Hematological Parameters in Pediatric-onset Systemic lupus Erythematosus and its association with disease activity

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Abstract
Background: Pediatric onset Systemic lupus erythematosus (P-SLE) is an autoimmune multisystem illness with disease occurrence before the age of eighteen. It is a highly complicated condition with a significant variability across individuals. Aim of the study: To assess hematological parameters in P-SLE patients attending to the Pediatric Rheumatology out-patient clinic in Minia University Children Hospital, as well as, admitted to the in-patient ward and to evaluate the relationship between these hematological parameters and activity of P-SLE disease. Methods: This study was a prospective cross-sectional study included 40 children diagnosed with SLE attending to the Pediatric Rheumatology out-patient clinic in Minia University Children Hospital, as well as, admitted to the in-patient ward, from August 2020 to January 2022. Also, 40 apparently healthy children were included as a control group. They are age and sex matched, with the children having SLE. All enrolled Patients were subjected to: Detailed history taking, complete clinical examination, laboratory investigations including: complete blood count (CBC).

Results: Both Patients with mild disease activity and Patients with moderate to high disease activity had significantly lower hemoglobin level than controls (P= 0.004 and 0.04 respectively), but there is non significant positive correlation between Hb level and SLEAI score as r = 0.382 and p = 0.142. Conclusion: Children having Systemic lupus erythematosus are more likely to have lower hemoglobin level than healthy children which may result in high morbidity in P-SLE, but lower hemoglobin level may not be closely associated with P-SLE disease activity.

Keywords; Systemic lupus erythematosus; autoimmunity; Rheumatology; hematological disorders.

Introduction
Pediatric onset Systemic lupus erythematosus (p-SLE) is an autoimmune multisystem illness with disease occurrence before the age of eighteen.1 It is a highly complicated condition with a significant variability across individuals.2

P-SLE is usually a more serious disorder involving renal, neurological and hematological systems, resulting in lifelong damage compared to adult-onset lupus patients3. Pediatric-onset SLE has a widely diverse presentation and clinical outcomes.

Consequently, diagnosis might be problematic. It ranges from relatively mild illness to severe, life-threatening manifestations. Countless symptoms, such as headaches, oral ulcers, arthralgia, fever and weight loss, are non-precise and occur in children for a diversity of reasons. Major organ involvement is dominant, with renal affection being the most common. Lupus nephritis (LN) is present in up to 80% of patients, with up to 19% having end-stage renal failure4.5.6

Rheumatologists as case managers, dermatologists, nephrologists, hematologists, neurologists, radiologists, immunologists, gastroenterologists, cardiologists, endocrinologists, and infectious disease experts are typically required due to the complexity of p-SLE with multi-organ involvement7.
Patients and methods
This study was a prospective cross-sectional study included 40 children diagnosed with Systemic Lupus Erythematosus attending to the Pediatric Rheumatology outpatient clinic in Minia University Children Hospital, as well as, admitted to the in-patient ward, from August 2020 to January 2022.

Also, 40 apparently healthy children were included as a control group. They are age and sex matched, with the children having SLE.

The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was calculated for all children with SLE. Activity categories have been defined based on SLEDAI scores

The subjects of the study were grouped accordingly into the following three groups:

- **Group (A) [Mild activity]**
  this group includes children with SLE with SLEDAI score less than or equal to 5.

- **Group (B) [Moderate-high activity]**
  this group includes children with SLE with SLEDAI score greater than or equal to 6.

- **Group (C) [control]**
  this group includes apparently healthy children.

Then included children were subjected to the following:

**A- Careful history taking including:**
Name, age, sex, residence, socioeconomic standard and family history of blood diseases.

**B- Full clinical examination:**
1. Vital data: respiratory rate, heart rate, blood pressure, temperature.
2. 2- Systematic examination including
3. Chest
4. Heart
5. Abdomen
6. Musculoskeletal System and Joints
7. Neuropsychiatric assessment

**C-Laboratory investigations:**
1. Complete blood count (CBC)
2. Renal Function tests
3. Liver function tests
4. Urine analysis
5. C-Reactive Protein (CRP)
6. Erythrocyte Sedimentation Rate (ESR)

Results
Table 1: showed that group A had significantly lower hemoglobin level than controls (P =0.004).

<table>
<thead>
<tr>
<th>Baseline data</th>
<th>Group A n = 20 Mean ± SD</th>
<th>Group B n = 20 Mean ± SD</th>
<th>control n = 40 Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>12.76 ± 2.46</td>
<td>11.88 ± 2.54</td>
<td>12.32 ± 2.51</td>
<td>0.502</td>
</tr>
<tr>
<td>Hb (gm/dL)</td>
<td>10.25 ± 0.83</td>
<td>10.5 ± 1.03</td>
<td>11.0 ± 0.98</td>
<td>0.008*</td>
</tr>
<tr>
<td>TLC (x10^3cells/mm^3)</td>
<td>7.28 ± 1.98</td>
<td>7.09 ± 2.65</td>
<td>6.68 ± 1.42</td>
<td>0.166</td>
</tr>
<tr>
<td>PLT (x10^3 platelets/mcL)</td>
<td>260.2 ± 65</td>
<td>207. ± 96.2</td>
<td>229. ± 67.5</td>
<td>0.101</td>
</tr>
</tbody>
</table>

Moreover, Group B had significantly lower hemoglobin level than control (p=0.04)

n = number, SD =standard deviation, Hb = Hemoglobin, TLC = Total Leucocyte Count, PLT= platelets
Hematological manifestations in systemic lupus erythematosus (SLE) are common and diverse. Their frequency varies in different populations.\(^{(11)}\)

The major findings of our study is that; Patients with mild disease activity (group A) had significantly lower hemoglobin level than controls (P= 0.004). Moreover, Patients with moderate to high disease activity (group B) had significantly lower hemoglobin level than controls (P=0.04), but there is non significant positive correlation between Hb level and SLEAI score as \(r = 0.382\) and \(p = 0.142\).

This was in agreement with Samohvalov et al., (2018) who found that anemia is present in approximately half of the people with active Systemic lupus Erythematosus.

Moreover, our results were in agreement with Giannouli et al., (2006) who found that hematological abnormalities are very common in systemic lupus erythematosus and anemia is found in approximately 50% of SLE patients.

On the other hand, our results were in disagreement with Samohvalov et al., (2012) who found that Anemia is closely associated with disease activity.

Also, our results were in disagreement with Beyan et al., (2007) who found that patients with high disease activity had significantly lower hemoglobin level than patients with low disease activity (P=0.018).

These hematological manifestations can be due to the disease itself, another concomitant disease or iatrogenic. Hemolytic anemia, leukopenia, lymphopenia and thrombocytopenia are incorporated into both the 1997 update of the 1982 American College of Rheumatology (ACR). Anemia is frequent, affecting more than 50% of patients throughout the course of the disease and it can be both immune and nonimmune mediated in SLE patients.\(^{(12)}\)

Anemia of chronic disease (ACD) is the most common type of anemia in SLE patients, responsible for about one third of the cases.\(^{(13)}\)

Autoimmune Hemolytic Anemia, Iron Deficiency Anemia, drug-induced myelotoxicity, and anemia due to chronic renal failure are also often detected.
Aplastic anemia, Pure Red Cell Aplasia, pernicious anemia, myelofibrosis, sideroblastic anemia, hemophagocytic syndrome occur less frequently\(^{(12-14)}\).

Anemia is associated with high morbidity in different clinical conditions. For example: developmental delay in children, changes in immunological status, high risk of infections. Anemia is an independent risk factor for the development of cardiovascular complications in general population\(^{(15)}\).

**Conclusion**

Children having Systemic lupus erythematosus are more likely to have lower hemoglobin level than healthy children which may result in high morbidity in P-SLE, but lower hemoglobin level may not be closely associated with P-SLE disease activity.

**References**