Anterior placental location influences onset and progress of labor

and postpartum outcome

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Abstract

Introduction: The aim of the study is to evaluate whether placental location at term is associated with delivery outcome.

Methods: A prospective study including 2354 patients with singleton pregnancy at term admitted for vaginal delivery was conducted. Placental position was determined before delivery by ultrasonographic examination performed transabdominally with women in the supine position. Maternal characteristics and delivery outcome such as premature rupture of membranes, induction of labor, mode and gestational age at delivery, indication for cesarean section, duration of the third stage, postpartum hemorrhage (PPH) and manual removal of placenta were correlated with anterior, posterior or fundal placental locations.

Results: Among women enrolled: i) 1164 had an anterior placenta, ii) 1087 a posterior placenta, iii) 103 a fundal placenta. Women with anterior placenta showed: i) a higher incidence of induction of labor (p= 0.0001), especially for postdate pregnancies and prolonged prelabor rupture of membranes (p<0.0001), ii) a higher rate of cesarean section rate for failure to progress in labor (p=0.02), iii) a prolonged third stage (p=0.01), iv) a higher incidence of manual removal of placenta (p= 0.003) and a higher rate of PPH in vaginal deliveries (p=0.02).

Discussion: The present study showed the influence of anterior placental location on the course of labor, with a later onset of labor, a higher rate of induction and cesarean section and postpartum complications. The reason for this influence on labor and delivery complications remains to be elucidated.

Introduction

Human placenta represents a "transient organ" that plays a key role during gestation, as the major determinant of pregnancy maintenance, fetal growth and labor onset [1, 2], through the production of substances acting as endocrine, paracrine and autocrine factors [3]. Placenta is responsible for exchange of all nutrients, oxygen, and fluid from mother to fetus and removal of fetal waste products [4]. It has also been called the ''diary of gestational life'' [5] an extremely appropriate description. Placenta may also provide valuable information on the cause and timing of many adverse events and conditions such as neurologic injury, fetal distress, infections, intrauterine growth restriction (IUGR), and demise, as well as identification of unsuspected maternal disorders, and primary placental disorders [5].

Given its role in mediating maternal-fetal signals, it has the ideal position at the interface between mother and fetus, to modulate these several biological functions during the course of pregnancy [6]. Indeed, placenta is an organ anchored to a uterine wall, reaching a total surface area for exchange of 11 m^2 at term [4]. In recent years it has been studied by ultrasound the location of placenta and its relationship with the internal cervical os during the course of gestation, showing a "dynamic placentation" [7]: the original location of the implanting blastocyst is modified during the course of its development. The factors that determine the site of nidation of human blastocyst are not fully understood. Human blastocyst normally implants in the upper portion of the uterus and then placentation begins [8]: anterior, posterior, fundal, right or left sides of uterus are all normal places for placental development [9, 10]. When placenta is attached lower down in uterus it is known as placenta previa, a situation which carries an increased risk of hemorrhage.

Whilst there has been extent research on abnormal placentation (placenta accrete) and low placental implantation, only a few studies have evaluated the other aspects of placental position and its possible impact on pregnancy and delivery outcome [11-15]. In fact, a link between low placentation and an increased risk of fetal growth restriction, abruption placenta, third trimester

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bleeding and postpartum hemorrhage (PPH) was shown [16-18]. Fundal implantation seems to increase the incidence of prelabor rupture of membranes and a shorter duration of the third stage [19, 20]. Lateral placental implantations have been associated with an increased incidence of preeclampsia, fetal distress in labor, abdominal deliveries and IUGR [12,13], while cornual implantations carries an increased risk of breech presentations [21,22]. Besides, women in labor with fetal persistent occiput posterior position had more frequently an anterior placenta [23, 24].

Therefore, the aim of the study was the association between placental location and unfavorable delivery outcome, in term of mode and gestational age of delivery, need of induction of labor, duration of the third stage, PPH and manual removal of placenta. The association between placental location and other parameters, such as maternal characteristics (age, pre-pregnancy BMI, BMI at admission, parity, mode of conception, prelabor rupture of membranes) and neonatal outcomes (fetal sex and weight), were evaluated.

Methods

A prospective study was conducted between January 2011 and December 2013 on all patients (n=2889) admitted consecutively to the University Hospital of Siena, at the Department of Molecular and Developmental Medicine, for vaginal delivery, both spontaneous and induced labor. The permission of the Local Human Investigation Committee was granted for the study.

Women with multiple pregnancy, elective cesarean section, preterm birth, maternal pathologies (uterine fibroids, uterine anomalies, coagulopathies, pregravidic diabetes and hypertension, severe preeclampsia), fetal congenital abnormalities, intrauterine deaths, third and fourth degrees vaginal tears and cervical tears were excluded from the study. Only women with fetus in cephalic presentation were included in the study.

For all patients, placental position was determined at admission, together with fetal presentation and amniotic fluid index, by ultrasonographic examination performed transabdominally with patient in the supine position. A sagittal view of the uterus was used to determine anterior and posterior location of placenta, while fundal placenta was visualized at the top wall of the uterus. Placentas occupying the left or right region of the anterior and posterior uterine walls were considered anterior and posterior, respectively.

Women with diagnosis of placenta previa, low lying placenta (a placental edge that is either less than 2 cm from the internal cervical os or implanted in the lower uterine segment, but not closer than 2-3 cm from the internal cervical os), abnormal placentation (placenta accrete, increta, percreta) or vasa previa were excluded [25].

Women admitted for induction of labor, presenting an unfavorable cervix (Bishop score less than 6) were induced by an intravaginal prostaglandin E2 pessary (dinoprostone; Propess 10 mg; Ferring AB, Limhamn, Sweden] while women with a favorable Bishop score underwent intravenous oxytocin administration [26].

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In all cases of spontaneous delivery, an active management of the third stage of labor was employed, including use of a uterotonic drug immediately following delivery of the fetus, transabdominal manual massage of the uterus, controlled cord traction and early cord clamping and cutting [27].

Clinical characteristics were registered, such as maternal age, BMI (pre-pregnancy, at admission), parity, mode of conception (spontaneous vs assisted reproductive technologies – ART), premature prelabor rupture of membranes (PROM), need of induction of labor, indication for induction, mode of induction of labor (vaginal prostaglandins or oxytocin), mode and gestational age of delivery, indication for cesarean section (CS), duration of the third stage, postpartum hemorrhage (PPH) and manual removal of placenta. After delivery, estimation of blood loss was made with measurement of blood collected in a graduate plastic drape. In case of cesarean section estimation of the amount of blood loss was invalidated by the presence of amniotic fluid, so this group of patients was excluded from the analysis concerning postpartum hemorrhage.

Finally, neonatal clinical variables (sex, weight) were recorded.

Statistical analysis

Analysis of data was performed using the GraphPad Prism version 5.00 for Windows (GraphPad Software, Inc, San Diego, California) and MedCalc® Package (Version 12.4.0.0). Data analyzed by descriptive statistics are presented as means and standard deviations (means ± SD). Statistically significant differences were evaluated using one-way ANOVA for quantitative data and Fisher's exact test or χ^2 test as appropriate for binomial variables. p values less than 0.05 were considered to indicate statistical significance. Logistic and multiple regression, with stepwise entry of covariates, were used to calculate odds ratio (OR), presented with 95% confidence intervals (CI) to evaluate the association between anterior placenta and statistically significant delivery outcomes.

Results

Among all women enrolled in the study 535 was excluded for the presence of exclusion criteria. The final study population was composed by 2354 at term pregnant women: i) 1164 with an anterior placenta, ii) 1087 with a posterior placenta, iii) 103 with a fundal placenta.

Among all patients, 26.8% underwent induction of labor, while 73.2% were admitted for spontaneous onset of labor. The major indications for induced labor were: postdate pregnancies, prolonged prelabor rupture of membranes, oligohydramnios, intrauterine growth restriction, pregnancy-induced hypertension and intrahepatic cholestasis of pregnancy.

Concerning mode of delivery, 87.5% had a vaginal delivery while 12.4% underwent nonscheduled cesarean section, for non-reassuring fetal heart pattern, malpositions, failure to progress in labor (arrest of descent or arrest of dilatation), failed induction, defined as failure to establish active labor after a cycle of treatment of intravaginal prostaglandin (one PGE2 controlled release pessary over 24 hours), or oxytocin infusion after rupture of membranes (if intact) up to 8 hours or intravaginal prostaglandins followed by oxytocin infusion.

Concerning maternal characteristics, no differences were shown between all groups regarding age, pre-pregnancy BMI, BMI at admission, parity and mode of conception *(Table 1)*.

Concerning obstetrics outcomes, a significant (p=0.03) correlation was found between more advanced gestational age at delivery and anterior placenta. Women with anterior placenta showed a higher incidence of induction of labor (p= 0.0001), with a OR 1.40 (95% CI 1.15 – 1.71), adjusted for age, nulliparity, prelabor rupture of membranes and gestational age. The need of induction was observed especially for postdate pregnancies and prolonged prelabor rupture of membranes (p<0.0001) with respect to other placental sites of implantation. A statistical significant correlation was observed between anterior placenta and cesarean section rate for failure to progress in labor due to an arrest of descent or an arrest of dilatation (p=0.02). On the contrary, the rate of PROM was significantly higher in women having a posterior placenta (p<0.0001), thus in multivariate analysis

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175 anterior placenta had a OR 0.78 (95% CI 0.66 - 0.94), adjusted for age, nulliparity and neonatal

176 weight *(Table 2)*.

177   Among women who had a vaginal delivery, the rate of PPH was significantly (p=0.02)

178 higher in women having an anterior placenta and the result is confirmed in the subgroup of women

179 with spontaneous onset of labor (p=0.002). Logistic regression analysis showed a OR of 1.36 (95%

180 CI 1.04 – 1.79), adjusted for parity, manual removal of placenta, duration of third stage and

181 gestational age at delivery. Besides, in women presenting an anterior placenta, prolonged third stage

182 (p=0.01) and manual removal of placenta were significantly more frequent (p= 0.003) *(Table 2)*.

183   Finally, comparing neonatal outcome between all the groups, newborns presented no

184 difference regarding sex and birth weight *(Table 2)*.

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Discussion

The present study showed a significant association between anterior placenta and a particular incidence of dysfunctional labor and postpartum problems. In particular, when placenta is located on the anterior wall of uterus the onset of labor occurs later, the rate of induction of labor is increased, especially for postdate pregnancy and prolonged prelabor rupture of membranes; also the incidence of cesarean section for failure to progress in labor is more frequent than in case of other placental sites implantation. Moreover, in anterior placenta was found a higher incidence of PPH in vaginal deliveries, even in spontaneous labors, with a prolonged duration of third stage and a higher incidence of manual removal of placenta.

The reason why an anterior located placenta could have an important influence on the dynamic of labor, both in its onset and in its progress, is unclear. However, these findings support the hypothesis that placental position may influence the mechanisms of uterine contractility. Previous observations suggested placental location instrumental in triggering the normal impulse for initiation of labor and correlating with the length of gestation [28]. Moreover, it is well known that anterior placental implantation site affects uterine contractility detected by trans abdominal electromyography (EMG), through the action on surrounding myometrial cells. In fact, a placental hormonal inhibitory influence on electrical activity of myometrial cells above the placental implantation site was previously hypothesized [29-31]. These observations support our results showing the higher need to induce labor for postdate pregnancy or prolonged rupture of membranes, indicating an alteration in the onset of labor; indeed, the highest rate of cesarean section for failure to progress in labor in case of anterior placenta suggests a dysfunction of the contractility mechanism, even in case of proper onset. Inefficient uterine contractions might often manifest themselves as fetal malposition because of failure to rotate [32]. In particular, persistent occiput posterior position was noted significantly more often after prolonged pregnancy and in presence of anterior placenta indicating a degree of prior inefficient uterine contractility during

labor [24]. Meanwhile, the influence of placental implantation site as one of the factors implicated in the onset of labor is supported also by our findings showing the association between posterior placenta and PROM. Moreover, a study showed that the risk of massive hemorrhage during cesarean section for placenta previa is largely increased if the placentation is anterior, independently of factors associated such as placenta accreta, previous CS, or a transplacental approach [33].

When placenta is located in anterior wall we also found a more frequent incidence of PPH, of manual removal of placenta and a prolonged duration of third stage than other placental locations. The fact that location of placenta at term may affect the duration of the third stage of labor derived from the observation that attachment of placenta to fundus uteri is an unfavourable location associated with increased rate of different deviations from normal labor [34,35]. However, the literature is poor and controversial.

During active labor myometrium thins symmetrically and then thickens asymmetrically after expulsion of fetus [36]. For many years, it has been stated the "fundal dominance", due to a combination of an electrophysiologic phenomenon and asymmetric uterine growth [37]. Before delivery, myometrial thickness is uniformly distributed, suggesting that the strength of uterine contractions during active labor is associated with a fundal dominance [36]. Once placenta is delivered, strong myometrial contractions bring the anterior and posterior walls of the uterus into close apposition, a critical process for uterine hemostasis and placental delivery [37]. A more recent, mathematic model showed that placental separation is associated with maximal myometrial strain [38]. Myometrial wall tension probably continues to be the highest at the implantation site, where the myometrium is thinner, immediately after the delivery of the fetus for placental detachment [39]. Thus, significant thickening of myometrium at the implantation site is a late phenomenon that occurs only after complete placental separation. Moreover, an asymmetric thick myometrium probably leads to a more weakly myometrial contractility in the anterior wall of uterus.

There is a body of published work that support some of our observations. The association between anterior position of placenta and a dysfunctional labor suggest a direct influence of placental tissue on uterine wall, probably throughout the mechanisms of abnormal uterine contractility. Indeed, dysfunctional labor usually suggests an abnormality in myometrial contractility. Ultrasound examination of the post-partum uterus in which placenta is retained reveals that whilst the majority of the uterus is well contracted, the myometrium located behind the placenta remains thin and uncontracted [40]. Probably this area failed to contract throughout the labor, leading to dysfunctional labor. A regional variation of uterine wall thickness according to uterine contractility during labor was demonstrated [39]. Large part of myometrium generates intrauterine pressure, while retroplacental myometrial thickness decreases, causing a "ballooning out" of this myometrium during contractions. The localized nature of this area of myometrial tocolysis suggest that placenta is producing a locally active tocolytic, probably progesterone [41]. Placental tissue may also modulate the effect of nitric oxide on spontaneous uterine contractility in pregnant rats enhancing inhibition of uterine contractility by agents that spontaneously release nitric oxide [42]. Further studies need to be conducted to understand the mechanisms that may contribute to the differences between placental position and PPH.

In conclusion, the present study, for the first time, showed the influence of anterior placental location at term on the course of labor, both on the onset and the progression. Parturition results from a complex process involving several hormonal and mechanical changes, leading to compliance of the uterine cervix and adequate activation of the myometrial contractility, and maternal, fetal and obstetrics factors are implicated. Understanding and accurate assessment of underlying determinants of labor, like placental implantation site and risks associated with anterior location, may add more information useful for an adequate management of labor.

266 **Declaration of interest statement**

267 The Authors declare no conflicts of interest.

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