# Serum Resistin Hormone In Protein Energy Malnutrition

***A THESIS***

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# نسبة هرمون الرزيستين في مصل دم الأطفال المصابة بسوء التغذية

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# Abbreviations

| | |
|---|---|
| ADSF | Serine/cysteine-rich adipocyte-Specific Secretory Factor" |
| ANG II | Angiotensinogen II |
| ARI | Acute respiratory infection |
| ASO | Antisense oligodeoxynucleotide |
| BMI | Body mass index |
| BN | Bulimia nervosa |
| CCAT | Calcium channel associated transcription regulator |
| CHI | Creatinine height index |
| C/EBP a | Enhancer-binding protein alpha |
| DM | Diabetes mellitus |
| CR | calorie restriction |
| ELISA | Enzyme-Linked Immunosorbent Assay |
| ET1 | Endothelin 1 |
| FA | Fatty acids |
| FFA | Free fatty acids |
| FAA | Free amino acids |
| FIZZ | Tissue-specific cytokines (found in inflammatory zones) |
| GH/IGF-I | Growth hormone/ Insulin like growth factor I |
| GLUT4 | Glucose transporter 4 |
| HDL | High-density lipoprotein -cholesterol, |
| HC | Head circumference |
| HOMA | Homeostasis model assessment |
| ICAM1 | Intracellular adhesion molecule-1 |
| IGFs | Insulin-like growth factors |
| IRS-1 | insulin receptor substrate 1 |
| IL-6 | Interleukin-6 |
| KWO | Kwashiorkor |
| MAC | Mid-arm circumference |
| M-CSF | Macrophage colony stimulating factor |
| mRNA | Messenger RNA |
| NCHS | American National center for health statistics |
| NFκB | Nuclear factor kappa B |
| NO | Nitric oxide |
| ORS | Oral rehydration solution |
| PAI-1 | Plasminogen activator inhibitor-1 |
| P. | Protein expression |
| PEM | Protein energy malnutrition |

| | |
|---|---|
| PI3K | Phosphatidylinositol-3-kinase |
| PKA | Protein kinase A |
| PKC | Protein kinase C |
| PMNG1 | Parasite induced Macrophage ± Novel. Gene 1 |
| PPARγ | Peroxisome proliferator-activated receptor γ |
| P-AN | Binge/purge subtype of anorexia nervosa |
| RBP | Retinol-binding protein |
| Retn | Human resistin gene |
| RELMs | Resistin like molecules |
| RT-PCR | Reverse transcription polymerase chain reaction |
| RV | Reference values |
| R-AN | Restrictive subtype of anorexia nervosa |
| SAA | Serum amyloid A |
| S.C | Subcutaneous |
| SFT | Skin fold thickness |
| SGA | Small for gestational age |
| SNP | Single nucleotide polymorphisms |
| SOCS-3 | suppressor of cytokine signaling 3 |
| SSCP | Single-stranded conformation polymorphism |
| sTNFR-p55 and sTNFR-p75 | Soluble receptors of tumor necrosis factor alpha |
| TBPA | Thyroxin-binding pre-albumin |
| TLC | Total leucocytic count |
| TNF-α | Tumor Necrosis Factor-α |
| TRF | Transferrin |
| TRAF3 | Receptor-associated factor-3 |
| TZD | Thiazolidinediones |
| VCAM1 | Vascular cell-adhesion molecule-1 |
| WHO | World Health Organization |
| Wt/Ht | Weight for height |

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# *INTRODUCTION AND AIM OF THE WORK*

Protein Energy Malnutrition (PEM) is the most deadly form of malnutrition. It is the primary or associated cause of around half of the nearly 11 million annual deaths among children under five, 30 000 each day **(Brundtland, 2005).**

Deficiency of a single nutrient is an example of under nutrition or malnutrition. Protein/energy malnutrition (PEM), for example, is manifested by inadequate dietary intake of protein and energy, either because the dietary intakes of these two nutrients are less than required for normal growth or because the needs for growth are greater than can be supplied by what, otherwise would be adequate intake for growth. however, PEM is almost always accompanied by deficiencies of other nutrients **(Heird, 2004)**

Malnutrition in general and dietary protein deprivation in particular are characterized in humans by a low basal plasma insulin together with low glucose levels **(Picarel-Blanchot et al ,. 1995).**

Resistin is a hormone secreted by adipose tissue. Among the hormones synthesized and released from adipose tissue (adiponectin, angiotensin, estradiol, IL-6, leptin, PAI-1, TNF-α, and resistin) **(Adeghate , 2004)**. Resistin is an adipocytokine that may link obesity with insulin resistance and diabetes. **(Steppan et al., 2001)** reported serum resistin levels to be elevated in obese mice and to be decreased by thiazolidinediones. They also showed that administration of antiresistin antibodies improved insulin sensitivity. However, subsequent studies produced disparate findings regarding the role of resistin in obesity and insulin resistance **(Way et al., 2001)**. Although serum resistin levels were

reported to be elevated in obese **(Azuma et al., 2003)**, and diabetic patients **(Zhang et al., 2003, Fujinami et al., 2004)** conflicting results were also presented **(Silha et al.,2003)**.

plasma concentrations of several mediators of the inflammatory cascade. (interleukin 6 (IL-6), C-reactive protein, and the soluble receptors of tumor necrosis factor alpha (sTNFR-p55 and sTNFR-p75)) was found to be greater in children with PEM. particularly in those with kwashiorkor (increased inflammatory reactivity may contribute to edema formation in edematous malnutrition) **(Sauerwein et al., 1997).**

Resistin has been shown to increase expression of several pro-inflammatory cytokines including (interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-12 (IL-12), and tumor necrosis factor-α (TNF-α) in an NFκB-mediated fassion **(Milan et al., 2002, Silswal et al., 2005).**

It has also been demonstrated that resistin upregulates intracellular adhesion molecule-1, vascular cell-adhesion molecule-1 and CCL2, all of which are occupied in chemotactic pathways involved in leukocyte recruitment to sites of infection **(Verma et al., 2003)** Resistin does indeed bear features of a pro-inflammatory cytokine and could act as a key node in inflammatory diseases with or without associated insulin resistance **(Nagaev et al., 2006)**. So Resistin can be of value in diagnosis and or prognosis of PEM .

Thus Our aim of the present work is to assess the serum resistin level in infants or children with PEM, before and after rehabilitation to examine the possibilities of its use as a diagnostic and prognostic tool and whether or not it correlates to severity of PEM .

# Protein Energy Malnutrition

## Definitions :

Malnutrition is a state of decreased intake of calories or micronutrients (vitamins and trace elements) resulting in a risk of impaired physiological functions associated with morbidity and mortality (**Spiekerman, 2000**).

Protein energy malnutrition (**PEM**) is a spectrum of conditions due to varying proportions of protein and calorie deficiencies (**Curran and Barness, 2004) .**

Since several vitamin and mineral deficiencies are associated with PEM, the American authors prefer to use the term multi- deficient disease (**Brasseur et al., 1994).**

Marasmus is the most common form of PEM. It is due to severe caloric depletion and is diagnosed in the presence of clinical muscle wasting, loss of subcutaneous fat and absence of edema **(Gernaat and Voorhoeve, 2000).**

Kwashiorkor (KWO) is a clinical syndrome which results from acute deficiency of proteins and inadequate caloric intake. It is diagnosed in the presence of edema, mental apathy and one or more symptoms or signs (hepatomegaly, diarrhea, hair discoloration, skin changes and muscle wasting) (**Gernaat and Voorhoeve, 2000).**

Marasmic kwashiorkor is a combination of chronic energy deficiency with acute or chronic protein deficiency (**Gernaat and Voorhoeve, 2000).**