International Journal of Medical, Medicine and Health Sciences
ISSN: 2517-9969
Vol:12, No:9, 2018

Evaluation of Systemic Immune-Inflammation Index in Obese Children

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***Abstract*—**A growing list of cancers might be influenced by obesity. Obesity is associated with an increased risk for the occurrence and development of some cancers. Inflammation can lead to cancer. It is one of the characteristic features of cancer and plays a critical role in cancer development. C-reactive protein (CRP) is under evaluation related to the new and simple prognostic factors in patients with metastatic renal cell cancer. Obesity can predict and promote systemic inflammation in healthy adults. BMI is correlated with *hs*-CRP. In this study, SII index and CRP values were evaluated in children with normal BMI and those within the range of different obesity grades to detect the tendency towards cancer in pediatric obesity. A total of one hundred and ninety-four children; thirty-five children with normal BMI, twenty overweight (OW), forty-seven obese (OB) and ninety-two morbid obese (MO) participated in the study. Age- and sex-matched groups were constituted using BMI-for age percentiles. Informed consent was obtained. Ethical Committee approval was taken. Weight, height, waist circumference (C), hip C, head C and neck C of the children were measured. The complete blood count test was performed. C-reactive protein analysis was performed. Statistical analyses were performed using SPSS. The degree for statistical significance was $p \leq 0.05$. SII index values were progressively increasing starting from normal weight (NW) to MO children. There is a statistically significant difference between NW and OB as well as MO children. No significant difference was observed between NW and OW children, however, a correlation was observed between NW and OW children. MO constitutes the only group, which exhibited a statistically significant correlation between SII index and CRP. Obesity-related bladder, kidney, cervical, liver, colorectal, endometrial cancers are still being investigated. Obesity, characterized as a chronic low-grade inflammation, is a crucial risk factor for colon cancer. Elevated childhood BMI values may be indicative of processes leading to cancer, initiated early in life. Prevention of childhood adiposity may decrease the cancer incidence in adults. To authors' best knowledge, this study is the first to introduce SII index values during obesity of varying degrees of severity. It is suggested that this index seems to affect all stages of obesity with an increasing tendency and may point out the concomitant status of obesity and cancer starting from very early periods of life.

***Keywords*—**Children, c- reactive protein, systemic immune-inflammation index, obesity.

I. Introduction

OVERWEIGHT and obesity have become severe health problems because of their associations with many chronic diseases. In severely obese people, high body mass index (BMI) values were found to be independently associated with an increased risk of death. Excess weight is also reported to be associated with increased cancer risk. Obesity is one of the top contributors of some cancer cases. In association with the worldwide expansion of obesity, a striking elevation in the number of young adults with obesity-associated cancers is being detected. In addition to this information, reports investigating new hypotheses for a connection between obesity and cancer are being carried out [1]-[4].

Obesity is described as one of the known modifiable causes of cancer [5]. It is reported to promote the risk of breast cancer in postmenopausal but not in premenopausal women [6].

There are also recent studies evaluating the matter from children point of view [7]-[9].

Systemic immune-inflammation (SII) index, -one of pretreatment inflammatory indices-, derived from platelet count and neutrophil-to-lymphocyte ratio is commonly used as predictor of prognosis and clinical outcome in patients with various cancers such as small cell lung [10], non-small cell lung [11], pancreatic [12], prostate [13], colorectal [14], gastric [15], [16] cancers as well as hepatocellular [17], [18], hepatitis B-associated hepatocellular [19], nasopharyngeal [20], esophageal squamous cell carcinomas [21]-[23]. Elevated SII index is also associated with a poor outcome in patients with solid tumors [24]. Association of BMI, diet-related factors and outcome in patients with several cancers is under investigation. *High sensitive* C-reactive protein (*hs*-CRP) is under evaluation related to the new and simple prognostic factors in patients with metastatic renal cell cancer [25]. Obesity is associated with chronic low-grade systemic inflammation. It seems to exit a correlation between BMI and *hs*-CRP.

The aim of this study is to evaluate SII index and CRP values in children with normal BMI and those within the range of different obesity grades [overweight (OW), obese (O), morbid obese (MO)] to detect the tendency towards cancer in pediatric obesity.

II. Patients and Methods

A. Patients

A total of one hundred and ninety-four children; thirty-five with normal BMI, twenty OW, forty-seven O and ninety-two MO admitted to Namik Kemal University, Medical Faculty Hospital, Department of Pediatrics participated in the study. Weight, height, waist circumference (C), hip C, head C and neck C measurements were taken. BMI values were calculated. Written informed consent forms were filled out.

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The study protocol was approved by Ethical Committee. Those with acute and/or chronic infection, inborn errors of metabolism were excluded from the study.

B. Obesity Classification

Body mass index values tabulated for age- and sex-percentiles prepared by WHO were used to constitute the groups. The children with their percentiles between 15th and 85th were included in the normal weight (NW) group. Those between 85th and 95th were considered OW. The percentiles of O children were between 95th and 99th. The children, whose percentiles were above 99 participated into the study as the members of MO group.

C. Laboratory Analyses

Basic hematological parameters were determined by the automatic hematology analyzer. Erythrocyte, leukocyte, platelet counts as well as their indices were recorded. Neutrophil-to-lymphocyte ratios were calculated. SII index values, which were based upon the lymphocytes (L), neutrophils (N) and platelets (P) counts of the individuals were calculated by using the formula; P*N/L. *hs* C-reactive protein was determined by immunological test system in a chemistry analyzer.

D. Statistical Evaluation

SPSS program was used to perform statistical analyses. Mean±standard error (SE) values were calculated. Statistical differences were determined by the appropriate tests. Correlation analyses were performed. $p \leq 0.05$ was the degree for statistical significance.

III. Results

A total of one hundred and ninety-four pre-pubertal children were included into the scope of this study. Figure 1 shows bar diagrams of SII index values varying with the obesity grades from NW to MO children.

Mean ± standard error of SII index values were calculated as 381±43 (*10^9/L), 430±48 (*10^9/L), 503±49 (*10^9/L) and 538±29 (*10^9/L) for NW, OW, O and MO groups, respectively. The corresponding values for *hs*-CRP were 2.1±0.9 mg/L, 2.5±1.1 mg/L, 3.4±1.0 mg/L and 4.6±1.1 mg/L.

SII index values were progressively increasing starting from NW to MO children. There is a statistically significant difference between NW and O as well as MO children ($p \leq 0.05$). No significant difference was observed between NW and OW children, however, a positive correlation ($r=0.458$; $p \leq 0.05$) was observed between SII index values of NW and OW children (Fig. 2).

MO constitutes the only group, which exhibited a statistically significant positive correlation between SII index and CRP ($r=0.261$; $p \leq 0.05$) (Fig. 3).

IV. Discussion

Obesity needs immediate attention in both developed and developing countries. Overweight and obese children have a higher likelihood of becoming obese adults. This disease with a low-grade inflammation may lead to health-related problems including diabetes, metabolic syndrome, dyslipidemia, and cardiovascular diseases.

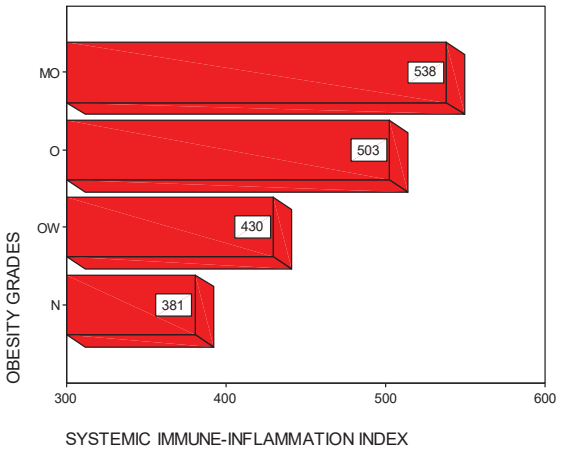

Fig. 1 Systemic immune-inflammation index values of normal weight, overweight, obese and morbid obese children

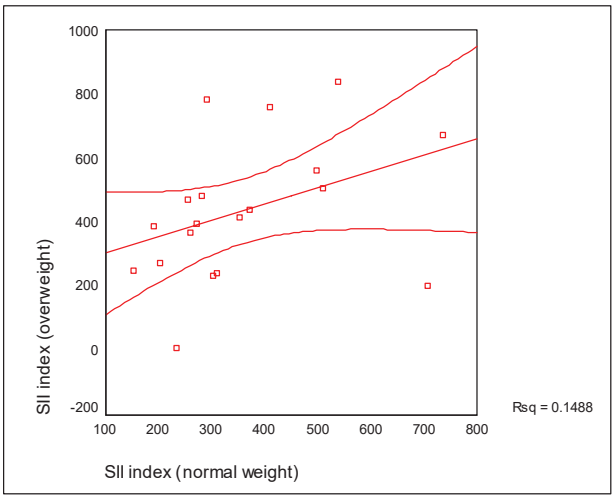

Fig. 2 Correlations of systemic immune-inflammation index values between children with normal body mass index and overweight children

Obesity is linked to risk for developing many forms of cancer. There is a long way from inflammation to cancer. Inflammation is a hallmark of cancer and is widely recognized to influence all cancer stages from cell transformation to metastasis [26].

Many reports concerning the alterations in hematologic parameters within the complete blood count analyses list have been reported during obesity, morbid obesity and metabolic syndrome. An association between body fat and hematologic parameters was introduced [27]. The importance of erythrocyte parameters as well as leukocyte subgroups, and also some ratios such as neutrophil-to-lymphocyte ratio have widely been investigated within this context [28]-[30].

Systemic immune-inflammation index is an index, which is

derived from some hematologic parameters and it is expected to give a notion about the severity and outcome of the cancer patients. It may have the potential to reflect the status of the inflammation also in obesity, which is a disease associated with low-grade inflammation.

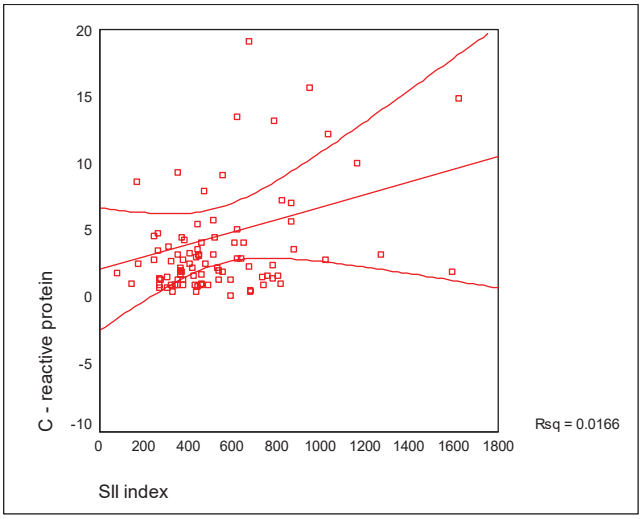

Fig. 3 Correlation between systemic immune-inflammation index and C-reactive protein values in morbid obese group

In several cancers, optimal cutoff points were defined for this index. In a study, it is suggested as a powerful prognostic indicator of poor outcome in patients with hepatocellular carcinoma. Patients were stratified into high (≥330) and low (<330) SII index groups. Patients in high SII index group were associated with vascular invasion, large tumors and early recurrence. Circulating tumor cell levels were significantly higher than patients with low SII index values [17].

In another study performed on patients with squamous cell carcinoma of the esophagus, the optimal cut-off values were calculated as 410 (*10^9/L). Patients, who exhibit values below this had a significantly better 5-year cancer-specific survival than patients with SII>410(*10^9/L) [22].

Another cut-off point was calculated as 340 in patients with colorectal cancer and it was reported that overall survival and disease-free survival were better in patients with low SII index [14].

In a report published this year, the cut-off value to distinguish high grade and low-grade gliomas was determined as 392 ((*10^9/L) [31].

In our study, SII index value for healthy children was found as 381±43 (*10^9/L). Comparison of this value with that of OW [430±48 (*10^9/L)], O [503±49 (*10^9/L)] and MO [538±29 (*10^9/L)] will lead to the outcomes supporting the obesity- cancer link during the very early periods of life.

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