Dr Catherine O'Sullivan - The burden of invasive GBS disease in young infants in the UK & Republic of Ireland 2014-2015

We were aiming to look at the current burden of Group B Strep in infants under 90 days, looking at cases from a sterile site, so for example, blood culture, or spinal fluid. We collected data via the BPSU, which I'll explain, through isolates sent in to reference laboratories and from laboratory notifications of cases. The BPSU stands for British Paediatric Surveillance Unit, which some of you may be familiar with. Essentially, it's a system where particular diseases are looked at for research and each month, paediatricians and neonatologists ask to notify if they've seen any of these cases. They do so and then researchers researching those conditions can contact them.

In terms of the cases as it stands at the moment we have 817 cases over the 13 months. That's 597 which I would call 'clinician cases' where we have detailed information from the clinician along with microbiological information and 220 where we just have the microbiology information. So that's 817.

We looked across the British Isles, so it wasn't just England and Wales, as you can see 80% of the cases were in England, with 6 to 7% in the Republic of Ireland and Scotland, and around 3% in Northern Ireland and in Wales. We did the study with the Health Protection and Public Health Agencies of these countries.

Looking at the onset of disease, which I'll mention several times, we looked at where the cases were early onset, so from birth to six days of age, or late onset, from seven days to under 90. We found a similar split to in 2000, though with slightly more late onset cases. So, just to get to the incidence, the incidence that we have at the moment is 0.89 per 1,000 live births. This is an increase from 2000 where it was 0.72. And as you can see, there is an increase both in early onset cases and late onset cases with particular note that the greater increase is in the late onset. This pattern is the same across all of the countries, so the increase in total incidence, early onset and late onset, but a greater increase in late onset, it's the same pattern in all regions.

Looking at some of the patterns with the information we have, if we look at birth weight, we can see that in the early onset cases we are seeing the larger babies, as maybe expected, the more term babies, and in the late onset, a lot more of the smaller babies, so the premature babies. And again, this pattern is the same as in 2000 and is the same across the

regions. And this, looking at birth weight, illustrates the same thing. We have the higher number of cases in the small babies in the late onset.

If we look at day of onset, so when did the babies become sick, you can note that babies who had early onset disease primarily became sick in the 24 to 48 hours. There's a slightly different spread with the babies who had late onset, but it's roughly around one month is the highest proportion and the median age for those babies getting late onset disease was 25 days which is slightly earlier than in 2000 where it was 29 but around that one month stage.

If we look at what we call the clinical syndrome, so whether the babies had a sepsis, a meningitis, a pneumonia or something else like an osteomyelitis, the division is very similar to in the past with a slight increase in meningitis. The pattern of seeing more early onset sepsis and less meningitis and more meningitis in the late onset, remains the same, so as you can see. In terms of the incidence of meningitis, the incidence in 2001 was 0.15 per 1,000 live births and preliminarily what we have now is 0.16. In a study done between 2010 to 2012 on neonatal meningitis, the GBS meningitis was 0.16 so it is as we expected from that study.

If we look at mortality, and again, this is the same across the regions, the overall mortality has fallen and the greatest fall in that mortality is in the early onset cases. So from the information we have at the moment, there were 37 deaths; 22 of those 37 were in late onset cases. When we look at when the children died, 98% of them died within a month of becoming sick. The median time of death was 3 days after they became unwell. Again, if looking at mortality across, you can see that is has fallen.

We wanted to look at serotypes and the serotype distribution, thinking about if there had been any changes in the past fourteen years, also keeping very much in mind the work that's going on with Group B Strep vaccines and which stereotypes will and won't be included. This is the serotype distribution by early and late onset disease and as you can see, and may not be surprised, primarily they are serotype 3 and 1A. This distribution is the same across the regions. Just to break it down to meningitis, again you see the same thing, primarily serotype 3.

To have a look at the demographics of the babies who became unwell, who were in the study, we found, as expected in the population really, so the split male to female and the ethnicity split. We had ethnicity available for around 63% of the cases and that was 75% White, then Pakistani, then African, then Indian, and that fits with what we know about the population.

There were 38 twins, most of those twins were not sets of twins, as in one twin got sick, not the other. We didn't have any triplets. In the previous study there were 39 twins; there were some triplets; but very little has changed there. Looking at the risk factors with

relation to those cases that are early onset, keeping in mind that this is preliminary data, and that for 220 of the cases we didn't have any of the clinician information, only whether they were early or late onset. We're still able to find some information, so for example, for those early onset babies where we do have clinician information, 29% of them had maternal pyrexia and/or suspected chorioamnionitis. Again it's early to say but it looks like we have picked up more carriage in this study than in the previous, for whatever reason, but a lot less prolonged rupture of membranes over 18 hours. And actually, looking at the prolonged rupture of membranes, the median time is a lot lower and the number that are over 18 hours is also a lot lower.

If we look at the mothers who received antibiotics during labour, if we look at the guidelines based on the risk factors, we find somewhere in the region of 100 to 130 who may have fitted criteria to receive antibiotics during labour. Of those we have information about who did receive, there were 61. That may not be that those other mothers didn't receive antibiotics but we don't have the information, or it may be that they didn't.

In terms of which antibiotics were given, from those where we know which antibiotic was given, this is the split. It's fairly as we might expect, there are a few combinations on there that would have been given not with the primary aim of preventing GBS, so for example the gentamicin and metronidazole but in the most part they are probably acceptable choices. The median time before delivery that antibiotics were given, in those we know about, is two hours pre-delivery. An awful lot of the antibiotics were given either in the half an hour before delivery, or in that hour to two hours.

To move away from the early onset cases to the late onset, just a few things of note: in terms of the number of late onset children who were neonatal intensive care unit in-patients, there were 21%. I think it's worth looking at this because where we're seeing this increase in late onset cases, in some cases that may attributed to there are more babies on NICU, or an increase in the prematurity rate.

But actually, although there were these 21% of whom one was not premature, it was a surgical baby, essentially 80% of the late onset babies were at home and most of them were term babies. There were 10 relapses, of those relapses there was one which was seven days post a course of treatment, the rest were longer, or further on. One of the babies who relapsed died, it was actually the baby's second relapse of suspected sepsis. In the first instance they were treated but there was no blood cultural growth and in the second and third, and the baby died on the third relapse. One of the babies had relapse has made a disability. The other eight, to our knowledge, were healthy at discharge.

I've mentioned meningitis before but just to say again, the incidence was 0.16 per 1,000 live births. That's where we take meningitis both where we have a proven growth in the spinal fluid, so a proven culture, but also where we have meningitis from the clinician, or from the lumbar puncture results. So for example, a baby may be extremely sick, may be having

seizures, may have imaging consistent with meningitis but may never be well enough to have a lumbar puncture, that would still be considered as meningitis. So you can see the divide there. Again that's fairly similar to in 2000, slightly more cases, but not a huge increase. The divide of early onset to late onset is pretty much the same.

Just in terms of whether we are missing a lot of cases of meningitis, because people are not having lumbar punctures, and also whether people are following guidelines that are out there about lumbar punctures, actually in the most part, they are. 84% of these babies had a lumbar puncture. Of the 13% who didn't, a lot of them actually did but they were unsuccessful or they didn't because the baby was too sick. So people are doing their lumbar punctures.

In terms of thinking about outcome, when we asked clinicians about outcome, we asked about outcome at discharge, though actually a lot of people have gone on to give further information than that, about seeing them in the future when they are older. We've found- so we've asked if the baby was healthy, if there was major or minor disability at discharge, we've also asked if there was uncertainty because, as you can imagine, when these babies are discharged from hospital there may be uncertainty about whether they will or won't go on to have problems in the future. We've found a slight increase, though not huge, from 2000 to now in terms of the number of babies where there was an uncertainty about if they would go on to have any problems. And again, as you'd probably expect, you see more disability and uncertainty is seen in the babies with meningitis. However, on a positive note, 78, or 66% of the babies with meningitis were classed as healthy at discharge.

So just in summary, in looking from 2014 to 2015, again preliminary, but what we have at the moment, we have an incidence of 0.89 per 1,000 live births which is an increase from 2000-2001 where it was 0.72. Also in those 14-15 years we have seen increased incidence across all countries. The greater increase is definitely in the late onset cases. However, on a positive note, we are seeing a lower overall mortality, in particular, lower mortality in the early onset cases. And looking to the future in terms of serotype distribution and vaccine coverage, if we were thinking along the lines of trivalent vaccine for example, which would be 1A, 1B and 3, 82% of these cases fit into those serotypes. If we were looking at a combined, so 1A, 1B, 2, 3 and 5, 94% of these cases fall into those serotypes, so some positive news for the future.

And I'd like to say thanks to everybody from all the Public Health and Health Protection Agencies who helped and all the microbiologists and paediatricians who have helped so much with all the information.