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Can color difference on the maternal side of the placenta distinguish between acute peripartum twin–twin transfusion syndrome and twin anemia–polycythemia sequence?

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ABSTRACT

Objective: To investigate the color difference between two placental shares in monochorionic placentas with acute peripartum twin–twin transfusion syndrome (TTTS) and twin anemia–polycythemia sequence (TAPS).
Methods: We evaluated all digital pictures of TAPS, acute peripartum TTTS and a control group of uncomplicated monochorionic placentas examined at our center. We determined the color intensity of the individual placental share on the maternal side of each monochorionic placenta using an image–processing program and calculated the color difference ratio (CDR).
Results: Digital pictures of 5 acute peripartum TTTS, 25 TAPS and 54 control group placentas were included in this study. The median CDR in acute peripartum TTTS was significantly lower compared to TAPS placentas, 1.20 (inter-quartile range (IQR) 1.05–1.20) and 2.50 (IQR 1.85–3.34), respectively ($p < 0.01$), and was comparable to the control group (CDR 1.11, IQR 1.05–1.22).
Conclusion: TAPS placentas have a higher CDR compared to acute peripartum TTTS placentas. Examining color difference on the maternal side of the placenta might help distinguish between acute peripartum TTTS and TAPS.

1. Introduction

Monochorionic twins share a single placenta and are connected to each other through vascular anastomoses, allowing inter-twin blood transfusion. Unbalanced net inter-twin blood transfusion can lead to various disorders, including chronic twin–twin transfusion syndrome (TTTS), acute peripartum TTTS and twin anemia–polycythemia sequence (TAPS).

Chronic TTTS, the most well-known form of TTTS, is characterized by the development of oligohydramnios in the donor and polyhydramnios in the recipient. This chronic form of TTTS occurs in 10% of monochorionic twin pregnancies and is most often diagnosed during the second trimester [1]. Acute peripartum TTTS results from a rapid and large inter-twin blood transfusion from donor to recipient through large anastomoses during delivery [2,3] and complicates 2.5% of the monochorionic twin pregnancies [4].

In contrast to acute peripartum TTTS, TAPS is characterized by a chronic and slow blood transfusion from donor to recipient through miniscule vascular anastomoses during the course of pregnancy, causing the donor to become anemic and the recipient to become polycythemic, without discordances in amniotic fluid [5]. TAPS may occur spontaneously (spontaneous TAPS) in 2–5% of the monochorionic twin pregnancies or after laser surgery for chronic TTTS (post-laser TAPS) in 3–16% of the chronic TTTS cases [6–9].

Distinction at birth between acute peripartum and TAPS may be difficult. In both cases, twins show a striking difference in skin color (a pale anemic donor and a plethoric polycythemic recipient twin) and a large difference in hemoglobin (Hb) levels (>8 g/dL) [4,5]. Nevertheless, the required therapeutic approach is different in acute peripartum TTTS and TAPS. Therefore, distinction between the two conditions is of utmost importance. Measurement of the reticulocyte count ratio and injection of the placenta with color dye

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are two methods currently used to differentiate between acute peripartum TTTS and TAPS [10–12]. However, reticulocyte count is not always measured and placental injection is a complex and time consuming procedure and is therefore only performed in specialized medical centers.

A previous study showed that measuring the color difference ratio (CDR) between the two placental shares of the maternal side can provide additional diagnostic information [13], as TAPS placentas are characterized by a large CDR. To date however, there are no reports on color differences in placentas from acute peripartum TTTS.

The aim of this study is to examine the CDR on the maternal side of acute peripartum TTTS placentas and to investigate whether this tool can help distinguish between acute peripartum TTTS and TAPS.

2. Method

All monochorionic diamniotic twin placentas with a clear digital picture of the maternal side evaluated at our center between 2002 and 2016 were included in this retrospective study, and subdivided into three groups: 1.) acute peripartum TTTS placentas 2.) TAPS placentas (spontaneous and post-laser) and 3.) a control group of uncomplicated monochorionic twin placentas. Some of the cases we included were already used in a previous study [13].

For the purpose of this study, digital pictures with insufficient quality or with incomplete Hb values were excluded. The quality of the picture was considered insufficient in case of unequal light exposure, low resolution, excessive light reflection or the presence of blood clots on the placenta.

TAPS was diagnosed using the following criteria: an inter-twin Hb difference >8 g/dL and a reticulocyte count ratio >1.7 or the presence of only miniscule anastomoses (diameter < 1 mm) detected through placental injection [14]. Diagnosis of acute peripartum TTTS was based on the presence of an inter-twin Hb difference >8 g/dL and no signs of TAPS or chronic TTTS (according to the internationally accepted standardized antenatal ultrasound criteria for TTTS [15]).

The following obstetric and neonatal data were retrieved from our database: gestational age at birth, antenatal intervention, mode of delivery, gender, birthweight, Hb levels and reticulocyte count at birth and the presence of anastomoses. The presence of anastomoses was examined through placental color dye injection. The primary outcome of this study was the color difference ratio (CDR) between the different shares of the maternal side of the placenta. CDR was calculated using an image processing program called Image J version 1.57. A step-by-step tutorial on calculating the CDR using Image J created by our institution can be viewed at: https://www.youtube.com/watch?v=_OSd6utv2Bw.

Data are reported as medians and interquartile rages (IQR). Since the size of the groups was small and data were not normally distributed, non-parametric tests were used. A Kruskal–Wallis test was applied to compare the results of the three different groups. To study the association between the inter-twin Hb differences an d CDR the Spearman rank correlate on test was used. A p-value < 0.05 was considered to indicate statistical significance. Statistical analysis was performed using IBM Statistics v23.0 (SPSS, Inc., an IBM company, Chicago, IL, USA).

3. Results

A total of 108 pictures of the maternal side were considered eligible for this retrospective study. We excluded 1 acute peripartum TTTS case due to an insufficient picture quality (blood clots and unequal light exposure). In the control group 23 cases were excluded because of insufficient picture quality (n = 2) and missing Hb values (n = 21). In total, 5 acute peripartum TTTS, 25 TAPS, and 54 control group placentas were analyzed. The TAPS group consisted of 14 spontaneous TAPS (56%) placentas and 11 post-laser TAPS placentas (44%). Fig. 1 provides an overview of the selection of the study population.

The median gestational age in the acute peripartum TTTS group was 37 weeks (IQR 33–37 weeks), 32 weeks (IQR 30–35 weeks) in the TAPS group and 35 weeks (IQR 32–36 weeks) in the control group. Baseline characteristics of the three groups are presented in Table 1.

Table 2 shows hematological characteristics and the CDR for the three different groups. Reticulocyte count ratio was measured in 60% (3/5) of the acute peripartum TTTS cases, 92% (23/25) of the TAPS cases and 41% (22/54) of the cases in the control group. In cases in which reticulocyte count ratio was not available, placental injection was used to fulfill the required diagnostic criteria for TAPS or acute peripartum TTTS. In agreement with the postnatal diagnostic criteria for TAPS, all TAPS cases had an inter-twin Hb difference >8 g/dL, median 12.7 (IQR 10.5–18.1), and a reticulocyte count ratio > 1.7, median 3.7 (IQR 2.5–5.0). In the acute peripartum TTTS group, all 5 cases showed an inter-twin Hb difference >8.0 g/dL and the median reticulocyte count ratio was 1.1 (IQR 1.0-*). In the control group, all 54 cases had an inter-twin Hb difference <8 g/dL.

*Upper quartile could not be measured since only three reticulocyte count ratios (1.0, 1.1 and 1.4) were available.

The median CDR in the acute peripartum TTTS group was 1.20 (IQR 1.05–1.20) compared to the median of 2.50 (IQR: 1.85–3.45) in the TAPS group and a median of 1.11 (1.05–1.22) in the control group ($p < 0.01$). There was no significant difference in CDR between spontaneous TAPS cases and post-laser TAPS cases ($p = 0.149$). Fig. 2 shows the maternal side of a control group placenta, acute peripartum TTTS placenta and a TAPS placenta. In Fig. 3, pictures of the maternal side of the placenta are shown for ascending CDR values to illustrate the increasing difference in color intensity.

In Fig. 4, the relation between CDR and inter-twin Hb difference for the acute peripartum TTTS, TAPS and the control group is depicted. All the CDR values of the TAPS group were larger than 1.5, except for one post-laser TAPS case (CDR = 1.3). In this case an inter-twin Hb difference of 9.3 g/dL was found, corresponding with TAPS stage 1 [11]. All control group cases showed a CDR <1.5, with the exception of one case (CDR = 1.5). This placenta belonged to a twin with selective intra-uterine growth restriction (sIUGR), with an inter-twin Hb difference of 3.8 g/dL and a high reticulocyte count ratio (3.7). In all acute peripartum TTTS cases a CDR <1.5 was found. Median CDR in the spontaneous TAPS group was 2.6 (IQR 2.0–4.7) and 2.1 (IQR 1.5–3.0) in the post-laser TAPS group ($p = 0.14$). As shown in Fig. 4, there was no correlation between CDR and inter-twin Hb difference in the control group ($R = 0.18$, $p = 0.098$) or the acute peripartum TTTS group ($R = 0.63$, $p = 0.253$). In the TAPS group, there was a positive correlation between inter-twin Hb difference and CDR ($R = 0.58$, $p < 0.01$).

4. Discussion

This is the first study reporting on color differences on the maternal side of acute peripartum TTTS placentas. We found a significantly lower median CDR in acute peripartum TTTS placentas compared to TAPS placentas ($p < 0.01$). Furthermore, all acute peripartum TTTS placentas had a CDR <1.5, whereas almost every TAPS placenta (except one) had a CDR higher than 1.5.

Our study suggests that inspection of the maternal side of the placenta may help distinguish between acute peripartum TTTS and