Challenging infections in pregnancy: a multiparametric approach

Marina Morgan

Abstract

Despite advances in medical knowledge, infection still kills pregnant women. Early signs of sepsis may be missed or overlooked by busy healthcare workers, some with little experience of infections, and it can be difficult to recognise symptoms in a woman where infections present in subtle ways. The pregnant woman's immune system is compromised and she may have other reasons for malaise, flushes, miscellaneous aches, nausea, vomiting and abdominal pain, all of which could herald sepsis.

This review is intended to cover basic microbiology germane to the diagnosis and understanding of infection, and combine this with microbiologically orientated aspects of clinical skills and pertinent history taking. These parameters, together with appropriate laboratory tests, can help the clinician spot infection early, and point towards the identification of the underlying causative agent. A review of antimicrobials, the place of immunoglobulin and other adjunctive therapies completes the multiparametric and pragmatic approach to diagnosis and management of serious infection in pregnancy.

Keywords immunoglobulin; influenza; necrotising fasciitis; pregnancy; toxic shock

Introduction

Maternal mortality in the lying in hospitals fell initially after the introduction of hand washing and emphasis on hygiene by Semmelweis in Vienna and Oliver Wendell Holmes in the USA, with most sepsis then attributable to Group A beta-haemolytic streptococci (GAS) With the introduction of sulphonamides and penicillin in the mid-20th century, mortality fell further. A resurgence of invasive GAS in pregnancy in 2006–8 produced an infection related mortality of 1.13/100,000 pregnancies, (CMACE report) leading to new 'Green top' guidelines, and a drive to educate healthcare workers about sepsis.

The subsequent MBRRACE report MBRRACE-UK: Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (2009–12 published 2014) found GAS-associated mortality exceeded only by swine influenza, with an overall infection mortality rate of 0.63/100,000 live births. The subsequent dramatic decline to an overall figure of 0.08/100,000 (data from the 2009–14 MBRRACE report published 2016), probably reflects a combination of increasing influenza vaccine uptake, implementation of various sepsis-related guidelines and mandatory education of healthcare staff to recognise sepsis. Details of the mortality attributable to individual organisms were omitted from the most recent report, but presumably include the usual GAS and Gram negatives with less influenza.

Morbidity rates are even more difficult to estimate, although the United Kingdom Obstetric Surveillance System UKOSS study 2014 suggested for each death there were some 50 patients with severe sepsis who survived.

Viral infections in pregnancy rarely produce sepsis, and there are numerous publications and guidelines available to consult on viral hepatitides, HIV, parvovirus and Herpes viruses. Zika virus exposure in pregnancy is leading to a plethora of publications, but who to test, what methodology to use and optimal management are the subject of fierce debate, out with the scope of this review. The devastating effects of influenza pneumonia in pregnancy will, however, be considered.

This review will concentrate on bacterial infections in pregnancies that are particularly problematic for clinicians, employing a clinical microbiologist's multi-parametric approach to their diagnosis, aetiology, and management.

Causes of infection (Table 1)

The major bacterial organisms causing fatal infection during pregnancy remain

Streptococcus pyogenes (GAS)

E. coli and coliforms – some multi-resistant

Streptococcus pneumoniae

Others, (mostly single case reports nowadays) include meticillin resistant *Staphylococcus aureus* (MRSA), *Mycobacterium tuberculosis* (MTB) *Clostridium septicum*, and unusual Gram negatives – *Serratia* spp, *Salmonella spp* and *Morganella morganii*.

Influenza

During 2009–12, a massive upsurge in influenza accounted for 43% of all infection-related deaths in pregnancy, thirty six women died, mainly because of H1N1, 'swine flu' (MBRRACE report), in stark contrast to only one death during the three years of the subsequent report (MBRRACE 16).

As with the general population, morbidity and mortality was associated with a BMI of >30, and additionally, pregnant women are susceptible because of a low immunoglobulin, IgG4. Contributory factors to maternal mortality included diagnostic delay, and being unvaccinated. 75% died untreated whist awaiting confirmation of the diagnosis.

Patients suspected of influenza should be tested immediately using viral Throat swab for Influenza PCR, barrier nursed and treated with antivirals before diagnosis confirmed, as per national PHE guidelines.

H1N1 ('swine flu') has a predilection for young women, multiparous and in the first or second trimester of pregnancy. Early delivery may be indicated during the third trimester of pregnancy. Comparatively few pregnant patients have been treated with ECMO for influenza, with an overall survival of 66% was reported from a large Australian and New Zealand Intensive Care Society series.

Pulmonary haemorrhage due to primary influenza or secondary necrotising pneumonia due to PVL-S *aureus* or GAS causes severe respiratory compromise with almost certain death.

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Please cite this article in press as: Morgan M, Challenging infections in pregnancy: a multiparametric approach, Obstetrics, Gynaecology and Reproductive Medicine (2017), http://dx.doi.org/10.1016/j.ogrm.2017.06.007

Causes of infection

Gram appearance	Morphology	Example	Site found	Presentation/associations
Gram positive (blue/purple stained) cocci	Chains of spheres	Streptococci e.g. GAS	Usually mucous membranes – throat, vagina	Skin and soft tissue infections (SSTI) Puerperal sepsis (GAS) Neonatal and maternal sepsis (Group B Streptococci (GBS))
		S. pneumoniae	Oropharynx	Respiratory infections
Gram positive cocci	Clusters (*staphyle in Greek-roughly translates as bunch of grapes*)	Staphylococci (aureus = Latin, 'golden')	Skin, mucous membranes, nose.	SSTI, toxic shock
Gram negative rods	Brick (rod) shaped	Coliforms/ *Enterobacteriaceae*	Gut reservoir	Intra-abdominal urinary tract infections (UTIs) Preterm Premature rupture of membranes Cerclage
Gram negative rods	Slender rods	*Pseudomonas aeruginosa*	Rarely healthy patients,	Catheter associated UTIs
Gram positive rods (aerobic)	Slender rods	*Listeria monocytogenes*	Gut, from unpasteurised animal products	Sepsis, meningitis in mother, Listeriosis in fetus (microabscesses – "*granulomatous infantiseptica*")
Anaerobes;				
1] Gram negative rods	Pink rods	*Bacteroides* spp	Gut, oral cavity	Abscesses
2] Gram positive rods	Blue/purple rods Spore producers, *produce exotoxins*	*C. difficile* *C. perfringens*	Gut Gut contaminated wounds, dead tissue	Antibiotic associated diarrhoea Gas gangrene

Table 1

Initiating Extra-Corporeal Membrane Oxygenation (ECMO) early can improve survival.

It can be difficult to differentiate influenza from exotoxin syndromes, given they can all produce myalgia, high temperature, prostration, diarrhoea and vomiting and conjunctivitis, as illustrated in Table 2.

Infections by site

Treatment of UTI in pregnancy

Hormonal changes cause muscular relaxation and urinary stasis with decreased bladder emptying. Gram-negative rods, mainly coliforms and in particular *Escherichia coli,* are major

Comparison of influenza and TSS

Influenza	Toxic shock syndrome (TSS) (*S. aureus*)	Streptococcal TSS (GAS)
Very acute onset of severe myalgia	Slower onset illness, myalgia	
Cough	Usu no cough	Usu no cough
High temp	High temp/low temp	High temp/low temp
Severe prostration	Confusion, prostration	Confusion, prostration
	Exotoxins – nausea D V	Exotoxins – nausea D V
No rash	100% rash if Staph (TSS)	10% rash if GAS (STSS)
	Multi-organ failure	Multi-organ failure
	May be vaginal origin but uncommon. Small wounds most common source.	May be vaginal origin Often soft tissue focus.
Low CRP (till bacterial superinfection)	High/rapidly climbing CRP	High/rapidly climbing CRP
Haemoptysis (if severe pneumonia)	Haemoptysis not associated with TSS, usually associated with PVL-S. aureus pneumonia	Haemoptysis with severe pneumonia, but GAS pneumonia is rare

Table 2

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