مركز الامراض الوراثية والايض
Genetic & Metabolic Diseases Center

جامعة القدس
Al-Quds University

# A Pilot Study on an Expanded Newborn Screening Program in Palestine. Phaseп

Genetics and Metabolic Diseases Center
Faculty of Medicine/Al-Quds University
**Samir Khatib, PhD**
**Amer Ayyad,MSc**

# Outline

1- Background & Introduction

2-Justification of the study

3-Research Objectives

4-Methodology

5-Results

6-Conclusion


Mediterranean Sea
Quneitra
GOLAN HEIGHTS
WEST BANK
Tel Aviv
Jericho
Ramalah
Jerusalem
Ashkelon
Beit Lahia
Hebron
GAZA STRIP
Gaza
Rafa
ISRAEL
Suez Canal
JORDAN
EGYPT
SINAI

# PALESTINE

مركز الامراض الوراثية والايض
Genetic & Metabolic Diseases Center

جامعة القدس
Al-Quds University

# Background

Population : 4.5 million.

61% West Bank, 39% Gaza

Birth Rate : 25.9/1000.

Screening Program began in 1994.

Tests done since then for PKU and CH only.

Methodology of testing for Phe and TSH : ELISA.

مركز الامراض الوراثية والايض
Genetic & Metabolic Diseases Center

جامعة القدس
Al-Quds University

# Background …..

**Statistics for 2013 (MoH):**

PKU 63,430 samples
21 positive

TSH 57,607 samples
27 positive

مركز الامراض الوراثية والايض
Genetic & Metabolic Diseases Center

جامعة القدس
Al-Quds University

# Background …..

## Positive Experience:

1. **Government commitment.**
2. **Public awareness.**
3. **Coverage nearly 100%.**

مركز الامراض الوراثية والايض
Genetic & Metabolic Diseases Center

جامعة القدس
Al-Quds University

# Background …..

**Constraints:**

1. Government  priorities.
2. Financial burdens.
3. Limited resources.
4. Lack of data.
5. Limited management/treatment .

# Introduction

At the present day there are not enough data available on metabolic and genetic diseases that are found within the Palestinian population. As indicated earlier, newborns in Palestine are being screened for phenylketonuria  and congenital hypothyroidism only by measurement of Phe and TSH levels, respectively. However, a number of other metabolic diseases have been recognized amongst the population, including amino acids, organic acids and fatty acids disorders.

# Justification of the study

The present study (Phase II) was conducted in an effort to investigate the possibility of finding four main types of organic acidemias (MMA, PA, GA1, and IVA) in newborns throughout the West Bank of Palestine by screening newborns for a number of acylcarnitine profiles that are associated with these disorders. In previous phases (I and III) of the study some amino acids and fatty acid oxidation intermediates levels were examined in blood samples of newborns.

# Research Objectives

*To assess the expanded screening tests among newborns of Palestine.

*To investigate the relationship between some demographic variables such as gender, kinship, district, and weight with three acylcarnitine levels.

*To establish the reference ranges for three acylcarnitines associated with the four main types of organic acidemias for the Palestinian newborns.

# Methodology

## *Study Design, Setting, Sample Selection, and sample analysis

A cross-sectional observational study design was done. The study covered all 12 districts of the West Bank in Palestine during the period between January 2012 and January 2013 where 4240 newborn blood samples were collected . Convenience sampling was used to recognize study participants of newborns. A pilot study was conducted before the actual study took place. Informed consent was taken from each parent participant. Analysis of acylcarnitine concentration in the samples was performed using tandem mass spectrometry (MS/MS) .

# *Data collection method

**Participating groups in the study and their respective roles**

**1 - The Palestinian Ministry of Health**

Provided health information for this study, in addition to collection of 80 samples from all the districts on a weekly basis for the duration of the study(one year).

**2 – Liege University/ Human Genetics Department, Belgium**

Its role was primarily to receive, analyze and send results for the collected samples to GMDC at Al-Quds University. Sample analysis was done by tandem MS/MS.

**3 - GMDC/ Al-Quds University**

A)Coordinated with the Palestinian MoH and Liege University.

B)Accumulated and analyzed all data for each collected and tested card .

# *Data Analysis

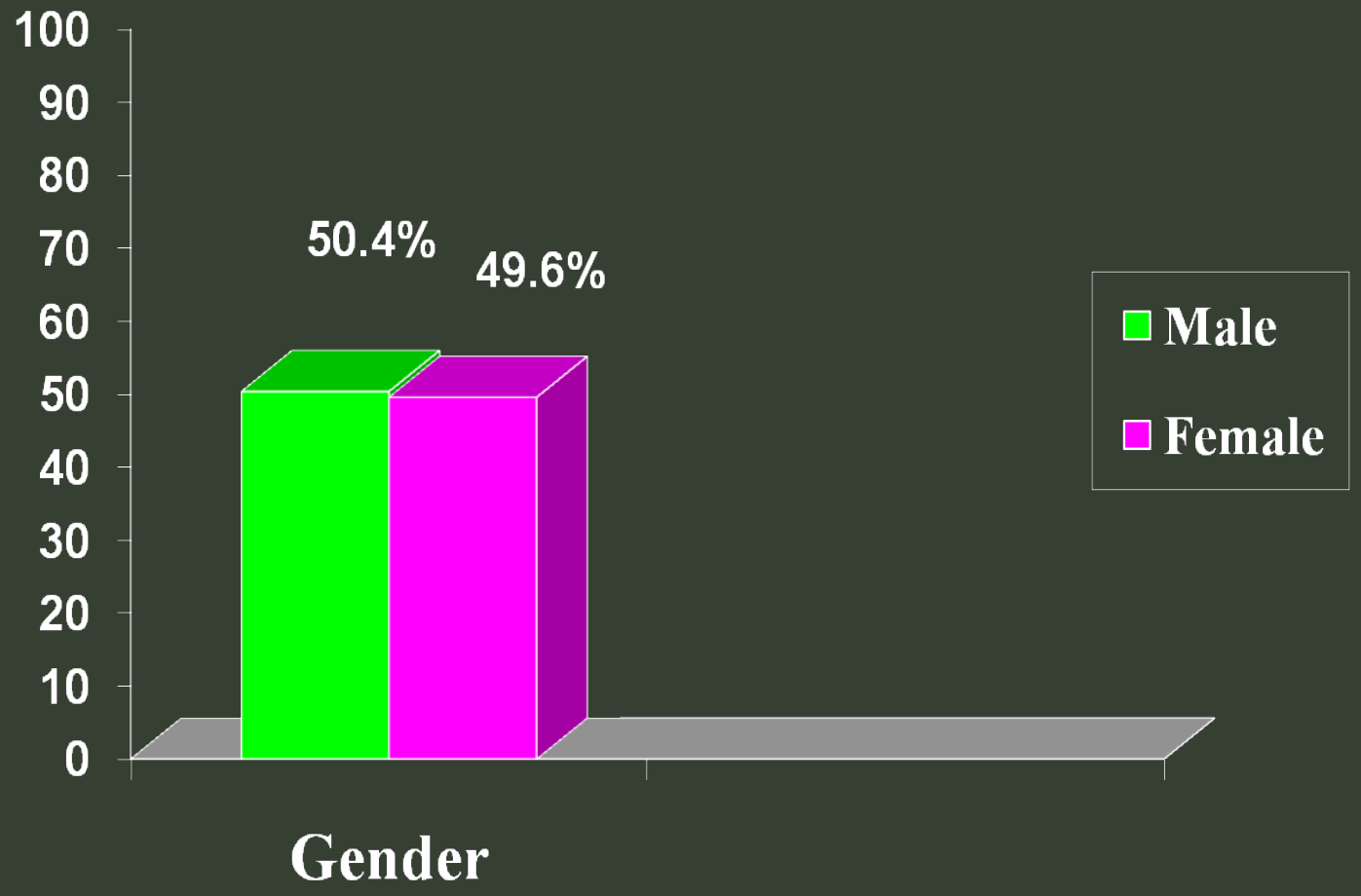
Statistical Package for Social Sciences (SPSS version 20) was used.

The reference range for each acylcarnitine level **(C3,C5-DC,C5)** was calculated based on the non- parametric percentile method **(CLSI (C28-A3)*).** Statistical relation between acylcarnitine levels and some of the demographic variables such as gender, kinship, weight, and district were examined by different statistical methods. P-values were considered statistically significant at **(P=<0.05)**.

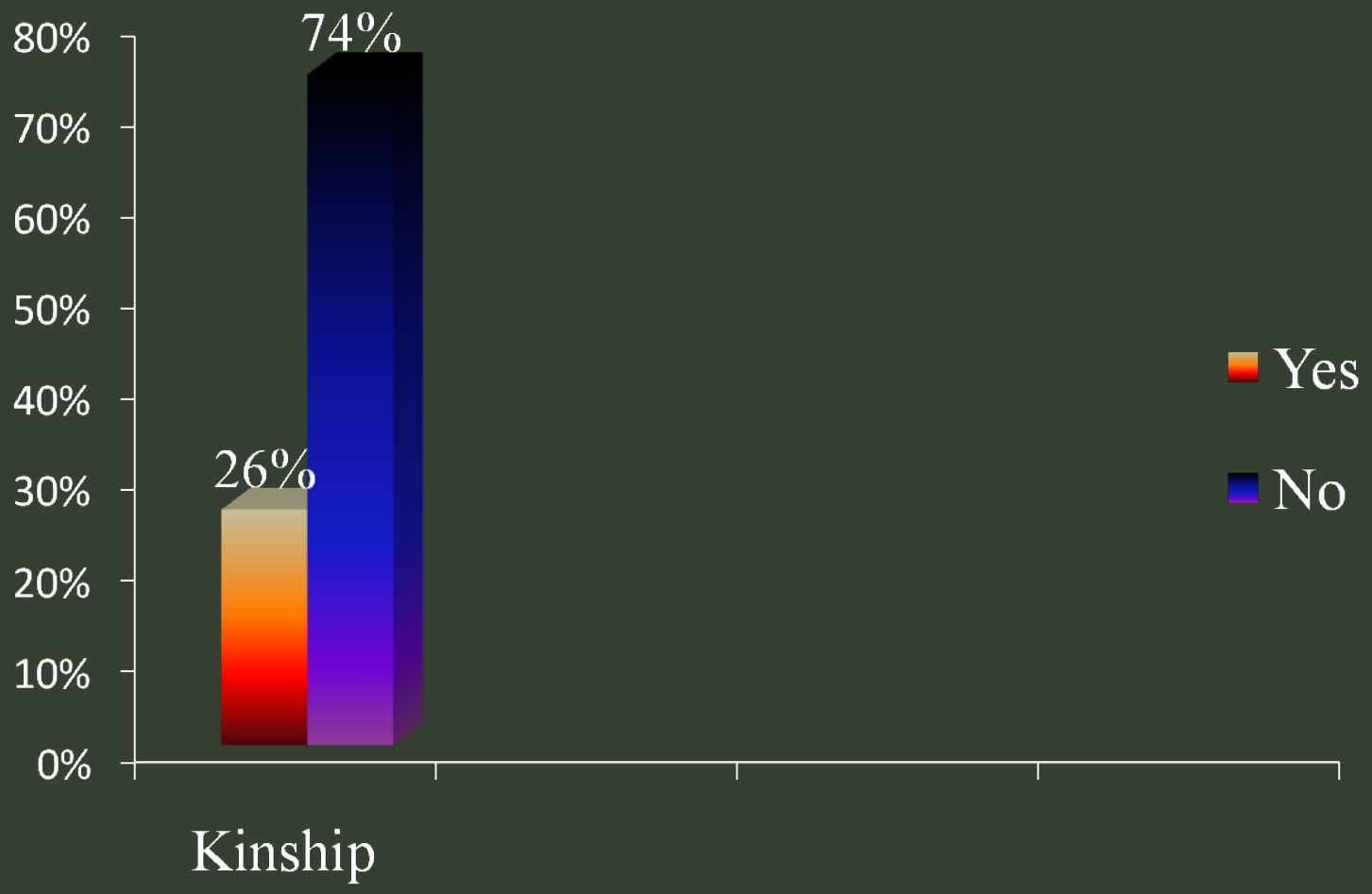
***Clinical and Laboratory Standards Institute, *Approved Guideline—Third Edition* (C28-A3), 2008.**

# Results

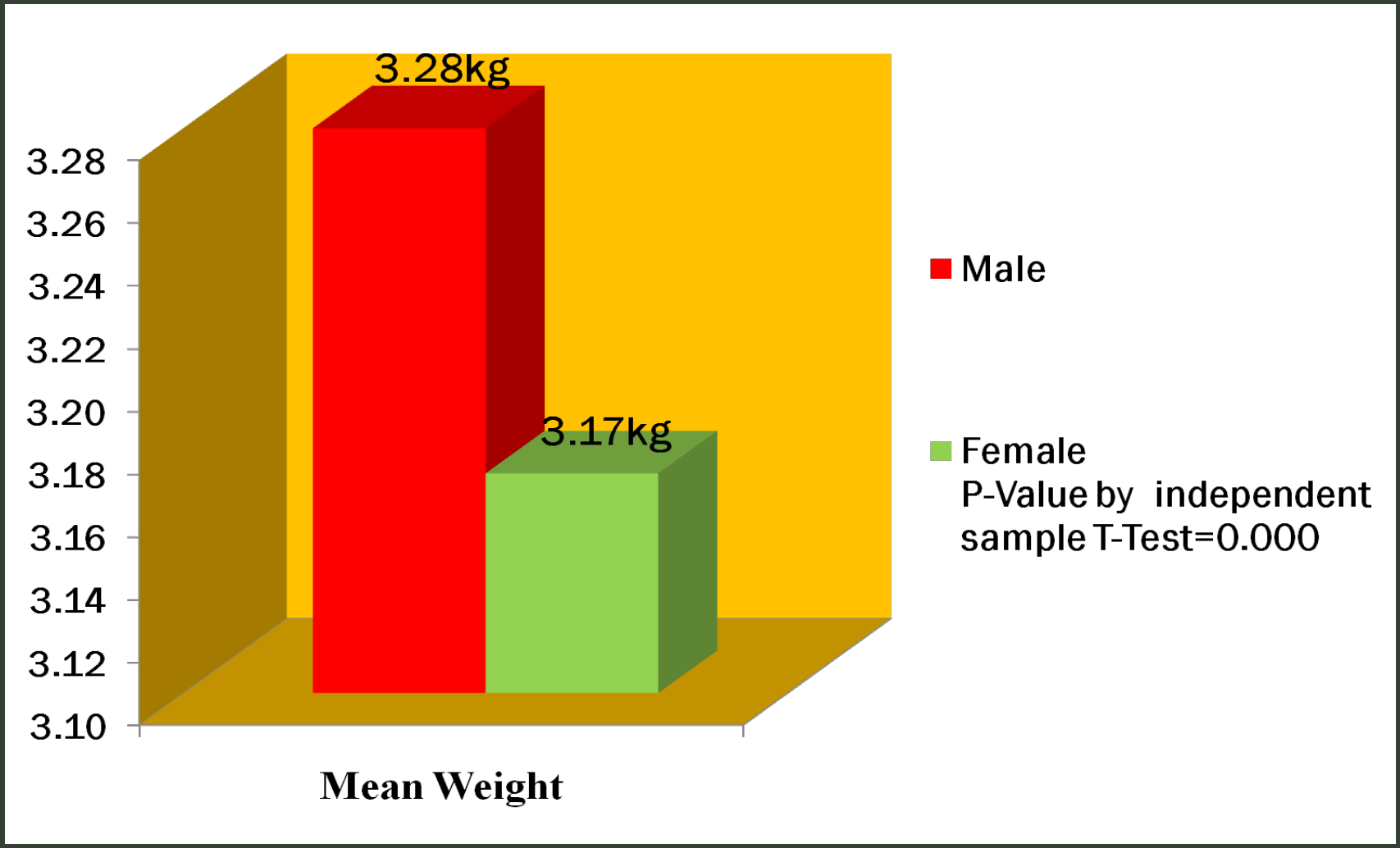
# Distribution of Newborns by Gender



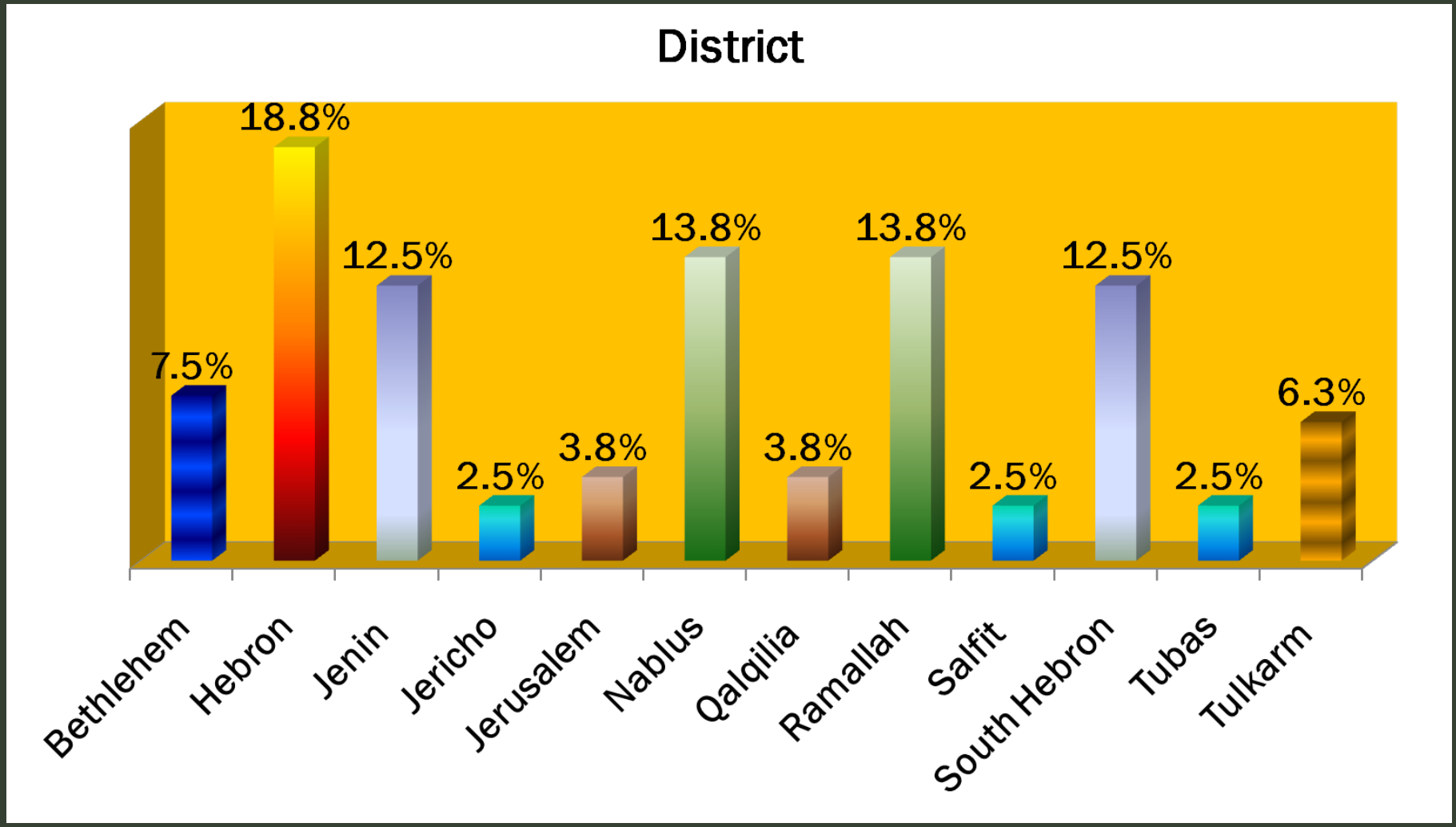
# Distribution of Newborns by Kinship



# Differences in the mean weight by Gender



# Distribution of Newborns by District



# Normal values for Acylcarnitines as provided by Liege University/Human Genetics Department

| Acylcarnitine | Normal value |
|---|---|
| C3-carnitine | <4.35 |
| C5-DC-carnitine | <0.56 |
| C5-carnitine | <0.85 |

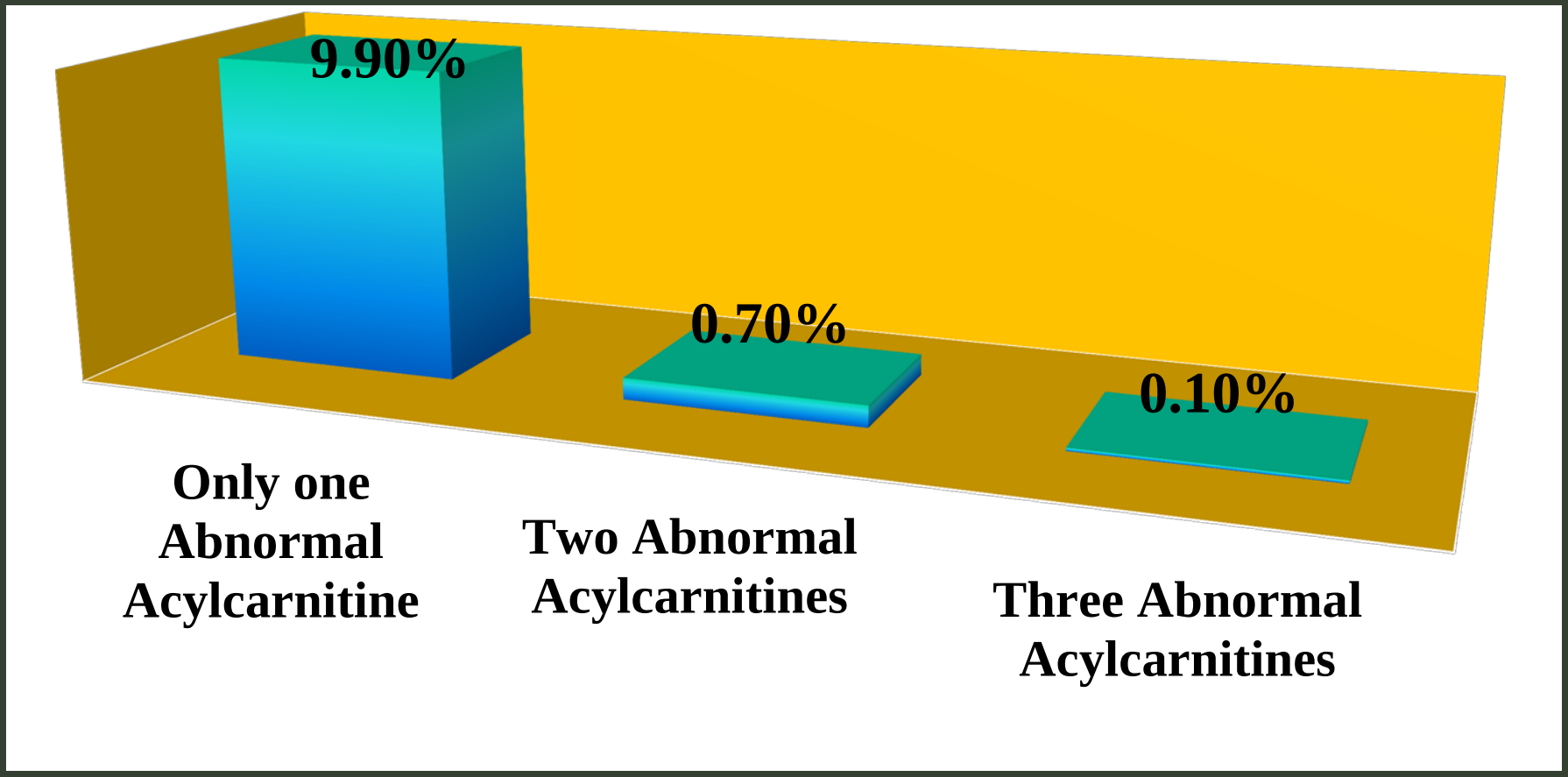
# Reference range of Acylcarnitines based on the Non- parametric percentile method CLSI (C28-A3)

| Acylcarnitine | Lower limit(µmol/L) | Upper limit(µmol/L) | Mean | Std. Deviation |
|---|---|---|---|---|
| C3-carnitine | 0.35 | 2.61 | 1.15 | 0.59 |
| C5-DC-carnitine | 0.05 | 0.26 | 0.13 | 0.05 |
| C5-carnitine | 0.10 | 0.41 | 0.21 | 0.08 |

# Distribution of Newborns by Acylcarnitine levels (Normal & Abnormal)

| Acylcarnitine | Normal | | Abnormal | | Total | |
|---|---|---|---|---|---|---|
| | Count | Row N % | Count | Row N % | Count | Row N % |
| C3-carnitine | 4078 | 96.2% | 161 | 3.8% | 4239 | 100% |
| C5-DC-carnitine | 4081 | 96.3% | 158 | 3.7% | 4239 | 100% |
| C5-carnitine | 4066 | 95.9% | 173 | 4.1% | 4239 | 100% |

# Distribution of Newborns by Different Status of Abnormal Acylcarnitine Levels



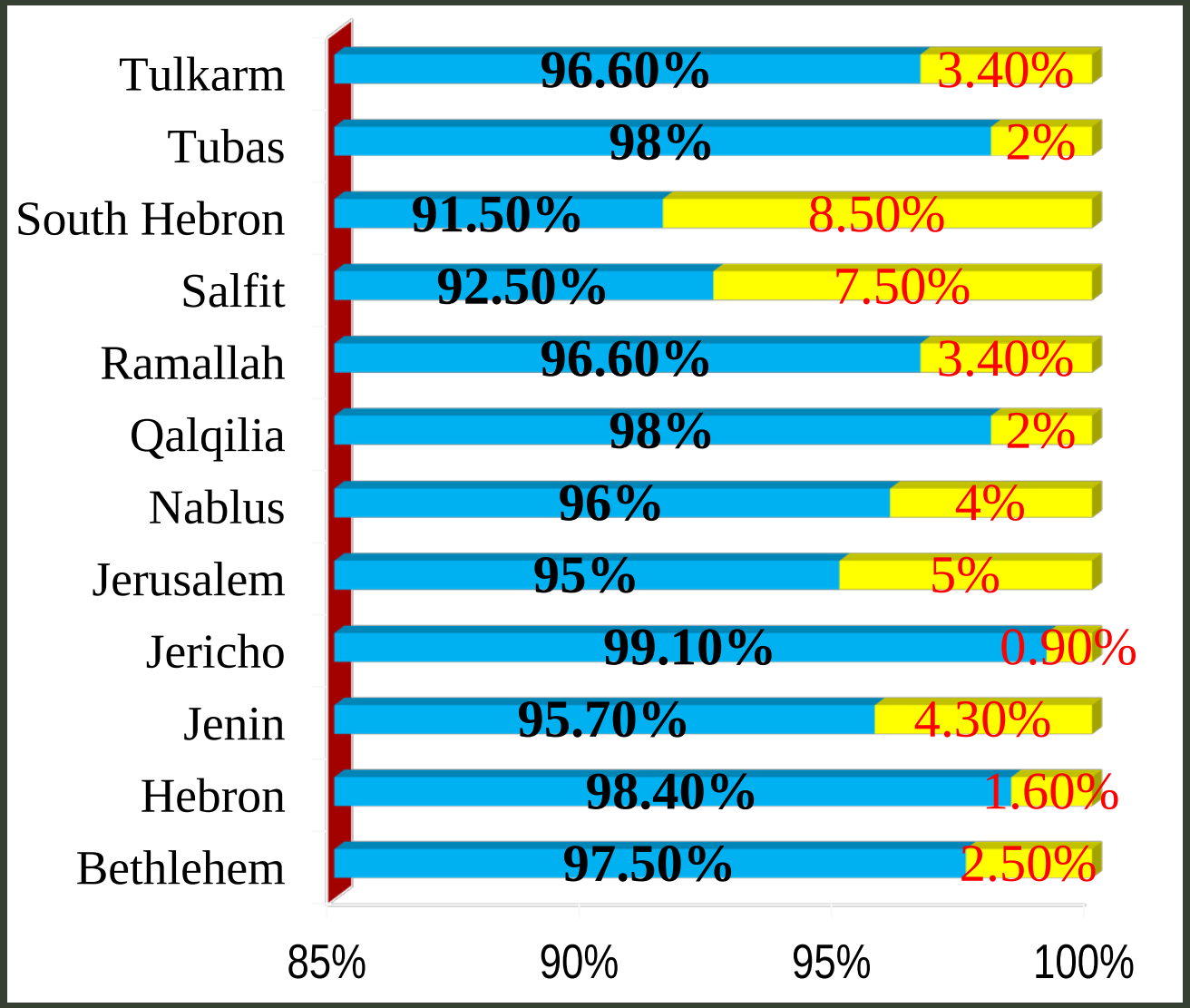
# Relationship between Gender and Mean Acylcarnitine Levels

| Acylcarnitine | Gender | N | Mean | Std. Deviation | Std. Error Mean | P-Value by independent sample T-Test |
|---|---|---|---|---|---|---|
| **C3-carnitine** | Female | 2135 | **1.22** | 0.78 | 0.02 | |
| | Male | 2104 | **1.17** | 0.66 | 0.01 | **0.029** |
| **C5-DC-carnitine** | Female | 2135 | **0.138** | 0.07 | 0.00 | |
| | Male | 2104 | **0.13** | 0.06 | 0.00 | **0.002** |
| **C5-carnitine** | Female | 2135 | **0.21** | 0.10 | 0.00 | |
| | Male | 2104 | **0.22** | 0.10 | 0.00 | **0.112** |

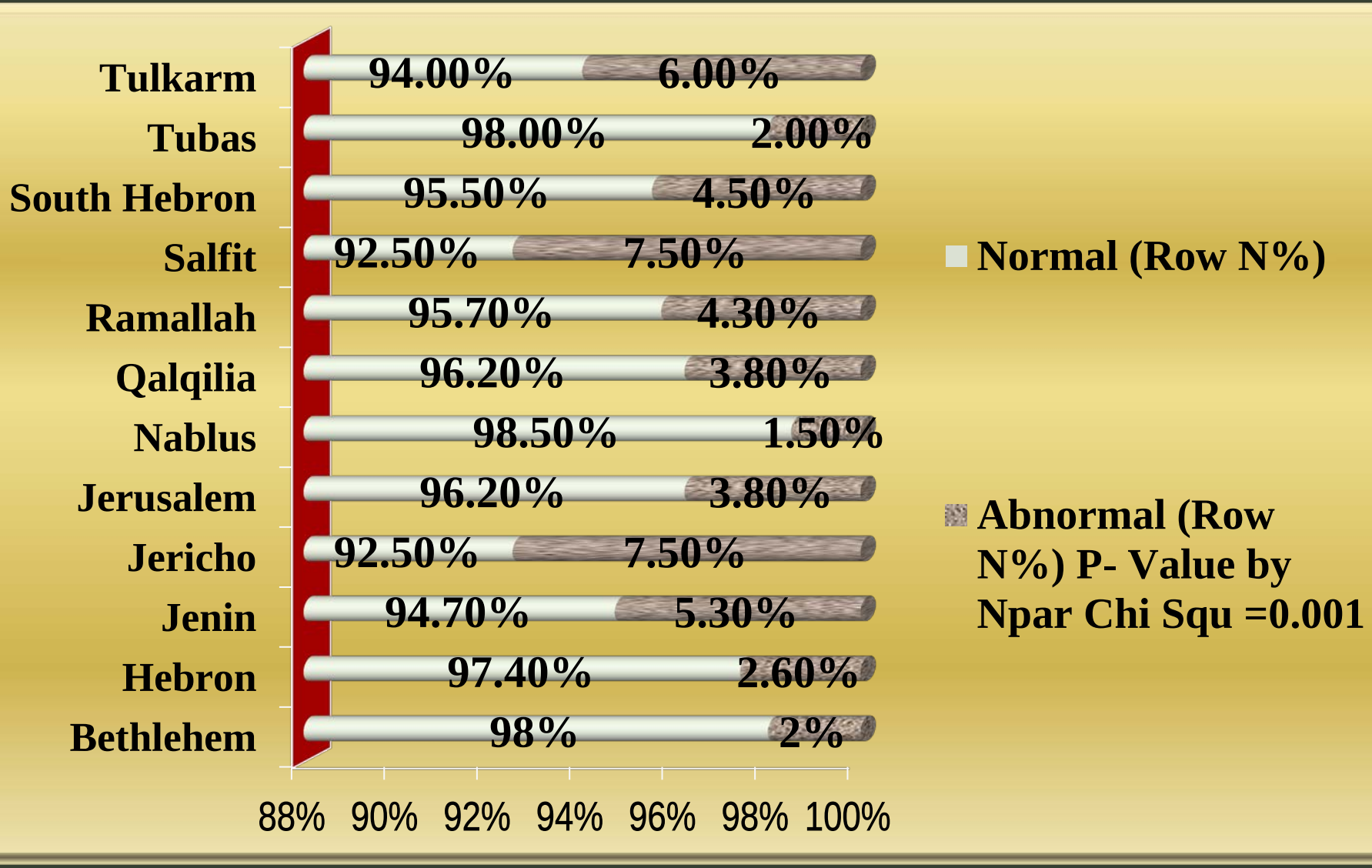
# Relationship between Mean Weight and Acylcarnitine Levels

| Acylcarnitine | Status | N | Mean Weight | Std. Deviation | Std. Error Mean | P-Value by independent sample T-Test |
|---|---|---|---|---|---|---|
| **C3-Carnitine** | Normal | 4077 | **3.2269** | 0.48797 | 0.00764 | |
| | Abnormal | 161 | **3.3102** | 0.51350 | 0.04047 | **0.034** |
| **C5-DC-Carnitine** | Normal | 4080 | **3.2336** | 0.48583 | 0.00761 | |
| | Abnormal | 158 | **3.1403** | 0.56295 | 0.04479 | **0.019** |
| **C5-Carnitine** | Normal | 4065 | **3.2312** | 0.48690 | 0.00764 | |
| | Abnormal | 173 | **3.2034** | 0.54053 | 0.04110 | **0.463** |

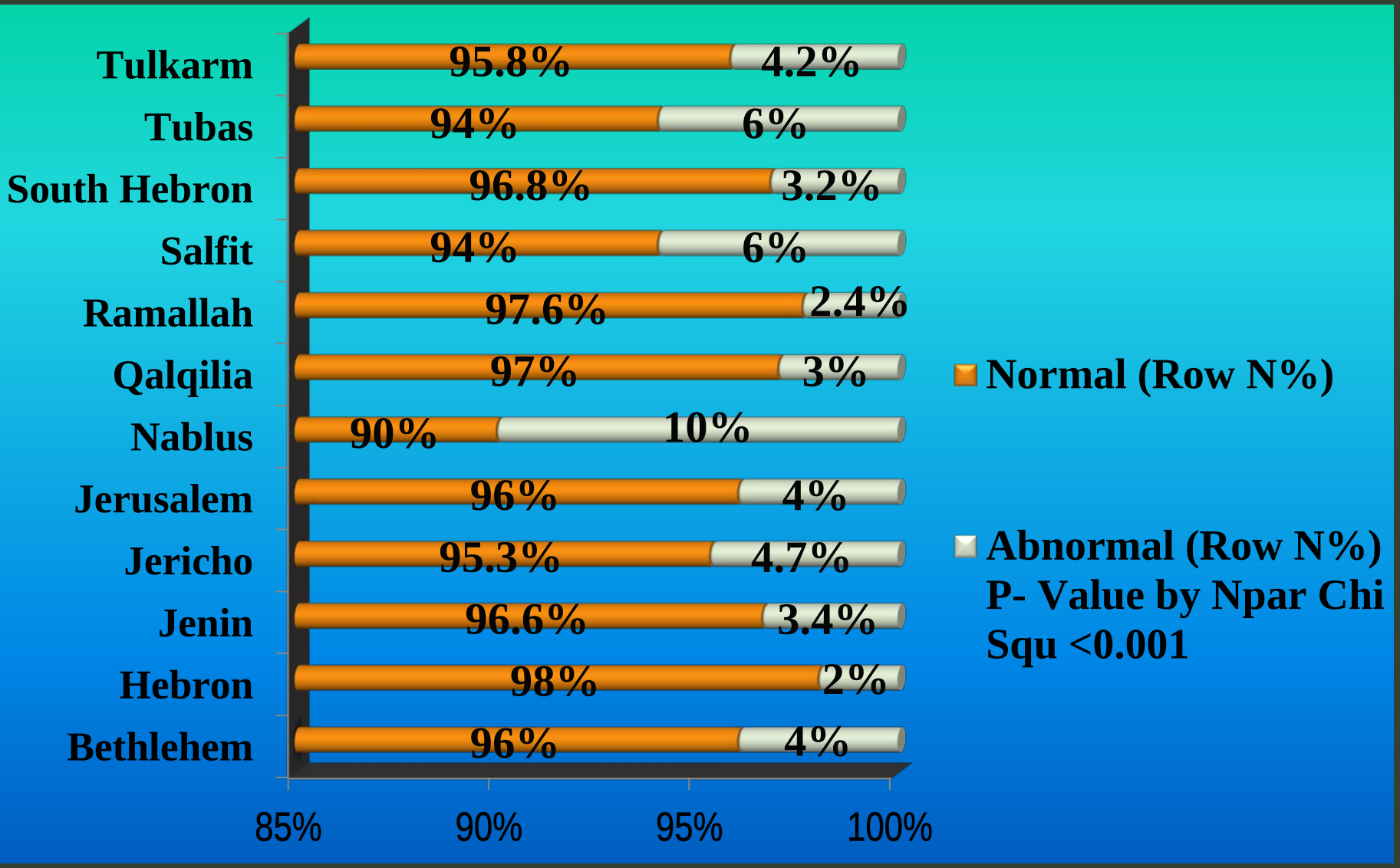
# Relationship between District and C3-carnitine Level



# Relationship between District and C5-DC-carnitine Level



# Relationship between District and C5-carnitine Level



# Conclusion

* Based on our established reference ranges for each analyte the results showed that 10.7% of the tested samples (455) had at least one acylcarnitine level in the upper 2.5% of the population.

* There is a significant relationship between mean weight and gender.

* There is a significant relationship between mean weight and most acylcarnitine levels.

* Neither gender nor kinship had any effect on the acylcarnitine levels, but there is a significant difference between most acylcarnitine levels mean and gender.

* There is a significant difference between districts and acylcarnitine levels.

* The study results support further assessment of the need to expand the existing newborn screening program in Palestine.

مركز الامراض الوراثية والايض
Genetic & Metabolic Diseases Center

جامعة القدس
Al-Quds University

# Acknowledgment


1. **Liege University / Human Genetics Department**

   **Prof V Bours, Dr R Schoos and Dr F Boemer**

2. **Palestinian Ministry of Health**