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The Importance of Erythrocyte Parameters in Obese Children

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***Abstract*—**Increasing prevalence of childhood obesity has increased the interest in early and late indicators of gaining weight. Cell blood counts may be indicators of pro-inflammatory states. The aim was to evaluate associations of hematological parameters, including hematocrit (HTC), hemoglobin, blood cell counts and their indices with the degree of obesity in pediatric population. A total of 249; -139 morbidly obese (MO), 82 healthy normal weight (NW) and 28 overweight (OW) children were included into the scope of the study. WHO BMI-for age percentiles were used to form age- and sex-matched groups. Informed consent forms and the Ethics Committee approval were obtained. Anthropometric measurements were performed. Hematological parameters were determined. Statistical analyses were performed using SPSS. The degree for statistical significance was $p \leq 0.05$. Significant differences ($p=0.000$) between waist-to-hip ratios and head-to- neck ratios (hnrs) of MO and NW children were detected. A significant difference between hnrs of OW and MO children ($p=0.000$) was observed. Red cell distribution width (RDW) was higher in OW children than NW group ($p=0.030$). Such finding couldn't be detected between MO and NW groups. Increased RDW was prominent in OW children. The decrease in mean corpuscular hemoglobin concentration (MCHC) values in MO children was sharper than the values in OW children ($p=0.006$ vs $p=0.042$) compared to those in NW group. Statistically higher HTC levels were observed between MO-NW ($p=0.014$), but none between OW-NW. Though the cause-effect relationship between obesity and erythrocyte indices still needs further investigation, alterations in RDW, HTC, MCHC during obesity may be of significance in the early life.

***Keywords*—**Anthropometry, children, erythrocytes, obesity.

I. Introduction

INCREASING prevalence of childhood obesity on a global scale has increased the interest in seeking some parameters, which may be the early and late indicators of gaining weight. Cell blood counts (CBCs) are components of hematological parameters and indicators of pro-inflammatory states. They seem to be associated also with metabolic syndrome (MetS) [1]. Obesity and factors related to MetS are not generally taken into account when evaluating a patient's CBC [2]. So far, white blood cells (WBCs) have been widely investigated in adults as well as pediatric populations. Red blood cell (RBC) indices have been investigated widely in adults, however, there are few studies performed on children and adolescents [1], [3], [4].

Hematocrit (HTC) is an important hemorheological parameter. It provides estimate of RBC proportion in a volume of blood [2]. Both HTC and obesity are strongly correlated with cardiovascular diseases (CVDs). HTC and mean corpuscular hemoglobin concentration (MCHC) play very important roles in preventing CVDs and anemia [5]. However, there is no study to explore the direct relationship of HTC as well as MCHC and obesity in pediatric population. In a similar manner, red blood cell distribution width (RDW), a measure of the variability in size of circulating RBCs, is associated with mortality and adverse outcome in selected populations with CVDs [6]. RDW has been associated with CVDs and inflammation in several conditions [7]. RDW, as an easy and quick measurable index, can predict early-stage renal function damage [8] and may be used as an early marker of CV risk in rheumatoid arthritis at disease onset, but not in patients with established disease [7]. RDW is a hematological parameter that has been studied in several clinical settings and has been found to be related to both anemia and inflammatory status. As obesity is related to increased inflammatory pattern, RDW was also analyzed within this context [9]. Since higher RDW is related with erythrocyte deformability and delayed RBC clearance, it could be associated with increased risk of a wide range of mortality and morbidity including CVDs [10], [11]. However, any study investigating the possible associations between RDW and early-stage obesity has not been reported in children yet. The objective was to evaluate the associations of hematological parameters, including HTC, HGB, RBC, WBC, platelet counts as well as their indices and subfractions with the degree of obesity in a cohort of pediatric subjects. This study was performed to detect any possible alterations in HTC, MCHC, RDW levels during early- and late- stages of obesity among overweight (OW) and morbidly obese (MO) children, respectively.

II. Materials and Methods

A. Patients

The study population consisted of a total of 249; -139 MO (BMI 27.3±3.9 kg/m^2), 82 healthy normal weight (NW) (BMI 15.8±1.1 kg/m^2), and 28 OW children (BMI 20.7±2.7 kg/m^2). Patients and controls consulted to Department of Pediatrics in Faculty of Medicine Hospital at Namik Kemal University (Tekirdag, Turkey) between 2011 and 2014 were included into the scope of the study. Their weights and heights were

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measured and body mass index (BMI) values were calculated. WHO BMI values designed for 5-19 year-aged-children and adolescents [12] were used as the values for determining the obesity criteria. The values obtained from the clinical examination were compared with the international reference data including percentile curves. The control group comprised volunteers, consisting of non-consanguineous relatives or friends of patients, who were age and sex-matched. The inclusion of patients and controls in the study was performed simultaneously, as sampling and analytical testing. Informed consent from the parents of all the participants and approval from Namik Kemal University, Faculty of Medicine Hospital's Ethics Committee for Clinical Investigations were obtained. This work complies with the principles of the Declaration of Helsinki. The exclusion criteria were malignant, hematological, infectious or inflammatory disease, previous thrombo-embolism, treatment with rheological drugs and secondary obesity (hypothyroidism, Cushing syndrome).

B. Measurements

Each child was anthropometrically measured following the physical examination and a detailed history taken from the parents. Head circumference (C), neck C of each child were measured in addition to weight, height, waist C and hip C. Shoeless children with thin issued clothing were measured for their weights by an electronic weighing instrument sensitive to 0.1 kg intervals. Shoeless children were measured for their heights by a portable stadiometer designed in 0.1 cm intervals, in a position that child looks at completely in the horizontal plane and in a position that her occiput, back, hip and heels are in contact with the vertical posterior plane. Other measurements were performed by a flexible, non-elastic tape. All the measurements were carried out by pediatricians. Each measurement was taken twice and the mean was recorded. Waist-to-hip ratio (whr) and head-to-neck ratio (hnr) were calculated.

C. Laboratory Methods

Venous blood was drawn from the antecubital vein between 8 and 10 a.m. after 12 h of fasting with a minimum stasis. Basic hematological parameters were determined by the automatic hematology analyzer; Pentra DX-Nexus (Horiba Medical ABX SAS, Japan). Fasting blood glucose was measured by spectrophotometric hexokinase assay, fasting insulin was detected by ECLIA (electro-chemiluminescence immunoassay) and C-reactive protein (CRP) was determined by immunological test system in a Roche COBAS C-501 chemistry analyzer.

Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index was calculated using fasting plasma glucose and insulin values [HOMA-IR= fasting glucose (mg/dL)* fasting insulin (µIU/ml)/ 22,5*0,0555)] [13] [14].

D. Statistical Analysis

The statistical analyses were performed using SPSS version 15 (SPSS inc. Chicago, IL, USA). Descriptive statistics were performed. Data were presented as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) and post hoc Tukey HSD tests were used to compare variables between groups. Differences were considered statistically significant at a p level of ≤0.05.

III. Results

A total of 249 children participated in the study. There were statistically significant differences between BMI values of the groups (p=0.000). No statistically significant differences were observed between the mean age values of MO (10.0±2.7 yrs), OW (10.6±2.9 yrs), and NW children (9.2±2.1 yrs), (p≥0.05).

Fig. 1 shows the values calculated for whr and hnr in MO (0.94±0.08 and 1.67±0.13), OW (0.90±0.06 and 1.88±0.20) and NW (0.87±0.06 and 1.94±0.13) children. There was statistically significant difference among the groups (p=0.000).

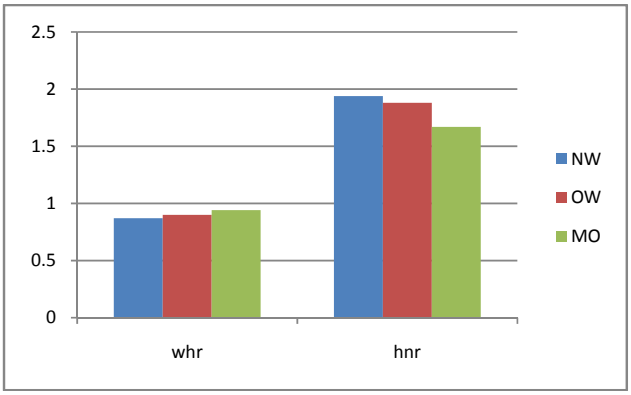

Fig. 1 Waist-to-hip (whr) and head-to-neck (hnr) ratios of MO, OW and NW children

Fig. 2 shows HOMA-IR values calculated for MO (2.77±2.19), OW (2.13±2.52) and NW (0.78±1.02) children. There was statistically significant difference among the groups (p=0.000).

No significant difference among the groups was detected for CRP values (p=0.123).

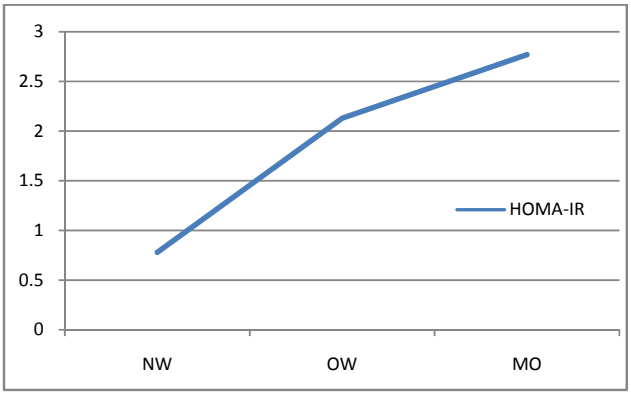

Fig. 2 HOMA-IR values of MO, OW and NW children

Hematological parameters in MO, OW and NW children were summarized in Table I.

TABLE I
MEAN±SD VALUES OF TOTAL AND DIFFERENTIAL LEUKOCYTES COUNTS, RED BLOOD CELLS AND PLATELET COUNTS AS WELL AS THEIR INDICES IN MO, OW AND NW CHILDREN

Parameters	Morbid Obese	Overweight	Normal weight	p
Wbcs				
wbc	8.2±2.0	8.1±3.5	8.0±4.2	0.281
neutrophiles	4.4±1.5	4.3±2.6	4.1±3.8	0.428
lymphocytes	2.9±0.8	2.7±1.0	2.9±0.9	0.378
monocytes	0.7±0.2	0.8±0.6	0.7±0.4	0.139
eosinophiles	0.2±0.2	0.2±0.2	0.2±0.2	0.589
basophiles	0.03±0.02	0.03±0.02	0.03±0.02	0.289
nly	1.6±0.6	1.8±1.4	1.6±2.2	0.894
Rbcs				
rbc	4.9±0.3	4.8±0.3	4.9±0.4	0.19
hgb	13.2±2.5	12.9±0.9	12.8±0.9	0.207
htc*	39.4±3.9	38.6±2.6	37.9±2.4	0.000
mcv	78.6±6.8	74.8±18.0	78.1±5.2	0.059
mch	26.3±1.8	28.7±10.7	26.5±2.2	0.125
mchc*	33.3±0.9	33.1±1.5	33.8±1.0	0.000
rdw*	14.1±1.2	15.0±5.8	13.8±1.1	0.024
Platelets				
platelet	342.8±67.0	345.6±87.7	318.7±89.1	0.133
mpv	8.2±0.7	8.5±0.7	8.0±0.8	0.455

wbc-white blood cell, rbc-red blood cell, hgb-hemoglobin, htc-hematocrit, mcv-mean corpuscular volume, mch-mean corpuscular hemoglobin, mchc-mean corpuscular hemoglobin concentration, rdw- red blood cell distribution width, mpv- mean platelet volume, nly-neutrophile to lymphocyte ratio
* $p \leq 0.05$

Statistically significant differences were observed for MCHC (p=0.042) and RDW (p=0.030) between NW and OW children whereas more significant differences were noted for MCHC (p=0.006) and HCT (p=0.014) between NW and MO children.

IV. DISCUSSION

Many researchers are in the need of finding some parameters as indicators of pro-inflammatory state upon investigation of children with obesity.

In this study, the aim was to interpret the RBC indices of OW and MO children in comparison with those of NW in the absence of any differences in total and differential WBCs as well as platelet counts and mean platelet volume. Overweight and MO children not having any MetS criteria were selected to be able to observe the marked differences between the groups if there is any.

Quite significant differences (p=0.000) between whrs as well as hnrs of NW and MO children were detected. Upon evaluation of hnr of these groups, also a significant difference between hnrs of OW and MO children (p=0.000) was observed. This difference was not detected for whr values of OW and MO groups. This finding suggests the preponderance of hnr over whr. HOMA-IR index values of all groups were found to be below 3.16, the cut-off value reported for children. However, an increasing profile towards morbid obesity was noted.

RDW might be a novel biomarker that reflects multiple physiological impairments related to atherosclerosis and coronary artery disease (CAD) [15]. RDW has been shown to predict CV mortality in various populations. Increasing RDW levels significantly increased risk of CV morbidity and all-cause mortality [16]. High RDW is a strong prognostic factor in patients with CVDs and associated with increased incidence of fatal coronary events [17]. In systematic reviews, the meta-analyses investigated the impact of RDW on the prognosis of heart failure and they reported that these patients with higher RDW levels may have poorer prognosis than those with lower RDW and are associated with increased risk of mortality and CVD events in patients with established CAD [15], [18].

In our study, RDW was found to be significantly higher in OW children compared to NW group (p=0.030). This finding is similar to the results of the study, which demonstrated higher RDW in obese adolescents [19], however couldn't be detected between the control and MO groups. These findings suggest that RDW can be considered as a surrogate marker of inflammation and, consequently, CV risk in obese individuals. RDW indicates a variation in the size of the red cell and is a quantitative measure of an isocytosis in microcytic MCV ranges [20].

In a recent study, the mean values of MCHC in overweight children were found to be significantly lower [3]. In another study performed on adults, RDW was higher while MCHC was lower in morbidly obese patients than in controls [9]. In our study, upon evaluation of MCHC values, significantly lower values have been detected in OW children (p=0.042) than those for NW. Statistical significance levels pointed out that the decrease in MO children (p=0.006) was more important than that in OW children compared to those in NW group.

In our study, increased RDW along with decreased MCHC were prominent during the early phases of obesity.

Higher levels of HTC, even within the normal range, were associated with an increased risk of developing heart failure in a long-term follow-up study [21]. Obese patients show increased HTC [22]. It has been suggested that elevated HTC levels may be positively associated with CV risk factors and thus, the combination of HTC values and CV risk factors may enable early diagnosis of CVDs [23].

In addition to these striking alterations in the early phases of obesity, differences in HTC values were also found between NW and MO children. HTC provides estimate of RBC proportion in a volume of blood [2]. HTC is a blood test that measures the percentage of the volume of whole blood that is made up of RBCs. This measurement depends on the number as well as the size of RBCs. As in our case, statistically higher levels were observed in MO children (p=0.014).

Our findings may serve as confirmatory evidence for the beginning of inflammatory processes of obese individuals even in children as the indicators of cardio-metabolic factors from early life.

It is suggested that the standard, clinically relevant hematological variables may be related to the underlying pathophysiological changes associated with Type 2 diabetes

[24]. Our findings have shown that they may also be related to those associated with obesity.

Though the cause-effect relationship between obesity and erythrocyte indices still needs further investigation, the elevated RDW, elevated HTC and reduced MCHC in obese children may be of significance to link obesity and CVDs.

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