HIGH FIBROBLAST GROWTH FACTOR 23 LEVELS INCREASE RISK OF SARS-COV-2 INFECTION AND MORTALITY IN END-STAGE RENAL DISEASE PATIENTS ON HEMODIALYSIS: A 3-YEAR FOLLOW-UP PROSPECTIVE COHORT

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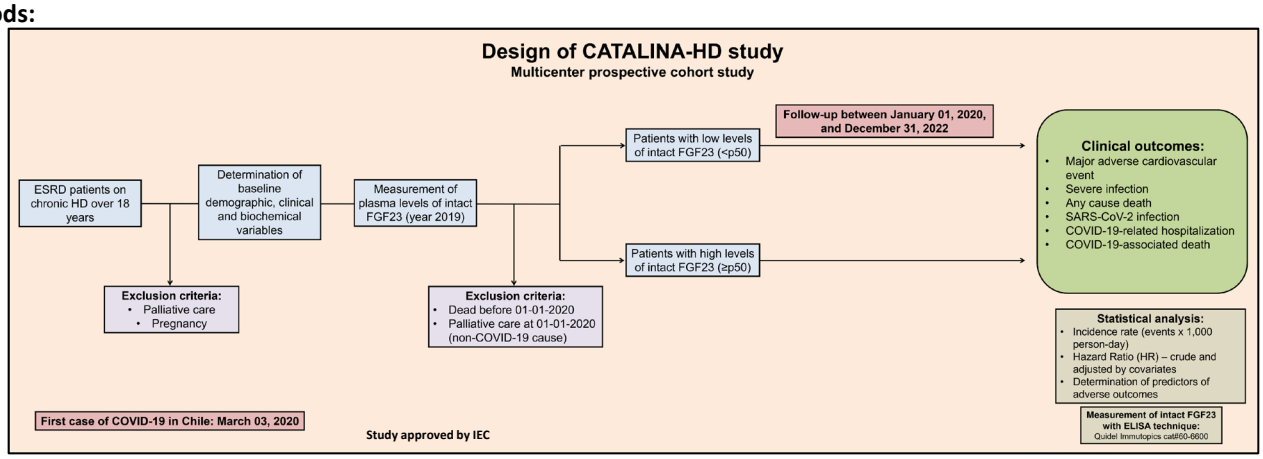
Introduction:

- End-stage renal disease (ESRD) patients have higher risk of severe infections and deaths compared to general population.
- Fibroblast Growth Factor 23 (FGF23) is a hormone that increases in ESRD and associate with higher CV and all-cause mortality.
- Experimental *in vitro* and *in vivo* studies indicate that FGF23 has immunosuppressive effects that increase infection risk.
- There is currently contradictory evidence on the association between FGF23 levels and risk of infection in ESRD patients.

Objective: To evaluate the association between baseline plasma FGF23 levels in the development of infection and adverse events associated with COVID-19 in patients on hemodialysis.

Methods:



Results:

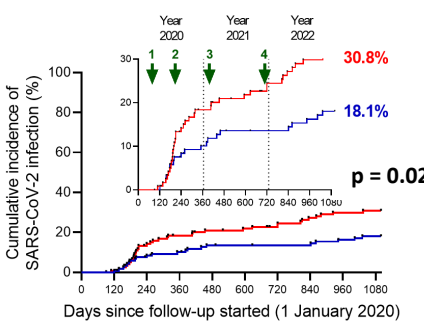
Baseline characteristics of patients

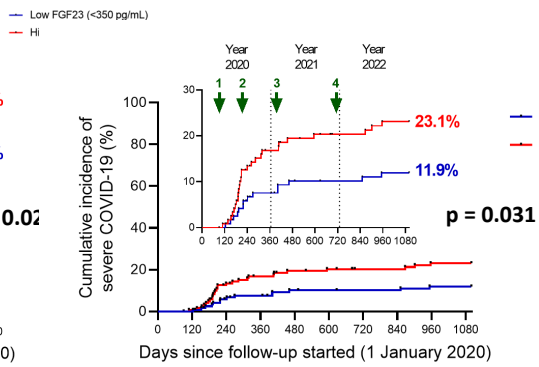
Baseline characteristics	Total cohort N	%
Total	243	100%
Sex		
Female (%)	120	49.38%
Male (%)	123	50.62%
Age group		
18-39 years (%)	8	3.29%
40-49 years (%)	37	15.23%
50-59 years (%)	66	27.16%
60-69 years (%)	95	39.09%
70-79 years (%)	31	12.76%
≥ 80 years (%)	6	2.47%
Comorbidities		
Diabetes (%)	110	45.27%
Hypertension (%)	218	89.71%
Heart failure (%)	40	16.46%
Vascular access		
Arteriovenous fistula (%)	140	57.61%
Hemodialysis catheter (%)	103	42.39%

Baseline characteristics	Total cohort N	%
Medications		
Angiotensin receptor blockers (%)	175	72.02%
Calcium channel blockers (%)	178	73.25%
Loop diuretics (%)	46	18.93%
Vitamin D analogs (%)	56	23.05%
Phosphate binders (%)	209	86.01%
Calcimimetics (%)	48	19.75%
Erythropoietic stimulating agents (%)	203	83.54%
Hemodialysis parameters		
Residual diuresis (%)	80	32.92%
Hemodialysis vintage (months)	25 [15-40]	
Dry weight (kg)	70,20 ± 7,66	
Single-pool Kt/V	1,31 ± 0,20	
Laboratory parameters		
Blood ureic nitrogen (mg/dL)	64,06 ± 12,70	
Intact parathormone (pg/mL)	565 [284-884]	
25-OH vitamin D (ng/mL)	19,05 ± 8,53	
Serum phosphate (mg/dL)	5,15 ± 1,08	
Total serum calcium (mg/dL)	8,22 ± 0,98	
Ferritin (ng/mL)	467,72 ± 168,45	
Hemoglobin (g/dL)	9,45 ± 1,33	
Intact fibroblast growth factor 23 (pg/mL)	319 [204-600]	

Baseline characteristics	Total cohort N	%
Clinical outcomes		
SARS-CoV-2 infection (%)	57	23.46%
COVID-19-related hospitalization (%)	41	16.87%
COVID-19-related death (%)	17	7.00%
COVID-19-non-related death (%)	29	11.93%
COVID-19-related hospitalization or death (%)	44	18.11%

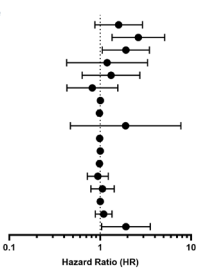
1.- First case of COVID-19 in Chile.
2.- End of the first COVID-19 wave in Chile.
3.- Initiation of anti-SARS-CoV-2 vaccination in Chile.
4.- First case of Omicron variant in Chile.





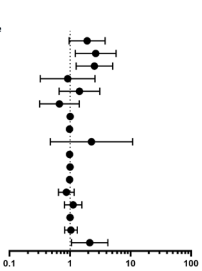
Risk factors of SARS-CoV-2 infection

Variable	Hazard ratio	IC 95%		p-value
Male	1.551	0.854	2.816	0.149
Age > 60 years	**2.634**	**1.360**	**5.101**	**0.004**
Diabetes	**1.909**	**1.051**	**3.465**	**0.034**
Hypertension	1.192	0.427	3.328	0.737
Heart failure	1.315	0.634	2.731	0.462
Residual diuresis	0.819	0.430	1.561	0.545
Dialysis vintage	1.004	0.991	1.017	0.568
Dry weight	0.973	0.938	1.008	0.128
spKt/V	1.904	0.469	7.738	0.368
BUN	0.987	0.963	1.010	0.261
Intact PTH	1.000	0.999	1.000	0.420
25-OH vitamin D	0.982	0.948	1.016	0.295
Serum phosphate	0.941	0.722	1.226	0.654
Total serum calcium	1.060	0.789	1.425	0.697
Ferritin	1.000	0.999	1.002	0.580
Hemoglobin	1.091	0.884	1.347	0.418
High iFGF23	**1.917**	**1.041**	**3.530**	**0.037**



Risk factors of severe COVID-19

Variable	Hazard ratio	95% CI		p-value
Male	1.913	0.963	3.800	0.064
Age > 60 years	**2.655**	**1.221**	**5.776**	**0.014**
Diabetes	**2.526**	**1.259**	**5.066**	**0.009**
Hypertension	0.913	0.323	2.583	0.865
Heart failure	1.433	0.660	3.110	0.363
Residual diuresis	0.668	0.314	1.420	0.294
Dialysis vintage	1.005	0.991	1.019	0.496
Dry weight	0.979	0.940	1.020	0.319
spKt/V	2.258	0.472	10.809	0.308
BUN	0.984	0.959	1.011	0.239
Intact PTH	1.000	0.999	1.001	0.866
25-OH vitamin D	0.982	0.945	1.021	0.363
Serum phosphate	0.869	0.645	1.171	0.356
Total serum calcium	1.125	0.807	1.568	0.487
Ferritin	1.001	0.999	1.003	0.558
Hemoglobin	1.034	0.813	1.315	0.783
High iFGF23	**2.116**	**1.058**	**4.232**	**0.034**



Conclusions:

- High levels of FGF23 are a risk factor for SARS-CoV-2 infection and severe COVID-19 in patients with ESRD.
- These results support a potential immunosuppressive effect of FGF23, which could contribute to the increased risk of serious infections in this group of patients.
- The potential role of FGF23 in the development of adverse events remains to be evaluated in translational and clinical studies.