The Hyper-Inflammatory Response in Adults with Severe COVID-19 Pneumonia Differs from the Cytokine Storm of Hemophagocytic Syndrome

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ABSTRACT In this review we described the values of commonly available HScore laboratory markers in patients with coronavirus-19 (COVID-19)-pneumonia associated cytokine storm syndrome (CPN-CSS) and compared results with those of other forms cytokine storm syndrome (O-CSS) to determine a pattern for CPN-CSS. Twelve CPN-CSS studies and six O-CSS studies were included. CPN-CSS typically obtained a single HScore value (e.g., aspartate transaminase > 30 U/L) while failing all other HScore criteria. A typical pattern for CPN-CSS was revealed when compared to O-CSS: lymphopenia vs. pancytopenia and increased vs. decreased fibrinogen. Findings, other than HScore commonly found in CPN-CSS studies, showed elevated lactate dehydrogenase, D-dimer, and C-reactive protein. Although CPN-CSS studies describe severely ill patients, the HScore markers are typically less toxic that O-CSS.

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KEY WORDS: coronavirus disease-2019 (COVID-19), cytokine storm syndrome (CSS), hemophagocytic syndrome, hemophagocytosis lymphohistiocytosis, macrophage activation syndrome (MAS)

The novel coronavirus-19 (COVID-19) was first reported in Wuhan, China, and rapidly grew into a worldwide pandemic. Some patients develop an acute severe respiratory syndrome characterized by fever, tachypnea, hypoxemia, and bilateral infiltrates on imaging studies. Laboratory findings demonstrate alarming levels of markers of inflammation [1,2]. Such values reflect a syndrome of hyper-inflammation often referred to as cytokine storm syndrome (CSS) [3-6]. In the pre-COVID-19 era, typical severe inflammatory syndromes, eliciting CSS, were classified as primary (genetic/familial) or secondary, namely hemophagocytic syndrome (HS) with infections such as Epstein-Barr viral infection, hemophagocytic lymphohistiocytosis (HLH) with malignancies such as lymphoma, or macrophage activation syndrome (MAS) with autoimmune diseases such as systemic juvenile idiopathic arthritis [7-9]. Machowicz and colleagues [7] delineated the differences between HLH and sepsis. Following this reasoning, delineated the differences between CSS associated with severe COVID-19 pneumonia (CPN-CSS) and CSS due to other (HLH, HS, MAS) etiologies (O-CSS). In particular, we focused on the lab findings in CPN-CSS versus O-CSS, as lab values are objective and available for most clinicians. The five laboratory criteria of the HScore served as a framework for the comparison [10]. Lab markers typically reported with CPN-CSS, however not included in the HScore, were considered as well. We hypothesized that delineating these differences would help clinicians understand whether the emerging hyper-inflammation is associated with CPN or perhaps associated with other conditions (e.g., sepsis).

We searched the literature for the following terms: cytokine storm syndrome, hemophagocytic syndrome, hemophagocytic lymphohistiocytosis (HLH), macrophage activation syndrome, HScore, HLH-04, COVID-19, nCov, SARS-Cov2, and combinations of these terms. Studies reporting lab values as means or medians for adult patients with CPN-CSS or O-CSS were included.

Patient inflammatory responses to coronavirus disease-2019 pneumonia varies, and in severe cases it is reported as a cytokine storm syndrome

The five laboratory criteria of the HScore [10], including the number of cytopenias (1, 2, or 3), values of ferritin, fibrinogen, triglyceride, and aspartate transaminase (AST), served as the skeleton for the comparison. Clinically or pathologically based HScore criteria were not considered. Markers of inflammation such as percentage of glycosylated ferritin, which is not widely available, was not considered. Laboratory markers commonly reported for CPN-CSS, such as D-dimer, C-reactive protein (CRP), and lactic dehydrogenase (LDH), were considered. Laboratory values of the more severe group of patients were typically considered.

We gathered laboratory values from included studies [1-23] into three tables [Table 1, Table 2, Table 3]. Numerical lab values of each marker derived from the studies were represented by an interval containing all the values. We summarized the relation between the representing interval of each marker in CPN-CSS and O-CSS.

Twelve studies reporting values associated with CPN-CSS and six studies reporting values associated with O-CSS were included in Table 1. Table values are given as median (and interval in parenthesis) or mean ± a measure of deviation. The thick line in the table (between AST and neutrophils count) separates the HScore laboratory markers from the other markers.

Although the inflammatory response in COVID-19 pneumonia (CPN) is significant, it is not as toxic as that found in hemophagocytic lymphohistiocytosis or macrophage activation syndrome

In CPN-CSS, most laboratory values failed to fulfill HScore criteria. Cytopenias were not observed in CPN-CSS. Ferritin level was increased (typical values < 2000 ng/L) but did not fulfill the HScore criteria. Fibrinogen levels were characteristically increased in CPN-CSS in contrast to the lower than normal level detected in O-CSS. AST levels were mildly increased in CPN-CSS, to a lesser degree than in O-CSS. Triglyceride levels were not reported in the reviewed CPN-CSS studies. Non-HScore lab markers, typically detected in CPN-CSS, included: increased levels of LDH, D-dimer, and CRP.

The inflammatory response in COVID-19 pneumonia (CPN) is characterized by increased levels of ferritin, fibrinogen, and aspartate transaminase. However, these markers typically do not reach the levels of HScore criteria

This qualitative comparison of the severity of the inflammatory response in CPN-CSS and O-CSS using lab profiles reveals that CPN-CSS is typically less toxic compared to O-CSS.

Laboratory values of severe CPN patients (N=26) from a recently published cohort of COVID-19 patients in Israel were consistent with our study findings: No bi-cytopenia were found; Ferritin level was only mildly increased (579.8 ng/L); AST was mildly increased (62.0 IU/L); lymphopenia was observed (0.8 absolute lymphocytes count [×109/L]); CRP (132.4 mg/L) and LDH (538.0) levels were elevated [24].

McGonagle et al. [25] found that CPN-CSS is distinct from HLH. Like our review, they found that the hypercytokinaemia characteristic of HLH is often associated with extremely high serum ferritin concentrations (≥ 10,000–100,000 ng/ml), whereas in patients with CPN, serum ferritin concentrations are typically in the 500–3000 ng/ml range, at least early in the disease course. Another clear distinguishing feature of HLH is liver function derangement, which can contribute to coagulopathy secondary to loss of liver synthetic function and is not typically seen in patients with CPN. Moreover, Ruscitti et al. [26] reported that two of the main features of primary or secondary HLH, the hemophagocytosis and the peripheral blood bi-or pancytopenia have not been clearly demonstrated in COVID-19.

CPN-CSS was considered to be part of the spectrum of hyerferritinemic syndromes in two reviews by Shoenfeld and Colafrancesco et al. A common pathogenic background is probably underlying to these conditions supporting the use of therapies that target crucial inflammatory mediators [27,28]. As such, Bridgewood et al. [29] have recently suggested that PDE4 inhibitors (PDE4i) may have potential beneficial immune-modulation for treating severe CPN-CSS.

LIMITATIONS

This study has several limitations. First, it is not a systematic review. Second, characterizing the inflammatory response in O-CSS is difficult as cases are quite rare [4] and etiologies vary, highlighting the diversity of this entity. Third, CPN-CSS is a novel disease, still under investigation and reports are accumulating by the day.

CONCLUSIONS

Despite limitations, this review delineates the lab profile of CPN-CSS and distinguishes it from the typical lab profile of O-CSS. It is clear that results should be considered with a grain of salt as CPN remains an emerging disease.

Table 1. Laboratory findings reported in severely ill patients with COVID-19 pneumonia and cytokine storm syndromes of other etiologies

Marker and normal values	CPN-CSS	O-CSS
White blood cells (4.5–11.0 × 109/L)	8.3 (6.2–10.4) Chen [11] 5.6 (4.3–8.4) Qin [12] 6.6 (3.6–9.8) Wang [13] 11.3 (5.8–12.1) Huang [2] 6.52 (4.30–7.73) Wang [14] 9.8 (6.9–13.9) Zhou [15] 3.4 (2.6–5.8) Young [16] 10.1 ± 6.3 Du [17]	On admission 3.3 (1.3–6.9), later minimum 0.9 (0.2–2.7) Knaak [3]
		CSS associated with sepsis usually leukocytosis Machowicz [7]
		On admission: NS:5.9 ± 4.4 , S:4.2 ± 2.2 Nadir or peak: NS:1.7 ± 1.9 , S:2.1 ± 1.1 Kaito [18]
Range:	**Normal to low**	**Low in HLH** **High in sepsis**

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	Take home message

Marker and normal values	CPN-CSS	O-CSS
Hemoglobin (13.5–17.5 g/dl for males 12.0–16.0 g/dl for females)	13.60 (12.55–14.45) Chen [11] 12.2 (11.1–12.8) Huang [2] 12.8 (11.7–13.6) Wang [13] 12.6 (11.5–13.8) Zhou [15] 13.2 (11.7–14) Young [16] 12.91 ± 2.54 Du [17]	6.7–11.4 At diagnosis: 8.4 (7.9–8.8). Later minimum 6.9 (6.4–7.6) Knaak [3] 8.7 ± 2.4 Dhote [9] On admission: NS:9.9 ± 2.7 , S:13.0 ± 2.1 Nadir or peak: NS:7.1 ± 2.0 , S:11.2 ± 2.6 Kaito [18]
Range:	**Normal**	**Low**
Platelets (150–450 × 109/L)	157.0 (134.0–184.5) Chen [11] 169.67 ± 48.95 Qu [19] 142 (119–202) Wang [13] 196 (165–263) Huang [2] 167 (144–215) Wang [14] 165.5 (107.0–229.0) Zhou [15] 156 (116–217) Young [16] 162.6 ± 108.9 Du [17]	6–52 Sepsis: 236.98 ± 19.37 Severe sepsis 196.37 ± 23.1 Septic shock 144.93 ± 25.31 Septic shock: 196 (127–332) Machowicz [7] At diagnosis 51 (23–96) Later minimum 18 (5–34) Knaak [3] 95 ± 12 Dhote [9] On admission: NS:82.6 ± 62.2 , S:146.3 ± 64.2 Nadir or peak: NS:23.0 ± 19.1 , S:113.3 ± 56.2 Kaito [18]
Range:	**Normal**	**Low to normal, Severe sepsis low**
Ferritin (20–250 ng/L for males 10–120 ng/L for females)	1598 (1425–2036) Chen [11] 800 (452–1452) Qin [12] 1435 (729–2000) Zhou [15]	Median 2367–25,720 and peak 6067–684,000 for adults. Machowicz [7] At diagnosis 16535 (9156–40800), Later peak 31674 (15121–87975) Knaak [3] 39,504 (1254–2,632,220) Birndt [4] **41,512 ± 78,465 Dhote [9]** In bacterial sepsis: Pneumococcal PN Median: 312–653 Sepsis Median: 432 (184–773) , 590 (429–771) Machowicz [7] 25,720 (626–684,000) Otrock [20]
Range:	**Increased from several hundreds to < 2000**	**In sepsis: Increased from several hundreds to < 1000 In CSS: Increased from thousands to tens of thousands**
Fibrinogen (1.5–3.5 g/L)	4.76 ± 1.73 Han [21] 6.32 ± 18.35 Du [17] 5.16 (3.74–5.69) Tang [22]	Usually levels are low < 1.5 Machowicz [7] septic patients: median > 5.5 in adults. Machowicz [7] sepsis: At diagnosis 2.6 (1.4–4.3), later minimum 2.0 (1.0–3.0) Knaak [3]
Range:	**Increased to approx. × 2 nl**	**CSS usually low < 2.0 , Sepsis > 4**
Triglyceride (30–135 mg/dl)	N/A	In HLH maximal values reach 310–1475 Machowicz [7] At diagnosis: 288 (197–438) Later maximum: 376 (245– 563) Knaak [3] 319 ± 300 Dhote [9] In many studies, values for adult patients with sepsis are much lower than the HLH criterion and do not or only moderately exceed levels of 180 mg/dl, Machowicz [7]
Range:	**N/A**	**In CSS usually increased**
AST (5–40 IU/L)	47.0 (28.0–74.5) Chen [11] 45.33 ± 12.90 Qu [19] 52 (30–70) Wang [13] 49.0 (29.0–115.0) Huang [2] 40.5 (24.0–62.0) Wang [14] 94.4 ± 263.3Du [17]	45–286 Lower range: 14–40 Upper range: 157–1489 Machowicz [7] At diagnosis: 171 (119–498) Later maximum: 495 (235–2732) Knaak [3] 286 ± 661 Dhote [9] On admission: NS:76.6 ± 84.7 , S:127.3 ± 285.3 Nadir or peak: NS:243.1 ± 187.6 , S:174.1 ± 284.8 Kaito [18]
Range:	**Increased to < 2 × nl**	**Increased to > 5 × nl**

	Take home message
	Extremely low hemoglobin should suggest a diagnosis other than CPN-CSS
	Low PLT (< 100 × 109/L) suggest O-CSS or sepsis
	Very high levels of ferritin (> 2000) suggest O-CSS. Sepsis and CPN-CSS obtain similar values
	In CPN-CSS and sepsis fibrinogen is increased where it is low normal or low in O-CSS
	In CPN-CSS values are often mildly elevated. If greater values are observed consider O-CSS

Marker and normal values	CPN-CSS	O-CSS
Neutrophils absolute count ×109/L	6.9 (4.9–9.1) Chen [11] 4.3 (2.9–7.0) Qin [12] 4.6 (2.6–7.9) Wang [13] 10.6 (5.0–11.8) Huang [2] 5.24 (2.90–6.44) Wang [14] 1.8 (1.2–3.7) Young [16] 8.765 ± 6.181 Du [17]	In HLH: 0.7–3.5 Lower level: 0–1 Upper level: 7.9–33.0 CSS associated with sepsis: 14 (8.8–16.6) sepsis and severe sepsis: 25.1 (14.7–32.4) septic shock. Machowicz [7] 2.4 ± 1.9 Dhote [9]
Range:	**Normal**	**Low in HLH, High in sepsis**
Lymphocytes absolute count × 109/L	0.7 (0.5–0.9) Chen [11] 1.16 ± 0.55 Qu [19] 0.8 (0.6–1.1) Qin [12] 0.8 (0.5–0.9) Wang [13] 0.4 (0.2–0.8) Huang [2] 0.61(0.37–1.00) Wang [14] 0.6 (0.5–0.8) Zhou [15] 1.1 (0.8–1.7) Young [16] 0.729 ± 0.419 Du [17]	0.54 ± 0.41 Dhote [9]
Range:	**Low**	**Low**
ALT [5–40 IU/L]	42.0 (32.5–50.0) Chen [11] 36 ± 19.52 Qu [19] 35 (19–57) Wang [13] 44.0 (30.0–70.0) Huang [2] 31.5 (23.0–52.0) Wang [14] 40.0 (24.0–51.0) Zhou [15] 72.9 ± 199.5 Du [17]	Median: 40–318 Lower range: 7–37 Upper range: 157–4100 Machowicz [7] 284 ± 847 Dhote [9] On admission: NS:76.6 ± 131.0 Nadir or peak: NS:229.3 ± 290.9 , S:184.4 ± 255.9 Kaito [18]
Range:	**Increased to < 2 × nl**	**Increased to > 5 × nl**
LDH (50–240 U/L)	537 (4335–707) Chen [11] 772.33 ± 292.13Qu [19] 435 (302–596) Wang [13] 400 (323–578) Huang [2] 518 (267–549) Wang [14] 521 (363–669) Zhou [15] 550 (512–796) Young [16] 646 ± 597 Du [17]	552–1314 Lower range: 28–399 Upper range: 2203–9290 Machowicz [7] At diagnosis 735 (422–2159), Later maximum 1779 (607–4995) Knaak [3] 1735 ± 1693 Dhote [9] 849 (179–7,220) Otrock [20] On admission: NS:766.9 ± 497.3 , S:774.5 ± 701.4 Nadir or peak: NS:1541.9 ± 1142.3, S:950.8 ± 673.2 Kaito [18]
Range:	**Increased to < 2 × nl**	**Increased to > 2 × nl**
D-dimer [< 0.5 µg/ml]	2.6 (0.6–18.7) Chen [11] 4.14 (1.91–13.24) Wang [13] 2.4 (0.6–14.4) Huang [2] 5.2 (1.5–21.1) Zhou [15] 19.11 ± 35.48 Han [21] 5.159 ± 4.679 Du [17] 2.12 (0.77–5.27) Tang [22]	A marker considered to be unhelpful for diagnosing HLH(23)
Range:	**Increased > × ~4 nl**	
CRP (< 8 mg/L)	139.4 (86.9–165.1) Chen [11] 57.9 (20.9–103.2) Qin [12] 81.55 (48.85–105.90) Wang [14] 65.6 (47.5–97.5) Young [16] 107.259 ± 117.215 Du [17]	A marker considered to be unhelpful for diagnosing HLH [23]
Range:	**Increased to ~8–10 × nl**	

ALT = alanine transaminase, ANC = absolute neutrophil count, CPN-CSS = COVID-19 pneumonia associated cytokine storm syndrome,
CRP = C reactive protein, LDH = lactate dehydrogenase, nl = normal, NS = non survivors,
O-CSS = cytokine storm syndrome associated with diseases other than COVID-19, S = survivors, WBC = white blood cells

	Take home message
	Low ANC suggest CSS from etiologies other than CPN. Very High ANC suggests sepsis
	Low Lymphocyte count hallmark of CPN-CSS but can be detected with O-CSS
	In CPN-CSS values are often mildly elevated. If greater values are observed consider O-CSS
	Values > 1000 suggest etiologies other than CPN-CSS
	In CPN-CSS D-dimer is usually increased
	In CPN-CSS CRP is usually increased

Table 2. Lab findings reported in severely ill patients with COVID-19 pneumonia

	Wu [1]	Chen [11]	Qu [19]	Qin [12]	Wang [13]
WBC (×109/ml)	8.32 (5.07–11.20)	8.3 (6.2–10.4)	N/A	5.6 (4.3–8.4)	6.6 (3.6–9.8)
Hemoglobin (g/dl)	N/A	N/A	N/A	N/A	N/A
Platelets (×109/ml)	187.00 (124.50–252.50)	157.0 (134.0–184.5)	169.67 ± 48.95	142 (119–202)	142 (119–202)
Ferritin (ng/ml)	1029.28 (546.26– > 2000)	1598.2 (1424.6–2036.0)	N/A	800.4 (452.9–1451.6)	N/A
Fibrinogen (g/L)	N/A	N/A	N/A	N/A	N/A
Triglyceride (mg/dl)	N/A	N/A	N/A	N/A	N/A
AST (IU/L)	38.00 (30.50–53.00)	47.0 (28.0–74.5)	45.33 ± 12.90	N/A	52 (30–70)
Neutrophils absolute (×109/ml)	7.04 (3.98–10.12)	6.9 (4.9–9.1)	N/A	4.3 (2.9–7.0)	4.6 (2.6–7.9)
Lymphocytes absolute (×109/ml)	0.67 (0.49–0.99)	0.7 (0.5–0.9)	1.16 ± 0.55	0.8 (0.6–1.1)	0.8 (0.5–0.9)
ALT (IU/L)	35.00 (21.50–52.50)	42.0 (32.5–50.0)	36 ± 19.52	N/A	35 (19–57)
LDH (U/L)	396.00 (320.00–521.00)	537.0 (433.5–707.5)	772.33 ± 292.13	N/A	435 (302–596)
CRP (mg/L)	83.00 (39.45–152.40)	139.4 (86.9–165.1)	N/A	57.9 (20.9–103.2)	N/A
D-dimer (ug/ml)	1.16 (0.46–5.37)	2.6 (0.6–18.7)	N/A	N/A	4.14 (1.91–13.24)

Values are given as median (and interval in parenthesis) or mean ± a measure of deviation. Thick line in the table (between AST and ALT) separates the HScore
ALT = alanine transaminase, AST = aspartate transaminase, CRP = C-reactive protein, LDH = lactate dehydrogenase, N/A = not available, WBC = white blood cells

Table 3. Laboratory findings reported in cytokine storm syndromes associated with diseases prior to COVID-19

	Machowicz (HLH) [7]	**Machowicz (Sepsis) [7]**
WBC (×109/ml)		Although in the SIRS criteria both patients with leukocytosis andleukopenia are included, the first group prevails. median ANC of 14 × 109 L in septic patients
Hemoglobin (g/dl)	6.7–11.4 Anemia < 9 good candidate for HLH	8.3-11.3
Platelets (×109/ml)	6–52	Sepsis: 236.98 ± 19.37 Severe Sepsis 196.37 ± 23.1 Septic Shock 144.93 ± 25.31 Septic shock: 196 (127–332)
Ferritin (mg/L or ng/ml)	Median 2367–25,720 and peak 6067–684,000 ng/ml for adults	Pneumococcal PN Median: 312-653 Sepsis Median: 432 ng/ml (184-773) , 590 ng/ml (429-771)
Fibrinogen < 1.5 g/L Depends on whether DIC is present	Usually levels are low < 1.5 but values differ among studies and groups and whether patients were transfused with plasma	Fibrinogen is an acute phase reactant and its concentration is elevated in septic patients. median > 5.5 in adults
Triglycerids (mg/dl)	In HLH maximal values reach 310–1475	In many studies, values for adult patients with sepsis are much lower than the HLH criterionand do not or only moderately exceed levels of 180
AST (IU/L)	45-286 Lower range: 14–40 Upper range: 157–1489	N/A
Neutrophils absolute (×109/ml)	0.7-3.5 Lower level: 0-1 Upper level: 7.9-33.0	14 (8.8–16.6)–sepsis and severe sepsis 25.1 (14.7–32.4)–septic shock
Lymphocytes absolute (×109/ml)	N/A	N/A
ALT (IU/L)	Median: 40–318 Lower range: 7–37 Upper range: 157–4100	N/A
LDH (U/L)	552–1314 Lower range: 28–399 Upper range: 2203–9290	N/A

Values are given as median (and interval in parenthesis) or mean ± a measure of deviation. Thick line in the table (between AST and ALT) separates the HScore
ALT = alanine transaminase, AST = aspartate transaminase, ANC = absolute neutrophil count, CRP = C-reactive protein, LDH = lactate dehydrogenase,

	Huang [2]	Wang [14]	Zhou [15]	Han [21]	Young [16]	Du [17]	Tang [22]
	11.3 (5.8–12.1)	6.52 (4.30–7.73)	9.8 (6.9–13.9)	N/A	3.4 (2.6–5.8)	10.121 ± 6.266	N/A
	12.2 (11.1–12.8)	12.8 (11.7–13.6)	12.6 (11.5–13.8)	N/A	13.2 (11.7–14)	12.91 ± 2.54	N/A
	196 (165–263)	167 (144–215)	165.5 (107.0–229.0)	N/A	156 (116–217)	162.6 ± 108.9	N/A
	N/A	N/A	1435.3 (728.9–2000.0)	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	4.76 ± 1.7301	N/A	6.321 ± 18.349	5.16 (3.74–5.69)
	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	49.0 (29.0–115.0)	40.5 (24.0–62.0)	N/A	N/A	N/A	94.4 ± 263.3	N/A
	10.6 (5.0–11.8)	5.24(2.90–6.44)	N/A	N/A	1.8 (1.2–3.7)	8.765 ± 6.181	N/A
	0.4 (0.2–0.8)	0.61(0.37–1.00)	0.6 (0.5–0.8)	N/A	1.1 (0.8–1.7)	0.729 ± 0.419	N/A
	44.0 (30.0–70.0)	31.5 (23.0–52.0)	40.0 (24.0–51.0)	N/A	N/A	72.9 ± 199.5	N/A
	400 (323–578)	517.5 (267.0–549.0)	521.0 (363.0–669.0)	N/A	550 (512–796)	645.8 ± 596.9	N/A
	N/A	81.55 (48.85–105.90)	N/A	N/A	65.6 (47.5–97.5)	107.259 ± 117.215	N/A
	2.4 (0.6–14.4)	N/A	5.2 (1.5–21.1)	19.11 ± 35.48	N/A	5.159 ± 4.679	2.12 (0.77–5.27)

lab markers (above) from the other markers

Knaak [3]	Birndt [4]	Dhote [9]	Kaito [18]	Otrock [20]
On admission: 3.3 (1.3–6.9) Later minimum: 0.9 (0.2–2.7)			On admission: NS:5.9 ± 4.4 , S:4.2 ± 2.2 Nadir or peak: NS:1.7 ± 1.9 , S:2.1 ± 1.1	
At diagnosis: 8.4 (7.9–8.8) Later minimum: 6.9 (6.4–7.6)		8.7 ± 2.4	On admission: NS:9.9 ± 2.7 , S:13.0 ± 2.1 Nadir or peak: NS:7.1 ± 2.0 , S:11.2 ± 2.6	
At diagnosis: 51 (23–96) Later minimum: 18 (5–34)		95 ± 12	On admission: NS:82.6 ± 62.2 , S:146.3 ± 64.2 Nadir or peak: NS:23.0 ± 19.1 , S:113.3 ± 56.2	
At diagnosis: 16535 (9156- 40800) Later peak: 31674 (15121–87975)	39,504 (1254–2,632,220)	41,512 ± 78,465		25,720 (626-684,000)
At diagnosis: 2.6 (1.4–4.3) Later minimum: 2.0 (1.0–3.0)				
At diagnosis: 288 (197–438) Later maximum: 376 (245–563)		3.19 ± 3.0		
At diagnosis: 171 (119 -498) Later maximum: 495 (235–2732)		286 ± 661	On admission: NS:76.6 ± 84.7 , S:127.3 ± 285.3 Nadir or peak: NS:243.1 ± 187.6 , S:174.1 ± 284.8	
		2.4 ± 1.9		
N/A	N/A	0.54 ± 0.41		
		284 ± 847	On admission: NS:76.6 ± 131.0 , S:122.1 ± 260.1 Nadir or peak: NS:229.3 ± 290.9 , S:184.4 ± 255.9	
At diagnosis: 735 (422–2159) Later maximum: 1779 (607–4995)		1,735 ± 1,693	On admission: NS:766.9 ± 497.3 , S:774.5 ± 701.4 Nadir or peak: NS:1541.9 ± 1142.3 , S:950.8 ± 673.2	849 (179-7,220)

lab markers from the other markers
N/A = not available, nl = normal, NS = non survivors, S = survivors, WBC = white blood cell