0:00

the session as well as the speakers sure

0:05

welcome everyone to the family planning and achieving reproductive success

0:10

session um before we get started i want to let you know that if you do

0:18

have any questions during the session to please enter them in the chat button bottom

0:23

of the screen I’m sure you've been doing this for other sessions so the same things apply here we are also asking you

0:30

to please keep your microphone muted so that we might have better

0:36

audio and video quality for the presenters and for everyone else that's attending

0:42

I’m pleased to introduce our speakers for this session first we have dr. juliana sanchez-gebb

0:49

she's an attending physician at the center for fetal diagnosis and treatment of children's hospital philadelphia and

0:57

an assistant professor of obstetrics and gynecology and surgery at the university of pennsylvania

1:04

pearlman school of medicine with her we have eric schindeloff abroad certified

1:12

genetic counselor at the center for fetal diagnosis and treatment at children's hospital in Philadelphia

1:19

erica dr. gebb it's my pleasure to turn the presentation over to you thank you so much we really

1:27

appreciate the opportunity to present to you here today um so we'll be talking about family

1:32

planning and achieving reproductive success with kidney disease

1:41

um so this is just the routine disclaimer uh and the disclosure we have no

1:46

conflicts of interest to disclose and these are just our bios that you nicely went through thank you so much

1:56

and so today in the talk we're going to speak about imaging findings in fetuses with cystic kidneys

2:02

i will talk about autosomal dominant polycystic kidney disease and autosomal recessive polycystic

2:08

kidney disease and we'll discuss a few cases we'll talk about the genetics of the two conditions

2:14

how they're similar and different and the maternal and fetal implications of pregnancies that are complicated by

2:20

these conditions and then we'll talk about the use of assisted reproductive technologies

2:25

in families with a history of ADPKD or ARPKD

2:33

so first to just go through some imaging findings that we see in fetuses with cystic kidneys

2:39

so you can see on the left hand side of your screen you see the normal renal system and we have the kidneys

2:45

here these are the ureters the tubes that drain the urine from the kidneys to the bladder

2:51

and then you pee out of your bladder here and these are the blood vessels that take the blood flow to the kidney

2:58

and then away from the kidney and so the blood goes into the kidney and as many people know it

3:03

if the kidney filtrates um the blood and holds onto things that you need to hold

3:08

on to and then gets rid of things that you don't need and puts them into the urine and for multiple different reasons

3:14

we can have cystic kidneys that occur during pregnancy um in the fetus and then also

3:20

it can be a maternal condition that is complicating the pregnancy and with cystic kidneys there can be

3:26

multiple different reasons why there are cystic kidneys that have formed sometimes it affects just

3:32

one side and it's because of a blockage or some sort of malformation of the one

3:37

kidney and which then usually develops into very large cysts or in other cases it can be a genetic

3:44

condition that can affect both kidneys symmetrically and can cause the kidneys to be enlarged or

3:50

were also replaced by cysts so when we see on what we see on

3:56

ultrasound we see on the left hand side here we have a picture of what the normal kidneys look like and you can see

4:03

this is from the side of the baby this would be the baby's head up here and then the bottom here and so you can

4:09

see the kidney here and the normal fetus and then this is a transverse view as if

4:14

we sort of cut the baby in half and took the top half off and looked from up above we would see

4:19

the kidneys here and they are you know sort of hard to pick up sometimes

4:26

they're not very bright usually um they're usually not filled with cysts not filled with

4:31

urine that has backed up into them so so they're sort of subtle and so things that we might see that are

4:38

different is we might see that the kidneys are bright like we see here these kidneys are just

4:43

echogenic we don't see any cystic changes of them but you can see they just look much more prominent than on this side here

4:51

other things we can see is that sometimes we see many cysts in the kidneys so just like that picture that i

4:57

showed you before we can see that there are multiple cysts that have replaced the kidney tissue here

5:02

on the left hand side whereas on the right hand side we still see the appearance of a normal looking kidney and this goes along

5:09

usually with with a multi-cystic dysplastic kidney

5:14

another thing we might see is that we might see that the kidneys are not only brighter than we would expect them to be

5:20

but that they're enlarged compared to the size that they would usually be and you can see here that this kidney is

5:26

is about this size and and then this kidney is much larger on this side and you can also see that within the

5:32

kidney tissue here we do see some cystic changes so this goes along with cystic kidneys

5:38

in the fetus and here's that transverse view again where we can see that the kidneys are taking up much more space in the

5:44

abdomen compared to what they take up in this

5:50

side other things we look for in order to

5:55

determine what kind of kidney disease the fetus has during the pregnancy or how severe it is

6:02

we look at the amniotic fluid we know that if there is normal amniotic fluid as you see here which is is the

6:08

black area here we know that the fetus is making a good amount of urine versus if the amniotic fluid decreases

6:15

like you see here where there's a much smaller pocket then we know that that that baby may not

6:20

be making as much urine um but sometimes it's hard to tell because sometimes people have leakage or

6:26

they're complaining of losing fluid and so then in those cases you have to make sure that they didn't

6:31

break their water and then the other thing you can look at is their bladder

6:39

um so here we see um that the bladder is on the left hand side

6:45

is um is filling and emptying you see that black part in between the two colored parts

6:50

is um is the bladder filling and emptying versus on the right hand side of the screen you

6:56

see that the bladder is empty there's no black fluid inside the bladder and these

7:02

are the blood vessels that normally go around the bladder and so this is a baby that is not making

7:07

urine anymore if you just see one moment in time where there's no black fluid

7:12

there you need to wait because the the baby could have just peed and then we're

7:17

not seeing the urine there because the baby just emptied the bladder but if you look over 30 minutes or over an hour and still the

7:24

bladder has not filled and the fluid around the pregnancy is low then you are suspicious that the

7:30

baby's not making urine which is often due to the kidney disease the other reason the bladder may not

7:36

feel as if there's a blockage up top so if one of those ureters were blocked then it can cause the kidneys to fill

7:42

with urine and and it can't get through are you using a

7:48

pointer I’m using like just the um the mouse but so you don't see it on

7:53

there don't no um I’m trying to figure out how i could use let's see

7:59

do you know how to have a real pointer i don't i mean i think these are the imaging I’m sorry um I’m done with the

8:06

imaging pictures so i think maybe i can look for a pointer if people have questions afterwards i can go back and

8:12

and find a pointer and and go and point things out okay great

8:18

um so this is the first case i was going to discuss um so this this pregnancy and the

8:25

patient came to us she was 28 years old she was already 34 weeks in pregnancy

8:30

and she had been told by her local provider that the fetus had cysts small cysts in the

8:36

kidneys and that they were concerned that after birth the baby would have respiratory failure

8:41

would not be able to breathe because of having the cystic kidneys because we know that

8:47

if there are cystic kidneys and there's no fluid around the pregnancy that does put the pregnancy at risk for

8:54

having respiratory failure in the fetus after birth but in this case the fluid was normal so we told her please come up and

9:01

and we'll evaluate you and see um what we think she had a past medical history of having a stroke at

9:08

age 17 it was thought to be related to smoking and using oral contraceptives and she was adopted

9:15

so her family history was really unknown so these are the imaging findings

9:22

so you can see on the left hand side you see that black fluid there between the the gray the light gray

9:28

parts that was the amniotic fluid so that looks normal and then you can see on the right hand side of the slide

9:35

you see the kidneys there look a bit brighter than we would expect them to be not super impressive but but

9:42

definitely a bit brighter and so then if we look a little bit closer we can see that on the left hand

9:48

side there are some cystic changes there's this bright area and kind of the the lower part let me try to get a

9:54

pointer let's see if i can um

10:02

i could probably google it does anyone know um who's who is moderating do you know how to get a pointer on

10:12

no but if you verbally explain that might be helpful okay fine so on the left hand side of the screen

10:17

we see the kidney from a side view and we can just see little black areas within the kidney

10:23

that are that are the cystic changes that was on the left kidney and then on the right kidney

10:28

you can see similarly but it's it's on the more right-hand side of that picture you can see the cystic changes whereas

10:35

on the left side of the picture it's more on the left-hand side of the picture that you see the cystic changes in the

10:40

areas where it's a bit brighter around them so that made us concerned that there was cystic kidney disease

10:46

in in this fetus but we did think that the amniotic fluid was normal so we felt optimistic about the the respiratory

10:52

outcomes and then actually we scanned her kidneys and and so this was the mom's kidneys

10:58

and you can see all of the black areas are our areas filled with fluid

11:03

and so we saw that that on the mom's kidneys she had multiple cysts on both of her kidneys

11:12

as we follow the pregnancy we found that the amniotic fluid remained normal um the mom ended up we so we

11:19

suspected autosomal dominant polycystic kidney disease for her so we did a work up to see how her

11:25

kidney function was and she had normal blood pressures normal kidney function we were also concerned about that

11:32

history of strokes because we know the association of aneurysms with autosomal dominant polycystic

11:37

kidney disease and so we we did a brain mri and that was fine and she ended up having an uncomplicated

11:45

remainder of the pregnancy and delivered at 38 weeks

11:50

the baby weighed seven pounds eight ounces at birth and had an uncomplicated postnatal course and just stayed in the

11:56

hospital for a couple of days with the mom and there were no respiratory issues or kidney issues

12:01

after birth and the infant has normal kidney function at three months of age

12:08

so the genetic counseling was very important to to talk to her about what was going on within her family and

12:14

also the implications for future pregnancies so erica you can take this part thank

12:21

you so in this case we have a lot of interesting factors one we don't know

12:26

the family history and we'll see when we talk a little bit further in some of our other cases about

12:31

autosomal dominant polycystic kidney disease even if we were to know her family history

12:37

there is a percentage of the time about 20 to 28 of the time where we don't have a family

12:42

history of polycystic kidney disease um and so that information is always helpful to look for clues but sometimes

12:48

even when we don't have it could be you know not being a red herring and not really telling us what we need

12:55

this patient also was a good patient from a genetic counseling perspective because we're always

13:00

thinking about when is the appropriate time to do testing and this patient presented a little bit

13:06

later in her pregnancy um and it because of insurance reasons because of thinking about invasive

13:13

testing was choosing to do testing um post-natally and so i was kind of working through that process for herself

13:19

and for the baby of course we know with autosomal dominant polycystic kidney

13:24

disease just like in the name there's a 50 recurrence risk if an individual is

13:29

affected by polycystic kidney disease meaning that in each pregnancy that she would have if this is her diagnosis

13:36

there would be a 50 chance that her child would also have the condition

13:41

we're going to talk a little bit more about that but because we don't know her mutation right now we'll kind of broadly talk

13:47

about the genes that are associated and i know there's other breakout sessions that will go over this as well

13:53

the two main genes that we think about with polycystic kidney disease in this form are pkd1 and pkd2 there are a few

14:02

other genes listed here g-a-n-a-b and d-a-n sorry d n a j b-11 which are

14:09

also associated with adpkd um to get testing for these genes we can

14:15

do this in a number of different ways and so prenatally that looks like doing invasive testing like chorionic villus

14:22

sampling or amniocentesis where we can get access to the baby's dna either through

14:28

placental biopsy with the cvs at 10 to 13 weeks or amniocentesis which is done

14:34

after 15 weeks where we get amniotic fluid which gives us access to babies dna

14:41

postnatally that can look like a blood test for either mom in this case or baby to assess the

14:46

molecular change it kind of just depends on when people feel most comfortable getting that test

14:52

and what are the other factors at play such as do we have enough amniotic fluid

14:57

to do that type of testing we often talk about multi-gene panels and because there are more genes than just pkd1 and

15:04

pkd2 we often do send a broad panel which includes all of these genes

15:11

in order to make sure we're really catching and being comprehensive in the way that we're thinking about disease

15:16

and molecular etiology of disease because if we just ordered pkd1 and pkg2

15:22

we would catch the majority of individuals about 80 percent of affected individuals have mutations in these

15:27

genes 80 to 95 but there is a handful of patients that have mutations in those other genes so it's

15:34

important to be comprehensive there are genotype phenotype correlations so that means that

15:40

the molecular etiology or the actual mutation can help guide guidance about the

15:45

disease we know that pkd1 changes are more associated with earlier disease

15:53

presentation that doesn't always mean in utero presentation it can mean things like presenting at age 50 instead

16:00

of presenting at age 70 but we do know that there's good literature to support that those

16:06

mutations in those genes present earlier in our lives and also something called truncating variants or truncating mutations are

16:13

more common to be associated with earlier disease onset in both pkd1 and pkd2

16:20

what that means truncating mutation means that you're kind of stopping the gene from having any

16:26

protein production it's like a huge stop sign where the body is supposed to read that gene

16:31

and so if you're stopping that and the protein cannot be made which is kind of what this schematic is trying to show

16:37

that if you're stopping all the way at the bottom where you see the words pkd1 and pkd2

16:42

nothing can get out of the cell and none of that protein that our body needs to make the kidneys function the way that

16:48

they're supposed to can happen and so those are more associated with earlier onset renal

16:54

disease as well as more significant findings in imaging

17:00

there are other genetic considerations we always think about as well sometimes you have deletions of

17:07

multiple genes in the area that sits right next to pkd1 and the most common that we think about

17:14

is the peak 81 and tubular sclerosis gene sit very close together so we can see

17:20

prenatally babies present with renal disease as well as heart findings or skin findings or brain

17:27

differences and that actually gives us a dual diagnosis of tuberous sclerosis and

17:32

polycystic kidney disease so we always have to kind of be thinking more broadly and there's another kind of concept

17:39

called somatic mosaicism where the mutation lives actually not in the germain or the ability to

17:47

pass on those genes but lives in certain cells in the individual's body

17:52

and so that can be another route we go if we are investigating disease etiology and we

17:57

can't find it in the more typical ways that we know you can advance this slide

18:03

great thank you okay that was awesome um now i will talk about the second case

18:11

so in for the second case we had a 28 year old woman she was 19 weeks and three days when she was referred to us

18:17

and she was referred for concern of the kidneys being bright and enlarged she had a past medical history that

18:24

appeared to be consistent with adpkd she had cystic changes noted in herself

18:29

at age 22 when she had an a renal ultrasound for a kidney infection

18:34

she had no history of high blood pressure however she had a sister that had a clinical diagnosis

18:40

of adpkd after having a kidney ultrasound at age 30 that was performed due to the family

18:45

history and it did show multiple cysts on both kidneys the and she also had a mother with

18:51

kidney failure that necessitated transplant in her 50s and there was no familial mutation known

18:58

at the time and there was no family history of aneurysms

19:03

so when we saw her we saw that the the picture on the left hand side of the slide you can see

19:09

where the areas are measured those those two the little x's that you see

19:14

those are the kidneys in the transverse view so they were a bit bright and also a bit enlarged for this

19:20

stage in pregnancy on the right hand side you see again that the kidneys appear to be

19:26

bright and enlarged and then the the black area and in the center is the area where

19:32

some urine has backed up into the kidneys that can really be a normal variant but

19:38

we did we were concerned about the family history as well as the brightness of the kidneys

19:45

during follow-up we saw her and the the kidneys became markedly enlarged so again you can see those x's on the left hand side of the

19:52

screen where the the kidneys are being measured and they they became very big where they

19:57

were taking up a lot of the abdomen and then on the right hand side of the slide you see those

20:03

those little x's that's measuring the amniotic fluid so the amniotic fluid actually stayed normal during the

20:08

pregnancy which was very reassuring for the pulmonary outcomes or the breathing outcomes

20:16

during the course of the pregnancy the the baby did become growth restricted which we know can happen sometimes in

20:22

in when the mom has autosomal dominant polycystic kidney disease and the amniotic fluid stayed normal the

20:29

mom did develop high blood pressure and the condition called preeclampsia which occurs in pregnancy when you have

20:36

high blood pressure and protein in the urine and she was delivered at 35 weeks for

20:41

the preeclampsia um the baby at birth was three pounds 12

20:48

ounces needed a tiny bit of respiratory support but that was really more because of the early delivery versus

20:55

the kidney disease and the baby did end up staying in the neonatal intensive care unit for one month and

21:02

developed high blood pressure at about six months of age and was started on medications and then the the kidney function is

21:08

still normal at three years of age so this compared to the last case we see an earlier onset

21:14

of high blood pressure in an earlier time period of needing medication for treatment related to the kidney disease

21:23

so for her genetic counseling so for her genetic counseling we are

21:29

able to know her mutations and i think that the description that dr jeb just gave is really wonderful because we're

21:35

going to be able to tie in the genetics to how that actually impacted um disease presentation and management

21:42

and really just understanding the why a lot of times people will ask you know what's the utility in doing genetic

21:48

testing um if we know this is going on in our family and we know this is a risk and certainly that is a personal decision

21:54

for every family but sometimes it can actually give additional clues not only for

22:00

what's the chances it's going to happen again and what might this look like but how might this play out in my own

22:05

health care and how much how might this play out in my child's health care and so

22:10

what you're looking at here is kind of the results of the baby's genetic testing and when we think about dominant

22:16

conditions we're usually thinking that one of the genes is working the way that it's supposed to

22:21

work and one of the genes has a mutation we get one copy of a gene

22:26

from our mom one copy of a gene from our dad so we always have two in dominant conditions we just need one

22:33

two of those copies to have a change to show some type of symptom but what you're looking at here is that

22:39

the baby actually had two mutations so the first mutation is this pkd1

22:44

truncating deletion you don't have to worry about letters or numbers but what we learned from the previous

22:50

slides is that truncating mutations or deletions are again those big stop signs that are

22:55

saying hey I’m not going to make this protein that I’m supposed to make and the kidneys are not going to work

23:01

the way that they're supposed to work because of that and usually like we said they presented

23:07

a bit earlier in our lifetime which fits with this patient's family history and obviously fits with the in utero

23:13

presentation but what's also interesting is when we did this testing we found another change

23:18

this is something called a missense variant which is not so important to know the verbiage but really what that

23:24

means is that one amino acid was supposed to be made and instead another amino acid was made um

23:31

what's interesting and what is so fascinating about genetics is you really have to kind of dive into the

23:37

literature look at other people who have presented with these findings to understand what they mean and what we see is that this

23:44

specific change is actually present in the general population at very low levels but we do

23:49

see it about .4 of the time in specific variations

23:55

um it is known specifically though as a modifier gene and modifier genes are becoming more and

24:01

more talked about in the world of genetics but this modifier gene when it is

24:06

present on the opposite uh gene so like we said we have two copies for this baby one copy had the truncating

24:13

deletion and the other copy had this missense variant the copy from mom who also had the

24:19

polycystic kidney disease had the truncating deletion which explained her symptoms and the family history

24:25

and interestingly the copy from dad had this missense variant

24:31

what was so interesting about that is dad did not have a history of kidney disease and nor did we think he would

24:37

but when we see this missense variant and we see a known truncating deletion

24:43

together where we are able to see that things like high blood pressure and things like

24:48

the cyst usually happen much earlier in a person's life because this modifier gene

24:54

um causes that effect to happen and so it can be really important to kind of understand that information

25:00

when you're understanding how to how to manage this baby and you know what challenges and what

25:06

strengths may be ahead for the baby

25:14

and then just to speak since i think this is our last case about autosomal dominant polycystic kidney disease

25:20

um you know there's a couple of factors that we are we always think about um

25:26

one being that disease can present in utero um though we know it's not very likely

25:32

and i see questions coming up in the chat and i know we'll talk about it a little bit after we're done with the slides

25:38

um but we know that that's not always the case right that's not often what we're counseling about we're thinking about adults

25:43

presenting with this condition but it certainly can happen if that happens it could be because of things like modifier genes playing into

25:51

a family history it could be things like a contiguous gene deletion where somebody has tubular sclerosis

25:58

which is way more likely to present in the in utero time period um so there could be a few different things going on and it's

26:04

really important to explore that to really understand the risks to the baby and to understand you know the whole

26:10

picture the comprehensive picture of what's going on the other piece to speak to family histories is that disease variability

26:17

can exist and can be very different for people who even have the exact same mutation

26:23

and so like for this family where we're seeing mom who's really only presenting with cysts later in life

26:28

um and her sister who's presenting with cis maybe in her 30s now we're seeing a baby presents they

26:34

all have the same mutations but what else is going on that's making them unique in this case it was the modifier gene

26:39

that's also helping that um but we certainly see even in sibling pairs or identical twins that have the

26:46

exact same mutation different um disease phenotypes that play into

26:51

uh into practice and that's just because in genetics there's so many other factors

26:56

aside from the mutation that make things present themselves or make things not present themselves so that

27:02

variability definitely exists as we touched upon before about 28 of patients have no

27:07

known family history and sometimes when we're doing the family histories um which can seem very cumbersome to ask

27:13

and answer all those questions sometimes we find little little clues that maybe somebody just hasn't been evaluated by a nephrologist

27:21

or when we look back we think okay maybe if we did some imaging we would kind of see this somewhere

27:26

but a lot of times you know in those families we're not seeing a family history and so we can't always rely on

27:32

that information and then just like all of this is kind of individualized

27:37

atypical kidney imaging can also present in upwards of 20 of patients so in genetics that just

27:43

really tells us that we have to look broadly even if we do feel confident about the diagnosis

27:48

just to make sure that we're being comprehensive we're not missing anything and that we're really guiding families in the right way

27:54

and not just oh this is how this image looks and this is how we're going to you know follow you we want to really

27:59

look at everything and make sure that the imaging if it will make sure that it's not atypical essentially

28:05

and fitting with the disease genotype or the molecular etiology that may be guiding the

28:10

symptoms great I’m sorry the chat is like i can't

28:17

advance it because of the chat one second um

28:25

okay so in terms of overall maternal and fetal indication implications so the the main question

28:31

we we ask ourselves is um you know first step in the genetic testing after we do the amniocentesis

28:37

and we identify a mutation in the fetus then we we test the parents unless the the parents one of them has a

28:44

known history of adpkd then we test both of the parents if the mom indeed has is the one

28:50

with adpkd then we know that during the pregnancy she'll have a higher risk of high blood pressure

28:56

of developing preeclampsia and then there is controversy over whether it actually can

29:02

make your kidney function worse in pregnancy um we think that that probably not for

29:07

one or two pregnancies when they look at people who have had a lot of pregnancies so four or more

29:13

they find that there is a higher rate of deteriorate kidney deterioration but

29:19

those patients are also older so it may just be that that's the time period when they would have had kidney deterioration

29:25

anyways so it can be hard to tease that out if one of the parents does have the

29:30

mutation and is affected by adpkd then there's that 50 recurrence risk for

29:35

each pregnancy in terms of the fetal risks we know that there's a risk of intrauterine growth

29:40

restrictions so the pregnancies have to be followed closely with growth scans in addition to to looking for fluid and

29:47

that's whether or not the baby has the mutation so even if the the baby didn't have the mutation was

29:53

unaffected there can still be the intrauterine growth restriction and preterm delivery just because the mom has the condition

30:00

if the dad has the condition then these risks aren't there and then if the amniotic fluid stays

30:06

normal usually the kidney disease doesn't develop until later in life so we would anticipate a normal delivery

30:12

and a normal postnatal outcome and just follow-up care in childhood but in the more severe cases like the

30:19

one we discussed there is this risk for for low fluid and and even respiratory failure in the most severe cases

30:26

or if the if the fluid stays normal then there can be no problems with respiratory issues

30:32

after birth but there can still be this risk for early high blood pressure and kidney insufficiency

30:39

so in terms of recommendations this was a really nice article that i put in here and just going through what the

30:45

recommendations are for women with adpkd so if you're not

30:50

planning to get pregnant it's important to to have a good method of contraception and

30:55

to have that time period for genetic counseling so you can look into what mutation is in your family

31:00

and and decide whether you would want to do pre-implantation genetic diagnosis which

31:06

we'll talk about um in an upcoming slide but whether you would want to do genetic testing and

31:11

have your pregnancy conceived via in vitro fertilization to avoid the mutation

31:17

in the fetus alternatively some people who don't go through in vitro fertilization

31:22

just opt to have a chorionic villus sampling at around 11 weeks of pregnancy

31:27

and so that's another way you can find out if the fetus has the mutation earlier rather than later in the pregnancy

31:33

and then this is very individualized so if you look on the left hand side of the slide you see if you're contemplating

31:39

pregnancy it's really important to go to your doctor and to go to a maternal fetal medicine specialist so that they

31:46

can risk stratify you and so you know people will ask you know what's the rate of getting preeclampsia or

31:52

or having complications in pregnancy and it's very related to the kidney function at baseline

31:57

so if there's already high blood pressure and protein in the urine then there's a very high risk that that's going to get worse during the

32:04

pregnancy versus if that is not the if that's not present then it's a much lower risk of developing preeclampsia

32:10

during the pregnancy so it's important to have really individualized recommendations and individualized care

32:16

and you also want to make sure if there's a family history of aneurysms or even just in general to to have evaluation for

32:23

that to to make sure that that's not going on because that could be dangerous during pregnancy and we always talk about the genetic

32:29

counseling and and discuss timing so sometimes people want to

32:34

have their pregnancies when they're a bit younger before kidney disease develops or if you're close to needing dialysis

32:42

and transplant then you may opt to actually have a transplant and then defer the pregnancy until after the

32:47

transplant and we do have patients that either are on dialysis and pregnant

32:52

which the dialysis frequency usually has to be increased or who have had a transplant and had

32:58

successful pregnancies and so these are all things to think about and if you're not planning to get

33:04

pregnant just use good birth control and then if you are actually pregnant we need to change your medications a bit

33:12

so right when you're trying to get pregnant the the um we take off some the arbs and then when you're actually

33:19

pregnant or if you can tolerate it before the pregnancy then will take away any ace inhibitors

33:25

and that's because those two medications can be toxic to the fetal kidneys even if the fetus doesn't have any renal

33:31

disease and then the pregnancy is high risk and followed very closely

33:37

so now we'll move on to ar pkd so this patient is a 23 year old she

33:43

came to us at 20 weeks and three days of pregnancy her pregnancy unfortunately was complicated by a prior pregnancy with

33:50

arpkd and she had had chorionic villus sampling this pregnancy that identified the same mutation

33:56

in her prior pregnancy she had had a delivery of a five pound ten ounce female infant with enlarged echogenic kidneys

34:03

and no amniotic fluid and unfortunately that baby passed away in the first day of life from

34:09

respiratory failure her and her partner had no family history of high blood pressure kidney

34:14

disease or any aneurysms we have 10 minutes remaining in this session okay

34:21

at her initial meeting and we saw that the kidneys looked a little bit bright but not too impressive you see where

34:26

these two x's are on the left-hand side of the sling screen you see those two x's on on either side of

34:32

both kidneys there and then on the right hand side of the screen you see sort of the bright area going down the

34:37

middle of the fetus that's the spine and then on either side you can see the kidneys and they're they're a little bit

34:43

bright but but not super impressive but during follow-up at the end of

34:48

pregnancy you can see on the screen on the left hand side that the the kidneys are

34:53

markedly enlarged they're they have bright dots in them and they're also taking up almost the whole

34:58

abdomen um both of the kidneys and so they're very enlarged which is what we generally see with ar pkd

35:05

and then we also saw that on the the right hand side of the slide you see that collapsed bladder that we

35:11

talked about before where there's no black in the center between those two bright lines and so the we

35:17

looked for an hour and we didn't see any urine going into the bladder and the fluid around the pregnancy was

35:23

not there anymore and so we knew since the fluid is usually the baby's urine and we didn't see the the bladder

35:29

filling anymore we knew that the fetus was no longer making urine

35:36

so unfortunately by 29 weeks she developed no amniotic fluid the baby was also

35:42

growth restricted and there was malpresentation which can often happen because the fetuses are often reached earlier in

35:50

the pregnancy but if fluid remains normal then they usually can turn head down before the end of pregnancy and a

35:55

vaginal delivery can be done but in her case or in in cases where fluid goes away then usually mouth

36:01

presentation is a common um issue and she had a cesarean delivery at 36 weeks because of

36:06

preterm labor with breed presentation the baby weighed four pounds 13 ounces

36:12

at birth and unfortunately it was similar to her last pregnancy where where the baby despite all of our

36:18

efforts passed away because of cardiac arrest and respiratory failure

36:24

so for her genetic counseling erica so for autosomal recessive polycystic kidney disease both parents need to be

36:30

carriers to have a baby that would be affected and if both parents are carriers which in the general population it's about

36:37

it's about 1 in 70 people are carriers for autosomal recessive polycystic

36:42

kidney disease if both parents were carriers there's about a 25 chance that their baby would

36:48

be affected with the condition this couple had been to us in their prior pregnancy as well

36:54

and we were able to identify mom's mutation but we actually weren't

36:59

able to identify dad's mutation we had to do a separate analysis something called linkage study

37:04

which we'll talk briefly about for ivf to find that i bring that up because it is important

37:10

to kind of not stop the exploration if you're in a situation where we can't find a mutation to keep

37:16

looking and work with the genetic specialists to do so especially for pkd it's a little bit

37:22

different than adpkd only 75 percent of cases are associated

37:27

with the most common gene pkhd1 there's a second gene dzipil

37:33

that is also associated but only accounts for about a handful of cases so there is a larger amount of people with

37:39

this condition who don't know their molecular status and that's obviously very challenging when we're talking about doing

37:45

genetic testing or ivf because we might not know the action mutation for this for these patients unlike adpkd there's

37:53

no genotype phenotype correlation so there's not one mutation that makes things present earlier or later

37:59

and everybody who has the mutations you know if they have two mutations are affected with this condition we'll show

38:05

some symptoms of this condition what also can make genetic testing a bit challenging for

38:10

ar pkd is the idea of low amniotic fluid and so this mom was very savvy had a

38:18

chorionic villus sampling which is a placental biopsy so we were able to get

38:23

access to the baby's dna but if we do have patients who present a bit later and don't have any amniotic fluid to

38:30

test because of the kidney disease then we have to kind of wait until after the baby is born to do testing

38:36

next slide okay and so the maternal and fetal implications are a bit clearer for arpkd

38:44

um just that the caesarean for maternal the caesarian is likely to be necessary because of malpresentation

38:50

and then the autosomal recessive inheritance like erica talked about the fetal risks there's a risk of

38:55

intrauterine fetal demise because of no amniotic fluid which can lead to a cord accident and

39:00

there's this risk of respiratory failure after birth due to the lack of the amniotic fluid

39:05

and so now we'll just briefly touch on reproductive technologies and then answer questions

39:12

so we often talk about you know you can conceive naturally and then test a pregnancy um to

39:19

determine if the baby is affected molecularly but some parents want a bit more you know control and understanding of that

39:25

information and their risk before they are actually pregnant and so there is the option of in vitro fertilization with the

39:32

technology called pgtm which is pre-implantation genetic testing and the m

39:37

stands for molecular testing so this is a technology we specifically use for molecular conditions like adpkd and

39:45

arpkd where we know the familial mutation and we know that we're at risk for one condition how this process works

39:53

is that they a family would undergo ivf um where they would establish

40:00

you know viable embryos those embryos would then receive an embryo biopsy at

40:05

either five cells big or eight cells big and that biopsy would then be sent to a genetic

40:11

testing lab that process usually takes place over a period of four to eight weeks where the lab

40:17

establishes if they can find them familial mutation and then how many embryos would be

40:24

affected with that mutation and then the family can decide if they want to implant embryos who are

40:30

unaffected um or for some recessive conditions embryos who are carriers and

40:35

every family determines those things a bit differently based on their preferences

40:42

there are very specific considerations for doing this type of testing each each case so every family who goes

40:50

through pgtm for a molecular condition is a case by case because a specific protocol or specific recipe

40:58

for each family needs to be created in this process this consultation and

41:03

understanding of the testing process happens way before the ivf so usually someone meets with a

41:09

reproductive endocrinologist or an ivf team they make a referral to a genetic testing or genetic counseling

41:16

service they talk through all of these steps before the family even begins any medications or moving forward with ivf

41:23

treatment just to see if they have all the information that they need and oftentimes with this process we have

41:29

to get samples from mom and dad and sometimes we even have to get samples from grandparents if they're available or other family members

41:35

to act as a family tree kind of a molecular family tree and reference

41:40

the mutations in the family have to be known so when we were talking about arpkd and talking about sometimes people

41:46

don't know their actual mutation because we can't find it that becomes a bit of a challenge there

41:52

are some ways we can work around that but generally this process works best when the individuals in the family know the

41:58

mutations or if they don't know them we can go through genetic testing and find them

42:03

um we have two minutes remaining in the session sure this is our last question and in order

42:10

to do this process we need to make copies of the dna and then we need to be able to do that testing which like i said can take some

42:16

weeks to do but this process is a really helpful process for our families to be able to

42:22

kind of just have good understanding and empowerment about making decisions about their reproductive health

42:28

and now we can open it up for questions you had some really great questions come through in the chat

42:34

thank you erica and dr gibb so let me try and get through as many

42:39

questions as we can in the period of time that we have left first question that came across is when

42:46

speaking with a genetic counselor and they seem fairly aware of pkd but is there a good source resource you

42:53

would recommend when meeting with these counselors i i would say i mean there's there's

42:59

great resources gene reviews is a really nice resource that's published and curated by many

43:05

genetic specialists that walks through each stage of polycystic kidney disease recessive and

43:10

dominant and many other conditions so they should know that but you could certainly guide them to that

43:16

thank you any thoughts on the effect of epigenetics and pkd

43:22

so epigenetics is a an evolving topic i think the the idea of modifier genes the idea

43:29

of disease variability within families comes from the thought of thinking about epigenetics

43:35

um i think every time we feel like we have a grasp on epigenetics we realize we don't know as much as we think so i

43:40

i think it's an excellent question i think it's a great thought because everybody's moving in that direction but i think more to come in my own opinion

43:47

more to come there okay and let's wrap up with one quick

43:52

question uh what is the chance for severe infections post delivery in the mother

43:59

i mean i would say not super super high definitely over the baseline particularly if

44:04

there's kidney disease or definitely if there's been a transplant there's any kind of steroid use or that sort of

44:09

thing then it is a higher risk than than baseline but generally not super

44:15

high we usually recommend screening with urine analysis and urine cultures every trimester at least and so

44:21

hopefully you've identified any infections that are in the urinary system before that and then we give

44:26

prophylactic antibiotics during caesareans and so that decreases that risk

44:31

okay thank you that's all the time we have for questions uh i want to thank both

44:38

dr gebb and erica for sharing their time with us today and their expertise thank everyone also for attending this

44:46

please don't forget to take the survey for this session we really do want to hear back from you

44:52

so that we can keep improving upon these conferences so before we leave

44:58

this session we next have a mindfulness break which is coming up you can just stay here and have that mindfulness

45:04

break go grab some lunch or a snack take some

45:10

time to go visit our exhibit halls and when you're ready to leave this zoom

45:15

breakout you can navigate back to the platform page and choose where you want to go next

45:21

great thank you and if anyone has any questions you can feel free to email us our emails are right here and we're happy to

45:27

answer whatever we can um thank you so much for inviting us thank you for having us okay

45:34

uh you'll find our exhibits by clicking on the exhibitor button in the top of the home page the next

45:41

session is genetics how your genes impact your family tree you'll find this session under the

45:46

general sessions tab and it will begin at one o'clock central time

45:52

thanks again for joining us and enjoy the rest of the conference

46:01

you