Chapter

Common Indications and Techniques in Prenatal MRI

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Abstract

Fetal and perinatal diagnostic imaging with MRI has evolved and expanded during recent times, allowing more widespread use and availability. Common indications are for neurodevelopmental conditions that are inconclusive with ultrasonography. The modality is pivotal in treatment planning for *in utero* interventions, such as repair of neural tube defects, and for particular obstetrical complications. The technique is also useful for identifying neurological sequelae from conditions like congenital heart defects and maternal viral infections. Many other applications are not indicated for routine use, particularly due to the high cost, but show much promise in research applications. Recently, complications associated with COVID-19 have been an area of interest, with prenatal MRI cohorts and case studies reporting obstetrical complications and neurodevelopmental effects. This review is aimed at highlighting common indications for the use of MRI in maternal-fetal medicine, including the MRI sequences and physics often implemented. Also, an in-depth analysis of the SARS-CoV-2 virus is discussed; in addition to pregnancy-related complications and the role of prenatal MRI in diagnosis and treatment.

Keywords: prenatal MRI, fetal MRI, birth defects, obstetrics, radiology, COVID-19

1. Introduction

Infection, preterm birth, and perinatal complications including asphyxia are among the leading causes of neonatal deaths worldwide [1, 2]. Neonatal and antenatal mortality and morbidity is most often associated with preterm birth that can result in respiratory complications, developmental abnormalities, and high-risk of infections [3, 4]. Infection has been reported in approximately 23% of worldwide neonatal deaths with an estimated 84% of instances being preventable with proper medical treatment [1, 5]. Preterm birth results in the majority of neonatal morbidity and mortality, is the direct cause of approximately 35% of neonatal deaths worldwide, and is the major risk factor for all types of neonatal deaths [1, 3, 4, 6]. Hypoxic birth asphyxia is expected to cause approximately 30% of worldwide neonatal mortality, identified by the inability to perform voluntary breathing at birth, can be observed intrapartum with techniques including Doppler ultrasound

and auscultation, and can be diagnosed by an arterial pH in the umbilical cord less than 7.2 [7].

Some of the most common birth defects include congenital heart disease (CHD), down syndrome, and neural tube defects. Congenital cardiac complications are the most common form of congenital abnormalities, with an estimated worldwide prevalence in about 0.8% of all live births, resulting in approximately 1/3 of all congenital abnormalities that cause significant medical and social consequences [8, 9]. Down syndrome is expected in about 1 in 400–1500 births, is the most common chromosomal abnormality, can be diagnosed early in pregnancy with chorionic villus sampling or amniocenteses, and predominately results from trisomy of chromosome 21 [10]. Global neural tube defect prevalence is estimated at 0.05–1% of live births, are characterized by improper closure of the neural tube during fetal development, are commonly asymptomatic, with spina bifida being the most common type, of which the most severe is myelomeningocele [11–13].

The understanding of normal *in utero* fetal brain development is still largely unknown, with techniques like magnetic resonance imaging (MRI) being uncommon in absence of disease [14]. Fetal MRI has allowed better understanding of the physiological processes involved with normal neurodevelopmental maturation, *in utero* and *ex utero* comparison, the underpinnings of congenital disease mechanisms, and long-term outcomes for specific conditions [14–17]. In the clinic, fetal MRI is often undertaken after referral from a maternal-fetal medicine specialist and indicated to help in diagnosis of particular conditions, management of known conditions, and to provide additional information for pregnancies considered for termination [9]. MRI is indicated after inconclusive results with ultrasonography, for a variety of structural abnormalities related to fetal development, particularly for imaging and identification of anomalies of the central nervous system, prior to fetal surgery, and for particularly difficult deliveries [18–21]. Fetal MRI is generally used in addition to ultrasound, primarily due to the relative cost, and can be complicated by fetal motion, wrap-around artifacts limiting the field-of-view, and from multi-slice magnetization transfer from off-resonance artifacts between adjacent slices [22]. Fetal MRI is often performed at a 20-week ultrasound scan [9]. Recently, the MERIDIAN study found that ultrasound provided accurate diagnosis of fetal brain abnormalities at 70% and 64% above and between 18 and 24 weeks, respectively; while fetal MRI in combination with ultrasound increased the accuracy to 92% and 94%, respectively [23]. Clinical radiologists report common referrals to include neurological diagnosis, treatment planning for *in utero* surgery, imaging of congenital masses, and imaging of congenital cardiac defects [24].

2. Fetal MRI sequences and safety for imaging neurodevelopmental and cardiac anomalies

MRI sequence for fetal brain analysis include functional imaging, structural imaging, and diffusion imaging [25]. The predominant sequences used in fetal MRI are single-shot T_2W (SST2W) sequences, such as rapid acquisition with relaxation enhancement (RARE) sequences on Bruker, Single-Shot half-Fourier Turbo Spin Echo (SShTSE) on Philips, Single-shot Fast Spin Echo (SSFSE) on General Electric, and half-Fourier acquisition single-shot turbo spin echo (HASTE) sequences on Siemens, with protocols provided by the MRI vendor [22, 26]. These T_2W sequences are quick enough to be acquired without sedation and are common for neuroanatomical fetal

imaging; [9] with other common sequences being T_1W to view hemorrhaging, perfusion MRI, diffusion MRI, and spectroscopy [9, 22]. Default SST2W sequences are generally capable of good image generation with 1x1x4 mm voxel size; using half-Fourier acquisitions, with refocusing pulses with flip angles between 120°-150° [22]. Though difficult to implement, diffusion-weighted imaging (DWI) allows identification of ischemic brain lesions, while T_1W images can provide improvement over T_2W for detection of calcifications, fat, and hemorrhaging [26].

Fetal cardiac sequences are often balanced steady state free precession (bSSFP) and HASTE to encompass small voxel size and reduce acquisition times needed to avoid motion artifacts, with bSSFP being particularly beneficial for imaging blood vessels and cavities containing fluid [26, 27]. Fetal cardiac MRI can be used to view structure, function, vasculature; in addition to performing quantitative MRI measurements including blood flow velocity and oxygen saturation [27]. Blood oxygen level-dependent (BOLD) functional MRI sequences have shown useful for illustrating the improvement of fetal oxygenation during maternal respiratory oxygen therapy for fetuses with impaired cerebral oxygenation resulting from certain types of CHD [28]. Abnormal placenta pathology has been linked with high rates of CHD and is a possible compounding factor for higher severity brain lesions [29]. Neurological implications are not distinct from CHD. Impaired cardiac development is linked with mild brain injury, delayed maturation, shorter gestational age, and smaller brain volumes [30, 31]. Fetal cardiac MRI complications include the smaller size of the fetal heart, lack of gating technologies, and higher heart rate [27].

The primary safety concerns in fetal MRI involve radiofrequency exposure in terms of specific absorption rate (SAR), high acoustic noise, and possibility of peripheral nerve stimulation [22]. MRI is generally considered safe during pregnancy with no evidence of harming the fetus, but is typically not recommended when the fetus is less than about 13 weeks gestational age, and gives best information after completion of organogenesis [22]. The United States Food and Drug Administration (FDA) fetal MRI SAR limit is set at 4 $W.kg^{-1}$ [22, 32]. Fetal MRI scans are usually recommended to be performed at 1.5 T, and as a "golden rule", remain below 25 seconds [20, 22]. 3 T fetal MRI is often used only within research settings because the SAR is four times higher than at 1.5 T; with the upper limit generally at 4 T for research applications [9]. Although, some institutions perform routine 3 T fetal imaging during the late second trimester and throughout the third trimester [33]. Contrast enhancement is not recommended in fetal MRI, thought to enter into the fetal vasculature, passing through the renal system, before emptying into the amniotic fluid [9, 34].

3. Common neurodevelopmental indications for Fetal MRI

Prenatal MRI is most routine for neural abnormalities because of the improved capability for fetal brain scans. In addition to treatment planning of delivery complications, a variety of conditions have high diagnostic rates with fetal MRI, including diagnosis for mild to moderate ventriculomegaly, a variety of neural tube defects, posterior fossa malformations, and twin-to-twin transfusion syndrome [9, 35]. A USA retrospective study for fetal neurology consultations (n = 94) with diagnostic MRI over 14 months reported the most common conditions were posterior fossa malformations, agenesis or dysgenesis of the corpus callosum, congenital acqueductal stenosis, ventriculomegaly, isolated malformations of cortical development, and holoprosencephaly at 19%, 15%, 14%, 11%, 8.5%, and 6%, respectively [36].

Malformations of cortical development are a collection of developmental malformations resulting from disruption during one of the stages of cerebral cortex formation, often causing cognitive impairment, cerebral palsy, and epilepsy. The cortical development occurs in three major stages, including neuronal stem cell proliferation, neuronal migration along radial glial fibers or axons to the developing cerebral cortex, and neuronal organization [37]. Malformations due to abnormal neuronal stem cell proliferation include microcephaly, megalencephaly, and cortical dysplasia. Malformations during neuronal migration and failure for proper cessation of neuronal migration, include: periventricular heterotopia, subcortical band heterotopia, classic lissencephaly, and cobblestone lissencephaly. While, neuronal organization abnormalities include polymicrogyria and schizencephaly [37, 38]. Historically, autopsy or surgical tissue samples were used for diagnosis of these conditions, being difficult to diagnose with ultrasound. MRI has greatly improved the ability to diagnose these conditions during development, rather than in childhood [39]. Retrospective assessment of cortical development malformations has shown high diagnostic accuracy of fetal MRI when compared to postnatal MRI [40].

Ventrigulomegaly is characterized by dilation of the cerebral lateral ventricles during fetal development. Congenital hydrocephalus is a type of ventrigulomegaly that results specifically from increased cerebrospinal fluid pressure, which causes birth defects resulting in abnormally large head size and many other anomalies, and most frequently results from aqueductal stenosis from outlet obstruction in the third ventricle [41, 42]. An illustration of hydrocephalus is shown in **Figure 1**. Characteristic findings seen postnatally are not often observed prenatally, such as aqueduct funneling or obstruction. Fetal MRI diagnostic indicators, for disease severity from aqueductal stenosis, include the extent of enlargement in the lateral and third ventricle, increased size of the third ventricle of inferior recesses, and observance of diverticulum outpouching in the lateral ventricles [43]. A cohort at the national maternity hospital in the Republic of Ireland reported suspected ventriculomegaly as the most common indication for fetal MRI at the facility, with severe ventriculomegaly (exluding termination) showing a 72% survival rate (n = 74) and a 65% rate for cesarean delivery (n = 72) [44].

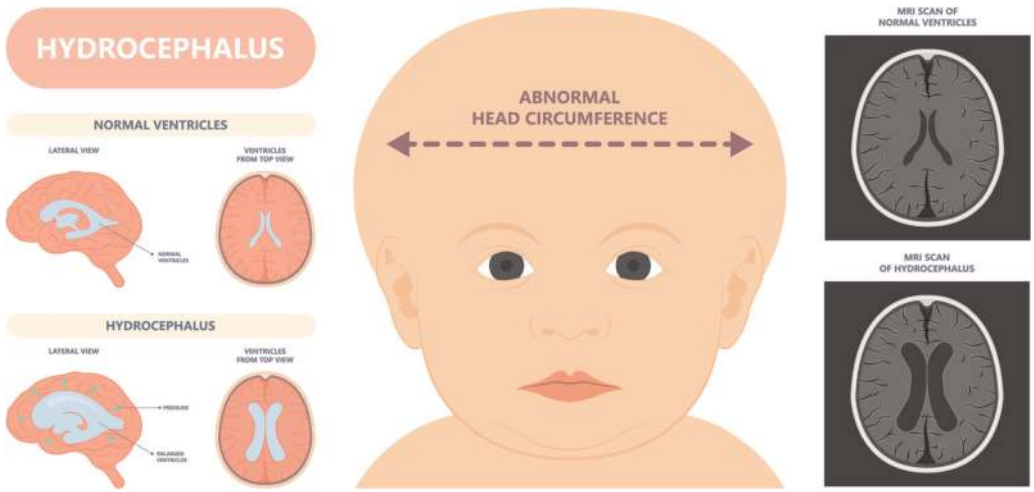

Figure 1.
Illustration of hydrocephalus with MRI. Rumruay/shutterstock.com

Failure of neural tube closure during development results in a variety of neural tube defects, causing spinal anomalies in cases of spinal dysraphism like spina bifida; or cranial anomalies like with anencephaly, characterized by absence of a major portion of the cranium. Though, anencephaly is less indicated for MRI [45]. Distinguishing characteristics of common types of spina bifida are shown in **Figure 2**. Worldwide incidence varies geographically, but estimated on average about 0.1–1% of live births, with anticonvulsants correlating with increased risk, and folic acid associated with reduced risk of neural tube defects [45]. Spinal dysraphism occurs from improper closure of the spinal cord and surrounding membranes during fetal development, and can be classified by open or closed. Closed spina bifida accounts for about 15% of instances, with spina bifida occulta as the most common form, and is usually asymptomatic [33]. Open spina bifida accounts for about 85% of open spinal dysraphisms with myelomenengocele (MMC) and myelocele being predominant, and nearly always presents with Chiari type II malformation [33]. The randomized MOMS trial compared spina bifida outcomes from fetal surgery compared to surgery after delivery, with fetal MRI playing a pivotal role in treatment planning. Outcomes showed fetal surgery for MMC allowed less need for cerebrospinal fluid shunt placement, improved cognitive function in early childhood, though higher risk of preterm birth was observed in the fetal surgery group [33, 46, 47].

Posterior fossa anomalies are characterized by neurodevelopmental malformations in the posterior fossa of the skull cranial cavity. Posterior fossa anomalies are some of the most frequent indications for fetal MRI, occurring in approximately 1 in 5000 live births, encompass a broad spectrum of conditions, and can be categorized as developmental disruptions and malformations [48, 49]. Posterior fossa anomalies include: mega cisterna magna, Blake's pouch cyst, Dandy-Walker malformation, arachnoid cyst, Joubert syndrome, rhombencephalosynapsis, and Chiari malformation [50]. The malformations can present with either an enlarged cyst appearing with abnormally

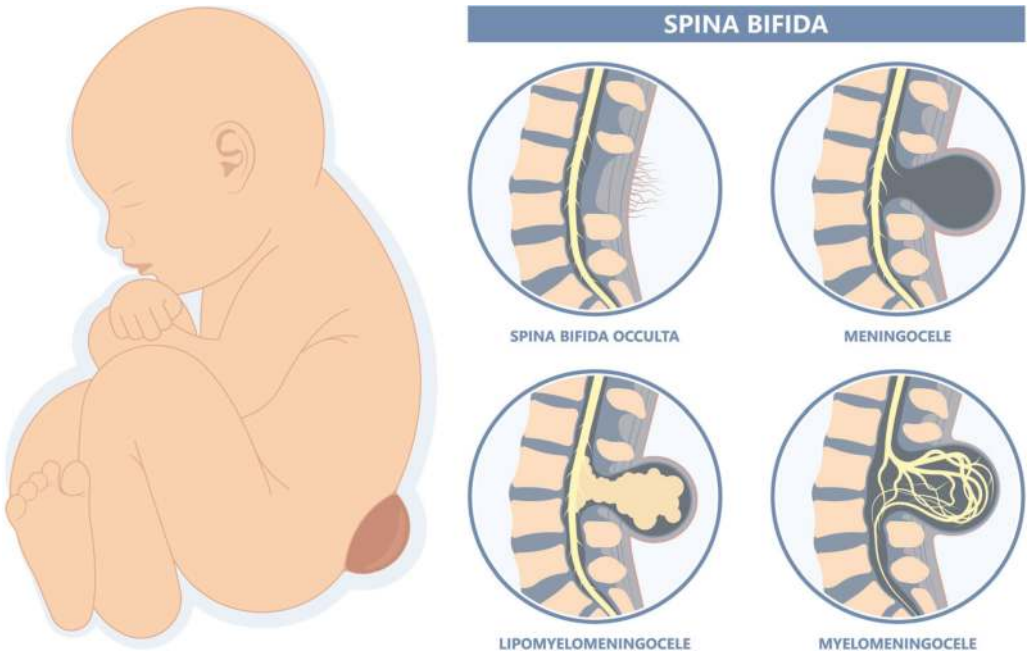

Figure 2.
Comparison of spina bifida subtypes. Rumruay/shutterstock.com

high retrocerebellar fluid, such as in Dandy-Walker malformation, mega cisterna magna, and Blake's pouch cyst. Or the malformations cause an unusually small posterior fossa such as in Dandy-Walker variant [51, 52]. The most common reported malformation is generally Dandy-Walker malformation, presenting with macrocephaly in 90–100% of children within months of delivery [49]. Comparison of fetal MRI and fetal ultrasound images in the diagnosis of Dandy-Walker malformation is shown in **Figure 3**. Prognosis of these conditions is highly influenced by concomitant anomalies, with co-occurring conditions like agenesis and cerebral hypoplasia often resulting in cognitive impairment. Other conditions like mega cisterna magna without hydrocephalus typically result in normal development [50]. In a USA retrospective cohort for ultrasonography referrals for fetal MRI involving posterior fossa anomalies (n = 180), the most common indications for fetal MRI were Dandy-Walker continuum (Dandy-Walker malformation in addition to Dandy-Walker variant) at 42%, mega cisterna magna at 22%, with a change in diagnosis in 70% of cases, and 60% agreement between fetal MRI and postnatal MRI [54].

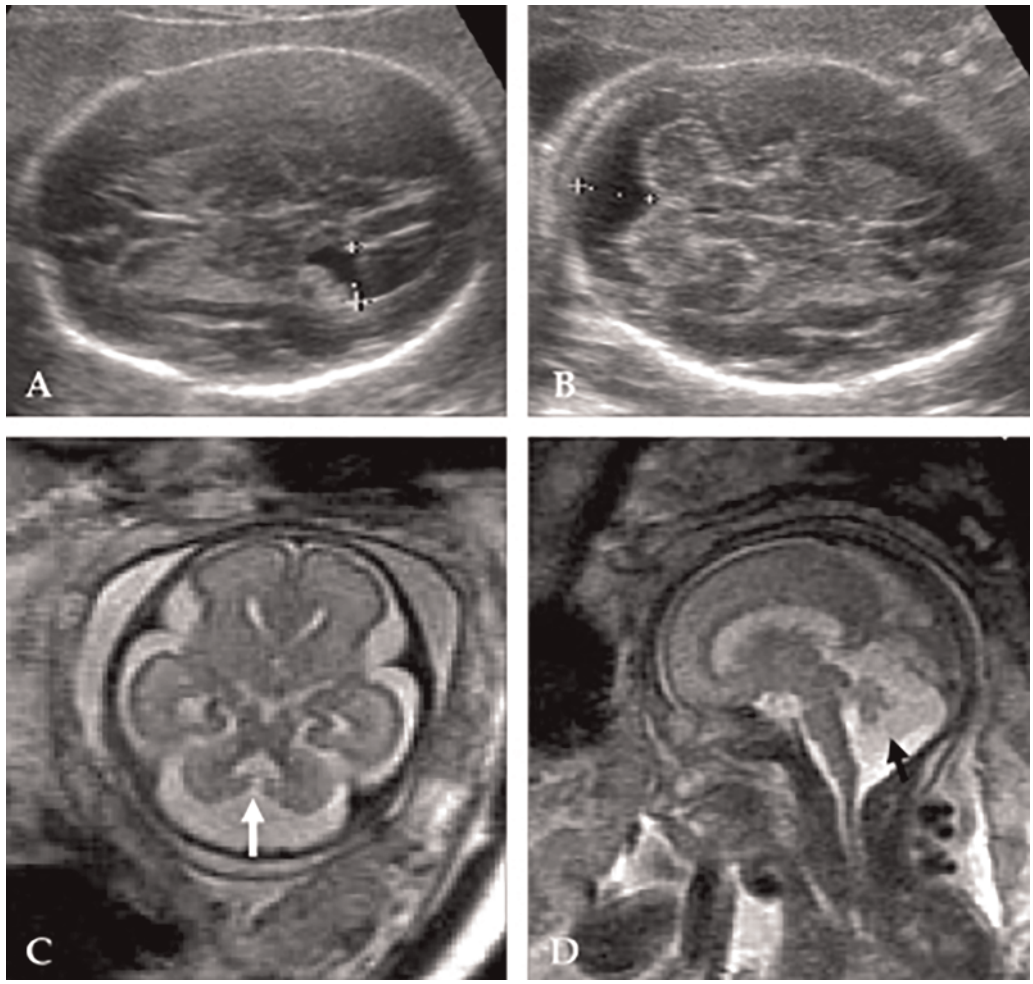

Figure 3.
Dandy-Walker malformation in a 26 week fetus, first suspected as Dandy-Walker variant with ultrasonography, and confirmed as Dandy-Walker malformation with T2W HASTE MRI. A) Ultrasonography illustrating mild ventriculomegaly B) ultrasonography image illustrating cisterna magna that is abnormally large. C) MRI image illustrating direct connection between the cisterna magna and 4th ventricle. D) Sagittal MRI of abnormally large posterior fossa. Reprint Sohn et al., 2008 under CC BY-NC 3.0 [53].

The corpus callosum is a white matter commissural nerve tract, connecting cortical regions of left and right hemispheres, and composed of myelinated axons that allow action potential propagation [55]. The corpus callosum forms between gestational weeks 11–22, is composed of five distinct regions, and hyperplasia or hypoplasia of these regions is termed callosal dysgenesis, while total absence is deemed callosal agenesis [56]. Agenesis of the corpus callosum rarely occurs in complete isolation, and generally occurs in combination with other disorders. MRI can provide more detail for the extent of the condition than ultrasonography alone [55]. This allows confirmation that the corpus callosum is intact and visualization of co-occurring and associated malformations [9]. Diffusion tensor imaging and fiber tractography in developing research applications has greatly improved the understanding of the neuronal tracts of the corpus callosum, and complications associated with different degrees of agenesis [55]. Tractography has allowed characterization of normal developmental patterns for the nerve bundles of the corpus callosum with increasing gestational age, showing an increase in volume and fractional anisotropy, with a decrease in apparent diffusion coefficient [57].

In twin-to-twin transfusion syndrome, unequal blood supply to the fetuses leads to demise of one twin. Untreated cases have dismal survival rates [58]. The condition indicates diagnostic fetal MRI due to improved capabilities over ultrasonography for identifying ischemic lesions and neurodevelopmental abnormalities. The condition often warrants intervention including serial amniocentesis or *in utero* fetoscopic laser ablation of the blood supply of the surviving twin [18]. This condition is hypothesized to be the cause of death for two fetuses found in the tomb of King Tutankhamen, whom are believed to be his two stillborn twin daughters [59, 60].

4. Common cardiac indications for Fetal MRI

Ultrasonography is the primary imaging modality for monitoring and diagnosis in both congenital and acquired pediatric heart disease and antenatal complications [61]. Ultrasonography and MRI have been determined safe for fetal imaging, but suggested to be used prudently, with common concerns and power limits due to potential tissue heating and acoustic damage [62]. Fetal cardiac MRI can improve outcomes by allowing earlier preparation of treatment procedures [63]. The American Heart Association (AHA) and British Association of Perinatal Medicine (BAPM) suggest neonatal MRI for newborn patients with high-risk CHD in combination of evidence for intracranial hemorrhaging or parenchymal brain trauma, though not recommended for routine use for CHD [9].

CHD is the most common form of congenital abnormalities, occurring in about 0.6–0.8% of live births, with as much as half of the patients requiring open-heart surgery, and is associated with high rates of neurodevelopmental problems [9]. CHD is associated with high neonatal morbidity, particularly in preterm infants [64]. Some of the most common congenital heart abnormalities include atrial septal defects, ventricular septal defects, Tetralogy of Fallot, patent ductus arteriosus, and pulmonary stenosis [65, 66]. A depiction of several types of congenital heart defects is shown in **Figure 4**. Ventricular septal defects are the most common congenital cardiac anomaly, often requiring surgical repair, though a high percentage will also spontaneously close with age [66–68].

Prenatal cardiac MRI for CHD has generally been limited to a research setting [69]. This has been due to factors including inability to perform electrocardiogram gating,

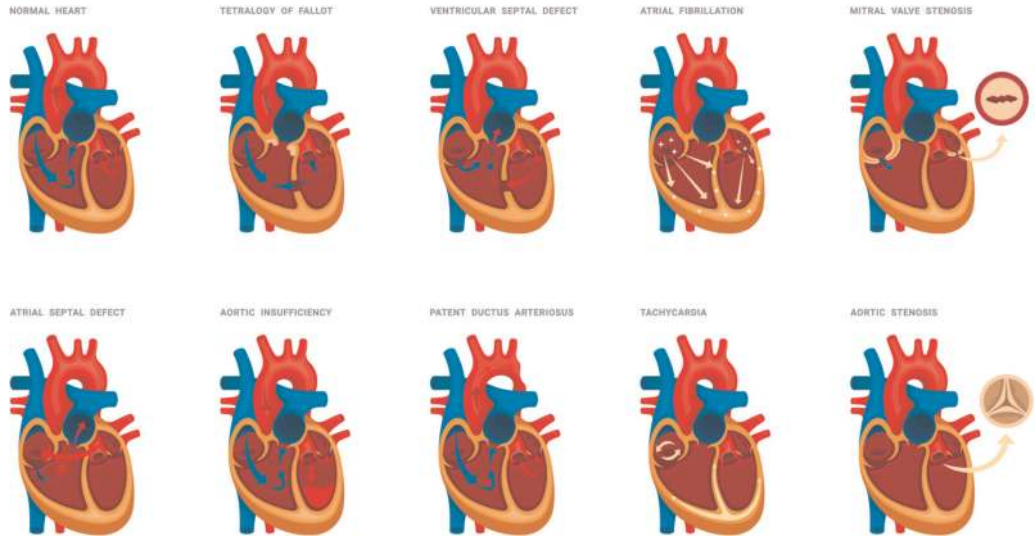

Figure 4.
Illustration of common congenital heart defects. N.Style/shutterstock.com

fetal motion, insufficient safety data, and the relatively small size of the features of the fetal heart [70, 71]. Prenatal cardiac MRI allows evaluation of cardiac anatomy, cardiac function, vascular anatomy, flow quantification, and oxygen content [69].

Recent advances has allowed image reconstruction techniques to obtain high-resolution 3D MRI of the fetal heart to assess for congenital heart defects. 3D MRI with motion-corrected image registration was shown in a cohort study to significantly increase visualization and diagnosis of major fetal vascular heart defects in late-gestational age fetuses, when compared to 2D MRI [72]. Additionally, Doppler ultrasonography has shown capable of performing cardiac gating of the fetal heart to generate high-quality bSSFP cine images [73].

A cohort study reported the use of a non-contrast velocity-selective arterial spin labelling (VSASL) sequence to assess placental perfusion in fetuses with CHD compared to fetuses without CHD [74]. The study found decreased global perfusion and increased variation of regional perfusion were linked to increasing gestational age in CHD fetuses. The results also suggest that early placental perfusion may increase to compensate for the heart defect.

A Chinese retrospective study reported findings in 1379 confirmed cases for fetal cardiac MRI from 2005 to 2019, referred after echocardiography could not show the four cardiac chambers in addition to ventricular outflow [75]. Imaging sequences were SSFP, real-time cine SSFP, non-gated phase contrast sequences, and SSTSE. The findings were normal in 92.5% of cases, 5.1% presented with CHD, and 2.4% were diagnosed with an alternative heart condition. In the CHD cases, 56% received correct diagnosis with MRI, which was similar to other studies, as prenatal detection rates for CHD for patients that eventually underwent congenital heart surgery, have tended to be low and less than 50% [76].

5. MRI in Fetal surgery

Most conditions are best treated when the fetus is delivered at term; however, certain instances warrant the use of *in utero* fetal surgery [77]. Traditionally, this has

been limited to cases of high likelihood of mortality for the fetus without intervention, as the technique is high-risk of morbidity and mortality to the mother. More recently, fetal surgery has allowed interventions for improved life quality [78]. MRI has proved beneficial for fetal surgery planning when indicated for conditions, including fetal tracheolaryngeal airway obstruction, congenital diaphragmatic hernia, congenital pulmonary airway malformation, myelomeningocele spina bifida, congenital heart defects, and lower urinary tract obstruction [77, 78]. Additionally, fetal MRI has shown useful to assess effects of fetal myelomeningocele repair, by comparison of before and after MRI images to uncomplicated fetuses of the same gestational age [79]. Also, MRI has shown beneficial in patient selection for fetal intervention prior to EXIT delivery in congenital high airway obstructive syndrome [80].

6. Fetal MRI for pregnancy complications

Again, ultrasonography is recommended as the first imaging modality, but MRI is often indicated in a variety of maternal obstetric and non-obstetric complications during pregnancy, including placental adhesive disorders, placental abruption, prognosis of uterine rupture, restricted circulation in placental bed disorders, placental insufficiency, acute appendicitis during pregnancy, prediction of preterm labor, ovarian cysts, and urolithiasis [18, 81]. Additionally, MRI is indicated in treatment planning for difficult deliveries, such as those that require the EXIT procedure due to fetal airway obstruction [9]. Moreover, the technique has proved useful in risk scoring for massive intraoperative hemorrhage in patients with previous cesarean sections and exhibiting placenta previa and accreta [82]. Fetal MRI was recently used in a randomized control trial to assess fetal neurodevelopmental improvement for supplemental pomegranate juice in pregnancies with intrauterine growth restriction [83].

7. Fetal MRI for viral infections

Prenatal MRI is useful for diagnosis of complications associated with maternal viral infections, including the more recent complications associated with SARS-CoV-2 infection.

7.1 Prenatal MRI for complications from viral infections other than SARS-CoV-2

A variety of fetal complications arising from viral infection can be imaged with MRI, particularly for identifying neurological sequelae, but also for conditions including fetal ascites, hydrops, cardiomegaly, and pericardial effusion [84]. Fetal MRI can be indicated for diagnosis of suspected neurotropic pathogens, such as cytomegalovirus, Zika virus, and toxoplasmosis [85–88]. Cytomegalovirus is a member of the Herpesviridae family, the most common vertically transmitted congenital viral infection, and the most common infection that results in deafness and intellectual disability in children [89, 90]. MRI and ultrasonography can identify fetal brain lesions resulting from cytomegalovirus infection. MRI diagnosis of infection-related complications allows the possibility of treatment planning for investigational therapies, including antiviral therapy such as Valaciclovir or hyperimmunoglobulin therapy, in the neonates and in fetuses [18, 91, 92].

7.2 Prenatal MRI for complications involving the SARS-CoV-2 virus

SARS-CoV-2 is a positive sense, lipid-enveloped, single-stranded, RNA coronavirus that causes both upper and lower respiratory tract infection, which can result in severe pulmonary inflammation and pneumonia, in a condition denoted human coronavirus disease or more recently COVID-19 [93–95].

SARS-CoV-2 relies upon two types of entry pathways to enter cells through the interaction of the virion spike (S) protein with angiotensin-converting enzyme 2 (ACE2), with release of internal RNA within the cell occurring after cleavage of the S-protein subunits [95]. After binding to ACE2, if transmembrane protease serine 2 (TMPRSS2) is present on the cell surface, the cleavage event occurs through TMPRSS2 and furin, initiating membrane fusion and fusion pore formation on the cell membrane, and release of viral RNA into the cellular cytoplasm [95]. Alternatively, if little or no TMPRSS2 is present on the surface, the clathrin-mediated endocytosis occurs and the virus is internalized intracellularly within endolysosomes, followed by a cathepsin-cleavage event within the endosome, resulting in membrane fusion and release of the viral RNA into the cell cytoplasm [95].

The BNT162b2 (Pfizer, BioNTech) and Spikevax (Moderna, NIAID) are both mRNA-based vaccines that encompass an mRNA strand encoding the spike protein for the original Wuhan-Hu-1 strain, in a liposomal mRNA-lipid nanoparticle, which has a notable ability for large-scale production [95, 96]. The vaccine causes cells to encode the vaccine mRNA to produce spike proteins that are then expressed into the cell membrane. This causes an antibody response that identify these spike protein antigens as a foreign body, stimulating a B-cell and T-cell lymphocyte response to produce antibodies that will tag future spike proteins from SARS-CoV-2 viremia [97]. The viral mutations of these spike protein antigens result in reduced efficacy of the vaccines to induce a immunogenic response. Because mRNA vaccines require antibody neutralization of viremia, mutations in the spike proteins can allow variants to exhibit resistance to the vaccines, potentially causing more severe infections, higher transmissibility, and the possibility of re-infection in vaccinated individuals [98, 99].

A prospective U.K. cohort found 0.5% incidence of SARS-CoV-2 infection during pregnancy that required hospital admission (n = 427) [100]. Of the patients that delivered or experienced pregnancy loss at the time of the article (n = 262), 10% required intensive care unit (ICU) admission and death occurred in 1.2%. From the SARS-CoV-2 positive pregnancies with live born births, 59% had cesarean deliveries and 25% of neonates were admitted to the neonatal intensive care unit (NICU). Preterm delivery occurred in 25% of cases, most of which were induced labor due to COVID-19 complications, and 5% of neonates were COVID-19 positive within 12 hours of birth.

Pregnant women are at high risk of developing severe COVID-19 compared to non-pregnant women, in terms of adjusted risk. Comparing COVID-19 positive pregnancies with non-COVID-19 pregnancies, studies have observed a factor of 3 increase in ICU admissions and invasive intubation with mechanical ventilation, a factor of 2.4 increase in odds for extracorporeal membrane oxygenation, and 70% increase in death [101]. Severe COVID-19 complications are linked with increased rates of preterm birth, hypertensive disorders, and cesarean births [101]. Studies have linked COVID-19 with significant increased mortality for mothers post-delivery and in neonates; particularly for symptomatic patients and those with underlying comorbidities [102, 103]. Neonatal outcomes have been reported as generally favorable, with about half of cases being asymptomatic; though, neonates and children less than one year of age are thought to possibly exhibit higher risk of acute respiratory failure than other children [104].

Risk of vertical transmission of SARS-CoV-2 from mother to fetus is considered low, with the primary transmission to the neonate being through horizontal transmission [101, 105]. Although, at least one case study has confirmed vertical transplacental transmission [106]. There is little evidence for transmission of SARS-CoV-2 through breast milk to the neonate, but pasteurization has been shown to inactivate the SARS-CoV-2 virus and might be considered in specific cases for positive SARS-CoV-2 mothers [101, 105, 107]. Transmission between members of the same family cluster is the primary means of infection from SARS-CoV-2 in children [108]. Infection in children and adolescents has tended to result in milder symptoms and good prognosis, in general [109].

The American College of Radiology (ACR) has suggested limiting the use of MRI to only cases that are absolutely necessary, for COVID-19 positive patients and those suspected of infection [110]. The use of fetal MRI for COVID-19 positive mothers does not have a common indication for routine use and has mostly been reported as case studies or small cohorts. Fetal MRI has been used in cohorts to assess possible neurodevelopmental damage in the fetuses of mothers with SARS-CoV-2 infection during early pregnancy, with results showing no abnormal findings [111]. However, a case study of *in utero* transplacental transmission did reveal white matter damage in a neonate, causing placental inflammation in the mother, and ill-effects in the neonate, including bilateral gliosis and white cortical matter damage on MRI from which the infant slowly recovered [106]. A cohort of 34 pregnant patients assessed lung volume with fetal MRI for complications associated with infection in mildly symptomatic SARS-CoV-2 positive mothers. The study found that the fetal lung volume to body weight ratio was noticeably reduced, particularly when the infection occurred during the third trimester; though neonates did not exhibit respiratory distress [112]. Many cases studies are reported for MRI diagnosis of non-obstetric complications of pregnant COVID-19 patients for a variety of common complications, such as stroke [113] and appendicitis [114].

A significant increase in obstetrical complications in COVID-19 has been observed, compared to non-COVID-19 pregnancies. Studies have shown higher rates of fetal deaths, maternal deaths, ICU admissions, preterm births, and cesarean deliveries. These outcomes highlight the benefit of vaccination during pregnancy, to reduce the risk of maternal and fetal complications [101].

8. Conclusions

Prenatal MRI offers useful complementary diagnostic information to ultrasonography, particularly for neurodevelopmental complications. The technique can be used for diagnosis, for guiding treatment decisions, and to counsel parents for scenarios like potential termination. MRI has been determined safe for fetal health, though low field strengths and non-contrast imaging are generally used, as these scenarios are lower risk to the fetus. MRI can improve diagnostic accuracy for neurodevelopmental and cardiac anomalies when used in conjunction with ultrasonography, but factors like additional cost limits the number of indications for prenatal diagnosis. Studies have shown increased rates of pregnancy-related complications in patients infected with SARS-CoV-2 during pregnancy. Although, studies with fetal MRI for assessing fetal developmental complications due to maternal COVID-19 has been limited, but results have been reported in case studies and small cohorts.

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