Course Name :An Overview on Maternal Health Antenatal, Intranatal and Postnatal Care

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Week:04

Lecture:04

Hormones in pregnancy

Good morning students. Welcome to the next session for the NPTEL online certified course on the topic an overview on maternal health, the antenatal, intranatal and postnatal care. I am Dr. Barnali Ghosh, an obstetrician and gynecologist working as assistant professor at B.c. roy Medical College and Medical Research Center, IIT, Kharagpur. Today we are going to discuss regarding the hormones in pregnancy. The concepts covered in today's class will be the hormones being secreted from the placenta of which the most important being the human chorionic gonadotropin or HCG, human placental lactogen, the different growth factors produced from placenta, estrogen and progesterone production from placenta and a little bit regarding the hormonal influences required for the maintenance of lactation following delivery.

The keywords for today's class are as follows right. Now coming to the hormones of placenta. Placenta acts as an endocrine organ during pregnancy and you know the hormones secreted can be divided primarily into steroid hormones and the peptide hormones right. Coming to the steroid hormones mainly they are the estrogen, the progesterone and the corticosteroids and the peptide hormones secreted from the placenta.

Now the main peptide hormones are number one the HCG or human chorionic gonadotropin, then human placental lactogen, corticotropin releasing hormone right CRH. IGF is the insulin like growth factor. The different growth factors released from the placenta. They are the insulin like growth factor, the vascular endothelial growth factor and the placental growth factor. And also is the soluble FMS like tyrosine kinase 1 right and another important hormone can be added here that is the relaxin.

So these are the peptide hormones and all these hormones taken together it helps in the continuation of pregnancy and thereby help in growth and development of the fetus right. So these will you know help in the different physiological changes occurring in the mother's body. Coming to the first and most important hormone of pregnancy that is the human chorionic gonadotropin. So right from the name itself you can deduce human. It is produced by the human placenta.

Chorionic produced from the chorionic structures right. So it is produced from syncytiotrophoblastic cells of the chorionic villi and gonadotropin. What are the gonadotropins? They are the FSH and LH. Thus HCG also has gonadotropin like activity. Now coming to the structure it is a glycoprotein meaning it is a polypeptide chain attached to a carbohydrate moiety.

And to note that it has the highest carbohydrate content among all the hormones present in the human body. Approximately you know the carbohydrate content is 30% and thus it is called as the sweetest hormone of the human body. It has 2 subunits. The alpha subunit which is nonspecific. Why it is nonspecific? Because it has structural similarity with other certain hormones.

And whereas the beta subunit is specific and detection of this beta HCG in the maternal serum or maternal urine is a confirmation of pregnancy right. Now similarities. Now I have already talked this alpha subunit is nonspecific and it is similar to number 1 the LH, number 2 the FSH and number 3 the TSH. So, there are structural similarities with these 3 hormones and thus it has also LH like activity, FSH like activity and TSH like activity right. So, this is a pictorial diagram where you know the syncytiotrophoblastic cells of the placenta secrete the HCG which has 2 subunits.

The alpha subunit which is nonspecific with similarities to LH, FSH and TSH whereas, the beta subunit is specific for pregnancy. And it is excreted in maternal urine when it is detected in the urine by the urine pregnancy test it is a confirmation of pregnancy right. So, pregnancy confirmation done by detection of beta HCG in maternal urine and it is nothing, but a sandwich ELISA test. It is done with the first morning urine sample because HCG is highest in the first voided morning sample right. And the reading should be taken within 2 to 5 minutes and not beyond 10 minutes right.

The threshold for urinary beta HCG is 20 to 50 milli international units per ml right. So, this is the UPT card you know NISHCHAY. NISHCHAY is a government supplied UPT card NISHCHAY KIT. And here you place the urine, here you place the urine approximately 2 to 3 drops of urine and if one pink line is visible then the result is negative. If two pink lines are visible then it is positive for pregnancy right.

Now, this is estimation of beta HCG in the urine. If we come to maternal serum beta HCG estimation it has two types of test one is qualitative which can detect as low as 5 to 10 milli international units per ml or less. And there is a quantitative assay which can detect know up to 1 to 2 milli international units per ml. Here I want to add one thing when do we get this you know beta HCG in the maternal serum and in the maternal urine. So, say this is the uterus and the developing embryo has entered the uterine cavity from the fallopian tubes on day 4.

Then it gets implanted into the decidua and you know there will be formation on day 6 and it will lead to the formation of you know syncytiotrophoblast and cytotrophoblast from. This happens this differentiation of syncytiotrophoblast and cytotrophoblast happens on day 7. And production of HCG beta HCG in maternal serum occurs from day 8 of fertilization right. So, beta HCG is secreted from the syncytiotrophoblast and it is you know present in the maternal serum on day 8 of fertilization. And that means what? So, we know the day of ovulation is the day of fertilization which is day 14 of the cycle.

So, 14 plus 8 is day 22 of the cycle very important. So, if this is the menstrual cycle the female had menses and then on day 14 there was ovulation and fertilization with the sperm leading to zygote formation and on day 22. So, on day 22 we can measure beta HCG in the maternal serum. Thus we here this is the day 28, this is the day of her missed period. So, you can see from here that we can detect pregnancy even before the missed period.

We can detect it on day 22 of the cycle. So, approximately you know 5 to 6 days prior to the day of missed period. Before she has a missed period you know before that 5 to 6 days prior we can detect pregnancy by estimation of beta HCG in the serum. And on the day of missed period you know here is the presence of beta HCG in maternal urine right. So, in maternal urine beta HCG comes on day 13 of fertilization which is day 27 just one day prior.

So, on day 28 when the patient comes to you with a history of her missed period you go for a UPT and you know you measure the beta HCG in the urine of the mother. And if it comes out to be positive then you tell her that yes you have a pregnancy right. So, this is how we go for pregnancy confirmation ok. Next coming to the concept of half life and doubling time. Half life of beta HCG T half is 36 hours.

To note T half of LH is only 2 hours. So, HCG you know has similarities of with LH has LH like activity and has a longer half life right. Now, what is doubling time? The level of beta HCG in mother's blood it increases. Beta HCG gradually increases in the early phases of pregnancy right. And this increase it doubles the level of beta HCG doubles in 48 hours.

That means, the beta HCG on day 1 you measure beta HCG and then after 48 hours on day 3 you again measure beta HCG there will be a rise in beta HCG right. And this rise has to be more than 66 percent. Doubling not a total 100 percent, but at least 66 percent rise in beta HCG in 48 hours. So, this you know will confirm that what do you get from this. In 48 hours you see that the beta HCG in the mother serum has increased by 66 percent which confers that it is a intra uterine pregnancy with a viable fetus.

Very important. So, increase if it is by more than 66 percent in 48 hours we in we know we

deduce from this that yes she has a intra uterine pregnancy with a viable fetus. If say the increase is less than 66 percent in 48 hours what does that mean? Yes she has a pregnancy, but it is not viable the fetus is non viable number 1. So, that means, in case of missed abortion right and number 2 it can so happen that it is a case of ectopic pregnancy. In both these scenario you get a rise in beta HCG, but it is not you know what we want it is not as high as 66 percent it is less than 66 percent. Or it may so happen that you know with subsequent days there is fall in beta HCG.

The levels of beta HCG are gradually decreasing then there is a chance of pregnancy failure right. So, it is a case of early pregnancy failure or you know pregnancy on the process of expulsion. So, these are the 3 you know scenario where you have to deduce infer from the levels of beta HCG checked between 48 hours. Another thing to note here is the rise in the beta HCG. So, we have already told that in the early pregnancy beta HCG levels goes on increasing.

First it is started from day 8, day 8 of the fertilization beta HCG comes in the maternal serum which corresponds to day 22 of the cycle right. And from then it will go on rising, rising at a rate you know doubling in 48 hours right and it will reach a peak. This peak is approximately at 8 to 10 weeks of gestation 60 to 70 days. So, this is the peak which is attained at around 60 to 70 days following her menses right. Then there will be a slight decline and after that it becomes constant from 16 weeks.

From 16 weeks the level of HCG remains constant all throughout the pregnancy and around 32 weeks, around 32 weeks there will be a slight secondary peak. This is the most important, but here there is a slight secondary peak at around 32 weeks and then it will remain same or constant up till delivery. Say here is the delivery around 38 weeks. So, here is the delivery, it remains constant up till delivery and then abruptly it falls to normal following 2 weeks from delivery. So, 2 weeks postpartum the beta HCG normalizes it goes down right.

So, this is the graph of beta HCG. Now there is a peak at 60 to 70 days around 10 weeks and then it will become constant from 16 weeks remain at that constant level. A slight secondary peak occurring at 32 weeks and then remaining constant for up till delivery. A following delivery within 2 weeks it normalizes right. So, that is regarding the you know beta HCG levels in the maternal serum.

Now coming to the functions of HCG. Number 1 function is corpus luteum rescue. What does that mean? In a normal female you know this in a normal female when she is you know having her menstrual cycle say this is the point of ovulation. Day 14 is the day of her ovulation. So, before these 14 days this is the follicular phase in the first half where the follicles are being recruited and they are gradually developing in size under the action of FSH. And this dominant follicle which is produced around day 14 it will you know rupture and there will be ovulation.

Following ovulation the graafian follicle now converts into corpus luteum say yellow colored corpus luteum. So, these are the corpus luteum and you know if this is under the action of LH right and following that up till day 21 the corpus luteum will be present. And then gradually it will get degenerated because there is no LH. This corpus luteum will get degenerated if there is no pregnancy. Say if during this cycle the female has become pregnant right.

So, there was fertilization between the ovum and the sperm in the female genital tract and the female has become pregnant. So, it will get implanted and beta HCG will start to be secreted in the maternal serum from day 8 right. From day 8 which is nothing, but day 22 of the cycle. Day 8 of fertilization mind it this is day 8 of fertilization which is plus 14 that is day 22 of the cycle right.

I hope you are understanding. So, up till day 21 up till day 21 the corpus luteum was maintained by the maternal LH. If there is no fertilization then the LH will decrease gradually and the corpus luteum will degenerate right. But if there is fertilization then on day 22 the beta HCG comes into action from day 22. And it will help to maintain the corpus luteum. There will be no demise corpus luteum will be maintained and it will help in the secretion of progesterone for another 2 weeks right.

Because this progesterone is required for the continuation of pregnancy. So, one of the most important function of a HCG is corpus luteum rescue which is nothing, but prevention of the corpus luteum demise right. So, this helps in secretion of progesterone from the corpus luteum for another 2 weeks up from which you know from 6 weeks the progesterone is then produced from the placenta called as the luteo-placental shift. Number 2 is HCG acting as a immunosuppressant it will decrease the immunological reaction of the mother and thus help to prevent fetal rejection from the mother side.

So, it has immunomodulatory effect. Then another important is the stimulation of the leading cells of the male fetus right. So, this beta HCG what happens to this beta HCG I will again here we will discuss. So, this beta HCG it has a peak at 10 weeks and this will act on the leading cells around 10 weeks it will act on the leading cells of a male fetus right. So, this has an LH like activity right. So, this LH like activity of beta HCG will activate or will you know help in stimulation of this leading cells which will release testosterone and this testosterone is required for the formation of male external genitalia right.

So, thus beta HCG has a role in the formation or development of the male external genitalia. So, it has a role in the development of sorry it has a role in the development of the male external genitalia by activation of the leading cells you know thereby helping in the production of testosterone. And lastly due to the TSH like activity it will stimulate the maternal thyroid and

you know this maternal thyroid will get stimulated it will secrete more thyroxine which is required by the fetus up to 11 weeks. The fetus is dependent on the mother for thyroxine for up to 11 weeks after which the fetal thyroid gland can itself you know produce thyroxine which is required for its growth and development. And this stimulation of maternal thyroid can be you know given a name called as gestational thyrotoxicosis right.

So, these are the functions which we have already discussed. It helps in the rescue and maintenance of corpus luteum during pregnancy which helps in the production of progesterone and continuation of pregnancy. And it also causes release of relaxin from the corpus luteum and this relaxin is a smooth muscle relaxant and helps in you know uterine quiescence right. So, there is no myometrial contractility thereby you know helping in pregnancy continuation. Number 2 is it helps in male sexual external genitalia differentiation through the activation of the leadic cells and lastly the stimulation of the maternal thyroid gland thereby helping in transfer of thyroxine to the fetus.

Now, the scenario or the cases where the HCG levels are higher than expected. Number 1 is in case of wrong date where you know the patient has forgot or has given a erroneous LMP. So, in that case you know the gestational age may be you know underestimated right. You have underestimated the gestational age calculated from the LMP and so it is not corroborating with the HCG levels right. Number 2 is in case of twin pregnancy or multiple pregnancy where there is more placenta, more trophoblastic tissue and more HCG production.

In case of molar pregnancy or in gestational trophoblastic disease where also there is more placental tissue, more syncytiotrophoblast, more production of HCG. In case of RH negative pregnancy erythroblastosis fetalis where the fetus has underlying anemia and to know compensate there is placentomegaly leading to increased secretion of beta HCG. And an important you know indicator of Down syndrome beta HCG increases in the second trimester in case of Down syndrome which is used as a screening test right. So, all these cases you know has raised levels of beta HCG and sometimes due to this high beta HCG it can cause thyrotoxicosis in mother. Maternal thyrotoxicosis because you know the TSH like activity of beta HCG.

And cases where the HCG levels are lower than expected again due to wrong date where it has been the gestational has been age has been overestimated right. In case of some chromosomal abnormalities like Edward or Patau syndrome which are nothing but Edward is trisomy 18 and Patau is trisomy 13 right. In case of abortion or ectopic pregnancy we have already discussed that the HCG rise is less it is lower than expected. Now, beta HCG disappear by 2 weeks after a normal delivery, but in case of molar pregnancy after suction evacuation the beta HCG you know normalizes by 8 weeks or 56 days. So, this is important because we need to follow up the patient you know for a longer period until the beta HCG normalizes in case of molar pregnancy right.

So, this was all regarding the most important human chorionic gonadotropin. Now, coming to another important hormone of the placenta that is the fumal placental lactogen HPL. It is also produced by the syncytiotrophoblast right. It is also produced by the syncytiotrophoblast of the placenta. It is a single polypeptide chain without any carbohydrate moiety and the weight is approximately 22000 dalton.

It is also called as HCS human chorionic somatomammotropin. So, from the name itself you can deduce it is human origin from the syncytiotrophoblast cells of the chorion and has somato that is growth hormone like activity and mammotropin that is prolactin like activity right. So, chemically and immunologically it is similar to prolactin by 65 percent and growth hormone by 96 percent right. So, it will help in growth of the mother. Number 2 it will you know help in breast development prolactin. So, lactogenesis or help in breast development which ultimately help in lactogenesis following delivery.

And third is it causes insulin resistance right. So, it you know is a diabetogenic hormone. A very important concept is this human placental lactogen it starts to rise from 3 weeks. From 3 weeks it is present in the maternal serum and it will go on rising throughout the pregnancy till 36 weeks. So, it is a constant rise for HPL and to mention here that you know it is compared to HCG the rise is maximum for HPL and you know the levels are maximum for any hormone in the human body.

HPL has a maximum level at 36 weeks right. T half of HPL is 20 to 30 minutes and production rate at term is 1 gram per day with maximum level of HPL found in maternal plasma followed by amniotic fluid and then the fetal blood right. So, this is the graph where representing the HCG which has a peak at around 10 weeks then it will decrease and around 16 weeks. 16 weeks there will be you know constant it becomes plateau for the rest of the pregnancy around 32 weeks there will be a slight secondary peak and then you know after delivery it decreases to normal by 2 weeks right. For HCG and in case of prolactin or HPL it starts from rising from third week of pregnancy and it will continue to rise continue to rise up till 36 weeks right. So, these are the graphical representation of the levels of the hormones in pregnancy.

Coming to the metabolic action of HPL, yes it helps in maternal lipolysis thereby increasing the circulating levels of free fatty acid which will act as a source of energy helping in fetal nutrition number 1 and also in maternal metabolism. Number 2 is it is a diabetogenic hormone that means, it helps it causes insulin resistance and thereby increases the insulin levels in the maternal blood. Insulin being an anabolic hormone helps in protein synthesis and transfer of amino acid to the fetus right. Also insulin resistance will increase glucose levels in maternal blood and this increased glucose in the mother's blood will help in its transfer to the fetus through placenta via facilitated diffusion right. And third is a potent angiogenic hormone helping in formation of fetal vasculature.

So, all this will be helping in the you know continuation of pregnancy. So, this was about the human placental lactogen. Now coming to the insulin like growth factor there are you know IGF-1, IGF-2 and IGF binding protein right. So, these are all produced from the placenta and mainly the IGF-2 or insulin like growth factor 2 is responsible for the fetal growth in intrauterine period. After the birth the growth of the baby is mainly by the growth hormone right.

So, this was you know a concept regarding the human chorionic gonadotropin or the hormone of pregnancy. Next we discuss the human placental lactogen which goes on increasing maximum at 36 weeks helping in insulin resistance, increasing the insulin levels in the maternal blood and thereby you know helping in anabolic state in protein synthesis right. So, this was regarding the HPL and lastly we discussed the insulin like growth factor helping in growth of the fetus. So, this was today's discussion. In the next class there will be continuation of the other hormones in pregnancy. Thank you.