

A Retrospective Chart Review Examining Ototoxicity of In-Utero Gentamicin Exposure

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Introduction

The incidence of acute pyelonephritis or chorioamnionitis in pregnancy is 1-2%. Both infections may be treated with gentamicin in combination with other antibiotics and can result in severe fetal and/or maternal complications if not treated. "Conventional" q 8 h dosing is used in ~17 pregnancies annually at Victoria General Hospital (VGH). In 2003 Schering's Garamycin® Injectable product monograph was amended to state the drug "may cause fetal harm when administered to pregnant women" and that "total irreversible bilateral congenital deafness in children whose mothers received aminoglycosides including gentamicin" has been reported. An extensive literature search yielded no case reports of auditory toxicity in infants exposed to gentamicin in utero and only one case of congenital deafness involving gentamicin was reported to the Canadian Adverse Drug Reaction Monitoring Program between Jan 1 1997 and Sept 30 2005. Gentamicin currently has an FDA pregnancy Category "C" rating meaning that it should be used when benefits outweigh potential risks to both mother and fetus.

Universal neonatal audiology screening was initiated throughout Vancouver Island Health Authority (VIHA) South Island in January 2002 using otoacoustic emissions and automated auditory brain stem response methods. Testing can detect gentamicin induced hearing loss in frequencies between 2000 and 4000 hz, a range important for language and speech development. The baseline incidence of audiologic deficits in newborns in VIHA South Island is ~3 per 1000 and approximately 7% of newborns screened will require outpatient follow-up screening at a community audiology clinic.

Objectives

Primary objective:

To determine if any infant exposed to gentamicin in-utero born between January 2002 and April 2006 demonstrated audiologic deficits on routine hearing screening

Secondary objectives:

To determine indication for gentamicin therapy and pregnancy outcome of mothers receiving gentamicin on antepartum unit at VGH. For live births, examine mean dose and duration of gentamicin therapy, concurrent use of other potentially ototoxic medications in mother while pregnant and again in neonate, value of gentamicin serum trough levels when obtained, mean gestational age of fetus when exposed and at birth, and proportion of neonates requiring special care nursery admission

Methods

Design: Single centre retrospective chart review

Inclusion Criteria: Patients admitted to antepartum unit at Victoria General Hospital between January 2002 and January 2006 who received at least one dose of intravenous gentamicin

Procedure:

- Obtained approval from VIHA Research Review and Ethical Approval Committee
- Searched pharmacy databases to identify patients who received gentamicin on the antepartum unit from January 2002 to January 2006
- Used medical record number to obtain patient charts and had medical records personnel identify baby by birth record in mother's chart
- Reviewed both mother and baby charts for audiology results and possible confounding factors such as family history, premature birth, low birth weight, birthing complications, exposure to teratogens or potentially ototoxic medications other than gentamicin both in utero and during neonatal period
- Collaborated with audiologist for data retrieval on live births and VIHA audiology statistics

Exclusion Criteria: None

Results

Table 1: Indication for Gentamicin Use n=53

Pyelonephritis/UTI	Chorioamnionitis	Other
48% (25)	31% (16)	21% (11)

Figure 1: Pregnancy Outcomes

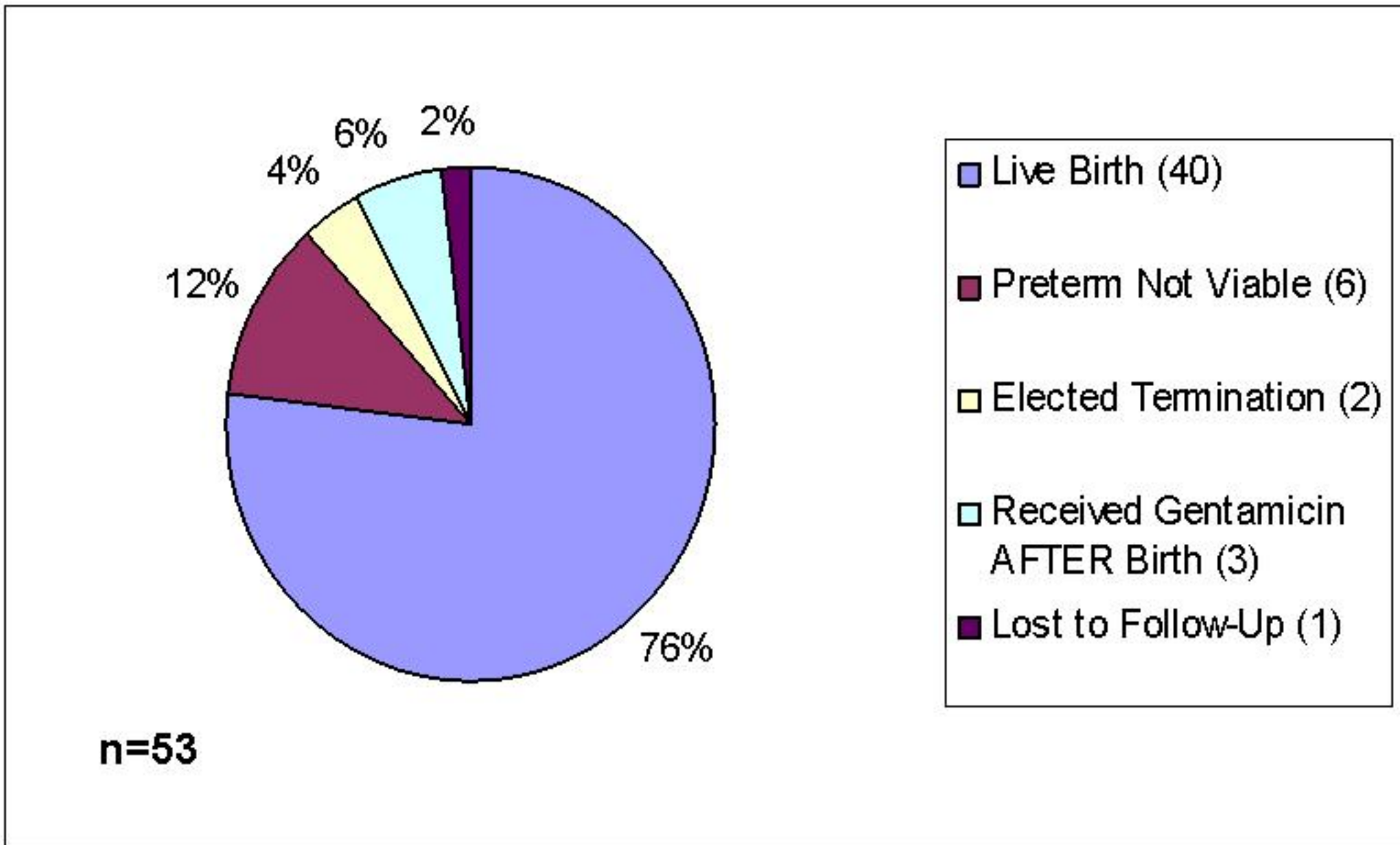
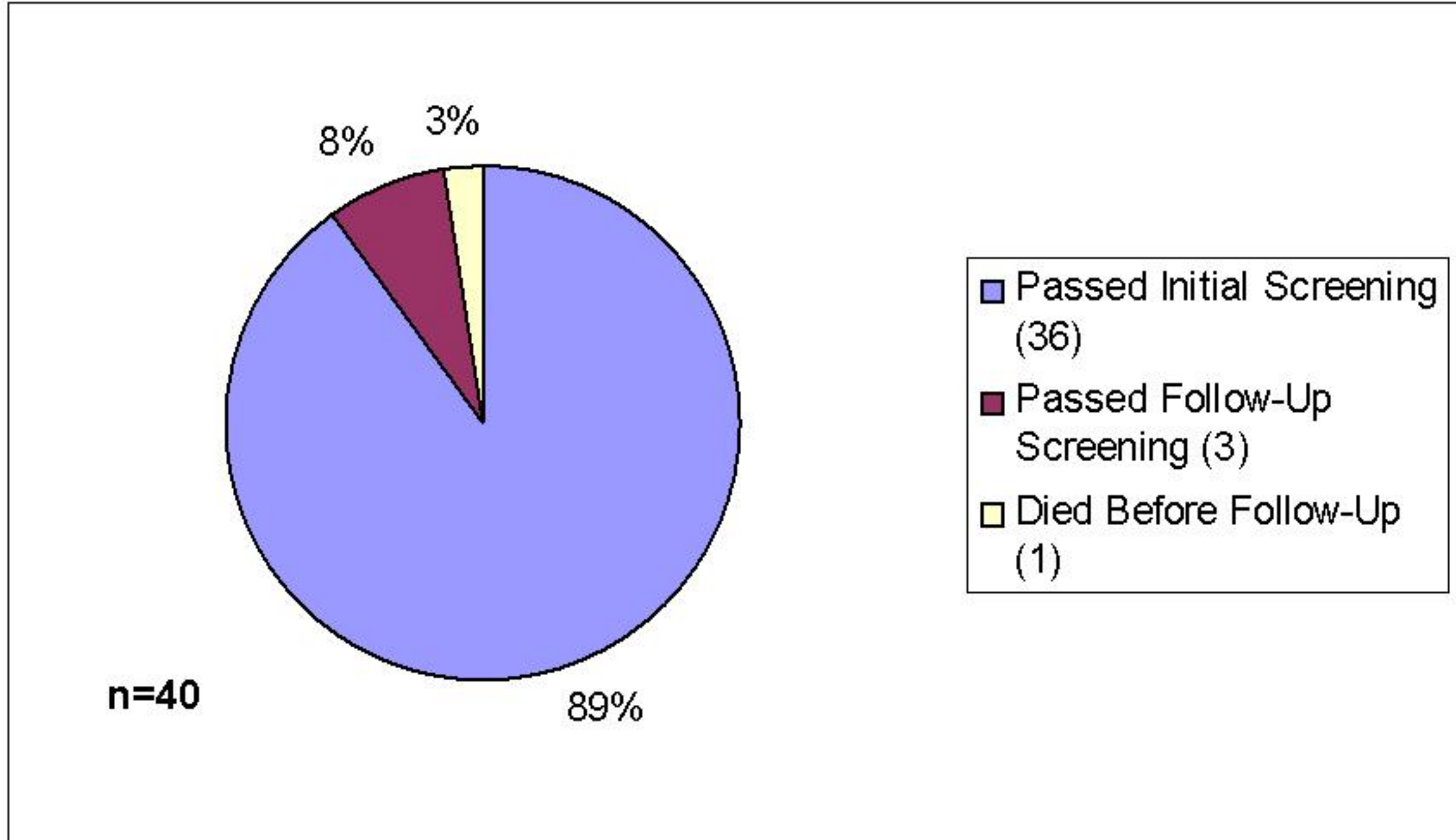


Figure 2: Primary Outcome – Audiology Results



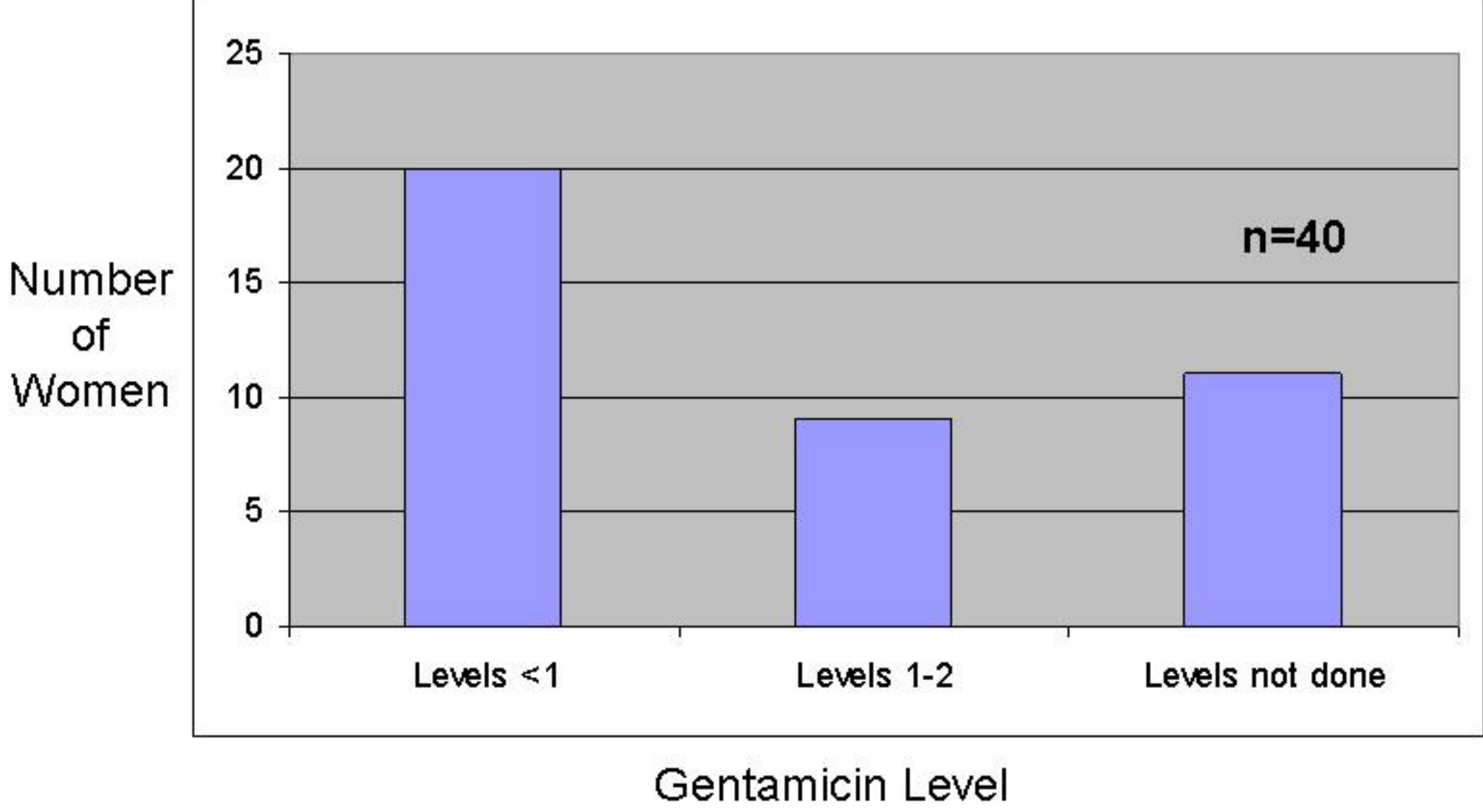
All gentamicin exposed infants PASSED their audiology tests

Table 2: Selected Secondary Objectives n=40

Mean Dose of Gentamicin	764 mg ± 600 mg
Mean Duration of Gentamicin Therapy	2.7 days ± 2.3 days
Mean Gestational Age at Exposure	28 weeks ± 6 weeks
Mothers Who Received Concomitant Potentially Ototoxic Medication	17.5% (7)
Gentamicin Serum Levels Obtained	72.5 % (29)
Mean Gestational Age at Birth	36 weeks ± 4 weeks
SCN Admission Required	30% (12)
Neonates Who Received Potentially Ototoxic Medications	17.5% (7)

Results

Figure 3: Maternal Serum Gentamicin Trough Levels



Discussion

•Three babies did not pass **initial** screening but went on to successfully complete follow up screening

•All three cases involved other confounding factors

•Baby #1 – born at 27 weeks; mother received additional potentially ototoxic medication (indomethacin 100 mg rectally, then indomethacin 25 mg po x 4 doses at 23 weeks gestation, and another indomethacin suppository at 26 weeks gestation); baby received gentamicin 2.3 mg iv q 24 h x 6 doses

•Baby #2 – born at 26.6 weeks and received gent 3.2 mg iv q 48 h x 5 doses and furosemide 2 mg iv x 2 doses

•Baby #3 – born at 38 weeks, otherwise healthy; mother had 3 courses of gent (total exposure of 2700 mg over 10.3 days) and one trough level between 1 and 2

•In order to show increase in hearing deficits due to in-utero gentamicin exposure from 5 in 1000 (North American average) to 7 in 1000 with 80% power and an alpha of 0.05, would need to study 11,629 women exposed to gentamicin during pregnancy

•Assuming gentamicin used in 0.005% of all pregnancies (current VIHA pattern), and Canada's birth rate remains stable at 337,856 births annually (2004-2005 data) would need 7 years of births to obtain 11,629 in utero gentamicin exposures

Conclusions

•Impossible to prove beyond reasonable doubt that gentamicin safe in pregnancy from ototoxicity perspective

•Pregnancies with infections severe enough to warrant the use of gentamicin are by nature complicated; 11.5% of pregnancies in this study ended in unplanned fetal demise

•When using gentamicin in pregnancy, must consider potential risks versus benefits to both mother and fetus

•Whenever possible, avoid repeated courses of gentamicin and concurrent ototoxic medications during pregnancy and neonatal period