Performance of serum apolipoprotein-A1 as a sentinel of COVID-19

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Background

Since 1920, a decrease in serum cholesterol has been identified as a marker of severe pneumonia (1), in particular the levels of high-density lipoprotein cholesterol (HDL) and a level below the median of its transporter, apolipoprotein-A1 (ApoA1), were associated with a two-fold increase in mortality in patients with severe sepsis (2). In February 2020 we observed in Pitié-Salpêtrière hospital in Paris, France, that patients hospitalized for Covid-19 had a specific profile of apolipoprotein-A1 decrease.

Aims

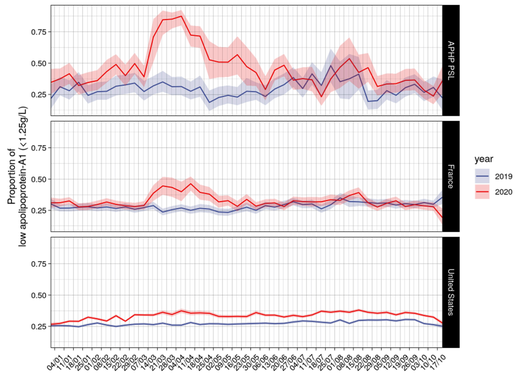
We have assessed the performance of serum apolipoprotein-A1 (ApoA1), to identify the early spread of coronavirus disease 2019 (Covid-19) in the general population and its diagnostic performance for the Covid-19. As a second purpose we evaluated the diagnostic performance of a multianalyte test including ApoA1.

Patients and Methods

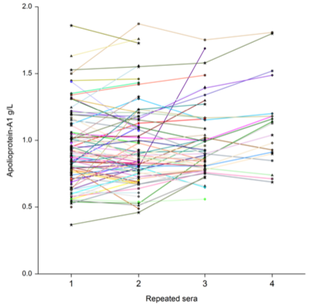
We compared the daily mean serum apolipoprotein-A1 during the first 39 weeks of 2020 in a population that is routinely followed for a risk of liver fibrosis risk in the USA (276,614 serum) and in France (27,490 serum) in relation to a local increase in confirmed cases, and in comparison to the same period in 2019 (337,092 and 36,442 serum, respectively). We prospectively assessed the sensitivity of this marker in an observational study of 136 consecutive hospitalized cases and retrospectively evaluated its specificity in 7,481 controls representing the general population. From the same population, a multianalyte test was constructed, combining ApoA1 and haptoglobin, a protein associated with inflammation, adjusted from age and sex.

Results

Proportion of low ApoA1 (<1.25 g/L) during the 39 weeks in France (national and hospital cohort) and US



Serum ApoA1 prospective 256 repeated measurements in patients with Covid-19



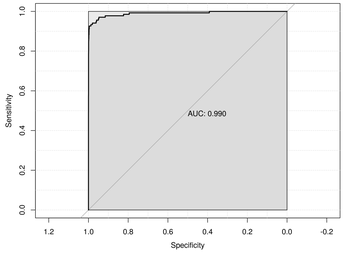
In the prospective recovery subset repeated measurements showed an increase of ApoA1 from 0.89 to 1.04 g/L in a median of 11 days (n=305; ANOVA P<0.01).

AUROCs ApoA1 and liver function tests. 136 Covid-19 cases and 7,481 controls.

Criterion	Count	AUROC	Standard Error	P-Value vs ApoA1	Lower 95%CI	Upper 95%CI
ApoA1 negative	7617	0.978	0.007	NA	0.957	0.988
Haptoglobin	7617	0.937	0.014	0.007	0.902	0.961
GGT	7617	0.540	0.029	<0.001	0.481	0.595
Alpha-2-Macroglobulin	7617	0.758	0.021	<0.001	0.715	0.796
Bilirubin negative	7617	0.712	0.028	<0.001	0.654	0.7623
ALT	7617	0.636	0.028	<0.001	0.579	0.688
AGE	7617	0.760	0.028	<0.001	0.699	0.801

ApoA1 at the 1.25 g/L cutoff had a sensitivity of 90.6% (95%CI 84.2-95.1) and a specificity of 96.1% (95%CI 95.7-96.6%) for the diagnosis of Covid-19. The area under the characteristics curve was 0.978 (95%CI 0.957-0.988). For a prevalence of 1.8% (136/7617; 95%CI 1.5-2.1) of Covid-19 cases, the positive predictive value (PPV) was 30.0% (95%CI 25.6-34.7) and the negative predictive value (NPV) was 99.8% (95%CI 99.7-99.9).

AUROC multianalyte blood test. 136 Covid-19 cases and 7,481 controls.



This score with he predetermined cutoff had a sensitivity of 97.1% (95%CI 94.2-99.8) and a specificity of 94.7% (95%CI 94.3-95.3) for the diagnosis of Covid-19. The area under the characteristics curve was 0.990 (95%CI 0.981-1.000). For a prevalence of 1.8% of Covid-19 cases, the negative predictive value (NPV) was 99.9% (95%CI 99.8-100) and the positive predictive value (PPV) was 25.1% (95%CI 21.4-28.9).

Conclusions

Apolipoprotein-A1 could be a sentinel of the pandemic in existing routine surveillance of the general population, as well as a candidate predictor of suspected Covid-19 in multivariate analysis in cases with a negative virological test (3). The combination of ApoA1 and haptoglobin has a very strong Negative Predictive Value (99.9%), enabling its usage as a first-line triage blood-based test for Covid-19.

References

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Disclosures

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