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Ethical considerations relevant to infections in pregnancy: Application to Sars-Covid-19

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Despite wide diversity and scope, the ethical dimensions relevant to infections in pregnancy remain little explored. Important questions span topics with personal or wider societal and public health impact. The conceptualization of the status and responsibilities of the pregnant woman and the legitimate limits of third-party interests are key determinants of our appreciation of applicable ethical obligations.

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Ethical statement

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Introduction

Pathogens and infections will continue to influence if not threaten human existence and a large part of medical effort is directed to combating their aftermath. Yet, infectious diseases have not attracted proportionate attention in ethical debate. This perhaps conforms to the observation referred to as the 10/90 divide, whereby less than 10% of resource is directed at 90% of the disease burden [1].

PubMed literature search (November 2019) using the terms ethics (or ethical), pregnancy and infections yielded 658 references. 144 of these were primarily concerned with ethics, including 105 articles on HIV/AIDS and 9 on the Zika outbreak. The sparse academic output leaves a number of areas inadequately explored. To date, there are no publications on the ethical concerns of Sars-Covid-2 pandemic as applicable to pregnancy.

Management of infections encompasses well-recognised clinical and laboratory-based attempts at diagnosis and treatment. In addition, there can be wider public health and health policy aspects concerned with prevention and containment. Compared to other affections of the body or mind, the means of preventing infections are often more clearly defined. Infections can spread rapidly, as in the case in outbreaks or epidemics. Immunization and the use of antimicrobials have implications beyond the individual. All of this invite consideration of the aims of treatment, and the interface with public health measures starting with disease notification. Determinations will necessarily evolve in relation to the prevailing conceptualisation of the individual and their place and duties in the wider society. This article outlines the areas with relevant ethical concerns but is not intended to resolve the many dilemmas that clinicians dealing with the current Sars-Covid-2 pandemic face. Resolving these matters is outside the scope of a single article.

Prevention

Many infections have limited, or short-term effects and medicine has achieved big success in relation to others. But some, including otherwise mild infections, can have serious and long-lasting impact during pregnancy. The notion that prevention is better than cure is deeply embedded in modern discourse and in health policy [2]. Prevention has inherent appeal but is necessarily constrained by the balance of burdens and benefits. Efforts aimed at prevention can entail significant sacrifice when patients constitute the disease reservoir at the centre of the infection cycle [3]. Patient behaviour, their willingness to be tested and to comply with stipulates are important determinants of their outcome, the infection cycle and the emergence of drug resistance. The boundaries between doctors’ commitment to the care of the individual and the desire to achieve public good can become blurred when it comes to testing and prescribing. When faced with
public anxiety, confidentiality and autonomy can give way to notification and enforcement.

Vaccinations can be central to prevention but their availability and efficacy vary. Achieving optimal levels of uptake requires trust, persuasion and motivation. The endeavour may entail measures designed to facilitate or encourage compliance, or more proactive measures targeting hard to reach groups. Despite their potential benefits, there are legitimate questions surrounding the framework and safeguards that need to be in place. Tension can arise at the interface with liberty, free choice and consent. Pregnancy could be linked to particular uncertainty, vulnerability and intense surveillance, which can strain the notion of autonomy. On the other hand, strong advocates of autonomy need to consider situations which threaten fetal welfare [4].

Efforts that aim to influence women’s behaviour can be contentious especially if they go beyond persuasion. Yet, there are advocates who support punitive measures including exclusion from access to services, compulsory treatment, directly observed therapy, or quarantine if optimal compliance is not realised or if the risk of contagion is high [5,6]. This calls for ethical scrutiny of policy, the role of clinicians, and of the locus of decision making and oversight.

The Harm Principle and safeguarding the community or the baby rather than benefit to the individual woman may be advanced as justification for intervention. There are echoes to Mill’s argument that ‘. . . the only purpose for which power can be rightfully exercised over any member of a civilized community, against his will, is to prevent harm to others. His own good, either physical or moral, is not a sufficient warrant’ [7]. But the justification or possible explanation articulated by Mill ought not be confused with a motivation for action. A ‘rightful’ act is one that can be justified, not one that ought to be undertaken. Much remains contingent on circumstances including the degree of harm, the nature of the disease, the degree of risk and importantly, the range of available options.

Still, a more accommodating stance may favour actions or intrusions by society if done to enhance public welfare or the welfare of the child. The spectrum of opinion includes those who view such interventions as legitimate, desirable or even necessary. Green argued that ‘it is the business of the state to take the best security it can for the young citizens’ growing up in such health’ [8]. Intervention may be placed in the context of ‘society’s effort to prolong life and promote health’ [9]. Some may place a responsibility on individuals to take part in collective efforts [10]. Article 25 of The Universal Declaration of Human Rights (1948) states that: ‘Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family’ [11]. This was also used as a basis for arguments in favour state intervention and corresponding obligations on citizens to enable achieving the aspired goal. Citizens’ obligations can be understood with reference to the correlativity thesis, which envisages reciprocity between the existence of rights and obligation [12]. This however raises wider questions related to the notion of rational assent and the responsibility of citizens on the one hand and the ethical principles needed to guide or delimit the extent by which health agencies can be part in any endeavour towards concordance.

Vaccination

Whilst effective against certain infections e.g. measles, tuberculosis and poliomyelitis, vaccines are not available against others e.g. malaria, or group B Streptococcus. Some vaccines are used for at-risk individuals e.g. hepatitis B, others are recommended for the entire population. High uptake of population-oriented vaccines creates ‘herd’ immunity, which requires 90–95 % uptake for high, and 80–85 % uptake for moderate contagion disease. Herd immunity benefits the small percentage who may have a contraindication to vaccination or those who have not otherwise been vaccinated. Overall, contraindications to any specific vaccine are rare, and lack of uptake is more likely to stem from passivity or deliberate choice. This creates inequity in the burden of risk and benefit. Minimizing own burden or risk in situations of high herd immunity becomes a tempting but, arguably, a self-centred choice. This can also create a dilemma for health care personnel when providing advice and brings into focus the tension between the desire to enable the exercise of individual choice and maintaining near universal uptake. Measures advocated to maximise uptake vary by the extent they employed persuasion, inducements or enforcement. Recently, the question of compulsory vaccination has come to the fore in relation to measles (in response to outbreaks) and influenza (vaccination of health care workers) [13,14]. Relevant here is that population vaccination campaigns are typically designed to deliver high-volume at low cost, with little information exchange between the parties at the clinical interface. The practical questions aside, there are challenging issues concerning social and individual responsibility. The emphasis on vaccination and prevention can influence the perception of those seen to have contributed to their illness.

Vaccines are rarely tested on pregnant women and manufacturers and regulators are likely to take a cautious approach when considering their use during pregnancy. This creates dilemmas for clinicians who have to consider the legal framework whilst balancing their ethical responsibility to individual women with societal interests. On the other hand, it is hard to see how meaningful consent could be achieved in scenarios where research and safety information are absent, rudimentary or unreliable. Inadvertent exposure creates the opportunity to understand the clinical course but are also the very situations where termination of pregnancy could be a consideration. Judgements have to be made in an information vacuum and can therefore only be rooted in heuristics.

Dilemmas arise when new vaccines are introduced during epidemics and imminent risk, as was the case in SARS (severe acute respiratory syndrome) or Ebola (Ebola haemorrhagic fever) and the new Covid-19 infection. These dilemmas, whilst applicable to the population at large, are particularly challenging in case of pregnancy because of the unknown and unquantifiable fetal risk.

Women who are unable or unwilling to follow clinical advice may place themselves and, in-turn, their babies at some risk. Whether non-concordance is voluntary can influence perception of moral agency. The status of pregnant women and unborn babies and the concern, interest or support afforded to them by society has changed over time and will necessarily continue to evolve in response to cultural and economic factors.

Lifestyle and the environment

Individual practices are relevant to the risk of certain infections. Some relatively minor lifestyle modifications can reduce risk e.g. hand hygiene, avoiding soft cheese to prevent listeriosis, measures to avoid toxoplasma. Avoiding contaminated food and drink or contact with affected individuals are commonly advised. But people vary in their ability to adhere to such stipulates even when the entailed opportunity loss is marginal.

Some aspects of prevention require resourcefulness or resources outside the reach of the individual or the community. But even when the requirements are known and accessible, prevention may not be achievable. Puerperal and postpartum sepsis still causes considerable morbidity and mortality worldwide despite the discovery of preventative measures more than a century ago. Tuberculosis remains a significant issue for underdeveloped
countries and for deprived populations in rich countries. Vector borne infections such as malaria remain endemic in many parts of the world. The Zika virus, also transmitted through insect bites, has resulted in significant outbreaks. Wound infections, including tetanus affecting the umbilical cord in new-born babies, remain an important challenge in developing countries. Other infections that could be sexually transmitted such as HIV, syphilis, chlamydia, gonorrhoea and hepatitis B are largely preventable and influenced by individual behaviour. Blood borne infections such as hepatitis C, hepatitis B and HIV are influenced by individual behaviour and the quality of medical facilities. Many diseases such as tuberculosis, measles and meningitis, as well as those causing pandemics such as SARS, pandemic influenza and the recent Covid-19 corona virus infection are transmitted through droplets. Vertical transmission from mother to baby can occur during pregnancy or labour and is influenced by maternal behaviour and by the quality of medical care. All of this raises ethical questions that span a woman’s responsibility to herself or to the unborn baby, the responsibility of health services in relation to those who are at risk because of factors within or outside their control, and the degree of acceptable risk to health care personnel themselves. There are wider questions concerned with the role of health care personnel and how they can balance their role in relation to individual good, societal interests and wider determinants of health. Sociodemographic determinants can influence susceptibility to infections and the ability of individual women to seek help. The relevance of these questions emphasises the challenges to depictions of health care professionals as narrowly confined to delivering benefit whilst observing confidentiality, autonomy and justice. An important question relates to the role of doctors in jurisdictions that require some diseases to be notified to authorities or where there is a risk of transmission to partners or contacts.

Much of the infection burden is preventable. This begs the question of moral responsibility and the duties of the woman herself and of society at large to the welfare of the baby or to future generations. This is a contentious area that has been valued differently by different cultures and jurisdictions. Mill’s standpoint referred to above views intervention as justifiable only if for preventing harm to others. But whether and how this may be applicable in pregnancy is debatable. First, the place of the unborn within this framework is contentious and second, because the exercise of power against a person’s will is a threshold that is unlikely to be relevant to situations where failure to comply with recommendations is the product of apathy or competing priorities, rather than it being a considered expression of autonomous choice. It is arguable whether the prohibition contained in Mill’s argument applies to interventions or intrusions short of coercive enforcement.

Relevant to the question of prevention of infections in pregnancy is the role and duty of pregnant health care workers who can be at risk of catching infection whilst caring from affected patients. A certain risk of contagion can be seen as inherent in providing health care. However, the level of acceptable risk is relevant to its degree, severity of consequence and the degree by which this may be mitigated. Thus, the level of acceptable risk it is a matter for debate.

**Diagnosis**

Not all infections result in manifest disease. Colonisation reflects the mere growth and multiplication of microorganisms in or on the host, without a host response or clinical expression. Clinical symptoms can bring the case to medical attention, but identifying subclinical affections or colonisation require targeted testing or screening.

Infections can remain asymptomatic despite ongoing deleterious effects e.g. asymptomatic phase of HIV, tuberculosis or hepatitis B or C. Methicillin-resistant Staphylococcus aureus (MRSA), Clostridium difficile (CDIFF) and asymptomatic bacteriauria are other clinically significant carrier states. Women who are carriers of β-haemolytic streptococcus can transmit the organism to the baby at birth leading to serious infections. Chlamydia can result in preterm birth or neonatal conjugicativis or pneumonia. There is evidence for a causative role of infection (including extraterine maternal infections e.g. pylonephritis, pneumonia and periodontal disease) and colonisation in preterm labour and prelabour rupture of fetal membranes.

One recommendation put forwards is for universal screening for HIV, hepatitis B and syphilis early in pregnancy and for selective prenatal screening targeting higher risk women for hepatitis C, chlamydia, gonorrhoea and tuberculosis [15]. The critique of health screening at the interface with personal liberty and self-determination is relevant here. In addition, there is a need to consider whether efforts directed at detecting infections is primarily focussed or motivated by concerns for the woman herself, her unborn baby or by other societal concerns such risk of contagion or cost. Whilst many of these issues are interlinked and can be relevant, it is important to analyse underpinning assumptions in order to appreciate their relevance or relative contribution to ethics deliberation.

Targeted screening requires judgements that blur boundaries as it confers advantage (and burden) selectively. Those not included within the programme may benefit from a universal service. Determinations around cut-off points or other selection criteria involve value judgements. The method of payment for services and the locus and mechanism for decision-making are relevant to deliberations.

Women may be asymptomatic whilst harbouring infections with significant implications. Hepatitis C infection for example is associated with preterm labour and delivery, intrahepatic cholestasis, gestational diabetes, and postdelivery neonatal abstinence syndrome. There is a risk of in-utero and intrapartum transmission. Until recently, hepatitis C had no effective treatment without a significant risk of teratogenicity. This, together with cost implications were used to argue against universal screening and in favour of selective testing for high risk women [16]. The more recent availability of protease and polymerase inhibitors raised the prospect of effective treatment during pregnancy [17] and generated calls for universal screening. The remaining uncertainties about safety in pregnancy and the fact that these drugs are not licensed for use during pregnancy, raise question of ethical and medico-legal import.

Relevant here is the way antenatal tests come to be administered as ‘routine’. Women often do not know the value or rationale for antenatal tests and rarely question them. The resource intensive provisions for opt-in HIV/AIDS testing introduced in the UK prior to the discovery of effective treatment have now been incorporated into routine care, with women able to opt-out. The distinction between opt-in and opt-out testing is rarely considered except for high profile illnesses.

**Management**

The effect of infections ranges from asymptomatic to severe or life threatening. The severity of fetal and maternal affection may not correlate. The fetus may remain unharmed - provided maternal survival - even where maternal infection is life-threatening e.g. swine flu in late gestation. Other infections can be more detrimental to the fetus e.g. rubella and CMV. Vertical transmission to the fetus can occur during pregnancy, childbirth or the puerperium. This provides different drivers for action and raises
the prospect of interventions, including caesarean section, aimed selectively towards fetal or maternal benefit. Tension can arise as treatments will have different implications for both parties. The effect of infection can also differ depending on gestational age. The risk of miscarriages or teratogenicity are relevant to early pregnancy. At later gestation, serious risks include preterm rupture of membrane, preterm labour and intrauterine fetal death. Some infections e.g. rubella and toxoplasmosis are linked to substantial lifelong impact.

Pregnancy termination continues to raise disagreement. Even where legally permitted, judgements based on fetal or maternal risk entail assessments of both the severity of affliction and the magnitude of risk. The evaluative nature of these decisions will necessarily entail differences in opinion. How to assure sound decision-making in these situations is a taxing question. Denial of abortion in the presence of infection can lead to tragic outcomes [18].

It is often the case that fetal welfare transcends self-benefit as a basis of maternal choice, but neither is a fail-proof determinant of compliance with prevailing orthodoxy. Failure to seek medical care can result in detriment to the patient, her baby or dependents. Health services and society may come to shoulder some of the ensuing burden. The unique interdependency poses questions about whether pregnant women have, or should be seen to have, moral (or legal) obligations to the unborn child. There are also questions about the derivation and extent of any obligations and their enforceability [4,5]. The questions raised here are linked to the status conferred on the unborn child, the pregnant woman and on ‘being pregnant’. This status varies in different societies and over time. Pregnant women often receive support or unique entitlements that facilitate their access to health care. Whether health care structure reflects societal values and how these structures ought to interface with individual choices are matters for debate, but understanding these points clarifies the framework in which healthcare professionals’ practice. Infections may be regarded as a matter for collective responsibility and endeavour or be consigned to individual resourcefulness or motivation. Whether societal interest is rooted in compassion, concern for the inescapable monetary or human cost, or in third party interest can have a strong influence. The approach adopted by different societies or healthcare systems will inevitably vary, but there will remain an inescapable need for collaboration in the face of outbreaks, epidemics or pandemics.

Moral dimensions relevant to the Covid-19

As Covid-19 became a major pandemic at the time of writing this article, this provided the opportunity to appraise how the outlined framework can provide a more complete account of the ethical dimensions relevant to pregnancy.

It remains the case that no vaccine or drug that protects against this highly contagious infection is available. Thus, prevention relies on individual actions e.g. handwashing, cough containment and environmental cleaning and the use of personal protective equipment (PPE) coupled with population level measures such as testing and contact tracing and social distancing. Many governments introduced population wide social distancing rules, stay-at-home orders, school and venue closures, and workplace restrictions. The ethical justification for these wide-ranging impositions is debatable as the risk of the disease and the burden of prevention affect people, including pregnant women, differently. It is questionable whether Mill’s harm principle can be relevant to situations where harm is neither imminent, direct or intentional or if it justifies restrictions on the pursuit of life routines. Some jurisdictions identified all or subgroups of pregnant women as requiring more stringent protection, social isolation or ‘shielding’. The burden on individuals and their ability or willingness to comply with these stipulates vary. Women who are unwilling or unable to observe recommendations pose a challenge and may endanger themselves, their baby or care providers which raises questions about moral responsibility.

Restrictions may also affect the availability or willingness of women to access health services. The risk of transmission in health care facilities or withdrawal of services can adversely affect outcomes. Whether imposed nationally or locally, such restrictions pose important challenges at the doctor-patient interface. Personal choice and health care professionals’ advocacy roles can become seriously strained under the clamour of collective good. The extent by which the duty of the doctors to individual women ought to be influenced, disrupted or substituted by public health considerations are matters for debate.

The risk of Covid-19 to health care workers is well recognised and entails ethical (and legal) considerations for employers and for policy makers. Individual practitioners face difficult ethical choices if tending patients entails personal risk. Pregnant health care workers need also to consider the need to protect herself and the fetus. At the core, these issues entail ethical choices rather than numerical calculations of risk.

Testing, isolating and contact tracing directed to the general good also entail impositions on liberty. The benefit for affected individual is less clear and the willingness to co-operate can vary between individuals and communities. This is particularly relevant as Covid-19 is a notifiable disease. Numerical risk estimates, whilst relevant to public health planning, are less meaningful as guides to ethical stance or to individual risk perception and behaviour. Similar considerations apply when considering access to tests done outside the direct therapeutic framework. Testing positive for Covid-19 usually entails the requirement for isolation of the index individual and their contacts, but this is unlikely to benefit asymptomatic or mildly symptomatic individuals. Situations arise where the rationale for testing is unclear or absent [19] raising questions about the ethical framework for doctors’ involvement especially when this entails competing demands on resources.

During the pandemic, much of the available diagnostic testing was directed towards public health rather than the clinical interface. This means that clinical management often proceeded with unknown infection status. Health care professionals face significant dilemma because of the limited availability of tests. The situation is particularly problematic in maternity care where much of the care cannot be delayed and because of the unique requirements of labour ward including prolonged close proximity. Members of staff can be the source of Covid-19 transmission to patients under their care. The need to reduce the risk of transmission involved changes to the way health professionals interact with women and the new born and also changes to standard antenatal care for example, the introduction of unevaluation remote consultations. In many ways, tackling the health crisis has resulted in major disruption to the wellbeing and health care provision for pregnant women, who perhaps are not at higher risk from the Covid-19 exposing a generational divide. Rather than being seen as inevitable, these disruptions ought to be regarded as a result of a particular value judgment that, in turn, had an ethical burden on health professionals. It is unclear whether or to what extent women are, or could meaningfully be, appraised of the potential implications of these disruptions.

The clinical manifestations of Covid-19 vary from the asymptomatic or mild to severe and life-threatening respiratory distress. Initial reports suggested favourable maternal and fetal outcomes but there have been reports of maternal mortality and also concerns about poor outcomes secondary to disruption of services or the introduction of remote consultations. Fetal effects of infections acquired early in the course of pregnancy remain
uncertain but there is evidence of viremia, placental pathology and the detection of viral RNA in solid organs and also of IgM in newborn babies. The effects on the fetus including long term neurodevelopmental implications will not be known for some time. This raises important ethical questions about managing infections under considerable uncertainty. Decisions may need to be made about the mode of delivery and its timing including cases that are remote from term in the absence of evidence that such intervention may stabilize deteriorating maternal health. Maternal anxiety or a request for a pregnancy termination can create a significant dilemma. In the absence of treatments known to be effective, those with severe symptoms have received a variety of drug therapies within or outside clinical research protocols. The framework for research participation will necessarily challenge the traditional understanding of informed consent and appropriate standards of safeguard needed for patients under condition of extreme desperation is a pressing consideration. Similar considerations apply in relation to clinical research on therapeutics and vaccines. It is unclear how ethics can guide clinical practice under conditions of extreme uncertainty and where the effects of infection can only be known in retrospect. Achieving benefit or best interest and avoiding harm may be rooted in hope rather than expectation. Decision-making becomes more testing at junctures that involve critical life and death decisions. For example, the prioritisation of ventilation and intensive care. Much of decision making in this area relies on likelihoods and probabilities which creates tension at the individual interface particularly given the reports of survival amongst those judged to be extremely ill. The degree of priority given to pregnant or postpartum women is rarely made explicit. Still, there is evidence of racial and age-related differences in outcome amongst peripartum women.

Finally, in during emergencies such as acute fetal distress the time required to don personal protection equipment or to allow for ventilation air exchange can significantly impact outcomes which places considerable burden on health care personnel when faced with choices that can put their own safety at risk.

Conclusion

This article highlights questions of the moral responsibilities of the pregnant woman, the legitimate limits of her autonomous choice and whether society has a right or duty to interfere in the name of welfare or public good in contentious issues that are relevant to prevention, diagnosis and management of infections in pregnancy. The impact of infections varies, and the severity of maternal affection may be at variance with the effect on the baby. The risk of transmission adds an important dimension. The unique status of pregnancy and societal interest in the welfare of the mother and baby may provide an impetus for intervention in the name of welfare. But this may conflict with maternal autonomy. Societal factors and interests can pose a challenge to health care professionals seeking to exercise their duty to the individual patient under their care. There is a risk that judgements be influenced by perceptions of maternal moral responsibility or by the various competing interests.

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