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# Noninvasive amniotic fluid sampling to establish PK of azithromycin in pregnancy



PRESENTER:  
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**BACKGROUND:** Pharmacokinetic studies to guide dosing of azithromycin (AZ) for pregnancy specific conditions, such as preterm premature rupture of membranes (PPROM), and data on accumulation of AZ in fetal compartment are lacking

## METHODS

- Prospective study of 5 pregnant women admitted with PPRM
- 1gram oral azithromycin dose one time administered on admission
- Amniotic fluid collected non-invasively from underwear lining pads ad lib
- LCMS/mass spectrometry used to quantify AZ concentration
- Luminex multiplex assay used to quantify TNFa, IL-1a, IL-1B, IL-6, IL-8, IL-10.
- Primary outcome: time/concentration profile of AZ in AF

## MAIN RESULTS

- Mean gestational age was  $27.5 \pm 2.3$ wk and BMI  $32.8 \pm 6.2$ kg/m<sup>2</sup>
- AZ successfully quantified in duplicate, coefficient of variation 17%. The lower limit of detection and quantitation was found to be 1 ng/mL and 10 ng/mL, respectively (Figure 1)
- AZ trended down and was <60ng/mL after day 3 (Figure 2)



# Azithromycin persists in fetal compartment for 7 days after single maternal dose, but may not be at adequate concentrations

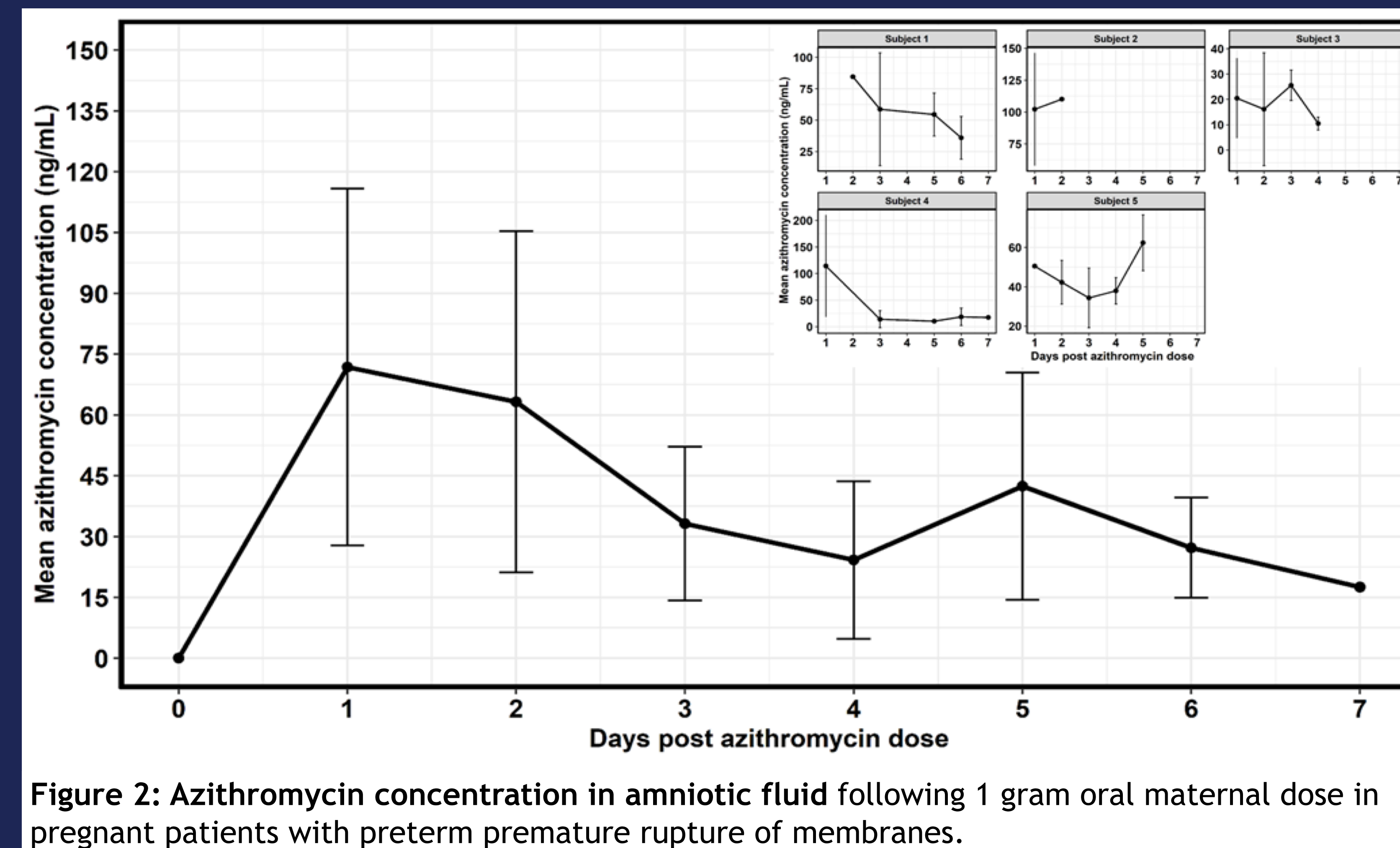
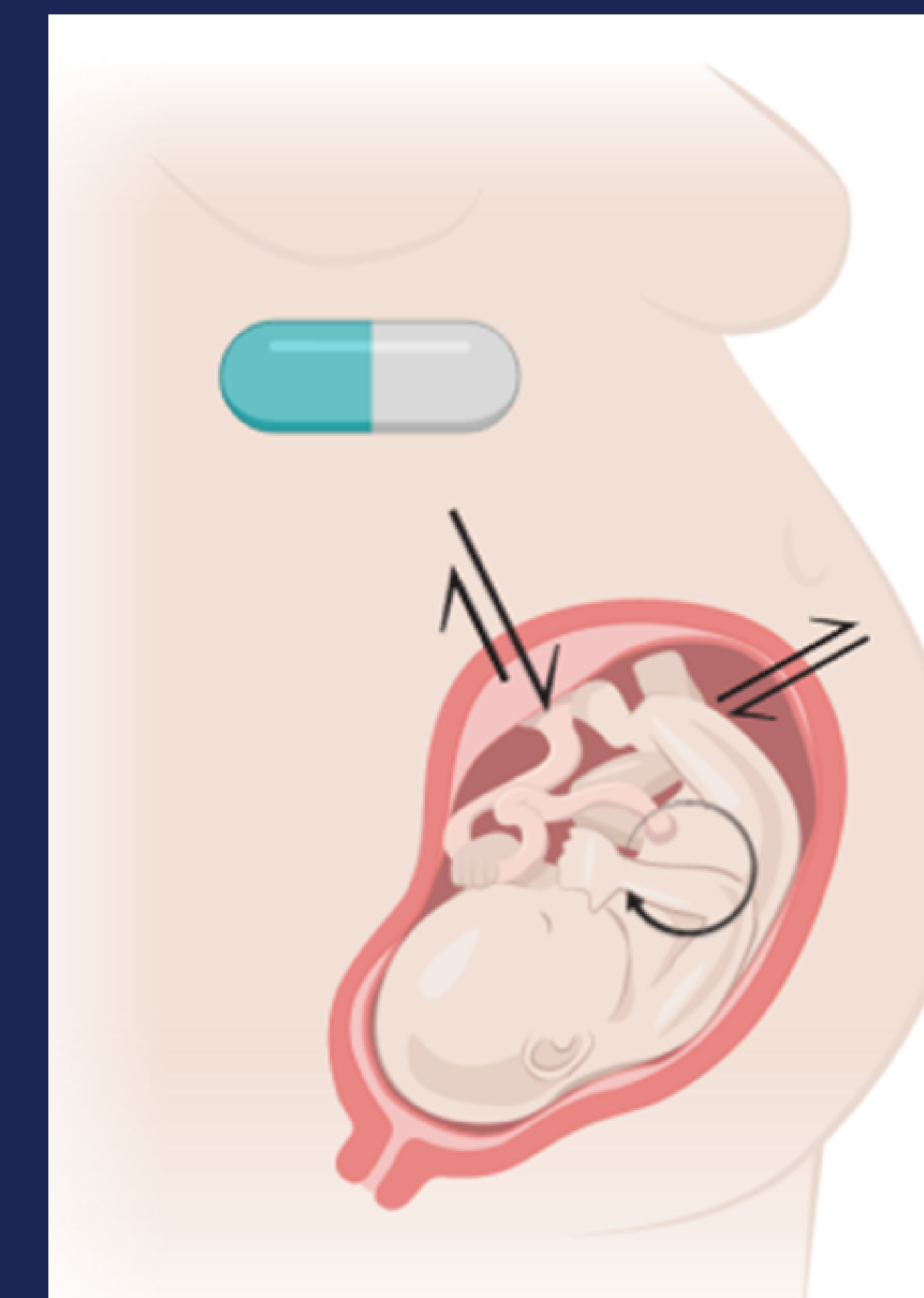


Figure 2: Azithromycin concentration in amniotic fluid following 1 gram oral maternal dose in pregnant patients with preterm premature rupture of membranes.



| Amniotic Fluid AZ (ng/ml) | Day 0 (0-24h) | Day 1 (24-48h) | Day 2 (48-72h) | Day 3 (72-96h) | Day 4 (96-120h) | Day 5 (120-144h) | Day 6 (144-168h) | Day 7 (168-172h) |
|---------------------------|---------------|----------------|----------------|----------------|-----------------|------------------|------------------|------------------|
| mean±SD                   | N/A           | 63±59          | 53±41          | 33±23          | 27±16           | 53±22            | 27±18            | 18               |
| CV (SD/Mean)              | N/A           | 0.94           | 0.77           | 0.70           | 0.59            | 0.42             | 0.67             | N/A              |
| Median [IQR]              | N/A           | 46[18-102]     | 42[19-97]      | 25[21-41]      | 21[7-42]        | 54 [45-71]       | 27[10-45]        | 18               |

Table 1: Azithromycin (AZ) concentration in amniotic fluid 1-7 days after a single one gram oral azithromycin maternal dose. There were no samples collected 0-24 hours for any participants so that data is not available (N/A). N= number of participants and n= total number of samples. CV: coefficient of variation. IQR: interquartile range

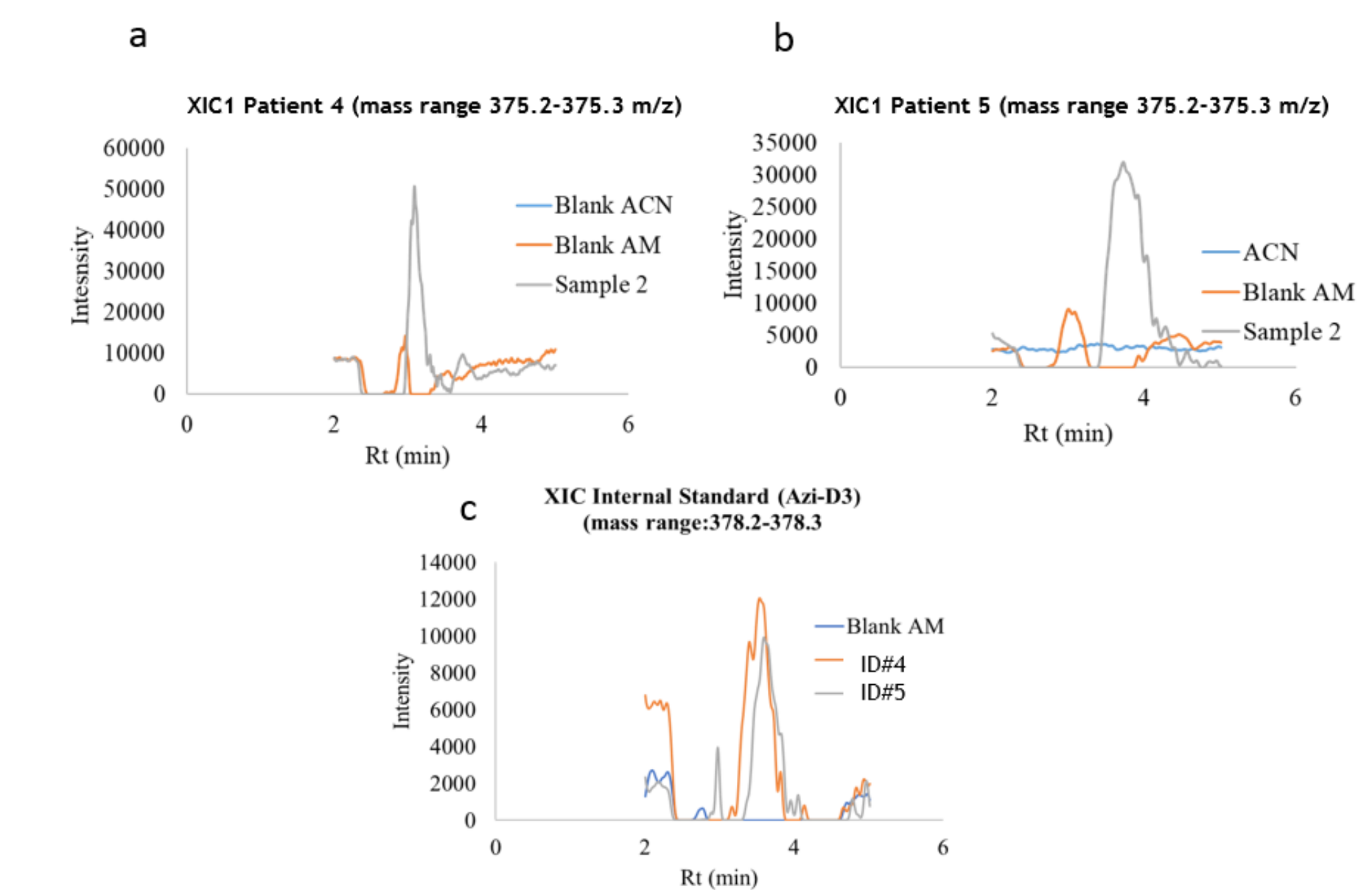


Figure 1: Representative LCMS chromatogram from a) Subject 4, b) Subject 5, and c) AZ-D3 internal standard

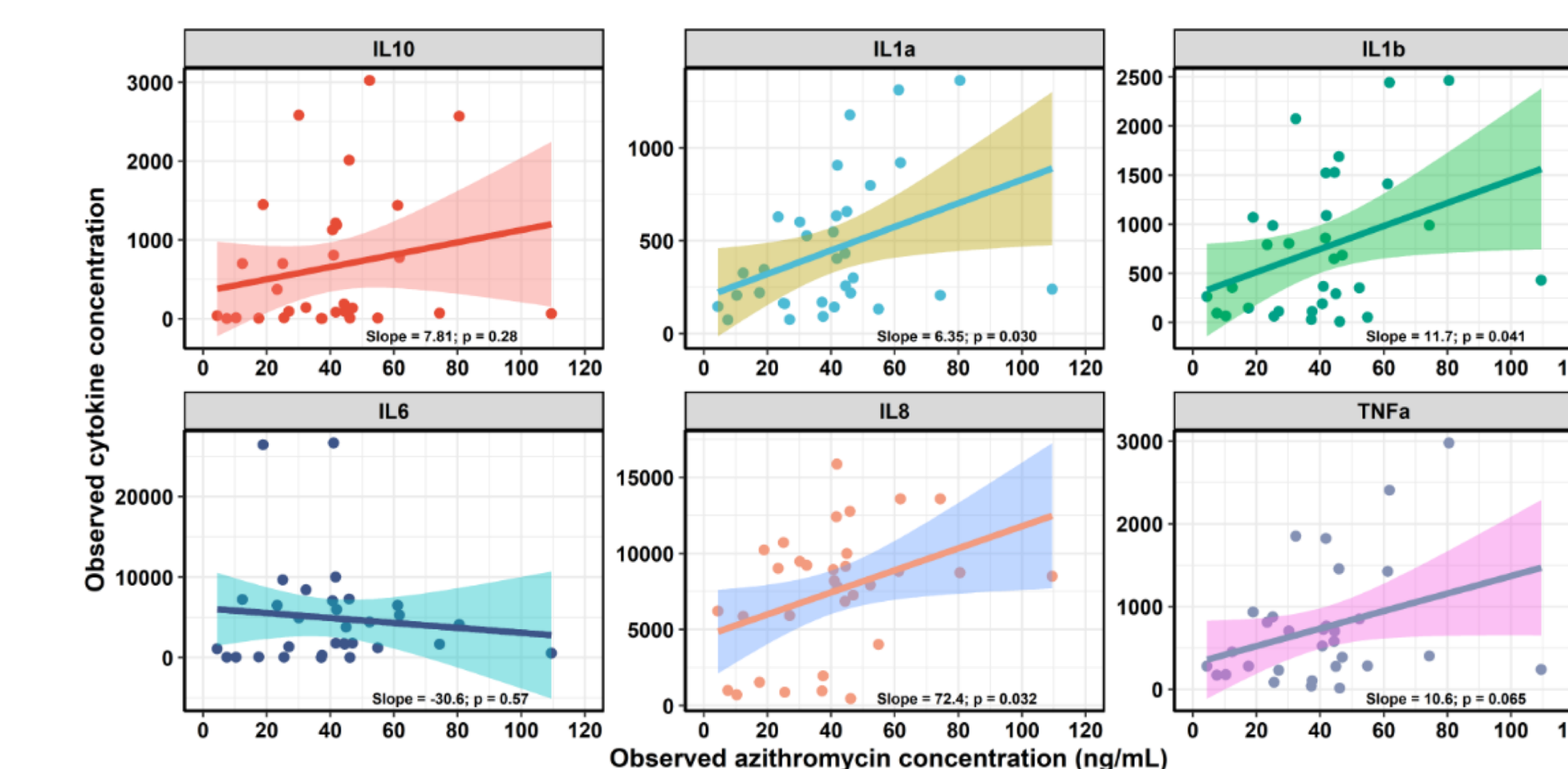


Figure 3: Azithromycin concentration was positively correlated with IL-8 ( $r=0.38$ ,  $p=0.03$ ), IL-1a ( $r=0.39$ ,  $p=0.03$ ), and IL-1b ( $r=0.36$ ,  $p=0.04$ ) in amniotic fluid. Azithromycin concentration was not correlated with TNFa ( $r=0.30$ ,  $p=0.07$ ), IL-6 ( $r= -0.06$ ,  $p=0.75$ ), or IL-10 ( $r=0.23$ ,  $p=0.2$ ) concentration in amniotic fluid.



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