**Investigation of factors involved in pathogenesis through case-control studies**

## TO DO: Practical activities. Case-Control Study.

### Aim and utility of this practical activity:

* To achieve the research protocol of the case-control study after a proposed scenario
* Analyzing data and presenting the obtained results
* Statistical and clinical interpretation of the obtained results

### Proposed scenario:

We assume that we have conducted a study on premature infants registered at public hospitals in Cluj-Napoca between December 2015 and December 2016 to identify the risk factors for neonatal sepsis. The data required for the study were collected from the medical records of newborns enrolled in the study. Two groups of subjects were compiled in the study: a sample of 100 preterm infants with clinically confirmed sepsis and a control group (116 premature neonates without sepsis).

*The inclusion criteria for cases were:*

* premature infants registered at pediatric or neonatal intensive care units of public hospitals in Cluj-Napoca with at least one of the clinical features: fever (≥37.5 ° C) or hypothermia (≤ 35.5 ° C), rapid breathing (≥ 60 breaths per minute), severe chest retraction, movements only when stimulated, seizures, lethargy or unconsciousness and
* at least 2 haematological criteria: total white blood cells (<4000 or >12000 cells/m3), absolute neutrophil number (<1500 cells/mm3 or >7500 cells/mm3), erythrocyte sedimentation rate (>15/1h), number of platelets( > 440 cells/m3) .

*The inclusion criteria for controls were:*

* premature infants who did not meet the criteria for sepsis and who were registered at neonatal pediatric or intensive care units of public hospitals in Cluj-Napoca

*Exclusion criteria:*

* newborns with congenital immune diseases or congenital malformations or those receiving immunosuppressive therapy

The data is available in the BD\_CMro.xlsx file available on the discipline's website: <https://www.info.umfcluj.ro/ro>

**Clinical question**: Does the *presence of chorioamniotitis* (= infection that occurs in the pregnant woman and which consists of the infection of the chord and amniotic fluid ->the membranes that surround the fetus) is *associated with neonatal sepsis in preterm newborns*?

* + 1. **Research protocol**
  1. Write the aim and objectives associated with this study:

**Aim:**

**Objectives:**

* 1. Write the research domain of this study:

### Domain of research:

* 1. Study type based on:

**Study type based on study objectives:**

**Study type according to the results:**

**Study type according to the technique used in the choice of groups:**

### What was the accessible population of this study?

#### **Accessible population:**

#### Describe the study sample:

##### **Study sample:**

##### *Inclusion criteria*

Demographics:

Clinical features:

*Exclusion criteria (applied to subjects meeting the inclusion criteria may be missing)*

Factors that induce errors (coexisting diseases / concomitant treatments):

Side effects:

Factors that make it difficult / impossible to obtain data:

Ethical issues:

The size of the sample:

6. Is the size of the selected sample sufficient? Respond to this considering that at an OR =3, a 13% chorioamniotitis frequency is in the control group, the study power of 80% and a control/case ratio = 1: 1 the estimated size (cases + controls) is 188 subjects (the Epiinfo program, the STATCALC option) can be used as a program for estimating the sample size.

#### **Is the size of the sample sufficient? (yes/no):**

7.Write the data collection method:

**• Based on the studied population:**

**• Based on the duration of data collection:**

**• Based on the grouping method:**

### Write the name and type of the variables measured in the study sample:

|  |  |  |  |
| --- | --- | --- | --- |
| **A. Qualitative** |  | |  |
| * Nominal | * Ordinal | | * Nominal dichotomial |
| **B. Quantitative** | | | |
| * Continuous | | * Discrete | |

1. Write the method you will use in the description of the data (variables) in the sample:

|  |
| --- |
| **Qualitative variables** (described by frequency table or sectoral graph, column / bars) |
|  |
| **Quantitative variables -**described by: 1) synthetic indicators in the format: mean ± standard or median deviation and quartile interval: median (quartile of order1; 3rd order quartile]; or 2) histograms - for distribution description, or 3) graph plot for normally distributed variables or 4) graph box and wiskers (box plot) for non-normal distributed variables |
|  |

1. Write the statistical method you will use in describing the association between neonatal septicemia and chorioamniotitis:

|  |
| --- |
| **Qualitative variables** (described by frequency table, sectoral graph, column / bars) |
|  |

1. Write the inferential statistic method that you will use in testing the association between neonatal septicemia and corioamniotitis:

|  |
| --- |
| **Qualitative variables** (independent groups: Chi Square Test if at least 80% of the theoretical frequencies are > 5, otherwise: Fisher's exact test, dependent groups: McNemar test) |
|  |

1. Write the medical indicator (relevant for the sample / study population) you will use to quantify the association between neonatal septicemia and corioamnotitis:

|  |
| --- |
| **Point estimator (95% confidence interval):** |

## Obtained results. Data analysis and presentation

### Perform the frequency table for chorioamniotitis (use EpiInfo – Frequencies – Frequencie of)

Table 1. Distribution of the chorioamnotitis on the study sample

**Perform a sectorial graph for neonatal sepsis (use EpiInfo – Graph - Pie, Main variable):**

Fig.1. Distribution of neonatal sepsis in the sample

**Table of contingency between risk factor and disease (use EpiInfo - Tables):**

Table 2. Distribution of the chorioamnotitis in cases versus controls

**Column Chart for the link between risk factor and illness (use EpiInfo – Graph – Bar, Main variable – exposure variable, Count %, Bar for each value or – dependent variable):**

Fig.2. Distribution of chorioamniotitis in cases versus controls

***Calculate the OR*** *(OR-cross product) and the associated confidence interval (from EpiInfo in the format: point estimator (95% CI lower limit-upper limit) - for details see examples Interpretations)*

**Find the value of p** (in EpiInfo - in the format: p = value - the name of the test used, with a maximum of 3 decimal places, if p <0.001 then write p <0.001):

## Data interpretation:

### 1. Interpreting the results from a statistical point o view:

Null Hypothesis:

Alternative hypothesis:

Rejected Null Hypothesis (yes/no). Explain why.

Point estimator interpretation (OR):

Interpretation of the confidence interval of 95% for OR:

### 2. Interpreting the results from a clinical point of view:

Point estimator (OR) size in clinical context (very important / moderate / minor)

The accuracy of the result based on confidence interval width (broad range - imprecise results, narrow range - accurate results)

Interpretation of confidence interval from a clinical point of view (clinically relevant relationship if both ends are of clinically significant value, relatively small, clinically relevant if both ends are of minor importance or clinically unclear link if one end of IC has significant clinical value and the other is not important).

## Take home messages

**How do we recognize a case-control study?**

*- grouping of subjects is based on the presence / absence of the disease*

*- are observational studies*

*- can demonstrate the link of dependece/association between factor and disease but can not prove causality*