

# Clinical Associations of Hypocomplementemia in Malaysian Systemic Lupus Erythematosus Patients

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## Background/ Objective

Complement plays a major role in systemic lupus erythematosus (SLE) and is included in the classification criteria and disease activity indices. A prospective study reported that low C3 is more important than low C4, in clinical and serological involvements. Our objective was to evaluate the relationship between hypocomplementemia and disease manifestations in Malaysian SLE population.

## Methods

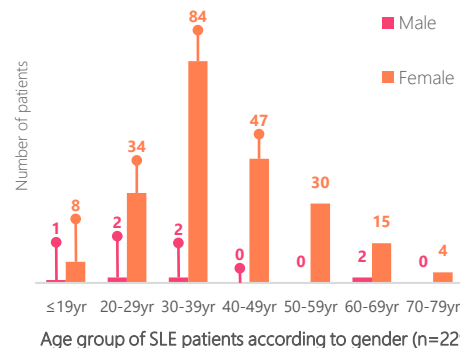
Retrospective cross-sectional study of all SLE patients attending Rheumatology Clinic Hospital Putrajaya between January 2015 and December 2020. Electronic medical records were reviewed.

- Persistent low complements: Minimum of 3 consecutive readings of low C3, C4 or both, without any subsequent return to normal range.
- Normal range: C3 (0.90- 1.80g/L) and C4 (0.10-0.40g/L)

## Results



Total analysed: 229 patients  
Majority were females (n=222)  
Median age: 37 ± 12.5 years  
Mean disease duration: 11.2 ± 6.4 years



Prevalence of either low C3 and/or low C4 (n=163)

71.2%

History of low C3 (n=125)

54.6%

History of low C4 (n=121)

52.8%

Persistently low C3 (n=30)

13.1%

SLE manifestations	Persistently Low C3 OR (CI)*	P value
Malar rash	1.14 (0.45-2.85)	0.777
Discoid rash	0.68 (0.15-3.10)	0.619
Photosensitivity	0.76 (0.21-2.72)	0.683
Oral ulcers	1.17 (0.37-3.68)	0.782
Arthritis	1.36 (0.59-3.10)	0.460
Serositis	2.64 (0.48-14.2)	0.242
Lupus nephritis	2.55 (1.21-5.16)	<b>0.008</b>
Cerebral lupus	0.86 (0.81-0.92)	0.488
Haemolytic anaemia	0.81 (0.81-0.90)	0.224
Leucopenia	1.62 (0.63-4.12)	0.305
Thrombocytopenia	1.32 (0.46-3.76)	0.603
Anti-dsDNA	3.01 (1.01-8.27)	<b>0.018</b>
Anti-Smith	0.44 (0.13-1.46)	0.177

### Persistently low C3

Nephritis and presence of anti-dsDNA.

Relationship between persistently low C3 and SLE manifestations.

	SLE manifestations	Low C3 only OR (CI)*	P value	Low C4 only OR (CI)**	P value	Both Low C3 and C4 OR (CI)***	P value
<b>Isolated low C3</b>	Malar rash	0.49 (0.13-1.81)	0.281	4.61 (1.64-12.9)	<b>0.000</b>	5.30 (2.92-9.58)	<b>0.000</b>
	Discoid rash	3.54 (0.75-16.5)	0.089	2.22 (0.47-10.4)	0.298	4.38 (1.71-11.2)	<b>0.001</b>
	Photosensitivity	0.81 (0.20-2.16)	0.763	3.13 (1.17-8.38)	<b>0.000</b>	2.87 (1.29-6.37)	<b>0.007</b>
	Oral ulcers	1.52 (0.34-6.68)	0.575	5.30 (1.20-23.3)	<b>0.000</b>	6.22 (2.62-14.7)	<b>0.000</b>
	Arthritis	3.96 (1.70-9.16)	<b>0.001</b>	3.54 (1.43-7.81)	<b>0.004</b>	2.82 (1.55-5.09)	<b>0.000</b>
	Serositis	0.27 (0.21-0.36)	<b>0.025</b>	0.73 (0.66-0.81)	0.398	2.27 (1.70-7.35)	<b>0.049</b>
<b>Isolated low C4</b>	Lupus nephritis	6.18 (1.97-19.4)	<b>0.001</b>	2.57 (0.78-8.99)	0.127	3.34 (1.97-5.66)	<b>0.000</b>
	Cerebral lupus	0.28 (0.21-0.36)	0.283	0.73 (0.67-0.81)	0.552	2.57 (0.47-1.41)	0.104
	Haemolytic anaemia	1.24 (0.11-14.0)	0.860	0.37 (0.16-0.88)	0.105	4.39 (1.10-17.4)	<b>0.023</b>
	Leucopenia	5.40 (1.68-17.2)	<b>0.002</b>	1.66 (0.52-5.32)	0.385	4.30 (2.09-8.83)	<b>0.000</b>
	Thrombocytopenia	1.75 (0.58-5.29)	0.310	5.72 (1.73-16.0)	0.002	2.24 (1.05-4.78)	<b>0.032</b>
	Anti-dsDNA	0.66 (0.26-1.69)	0.394	2.82 (1.02-7.87)	0.042	2.78 (1.54-5.01)	<b>0.002</b>
<b>Combined low C3 &amp; C4</b>	Anti-Smith	0.23 (0.07-0.74)	<b>0.011</b>	4.16 (0.86-20.1)	0.059	2.42 (1.48-3.97)	<b>0.000</b>

### Combined low C3 & C4

Mucocutaneous, renal, haematological, serositis, arthritis, anti-dsDNA and anti-Sm.

Relationship between a history of low C3, low C4 or both and SLE manifestations.

## Discussion

Low complements were reported in 47% to 67% of SLE patients [1,2] which is almost similar to our cohort (71.2%). Petri M. et al reported that low C4 is a weak marker compared to low C3 in terms of SLE associated clinical manifestations. In comparison to our findings, low C3 and combined low C3 and C4 were associated with many SLE manifestations, while low C4 was mainly associated with mucocutaneous involvement. Renal involvement was strongly associated with a low C3 and combination of low C3 and C4, but not with low C4 alone, which is similar to the previous study [1].

## Conclusion

In our cohort, low C3 and combined low C3 and C4 have a strong association with clinical and serological manifestations of lupus. Low C4 was associated with mucocutaneous manifestation.

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