration (MIC) tests by sub culturing to agar plates that do not contain the test agent.

It is not enough to just identify your organism. You also need to know what antimicrobial agents your organism is susceptible to.

Table 4.4. shows the susceptibility patterns of all *S. agalactiae* isolates to antibiotics. The susceptibility rate of *S. agalactiae* isolates to penicillin and, vancomycin in the present study was (100%). The results of the present study are nearly in agreement with that of study Khadijeh Nasri *et al.,* (2013), who reported isolated GBS Sensitivity to penicillin and vancomycin was100% .

Jannati , *et al.,* 2012 Showed all isolates were susceptible to ampicillin,vancomycin and penicillin. One isolate (1.7%) showed reduced susceptibility pattern to penicillin (MIC; 0.25 µg/ ml). There were 3 (5.3%) isolates semi- sensitive (0.25- 1 µ g/ ml) to erythromycin (2; 0.5µg/ ml and 1; 0.38 µg/ ml) and 2 (3.5%) isolates to clindamycin (1; 0.5 µg/ml, 1; 0.38µg/ml). Additionally,2 (3.5%) isolates were resistant to clindamycin (1;16µg/ml,1;2µg/ml).According to the disk diffusion test, 47 (83.9%), 8 (14.2%) and 7 (12.5%) isolates were resistant to Co- trimoxazole, ciprofloxacin and ceftriaxone respectively.

In our study showed that the sensitivity of GBS to Amoxicillin (100%), Chloramphenicol (94.44), clindamycin (94.11 %), Erythromycin(93.75), Ciprofloxacin(89.47), Cefatoxime (83.33). And all isolates were resistant 100 % to Doxycycline and oxacilline.

Decoster, *et al*., (2005) in belgie showed that all isolates were susceptible to penicillin, amoxicillin, cefazolin, cefotaxime, vancomycin and linezolid.We found resistance rate of 16.7% to erythromycin and 11.0% to clindamycin.

Persson.E. *et al* (1998-2001)in Sweden revealed that all isolates were sensitive to cefotaxime, meropenem, linezolid, vancomycin, moxifloxacin .Two strains displayed a slightly decreased susceptibility to penicillin G (MIC 0.25 microg/ml) also when tested by the broth dilution method. Two per cent were resistant to erythromycin and 1% to clindamycin. Strains with intermediate sensitivity to erythromycin and clindamycin increased over the 2 study periods. 68% were resistant to doxycycline, and the resistance rate for doxycycline increased over the 2 study periods.

Table 4.4. Susceptibility of *S. agalactiae* to antibiotics

No.of Isolates	P	AK	CTX	DA	E	VN	CRO	C	DO	OX
1	S	S	S	S	S	S	S	S	R	R
2	S	S	S	S	S	S	S	S	R	R
3	S	S	R	I	I	S	S	S	R	R
4	S	S	S	S	S	S	S	S	R	R
5	S	S	S	I	I	S	S	I	R	R
6	S	S	R	S	S	S	S	S	R	R
7	S	S	S	S	S	S	S	S	R	R
8	S	S	I	S	S	S	S	S	R	R
9	S	S	S	S	S	S	R	S	R	R
10	S	S	R	S	S	S	S	S	R	R
11	S	S	S	S	S	S	S	S	R	R
12	S	S	S	S	R	S	R	R	R	R
13	S	S	S	S	S	S	S	S	R	R
14	S	S	S	R	S	S	S	S	R	R
15	S	S	S	S	I	S	S	S	R	R
16	S	S	S	S	S	S	S	S	R	R
17	S	S	S	S	S	S	S	S	R	R
18	S	S	S	S	S	S	S	S	R	R
19	S	S	S	S	S	S	S	S	R	R

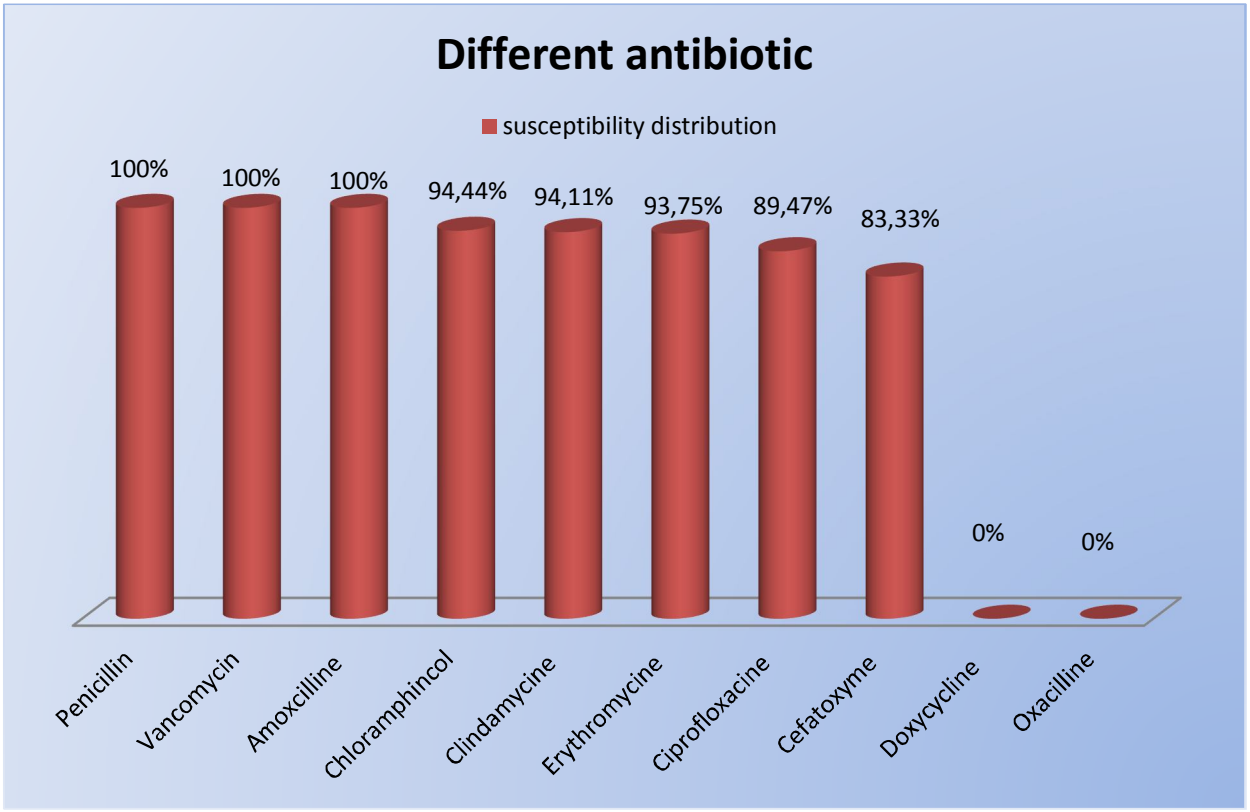


Figure 4.10. Susceptibility of Isolated GBS to the antimicrobial disc.

Shabayek *et al.,* (2009) in Egypt revealed that all isolates were susceptible to penicillin G, ampicillin and vancomycin. Resistance to cefotaxime was detected in three isolates (7.89%). Five isolates (13.15%) were resistant to erythromycin and nine isolates (23.68%) were resistant to clindamycin.

Joachim *et al.,* (2009) in Tanzania showed that all isolates were sensitive to vancomycin and ampicillin. Resistance to clindamycin, erythromycin and penicillin G was found to 17.6%, 13% and 9.4%, respectively .

Kimura *et al.,* (2013) in Japan showed that all 139 isolates were susceptible to penicillin G, ampicillin, cefotaxime, cefepime, and meropenem; no PRGBS isolates were detected. However, the rate of erythromycin and clindamycin resistance in the isolates were 10.1% and 5.0%, respectively . Arisoy *et al.,* (2003) in turkey revealed that None of the isolates were resistant to penicillin and ampicillin, whereas 21.2% and 9.1% showed resistance to erythromycin and clindamycin, respectively. González *et al.,* (2004) in pain showed that All the GBS (100%) were susceptible to penicillin, ampicillin, vancomycin.

At the end of this research i want to say that the result of my research might be different If the population of this research was people with higher socio-economic state for example if we did this research among the patients who visit to private hospital this result that we got changes . we can also say that according to recording information about patient most of them are rural patient includes in this research which indicate a low education level and having lower personal hygiene condition, which may enhance probability of this female to get this infection also this pregnant ladies were not followed by a specialist or didn't visit primary health care during the pregnancy .

Which means even if they got his infection no one will know about it and not discovered as long with the effect of it will be more clear during delivery and past partum period . As I mentioned during my presentation the effect of this microorganism should not be neglected so if pregnant women advised and educated to visit a physician or primary health care for regular checkup during pregnancy it will minimize occurrence of this bad result ,More of the patient samples had naturally delivery without surgery in this case if a GBS bacteria positive mother is not treated with antibiotics her baby can be exposed to GBS bacteria during a vaginal birth , once in contact with the baby ,the GBS bacteria can gain entry to to the babys body via mucous membran of the nose and mouth or through breaks of the skin, the GBS bacterial infection can spread throuh the babys blood to infect the other organ systems such as heart and lung throughout the baby.TV and media may get a role for this education and there advices because as we all know that prevention is much better than cure and also cost much less .

5. CONCLUSIONS AND SUGGESTIONS

5.1. Conclusion

Antibiotic resistance is a continually evolving and dangerous problem that requires immediate attention as well as future planning to impede a global health crisis. According to this study, we concluded the followings:

1. The occurence of positive colonization of *Streptococcus agalactiae* in vaginal swab obtained from 35 to 37 gestation age pregnant women was 12.10 %.
2. The rate of infection according to the age group was high in second and third decades.
3. Colony morphology, Gram stain, bacitracin test, catalase test, CAMP test, slidex strepto group test, wer good diagnostic parameter for identification of GBS.
4. The rate of colonization of *Streptococcus agalactiae* in the 35 to 37 gestation age pregnant women gestation age between 35s to 37 week was lower than colonization of GBS at delivery.
5. This study showed that isolated GBS were highly sensitive to penicillin, ampicillin and vancomycin, while the isolated GBS were resistant to doxycycline and oxacylline.

5.2. Suggestions

1. Its suggested for all pregnant woman to investigate vaginal swab for clonization of *Streptococcus agalactiae* at first, second and 35 to 37 gestation age.
2. Its suggested for pregnant women who were positive for GBS colony to recieved proper vaccination to decrease the risk factor for the newborn.
3. Its recomended to achieve blood culture of GBS colonization for the newborn of positive GBS colonization mothers to detect early new born infection.
4. It's suggested to use of penicillin G or vancomycin as a first-line drug in prophylactic treatment regimes against early-onset neonatal GBS disease.

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