ESHRE 2020 Virtual (5-8 July 2020)

Questions for the speakers

Session 36: COVID-19 - Lessons learned

Maternal-fetal vertical SAR-CoV-2 (COVID-19) viral transmission during pregnancies is possible and currently cannot be dismissed - Gulam Bahadur (United Kingdom)

Q: Maternal-fetal transmission is (maybe) possible, but are there any known adverse outcomes in relation to the foetus/newborn?

A: Yes. When a virus crosses the placenta and this is the worst-case scenario eg in CMV, parvovirus, ZIKA, rubella, and the risk of congenital abnormalities exist. With COVID-19 we are at the stage of establishing whether vertical transmission has occurred or not. It is therefore early to establish what sort of adverse outcome occur. Fetal death and miscarriages records are poor and because of the risks to clinicians and pathologist it is highly unlikely that infected and infectious tissue would have been kept especially when there is virtually near zero possibility for saying goodbye to the infected adults. In adults there is increasing interest in looking at the damage to the brain partly due to oxygen deprivation and efforts are being made to identify covid viral particles in cerebral tissue, just as what we are doing with the placenta.

The data presented give a strong steer that vertical transmission is occur (see the `triple witching hour' slide given the incubation period must pre-exist infection. Newer cases have since emerged and in one unpublished Mexican triplet positive case (all covid-19 positive) which suggests COVID-19 must now be placed in the very high-risk category (including the fact that maternal deaths are recorded. The ne Paris case shows beyond doubt that vertical transmission had occurred. Here they showed RT-PCR viral load is much higher in placental tissue, than in amniotic fluid and maternal or neonatal blood.

Now we need to establish the baseline figure and yes totally agree.

Q: Despite limitations, based on your systematic review is it possible to estimate a % for vertical transmission? It looks like it could be quite low.

A: It was important for me to show you how diagnostics works and be interpreted. We also went to lengths in bringing diagnostic conundrums in the male factor fertility and covid paper in RBMOnline recently. It shows most people publishing have simply not understood what they are doing, Three quarters of all tests being reported in this huge study made no comment on when the tests wen done and the slides which followed means there is a huge false negatives being reported In other words there must be far more positive cases. In the UK it is now estimated 5-10% of adult's population may well have contracted the virus.

So in terms of % vertical transmission we have a significant problem in gathering data as the basics of identification of positive cases is poorly practiced and understood. Since Jan 2020 to this time more than 500 publications have rapidly arisen and unfortunately these lacked proper controls or critical peer review. The test kits up to May 2020 were also based on the SARS 2013 virus and not specially to COVID -19. Many were using in house kits which had never been validated.

Bottom line is that we have a wrongful perception that vertical transmission of COVID -19 is low but we need to tease out all the poorly conducted tests – unfortunately means most of them. It took years to confirm placental damage an vertical transmission with Zika virus and yet it taken about 3 months to confirm cases with covid. This figure is bound to be low but high enough to be of serious public health concern.

Q: Have you any data on whether infected babies have displayed symptoms/abnormalities? is there an international follow-up of these infected babies?

A: We are grappling with case reports right now. Most likely symptoms are fever and breathing. Most cases reported here were mildly infected. The question arises as to what happens when the viral load is high? Whether there is long term damage due to oxygen deprivation in utero remains to be seem

Q: The maternal transfer of covid to fetus increases risk of mortality for the fetus?

A: Big question for the future. Even the mortality rates in pregnant women is under reported. We asked under special request to the UK Office of National Statistics (ONS) and they came up with zero pregnant women had died and no babies. Shocking to see they did not have information despite the huge government funding on covid related facts. Yet we know from another source (see our JBRA paper on Adverse effect in covid in pregnancy, Bahadur et al., 2020) that 5 pregnant covid infected women had unfortunately died. This separate source of data would only have cases where clinics would have volunteered to supply. Because of confidentiality reasons or unrecorded home deaths during the pandemic we need to be open for a much higher figure for mortality both maternal and fetal. Good data collection (good luck to ESHRE data collection – an excellent contribution) is essential and we are never really prepared for a pandemic f this nature. In the UK several years ago they ran a trail run on a pandemic and yet none of the findings ever came to light so we lost out on huge public expenditures where we could hve modelled and factored in deficits found there.

Yes, data collection is anther big wake up call here

Q: Do you think being symptomatic covid positive increases elective c-section rates? Is induction still ok?

A: No point in adding unnecessary procedures but this is for the mid-wife and doctor in charge to decide on a case by case basis

Q: for everyone: In case of 2nd wave of COvid, would these testing methods be introduced or IVF clinics would be most likely shut down?

A: Hopefully there will be more defined and better diagnostic testing reducing the level of false negatives. We know about the timing from day 1-5 will give false negatives from 100% to 67% for RT-PCR

Shutdown of IVF techniques would depend on where the risks and spreaders are coming from. Government clinics will inevitably have to be shutdown to reduce the footfall within hospitals. Private IVF clinics may well escape

Q: Does the covid infection affect women's ability to reproduce i.e. oocytes quality

A: Good question – nobody knows. Because ACES-2 receptor sites line the placenta previously infected women may well be vulnerable and this may affect the implantation of the embryos. No one has studied the oocyte quality post infection but I expect some compromise due to oxygen depletion in cells following SARS-CoV-2 infection and oocytes themselves too have ACE-2 receptor sites. We know from MERS (family of covid) and previous SARs strains of virus that miscarriages are higher and there is opportunistic microbial changes/infections to complicate and adversely affect pregnancies.

Q: What's the implication for vertical transmission in ivf?

A: Lethal damage and associated with congenital malformations where vertical transmissions are known (see my earlier slide). Vertical transmission is rare and the implications for the fetus are serious. It took years to establish ZIKA in placenta and yet we can establish the presence of COVID-19 in placenta (see my later slides)

Q: Is SARS-CoV2 seen in the fetal vessels inside the placenta (ie entering the fetal circulation)? Or is it sequestered only in the outer syncytiotrophoblast?

A: No it is entering the placenta and one later slide shows the damage on both sides of the placenta. In one case since I spoke RT-PCR viral load is much higher in placental tissue, than in amniotic fluid and maternal or neonatal blood. This case confirms (along with the cases I presented when factoring in the incubation period) that vertical transmission is happening and now being confirmed. Worrying findings. We need this fact to become more careful and counsel the patients

Q: SARS-CoV2 was apparently already in our regions from November 2019 onwards (and even earlier). What does that mean for our cryopreserved oocytes and embryos?

A: There should be no added risks to already cryopreserved oocytes, embryos or sperm. The risks post transfer of embryos need to be assessed as the pregnant woman can be infected away from the clinic and isolation. For this reason, the pregnant woman and partner must practice optimal safe living ie social distancing, travelling in off peak periods or working from home as much as possible. Difficult to be prescriptive here as we do not have case reports to work from

Q: Is it safe to have a pregnancy/deliver a baby during the pandemic?

A: These are unprecedented times and provided the couple and people around are living sensibly and following government guidelines do not be fearful of achieving a pregnancy – enjoy it

Q: Can these receptors be suppressed by any type of medication?

A: We have no safe and validated type of receptor suppressor. All chemicals may well have implications to the uterus, placenta and oocytes too as ACES 2 receptors sites are there too

Q: Should we follow sperm washing techniques as for HIV? Studies show the virus is found in semen

A: I would abandon the cycle if the man is SARS CoV2 positive as the risk to all operators is huge and not worth it. It will also lead to closing the clinic down if such practices were pursued. There is aerosol effect during sperm washing.

Q: What should we prioritize in the future studies related with the current pandemic, to further enhance the S& Q of the medical services that we provide?

A: To establish vertical transmission from mother to baby, level of miscarriage, my slides show that 75% of the babies tested DID not record the time and so most people testing and researching have not understood diagnostic testing and its limitations. Therefore, the number of cases is under estimated. Covid positive mothers have died and despite us asking the office of National statistics they indicated no women had died when another research group in the UK identified 5 pregnant women had died. We don't know how many more pregnant women had died in the general population and not reported. The cases are expected to be higher therefore and proper data collection during a pandemic is not always the priority when life saving procedures are being focused upon. We published these in JBRA 2020 Bahadur et al., Adverse pregnancy outcomes after COVID-19. There ought to be more IUI practice as it has lesser risks https://bmjopen.bmj.com/content/10/3/e034566.altmetrics

Oocyte/embryo quality after infection will be interesting

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I just want to thank all the participants asking such important and valid questions above. We need to work together to gain more defined information COVID-19 in pregnancy is going to be big area of concern and special practice. Thank you Gulam Bahadur