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# Recurrent preeclampsia in a pregnant woman with Klippel-Trenaunay syndrome: two cesarean deliveries and multiple extremity involvement - a case report and literature review

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## Abstract

**Background** In this study, a total of 17 patients with Klippel-Trenaunay Syndrome (KTS) and pregnancy were evaluated. The patients were divided into two groups: those with organ involvement (10 patients) and those without organ involvement (7 patients). The clinical findings, complications, and treatment approaches between the two groups were compared, and the effects of KTS on the pregnancy process and potential risks were examined in detail. Significant clinical differences were observed between pregnant women with involvement of abdominal organs such as the liver, spleen, rectum, sigmoid, kidney, bladder, and uterus, as well as central organs like the brain, and those without such involvement. Organ involvement was defined as organ enlargement or venous anomalies detected by techniques such as ultrasound, magnetic resonance imaging (MRI), or computed tomography. Our literature review found that the risk of postpartum hemorrhage (PPH) was significantly higher in the group with organ involvement ($p < 0.05$). The presence of varicose malformations in organs such as the spleen, liver, and uterus was identified as an important factor increasing the risk of PPH. Therefore, close monitoring of coagulopathic disorders and taking precautions against thromboembolism in pregnant women with KTS is crucial. The case report discusses the complications and treatment processes experienced by a 26-year-old woman diagnosed with KTS and who developed preeclampsia during her two pregnancies. Complications such as preeclampsia and varices were observed in the first pregnancy, and intrauterine growth restriction (IUGR) and preeclampsia in the second pregnancy. Successful outcomes were achieved in both cases with a multidisciplinary approach and appropriate treatment methods. This study provides important information to understand the effects of KTS on pregnancy and the potential complications associated with this rare condition. Future studies will provide more information on the management of preeclampsia and other complications in pregnant women with KTS.

**Keywords** Klippel, Trenaunay syndrome, Preeclampsia, Pregnancy, Cesarean, Hemihypertrophy, Vascular malformation

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## Introduction

KTS was first described by French doctors Maurice Klippel and Paul Trenaunay in 1900 [1]. English dermatologist Frederick Parkes Weber described similar clinical features in 1907. Therefore, the syndrome is sometimes referred to as Klippel-Trenaunay-Weber syndrome [2].

KTS is a rare congenital disorder characterized by capillary malformations as reddish "port-wine stains" on the skin, venous malformations as varices and other venous enlargements, lymphatic malformations as abnormalities in the lymphatic system, and excessive growth and thickening of the affected limb [3]. This syndrome usually becomes clinically apparent at birth or early infancy, but in some cases, it can be diagnosed prenatally [4, 5]. In the diagnosis of KTS, low-flow venous malformations are detected by ultrasonography, while organ and extremity involvement is evaluated in detail by MRI [6]. Although the exact cause of KTS is not known, genetic mutations are thought to play a role. Specifically, somatic mosaic mutations in the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) have been associated with this syndrome [7]. PIK3CA mutations play a critical role in the pathogenesis of vascular anomalies, and the increased PI3K signaling caused by these mutations affects endothelial cell responses to fluid shear stress, leading to the development of various vascular disorders [8].

Cases of pregnant women with KTS are rarely reported, so the level of uncertainty is high when it occurs during pregnancy. KTS is a condition that increases obstetric risk and can particularly worsen thromboembolic and hemorrhagic complications [9]. A retrospective study conducted in 2019 examined 139 women with Klippel-Trenaunay syndrome. Of these, 75 had a history of pregnancy, while 64 were classified as nulligravid. The study is based on the medical records of patients evaluated at the Mayo Clinic in Rochester, Minnesota, between 1945 and 2018. The large time span and inclusion of a large patient cohort enhance the quality of the study. However, due to its retrospective nature, it has some limitations. Nevertheless, it provides important information about the risks of venous thromboembolism and bleeding associated with pregnancy in women with KTS [10]. Another study conducted in 2017 evaluated pregnancy and delivery complications in women with Klippel-Trénaunay syndrome. Sixty women reached through two tertiary specialist centers in the Netherlands and the Klippel-Trénaunay patient organization provided information about their obstetric histories through an online survey [11].

Although rare in the literature, cases of KTS complicated by maternal preeclampsia have been reported [12]. In our study, the clinical course and treatment of a 26-year-old woman diagnosed with KTS who developed preeclampsia in both pregnancies are discussed. Preeclampsia was diagnosed in both pregnancies upon detection of high blood pressure and +3 proteinuria in the urine, and both deliveries were performed by cesarean section. The patient was found to have ipsilateral hemihypertrophy, varicose enlargements in the uterine vessels, liver enlargement, and low-flow venous anomaly.

Parkes Weber syndrome is a congenital vascular malformation characterized by the presence of capillary, venous, lymphatic, and arteriovenous malformations. The presence of arteriovenous malformation is the main criterion distinguishing Parkes Weber syndrome from Klippel-Trénaunay syndrome, and this distinction is important for treatment strategy [13]. In our study, we also conducted a literature review using case reports and excluded cases that could be Parkes Weber syndrome. There are no prospective studies related to our topic. Retrospective studies did not meet our inclusion and exclusion criteria, so their data could not be used.

Our study is observational as it is based on a literature review and case reports [14]. This research aims to provide more information on the management of complications such as postpartum hemorrhage (PPH) and preeclampsia resulting from organ involvement in pregnant women with KTS, and to offer recommendations for clinical practice. There are limited studies in the literature examining the relationship between organ involvement and pregnancy complications in pregnant women with KTS. Therefore, this study emphasizes the importance of a multidisciplinary approach in pregnant women with KTS and highlights the points to be considered in the management of these patients.

## Case report

**First pregnancy and delivery process** A 39-week nulliparous pregnant woman, who was not previously registered at our hospital, presented to the Istanbul City Hospital Obstetrics Emergency Clinic with complaints of a headache. The patient had a childhood diagnosis of KTS and exhibited several characteristic features, including right-sided hemihypertrophy, asymmetry more prominent on the right side of the head and face, port-wine stains on the jaw and neck, swelling and edema in both legs (more pronounced on the right side), deformity in the right big toe, and difficulty walking during physical examination (Figs. 1 and 2). Transabdominal ultrasonography revealed a single fetus with a fetal heart rate of 152 bpm and an anterior placenta.

The patient's blood pressure was initially recorded at 150/80 mmHg; however, during follow-up, it peaked at 160/100 mmHg, meeting the criteria for preeclampsia. Laboratory analysis showed significant proteinuria (+3), while all other laboratory values, including hemoglobin (8.8 g/dL, indicating anemia; normal range: 12–16 g/dL), platelet count (239 × 10^9/L, normal), AST (33 U/L,

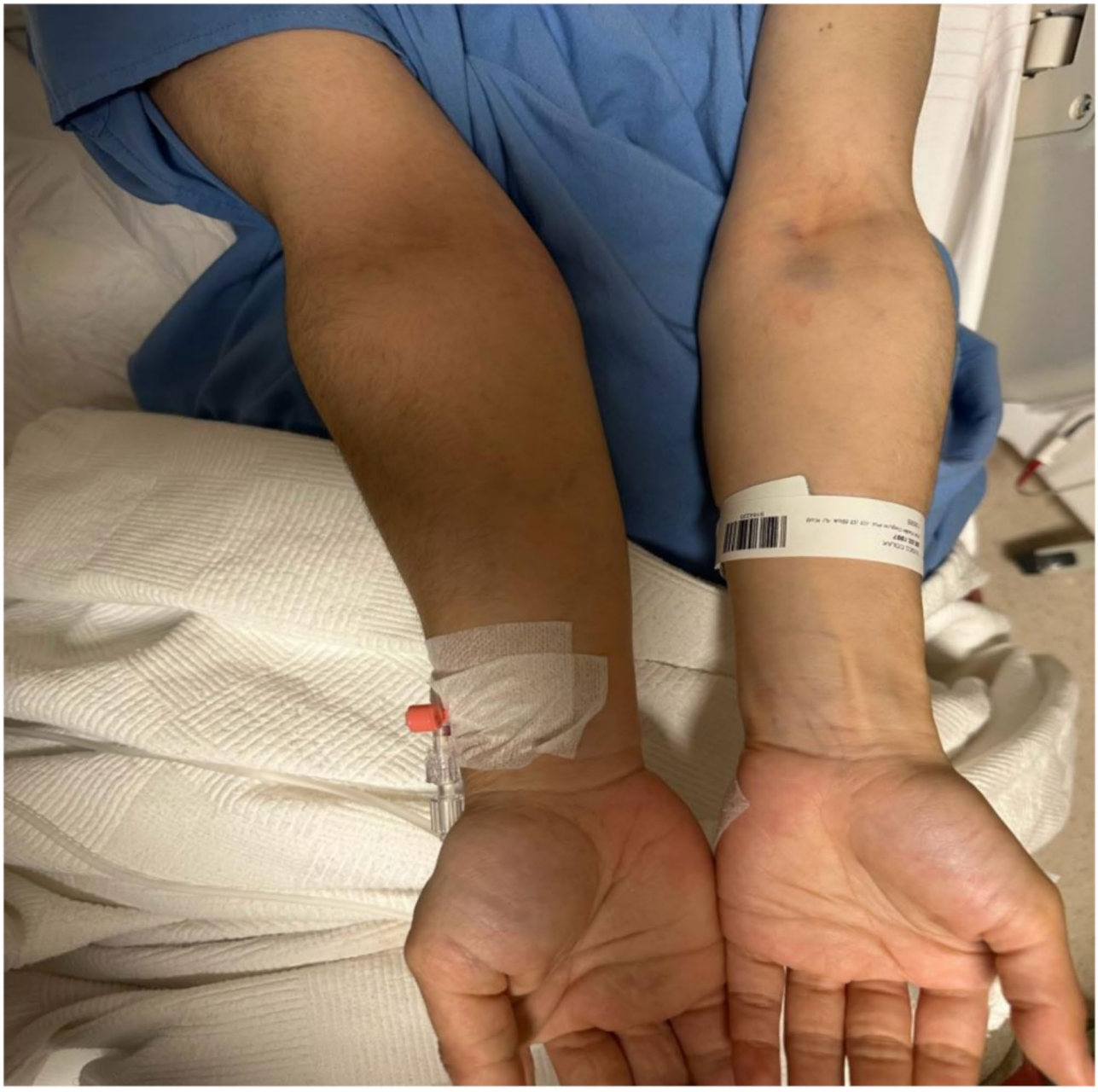

**Fig. 1** The right arm and forearm are thicker compared to the left arm

normal), ALT (9 U/L, normal), urea (17.1 mg/dL, normal), and creatinine (0.6 mg/dL, normal), were within normal limits. Based on the hypertension and proteinuria findings, a diagnosis of preeclampsia was confirmed, and magnesium sulfate (MgSO4) therapy was initiated with a 2 g/h loading dose, followed by maintenance therapy for 24 h.

The patient did not report a history of heavy menstrual bleeding. Considering the obstetric complications, no autoimmune testing, including antiphospholipid antibodies and thrombophilia screening, was conducted during the pregnancy. Additionally, no evidence of intracranial arteriovenous malformations was detected, either clinically or through imaging.

Consultations with cardiology, radiology, and vascular disease specialists were conducted. While color Doppler ultrasonography of the lower extremity venous system did not reveal deep vein thrombosis, varicose veins and thrombi were observed bilaterally. Considering the presence of genital varices and KTS findings, cesarean delivery was planned under spinal anesthesia.

The cesarean section was successfully performed, resulting in the birth of a healthy baby girl weighing 2730 g with an APGAR score of 8/9. Intraoperative

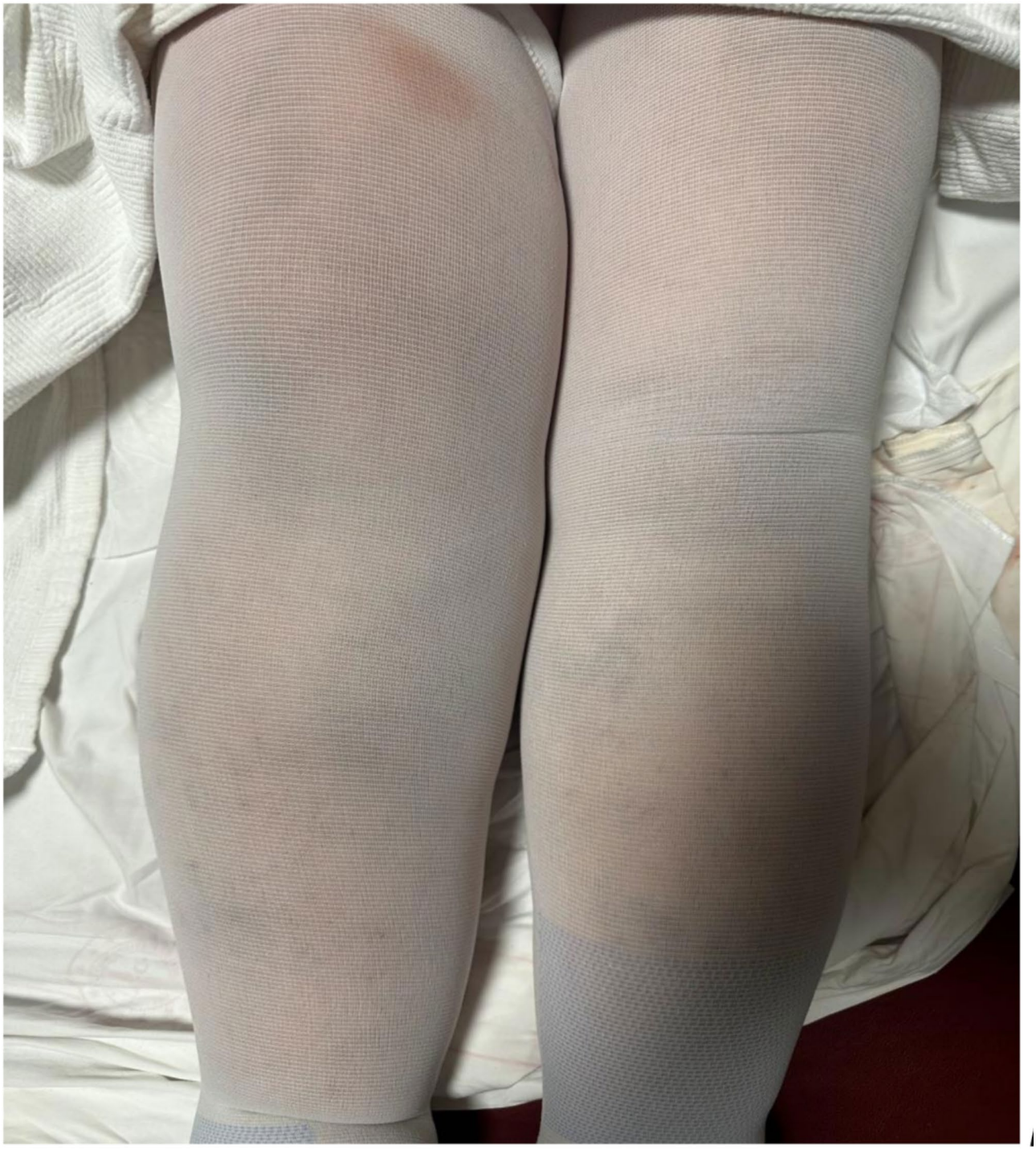

**Fig. 2** The right leg, with an anti-embolic varicose sock, is thicker than the left

findings included significant varices and hepatomegaly in the right abdominal wall, uterus, and pelvic region (Fig. 3). Postoperatively, the patient received anticoagulant therapy with low molecular weight heparin (LMWH) for one month. Abdominal MRI performed during the postpartum period confirmed mild liver enlargement and a fatty appearance (Fig. 4), with no evidence of arteriovenous malformations. The mother and baby were discharged in good health five days after delivery.

**Second pregnancy and delivery** The patient, who was followed up with intrauterine growth restriction (IUGR) at 34 weeks and 6 days of gestation, presented with complaints of vomiting and pain. The patient's blood pressure

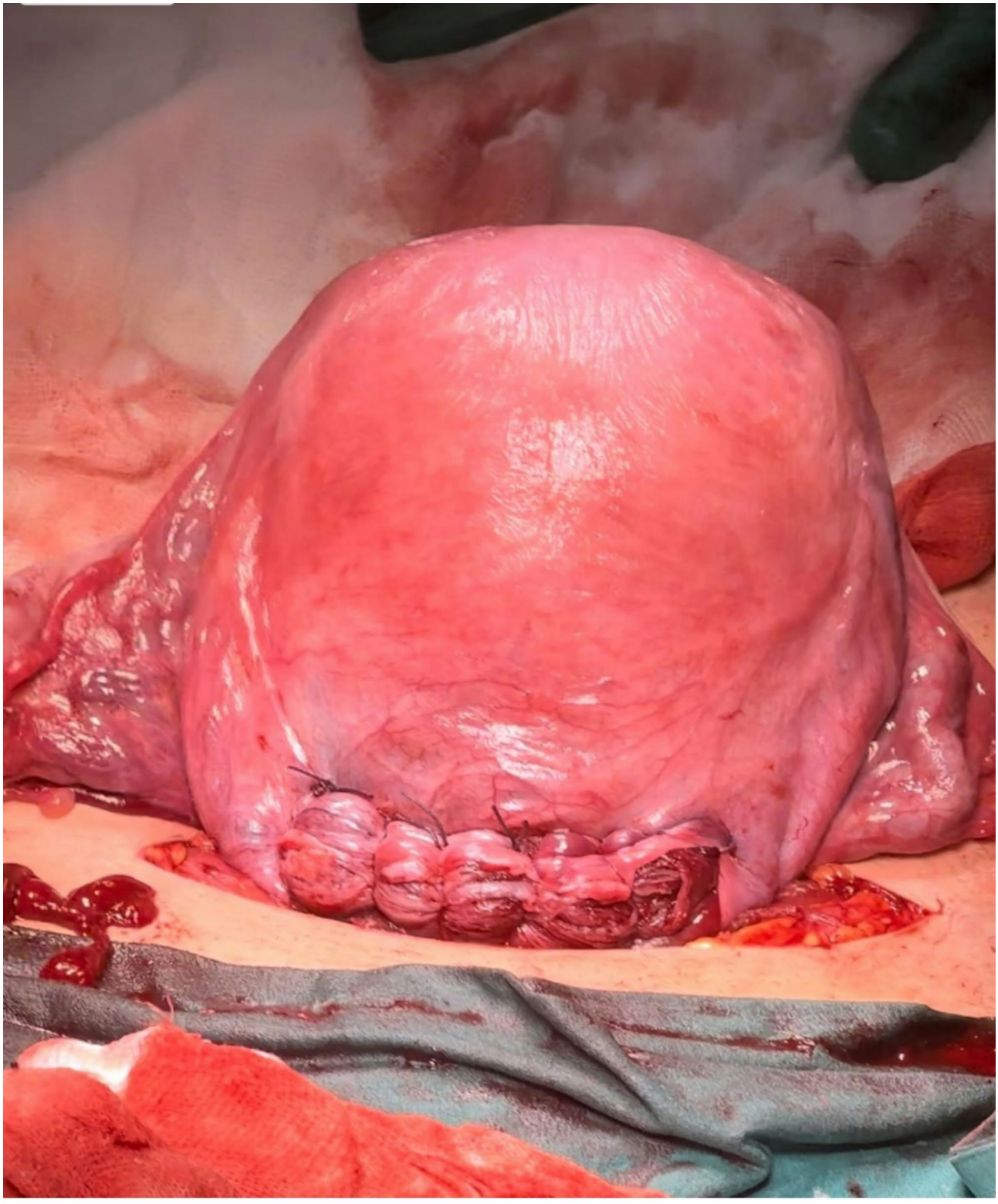

**Fig. 3** Varicose veins on the side of the uterus

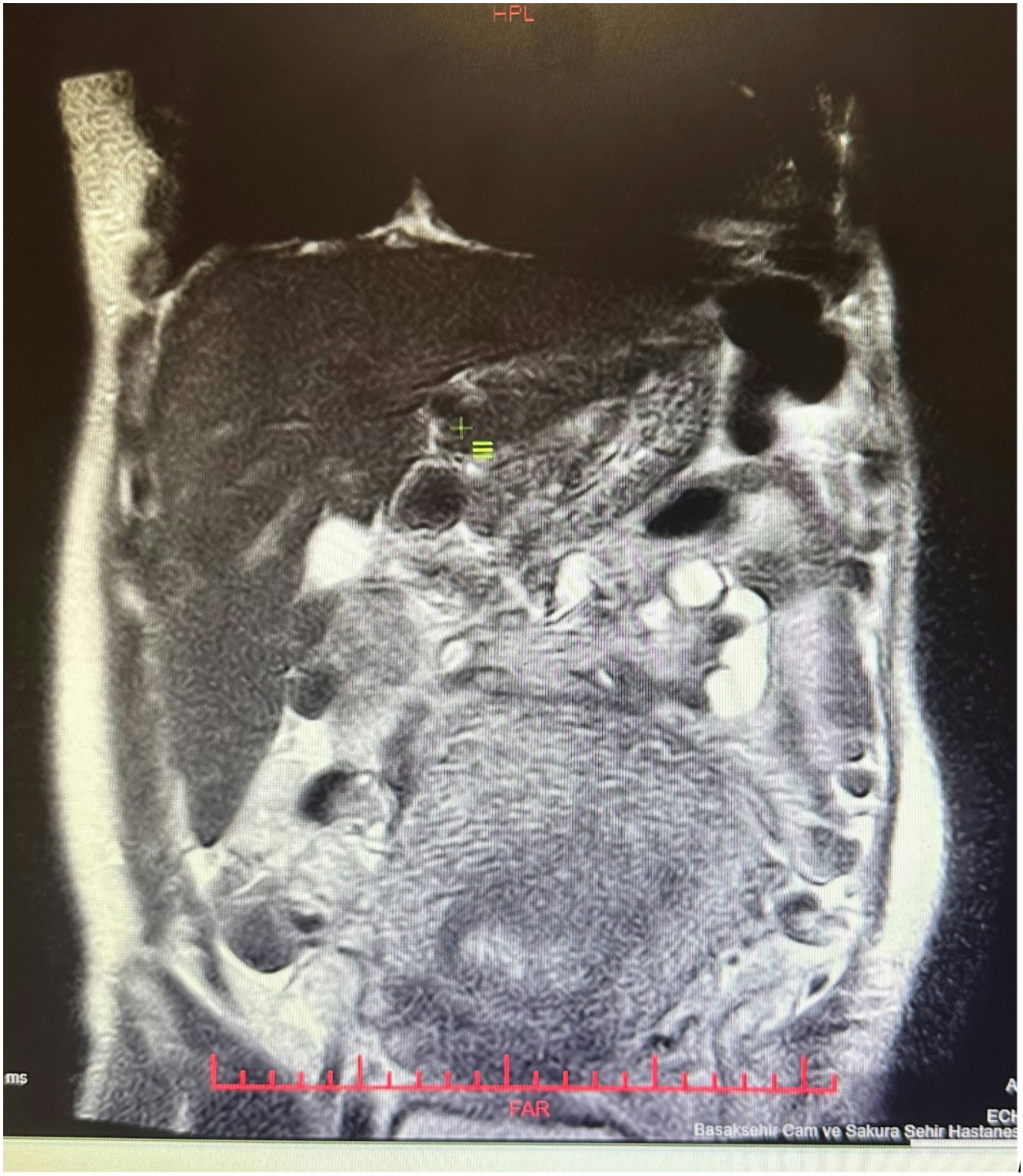


**Fig. 4** MR image showing hepatomegaly extending to the pelvis

was 145/96 mmHg, and she had been using LMWH (Low Molecular Weight Heparin) 0.6 ml 2 × 1 and antiplatelet therapy throughout her pregnancy. Fetal biometry measurements were recorded as BPD: 31 + 4, AC: 30 + 1 (264 mm, < 1 percentile), FL: 31 + 1, and EFW: 1690 g. These percentile values were calculated based on the last menstrual period. The umbilical artery Doppler PI was 0.90. The patient's urine showed + 3 protein. Due to headache complaints, magnesium sulfate (MgSO4) treatment was initiated with a loading dose of 2 g/h and continued

with maintenance therapy for 24 h. The patient was admitted for cesarean delivery under the indications of previous cesarean section, IUGR, and preeclampsia by the perinatology specialist.

Under general anesthesia, a healthy baby girl weighing 1850 g and measuring 43 cm with an APGAR score of 6/8 was delivered by cesarean section. Preoperative hemoglobin was 10.7 g/dL, urine protein was + 3, spot urine protein was 14,566, and protein/creatinine ratio was 19,743. Postoperative hemoglobin was 10.3 g/dL, creatinine was 1.36 mg/dL, and albumin was 23 g/dL. Proteinuria and hypoalbuminemia were noted; however, all other laboratory parameters, including renal and liver function tests, were within normal limits. Two ampoules of albumin replacement were administered. LMWH 0.6 ml 2 × 1 was started and continued for one month.

The placenta was reported as discoid in shape, measuring 21 cm in length and 1.5 cm in diameter, with a paracentral umbilical cord insertion. It was of normal consistency and weighed 231 g, with dimensions of 15 × 10 × 1.5 cm. The fetal surface appeared bluish-purple, with prominent chorionic vessels, while the maternal surface demonstrated complete but irregular cotyledons and areas of hemorrhage. Sectional analysis revealed congested parenchyma with patchy yellowish-gray areas. Histological evaluation showed findings consistent with maternal vascular malperfusion, including thinning of the syncytiotrophoblastic layer, thickening of fetal artery walls, and increased syncytial knots. The umbilical cord contained two arteries and one vein, with an umbilical cord index (UCI) of < 0.06. These findings provided significant insights into the severity of fetal growth restriction (FGR) in the second pregnancy and the pathophysiology of maternal complications. Placental assessment played a critical role in supporting the accuracy of management decisions and determining the timing of placental injury.

No acute deep vein thrombosis was observed in the deep veins. The right and left saphenofemoral junction (SFJ) diameters were measured as 14 mm and 10 mm, respectively. Varicose veins and some thrombi associated with the great saphenous vein (GSV) and small saphenous vein (SSV) were detected on both sides. Perforating veins were observed in the middle section of the cruris. No arteriovenous malformation was observed according to ultrasound and MRI results. After the patient's clinical condition and laboratory values improved, the mother and baby were discharged in good health.

This case demonstrates the complications experienced by a patient with KTS in two different pregnancies and the management of these complications. Complications such as preeclampsia and varices were observed in the first pregnancy, and intrauterine growth restriction and preeclampsia in the second pregnancy. Successful outcomes were achieved in both cases with a multidisciplinary approach and appropriate treatment methods. This case provides important information to understand the course and management of KTS during pregnancy.

## Materials and methods

**Data collection** The data used for the case report were obtained from the hospital information system. Information about the patient's age, medical history, and KTS diagnosis was collected. Complications experienced during pregnancy and treatment methods were detailed. The mode of delivery, postpartum complications, and treatment methods were explained. The patient's photos were taken with written consent, and the results were obtained from the hospital information system. Additionally, the patient provided verbal consent for her medical information to be used in this academic medical study.

**Literature review** In September 2024, a systematic search was conducted in the MedLine, Embase, and Cochrane Library databases without any date restrictions. This study conducted a literature review on KTS and pregnancy. The keywords used in the search were: "Klippel-Trenaunay-Weber syndrome and pregnancy," "pregnant," "expectant," "gravida," "delivery," "parturition," "birth." The databases used for the literature review and the results obtained are listed below.

Among the automation tools used, Rayyan was utilized as a systematic review tool to facilitate the rapid and easy screening of references. EndNote was used for reference management and duplicate detection. Covidence was used as a data management tool to facilitate the screening, selection, and data extraction processes of studies.

**PRISMA diagram** The search included the MEDLINE ($n = 1831$), Embase, Cochrane Library, and Google Scholar ($n = 661$) databases. A total of 2268 references were removed, with 2042 duplicates identified manually and 26 studies marked as unsuitable by automation tools excluded. The number of studies screened was 224, of which 72 were excluded. The number of studies sought for retrieval was 152, of which 117 were not retrieved. The number of studies assessed for eligibility was 35, of which 18 were excluded. As a result, the number of studies included in the review was 17 (Fig. 5).

Among the 18 studies excluded at the final stage, 5 were published under the name of KTS and pregnancy but were misdiagnosed due to the presence of arteriovenous malformations. Additionally, 7 studies did not have sufficient data on arteriovenous or venous anomalies. Furthermore, 6 studies did not have surgical, ultrasound, or MRI findings clearly demonstrating organ involvement.

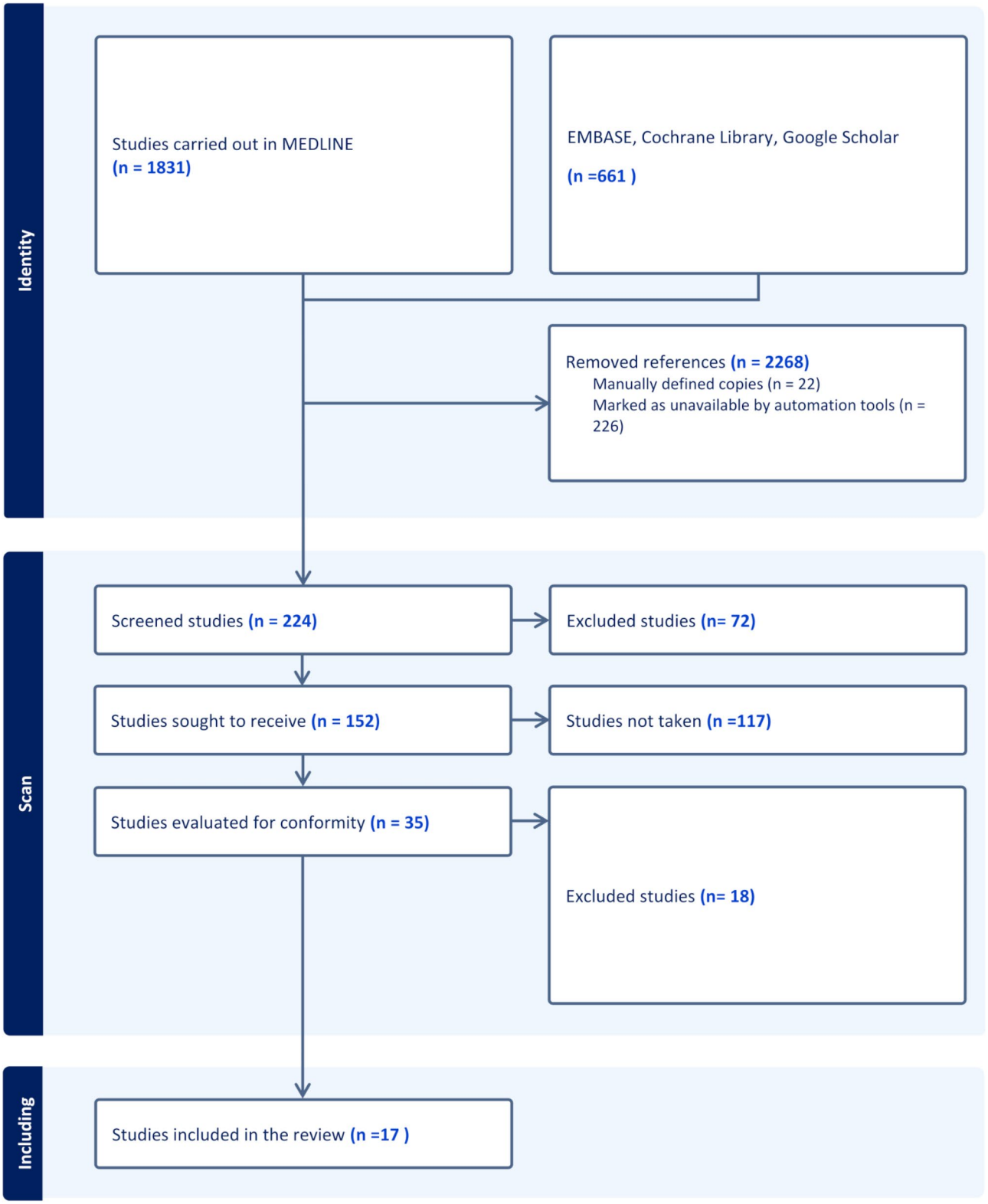


**Fig. 5** PRISMA scheme: literature review on kts and pregnancy

### Inclusion criteria

1. Patients diagnosed with KTS.
2. Patients who completed the pregnancy process and gave birth.
3. Pregnant women aged 18–45.
4. Primigravid and multiparous pregnant women.
5. Patients experiencing complications such as preeclampsia, gestational diabetes, intrauterine growth restriction (IUGR).
6. Patients receiving medical and surgical treatment.
7. Patients who gave birth vaginally and by cesarean section.
8. Fetal outcomes such as birth weight, APGAR score, neonatal complications.

### Exclusion criteria

1. Patients with arteriovenous malformations were not included in the study because these types of malformations have a different pathophysiology from KTS and require different clinical management.
2. Patients with Parkes Weber syndrome were also not included in the study because, although this syndrome may show similar clinical features to KTS, it is distinguished by the presence of arteriovenous fistulas and requires a different treatment approach.
3. Patients whose organ involvement could not be clearly determined were also not included in the study. This situation may be due to insufficient clinical information, incomplete imaging results (MRI or ultrasound), or diagnostic uncertainties. Patients whose organ involvement could not be clearly demonstrated were excluded from the study.

**Statistical methods** The Mann-Whitney U test was used for the analysis of quantitative independent data. The Chi-Square test was used for the analysis of qualitative independent data. Descriptive statistics of the data included mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was measured by the Kolmogorov-Smirnov and Shapiro-Wilk tests. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram was used for the literature review. SPSS 28.0 program was used for the analyses.

## Results

In this literature review, a total of 17 patients with KTS and pregnancy were evaluated. The patients were divided into two groups: those with organ involvement (10 patients) and those without organ involvement (7 patients). The clinical findings, complications, and treatment approaches between the two groups were compared, and the effects of KTS on the pregnancy process and potential risks were examined in detail. Significant clinical differences were observed between pregnant women with involvement of abdominal organs such as the liver, spleen, rectum, sigmoid, kidney, bladder, and uterus, as well as central organs like the brain, and those without such involvement. These differences significantly varied in terms of symptom severity, disease course, and response to treatment. Organ involvement was defined as organ enlargement or venous anomalies detected by techniques such as ultrasound, MRI, or computed tomography (Table-1).

Our literature review revealed that intra-abdominal organs, particularly the uterus, liver, rectum, sigmoid, spleen, and kidney, were generally affected. In two different case reports by Yara N and Atis A, brain involvement was detected as an extra-abdominal finding [15, 16]. Additionally, cases with bladder and kidney involvement along with the uterus were also presented [17, 18]. In a case reported by Water Meyer SR and Maciej Sadowski, only uterine involvement was observed. In this case, no abnormalities or disease signs were found in the patient's other organs, and only the uterus was affected [19, 20]. Zhang J and colleagues reported a case with only spleen involvement. This patient underwent a hysterectomy due to postpartum hemorrhage, but a splenectomy was not required [21]. In a case with only rectosigmoid colon involvement, hematochezia developed, and Argon Plasma Coagulation treatment was applied [22]. In Benson E's study, uterine and anal canal involvement was detected. Major postpartum hemorrhage was managed with Bakri balloon and Hayman suture [23].

In the case by Xiao L and colleagues, a patient with Klippel-Trenaunay syndrome had varicose malformations in the spleen, liver, and uterus, but delivered a healthy baby vaginally at 36 + 6 weeks of gestation, and the delivery process was uneventful. Blood loss was reported to be approximately 350 ml, and no blood transfusion was required [24]. In another study where uterine involvement was present but PPH did not develop, it was reported that patients did not experience postpartum hemorrhage complications [12]. In a study without organ involvement, postpartum hemorrhage (PPH) developed, and it was observed that this condition was not directly related to organ involvement [25].

Regarding fetal complications, one case of intrauterine growth restriction (IUGR) was observed in both groups. However, no significant fetal effect was observed in patients with KTS. This indicates that the impact of KTS on fetal development is limited. The study noted that fetal complications in pregnant women with KTS are rare and generally do not result in severe fetal effects [18, 25].

Pregnant women with Klippel-Trenaunay syndrome were evaluated with MR angiography performed before

**Table 1** Patients with KTS organ involvement

| Study Name | Age | Birth | Limb Involvement | Organ Involvement | Maternal Effect | Fetal Effect | Therapy |
|---|---|---|---|---|---|---|---|
| Wenpeng Xue | 26 | 39 + 0 weeks, vaginal delivery | Left lower extremity, PSW | None | Varicose veins, hypertrophy, thrombophlebitis | None | Oxytocin, heparin, elastic compression, general anesthesia |
| Chadha R | 19 | 37 + 3 weeks, cesarean delivery | Right lower extremity, PSW | None | Pulmonary embolism, cellulitis, lymphedema, septic shock, risk of DIC, PPH | IUGR | LMWH, warfarin, blood transfusion |
| González-Mesa E | 25 | 38 + 0 weeks, cesarean delivery | Left lower extremity, left thigh, left vulva, PSW | None | Varicose veins | None | Erythropoietin therapy |
| Güngör Gündoğan T | 33 | 39 + 0 weeks, vaginal delivery | Right leg, PSW | None | Varicose veins | None | LMWH, oxytocin |
| Tanaka R | 29 | 37 + 0 weeks, cesarean delivery | Right leg, PSW | None | Varicose veins | None | Heparin, elastic stockings |
| Sivaprakasam MJ | 18 | 35 + 0 weeks, cesarean delivery | Left leg, left groin, PSW | None | Preeclampsia, varicose veins | None | Heparin |
| Minguez JA | 31 | 38 + 0 weeks, vaginal delivery | Right leg, PSW | Cervix uteri | Cervical prolapse, vulvar edema, varicose veins | None | Sclerotherapy, polidocanol |

delivery. Hemangiomas and varices were observed in the extremities and abdomen, but no significant arteriovenous malformation was detected. In the group without organ involvement, a case report associated cervical prolapse with KTS, despite the absence of organ involvement such as the uterus. This indicates that KTS can lead to structural anomalies in the pelvic region, not limited to organ involvement [26]. In the group without organ involvement, studies reported starting LMWH treatment in the postpartum period due to the formation of vulvar and extremity varices. These studies suggested the prophylactic use of LMWH, considering that varices could increase the risk of thromboembolic complications [9, 27, 28]. In Wenpeng Xue's case, thrombophlebitis developed in the patient, but no pulmonary embolism was observed. This indicates that thrombophlebitis can be controlled without leading to more serious complications such as pulmonary embolism [29]. In one case, the mother developed pulmonary embolism, postpartum hemorrhage (PPH), and disseminated intravascular coagulation (DIC) risk. In another case, despite the development of preeclampsia, no significant maternal complication was observed in the group without organ involvement. These findings indicate that patients without organ involvement experience fewer severe complications during pregnancy and delivery (Table-2).

There was no significant difference in age between the groups with and without organ involvement ($p = 0.832$). There was no significant difference in gestational age between the groups with and without organ involvement ($p = 1.000$). There was no significant difference in the mode of delivery between the groups with and without organ involvement ($p = 1.000$). There was no significant difference in the presence of varices between the groups with and without organ involvement ($p = 1.000$). There was a significant difference in the incidence of PPH between the groups with and without organ involvement ($p < 0.05$). It was found that those with organ involvement had a higher risk of PPH (Table-3).

## Discussion

KTS is a serious congenital disorder characterized by capillary malformations, venous malformations or varicose veins, and hypertrophy of the affected tissues. Although the exact cause of KTS is not known, mutations in the PIK3CA gene are thought to be associated with this syndrome [30]. The incidence of genitourinary findings in this syndrome is 30%, and patients often develop degenerative joint disease at an early age. Management is largely conservative, with palliative treatment options including elastic compression therapy and laser therapy. In rare cases, surgery is performed. Gastrointestinal involvement in KTS patients is rare but can be life-threatening [31, 32].

**Table 2** KTS Non-Organ involvement

| Study Name | Age | Birth | Limb Involvement | Organ involvement | Maternal Effect | Fetal Effect | Therapy |
|---|---|---|---|---|---|---|---|
| Hofmann K | 34 | 38 + 3 weeks, cesarean delivery | Right lower extremity, PSW | Uterus, bladder, rectum | Hemorrhoids, thrombosis, thrombophlebitis, DVT, varicose veins, PPH | None | LMWH prophylaxis, PPH management |
| Benson E | ? | 39 + 0 weeks, cesarean delivery | Left lower extremity, PSW | Uterus, anal canal | Major PPH, uterine trauma, atony | None | LMWH, Bakri balloon, Hayman sutures, transfus |
| Fuentes Carrasco M | 20 | 33 + 4 weeks, cesarean delivery | Lower extremities, PSW | Kidney, liver | Thrombocytopenia, worsened renal and hepatic function, PPH | IUGR, prematurity | Prednisone, LMWH, plasmapheresis |
| Xiao L | 31 | 36 + 6 weeks, vaginal delivery | Right lower extremity, PSW | Uterus, spleen, liver | None | None | LMWH |
| Zhang J | 26 | 39 + 0 weeks, cesarean delivery | Left lower extremity, PSW | Spleen | Late puerperal hemorrhage, PPH, DIC, hemorrhagic shock, peritonitis, sepsis | None | Blood transfusion, hysterectomy, bilateral internal iliac artery embolization, LMWH, warfarin |
| Keepanasseril A | 24 | 35 + 6 weeks, vaginal delivery | Right lower extremity, varicose veins, PSW | Recto-sigmoid colon | Hematochezia, anemia, varicose veins, rectal hemorrhage, PPH | SGA | Argon Plasma Coagulation (APC), blood transfusion |
| Yara N | 23 | 37 + 0 weeks, cesarean delivery | Left leg, PSW | Uterus, brain | Focal left-sided convulsion, varicose veins, PPH | None | LMWH, blood transfusion |
| Atis A | 30 | 38 + 0 weeks, vaginal delivery | Left arm and leg, PSW | Spleen, brain | Varicose veins, mega cisterna magna, ventricular system asymmetry | None | Antithrombotic therapy, leg elevation |
| Maciej Sotowski | 17 | 38 + 0 weeks, cesarean delivery | Lower extremities, PSW | Uterus | Varicose veins, vascular malformations | None | Heparin, elastic compression |
| Watermeyer SR | 21 | 39 + 0 weeks, cesarean delivery | Left leg, PSW | Uterus | Varicose veins, cervical prolapse, PPH | None | LMWH, elastic stockings, blood transfusion |

**Table 3** Comparison of Demographic and Clinical Characteristics of Patients with and Without Organ Involvement

| | | ORGAN INVOLVEMENT (+) | | | | ORGAN INVOLVEMENT (-) | | | | p | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean ± SD / n-% | | | Median | Mean ± SD / n-% | | | Median | | |
| Age | | 24 | ± | 5.8 | 24 | 25.9 | ± | 5.3 | 26 | 0.832 | m |
| Gestational age (days) | | 260.3 | ± | 14.7 | 266 | 263.4 | ± | 9.9 | 266 | 1.000 | m |
| Mode of Birth | CS | 6 | | 60% | | 5 | | 71.4% | | 1.000 | $X^2$ |
| | NSD | 4 | | 40% | | 2 | | 28.6% | | | |
| Varicose veins | (+) | 6 | | 60% | | 5 | | 71.4% | | 1.000 | $X^2$ |
| | (-) | 4 | | 40% | | 2 | | 28.6% | | | |
| PPH | (+) | 7 | | 100.0% | | 1 | | 14.3% | | ***< 0.05*** | $X^2$ |
| | (-) | 3 | | 0.0% | | 6 | | 85.7% | | | |

[m] Mann-whitney u test / [$X^2$] Ki-kare test

KTS is part of the PIK3CA-related overgrowth spectrum (PROS) disorders and is found alongside other disorders such as CLOVES syndrome and macrodystrophia lipomatosa. KTS is usually associated with low-flow vascular malformations and should not be confused with high-flow malformations such as Parkes-Weber syndrome [33]. Parkes-Weber syndrome is a congenital vascular malformation characterized by the presence of capillary, venous, lymphatic, and arteriovenous malformations. The presence of arteriovenous malformation is the main criterion distinguishing Parkes-Weber syndrome from KTS, and this distinction is important for treatment strategy [13]. The relationship between KTS and spinal arteriovenous malformations is likely erroneous and has not been reliably proven in the literature [34].

Skin-related complications are present in 45% of KTS patients, most commonly associated with lymphatic malformations, venous malformations in the genital area or feet [35]. Additionally, hemihypertrophy of the brain and cerebellar hemispheres has been detected in 18% of KTS patients, which is important for understanding the effects of KTS on the central nervous system [36]. A wide range of intracranial neurovascular anomalies, particularly in

the venous system, have been shown to be common in these patients [37].

During pregnancy, KTS can lead to serious complications. The literature reports that complications such as deep vein thrombosis, pulmonary embolism, severe PPH, and preeclampsia are common in pregnant women with KTS [17, 18, 23]. These complications require a multidisciplinary approach and can be successfully managed with careful obstetric management [21, 24]. Our study discusses the clinical course and treatment of a 26-year-old woman diagnosed with KTS who developed preeclampsia. The patient had hypertrophy on the right side, port-wine stains on the jaw and neck, swelling and edema in both legs, deformity in the right big toe, and difficulty walking. The patient, who showed symptoms of high blood pressure and headache during her pregnancies, delivered two healthy baby girls by cesarean section. Despite having uterine and liver involvement, the absence of PPH in our patient differs from the results reported in the literature. In this case, the effects of KTS on pregnancy, the management of additional complications such as IUGR and preeclampsia required a multidisciplinary approach and prevented maternal bleeding [25].

The literature reports organ involvement and related complications in pregnant women with KTS. For example, varicose malformations in organs such as the spleen, liver, and uterus can lead to severe bleeding [11, 16, 22]. In our case report, hepatomegaly and varicose veins in the uterus were detected. Patients with organ involvement have a higher risk of PPH and require careful management [9]. Our analyses revealed that the incidence of PPH was significantly higher in the group with organ involvement compared to the group without organ involvement ($p < 0.05$). This finding indicates that patients with organ involvement should be monitored more closely in the postpartum period. Particularly, involvement of organs such as the uterus, liver, and spleen is among the important factors increasing the risk of PPH. There was no significant difference in age ($p = 0.832$), gestational age ($p = 1.000$), mode of delivery ($p = 1.000$), and presence of varices ($p = 1.000$) between the groups with and without organ involvement. However, the risk of PPH was significantly higher in the group with organ involvement (Table-3). Notably, this study is the first to directly link vascular malformations associated with KTS to an increased risk of PPH, highlighting the importance of addressing these vascular abnormalities in clinical management.

The mode of delivery should be carefully planned considering the vascular abnormalities in the pelvic region. Cesarean delivery is often preferred to reduce the risk of complications from varices and other vascular abnormalities [28]. In our case, cesarean section was performed to minimize the risk of bleeding during vaginal delivery due to varices. The literature indicates that patients without vulvar varices can safely deliver vaginally, highlighting the importance of considering the patient's individual vascular condition when determining the mode of delivery.

The International Union of Phlebology Consensus Document emphasizes the importance of a multidisciplinary approach in the diagnosis and treatment of venous malformations and provides current information on multidisciplinary approaches in KTS management, the importance of genetic testing, treatment of low-flow vascular malformations, management of gastrointestinal complications, and new treatment options [38].

This study makes significant contributions to the limited number of studies examining the relationship between KTS and pregnancy. Our findings confirm the complication risks reported in the existing literature for pregnant women with KTS and emphasize the importance of multidisciplinary approaches in managing these patients.

The limitations of our study include its retrospective nature and small sample size. These limitations may restrict the generalizability of the results and highlight the need for larger-scale, prospective studies in the future.

## Conclusion

KTS is a rare and complex vascular malformation syndrome that requires careful management. Parkes-Weber syndrome, which should not be confused with KTS, is distinguished by the presence of arteriovenous malformations and requires a different treatment approach. During pregnancy, KTS can lead to serious complications such as preeclampsia, intrauterine growth restriction (IUGR), and PPH. This study discusses the clinical course and treatment of a woman diagnosed with KTS who developed preeclampsia. Our study emphasizes the importance of a multidisciplinary approach in pregnant women with KTS.

Genetic testing for PIK3CA mutations was not performed in this case due to the unavailability of routine genetic analysis for such mutations in our clinical setting. While PIK3CA mutations are known to overlap with the clinical features of Klippel-Trenaunay Syndrome (KTS) and contribute to the diagnosis and differentiation from conditions such as CLOVE syndrome, this limitation is acknowledged as a potential gap in the comprehensive evaluation. The lack of genetic testing highlights the need for advanced molecular diagnostic tools to ensure precise classification and guide genetic counseling for patients with similar presentations. Future studies incorporating genetic analyses could provide deeper insights into the pathophysiology and management of these complex syndromes [39].

Our literature review found that the risk of PPH was significantly higher in the group with organ involvement ($p < 0.05$). The presence of varicose malformations in organs such as the spleen, liver, and uterus is among the important factors increasing the risk of PPH. Therefore, close monitoring of coagulopathic disorders and taking precautions against thromboembolism in pregnant women with KTS is crucial.

In conclusion, although a direct causal relationship between Klippel-Trenaunay Syndrome (KTS) and pregnancy complications such as preeclampsia has not been robustly established in the literature, further research is needed to elucidate how the vascular abnormalities associated with KTS might contribute to the pathophysiology of preeclampsia during pregnancy. The management of preeclampsia and related complications in pregnant women with KTS necessitates a multidisciplinary approach. This study provides valuable insights into the impact of KTS on pregnancy, contributing significantly to the existing body of literature.

#### Abbreviations

| | |
|---|---|
| KTS | Klippel-Trenaunay syndrome |
| PPH | Postpartum hemorrhage |
| IUGR | Intrauterine growth restriction |
| MRI | Magnetic resonance imaging |
| CT | Computed tomography |
| LMWH | Low molecular weight heparin |
| PIK3CA | Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha |
| APGAR | Appearance, pulse, grimace, activity, respiration (newborn assessment score) |
| SFJ | Saphenofemoral junction |
| GSV | Great saphenous vein |
| SSV | Small saphenous vein |
| PI | Pulsatility index (doppler ultrasound pulsatility index) |
| APC | Argon plasma coagulation |
| SGA | Small for gestational age |
| DIC | Disseminated intravascular coagulation |
| PSW | Port-wine stain (hemangioma) |

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#### Author contributions
EA (Emrullah Akay) designed the study, collected the data, performed the analysis and interpretation, and wrote the manuscript. ADUG (Alime Dilayda Uzun Gül) collected the data, conducted the literature review, and contributed to the writing and editing of the manuscript. AT (Alper Türkoğlu) performed the data analysis and contributed to the writing and editing of the manuscript. All authors reviewed and approved the final manuscript.

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#### Data availability
All data generated or analyzed during this study are included in this published article.

## Declarations

#### Ethical approval and consent to participate
Our institution, Başakşehir Çam and Sakura City Hospital, states that ethical committee approval is not required for case reports. Written consent to participate was obtained from the patient.

#### Consent for publication
Written informed consent for publication was obtained from the patient. The patient was clearly informed about the publication of her medical data and images, and she voluntarily agreed to their use in this case report. The patient's identity has been kept confidential.

#### Competing interests
The authors declare no competing interests.

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